7.1
RF_PH_7_SUDHA

NCRP - ICMR - CANCER PATTERNS IN BANGALORE 1982-1989

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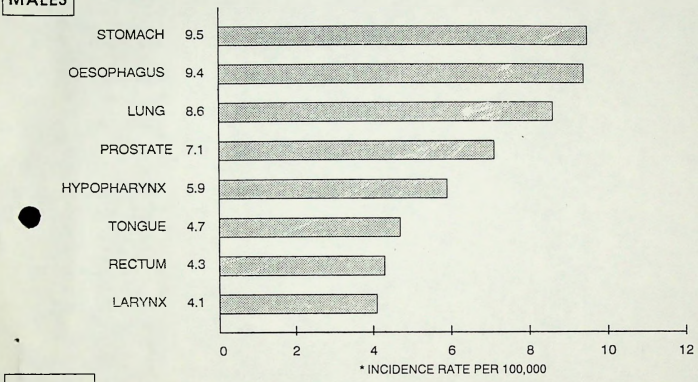
POPULATION-BASED CANCER REGISTRY BANGALORE *Sex : Female* *Year : 1989*

INCIDENT CASES OF CANCER BY MOST VALID BASIS OF DIAGNOSIS AND SITE (ICD.9)

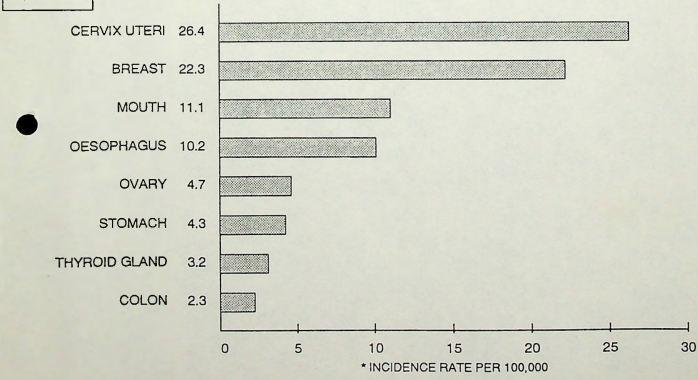
ICD 9TH	SITE	MICROSCOPIC n	%	X-RAY n	%	CLINICAL ONLY n	%	OTHERS n	%	D.C.O. n	%	TOTALS n	%
140	LIP	1	100.00	0	0.00	0	0.00	0	0.00	0	0.00	1	100.00
141	TONGUE	8	80.00	0	0.00	0	0.00	0	0.00	2	20.00	10	100.00
142	SALIVARY GLANDS	5	83.33	0	0.00	0	0.00	0	0.00	1	16.67	6	100.00
143	GUM	24	88.89	1	3.70	2	7.41	0	0.00	0	0.00	27	100.00
144	FLOOR OF MOUTH	3	75.00	0	0.00	1	25.00	0	0.00	0	0.00	4	100.00
145	OTHER MOUTH	68	80.95	3	3.57	9	10.71	0	0.00	4	4.76	84	100.00
146	OROPHARYNX	5	100.00	0	0.00	0	0.00	0	0.00	0	0.00	5	100.00
147	NASOPHARYNX	3	60.00	0	0.00	2	40.00	0	0.00	0	0.00	5	100.00
148	HYPOPHARYNX	7	58.33	1	8.33	3	25.00	0	0.00	1	8.33	12	100.00
149	PHARYNX ETC	1	50.00	0	0.00	0	0.00	0	0.00	1	50.00	2	100.00
150	OESOPHAGUS	75	71.43	12	11.43	12	11.43	2	1.90	4	3.81	105	100.00
151	STOMACH	27	56.25	4	8.33	11	22.92	0	0.00	6	12.50	48	100.00
152	SMALL INTESTINE	0	0.00	0	0.00	0	0.00	0	0.00	1	100.00	1	100.00
153	COLON	19	76.00	0	0.00	4	16.00	1	4.00	1	4.00	25	100.00
154	RECTUM	17	70.83	0	0.00	3	12.50	0	0.00	4	16.67	24	100.00
155	LIVER	4	33.33	0	0.00	2	16.67	0	0.00	6	50.00	12	100.00
156	GALL BALDDER	5	62.50	0	0.00	1	12.50	0	0.00	2	25.00	8	100.00
157	PANCREAS	4	36.36	2	18.18	1	9.09	0	0.00	4	36.36	11	100.00
158	RETROPERITONEUM	5	100.00	0	0.00	0	0.00	0	0.00	0	0.00	5	100.00
159	OTHER DIS SYS	2	50.00	1	25.00	1	25.00	0	0.00	0	0.00	4	100.00
160	NASAL CAVITY	4	100.00	0	0.00	0	0.00	0	0.00	0	0.00	4	100.00
161	LARYNX	6	85.71	0	0.00	0	0.00	0	0.00	1	14.29	7	100.00
162	LUNG	13	68.42	2	10.53	1	5.26	0	0.00	3	15.79	19	100.00
163	PLEURA	4	80.00	0	0.00	0	0.00	0	0.00	1	20.00	5	100.00
164	THYMUS	1	100.00	0	0.00	0	0.00	0	0.00	0	0.00	1	100.00
165	OTHER RES SYS	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
170	BONE	12	85.71	1	7.14	0	0.00	0	0.00	1	7.14	14	100.00
171	CONNECTIVE TISS	4	100.00	0	0.00	0	0.00	0	0.00	0	0.00	4	100.00
172	SKIN MELANOMA	1	100.00	0	0.00	0	0.00	0	0.00	0	0.00	1	100.00
173	SKIN OTHER	16	88.89	0	0.00	0	0.00	0	0.00	2	11.11	18	100.00
174	BREAST FEM	227	88.67	3	1.17	21	8.20	0	0.00	5	1.95	256	100.00
179	UTERINE UNS	5	71.43	0	0.00	0	0.00	0	0.00	2	28.57	7	100.00
180	CERVIX UTERI	253	86.94	0	0.00	33	11.34	0	0.00	5	1.72	291	100.00
181	PLACENTA	0	0.00	0	0.00	0	0.00	0	0.00	1	100.00	1	100.00
182	BODY UTERUS	21	95.45	0	0.00	0	0.00	0	0.00	1	4.55	22	100.00
183	OVARY	42	80.77	0	0.00	4	7.69	0	0.00	6	11.54	52	100.00
184	VAGINA	14	100.00	0	0.00	0	0.00	0	0.00	0	0.00	14	100.00
188	URI BLADDER	5	71.43	0	0.00	2	28.57	0	0.00	0	0.00	7	100.00
189	KIDNEY	5	100.00	0	0.00	0	0.00	0	0.00	0	0.00	5	100.00
190	EYE	1	100.00	0	0.00	0	0.00	0	0.00	0	0.00	1	100.00
191	BRAIN	20	71.43	3	10.71	0	0.00	0	0.00	5	17.86	28	100.00
192	NERVOUS SYSTEM	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
193	THYROID GLAND	46	97.87	0	0.00	1	2.13	0	0.00	0	0.00	47	100.00
194	OTH ENDO GLANDS	2	100.00	0	0.00	0	0.00	0	0.00	0	0.00	2	100.00
195	ILL DEF SITES	8	88.89	1	11.11	0	0.00	0	0.00	0	0.00	9	100.00
196	SEC LYMPH NODES	6	100.00	0	0.00	0	0.00	0	0.00	0	0.00	6	100.00
197	SEC RES ETC	7	87.50	1	12.50	0	0.00	0	0.00	0	0.00	8	100.00
198	SEC OTHER	4	57.14	0	0.00	2	28.57	0	0.00	1	14.29	7	100.00
199	PRIM UNK	1	1.25	3	3.75	0	0.00	0	0.00	76	95.00	80	100.00
200	LYMPHOSARCOMA	3	100.00	0	0.00	0	0.00	0	0.00	0	0.00	3	100.00
201	HODGKINS DIS	10	100.00	0	0.00	0	0.00	0	0.00	0	0.00	10	100.00
202	OTH LYMPHOMA	21	84.00	1	4.00	0	0.00	0	0.00	3	12.00	25	100.00
203	MULT MYELOMA	5	71.43	0	0.00	1	14.29	0	0.00	1	14.29	7	100.00
204	LEUK LYMPHATIC	8	88.89	0	0.00	0	0.00	0	0.00	1	11.11	9	100.00
205	LEUK MYELOID	23	88.46	0	0.00	0	0.00	0	0.00	3	11.54	26	100.00
206	LEUK MONOCYTIC	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
207	LEUK OTH SPE	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
208	LEUK UNS	4	40.00	0	0.00	0	0.00	0	0.00	6	60.00	10	100.00
	ALL SITESTOTALS	1085		39		117		3		161		1405	
	%	77.22		2.78		8.33		0.21		11.46		100.00	

BANGALORE - 1989
MOST COMMON FORMS OF CANCERS

MALES



FEMALES



* AGE–ADJUSTED (WORLD POPULATION)

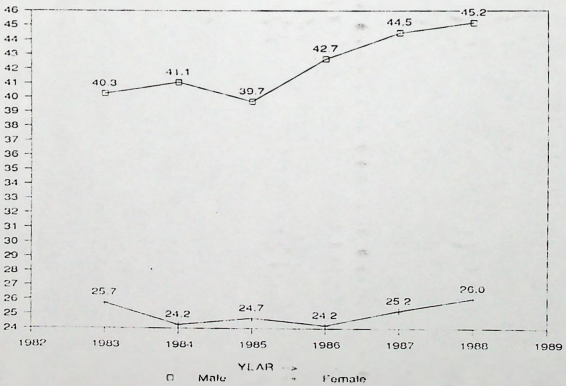
Trends Over Time

Table 6.3 gives the Age Adjusted Incidence Rates (AAR) and three year Moving Averages (MA) of tobacco related sites of cancer for different years. The same is graphically represented in Fig 6.1. There is a clear rising trend in the overall incidence of these cancers in males, whereas in females the rates are about the same over the years 1982 to 1989. The values of AAR for specific tobacco related sites is given in Tables 6.4 and 6.5.

Table 6.3
TOBACCO RELATED CANCERS - TRENDS OVER TIME : 1982 - 1989
ALL SITES OF CANCER ASSOCIATED WTIH USE OF TOBACCO - MALES AND FEMALES
Table gives figures of AAR and 3 year Moving Averages (MA) of AAR

YEAR	1982	1983	1984	1985	1986	1987	1988	1989	1982-89
MALE	38.11	41.92	40.73	40.51	37.94	49.68	45.90	39.94	42.08
MA	40.3	41.1	39.7	42.7	44.5			45.2	
FEMALE	27.35	23.58	26.25	22.86	24.93	24.79	25.83	27.47	25.40
MA	25.7	24.2	24.7	24.2	25.2			26.0	

Fig 6.1
TOBACCO RELATED CANCERS - TRENDS OVER TIME : 1982 - 1989
ALL SITES OF CANCER ASSOCIATED WTIH USE OF TOBACCO - MALES AND FEMALES
Figure shows line graphs of 3 year Moving Averages of AAR



Tobacco Related cancers (TRC):

Cancers of the oral cavity, pharynx, oesophagus, larynx, lung and urinary bladder are considered as the cancer sites related to Tobacco use. The paportion of these cancers by sex is shown below.

Tobacco related cancers by sex

	MALE			FEMALE			TOTAL	
SITE	NO.	% TO TRC	% TO ALL SITES	NO.	% TO TRC	% TO ALL SITES	NO.	% T TRC AL
Oral cavity	386	24.5	12.16	553	58.2	14.87	939	37.2
Pharynx	503	31.9	15.84	97	10.2	2.60	600	23.8
Oesophagus	318	20.2	10.01	238	25.0	6.40	556	22.0
Larynx	157	10.0	4.94	17	1.9	0.46	174	6.9
Lung	187	11.9	5.89	37	3.9	1.00	224	8.9
Uri.Bladder	24	1.5	0.76	8	0.8	0.22	32	1.3
Total	1575	100.0	49.6	950	100.0	25.5	2525	100.0
All sites	3174			3718			6892	

Tobacco related cancers constituted 37% of all cancers in both sexes. It accounted for about 50% of all cancers in males and 26% in females. No significant change in the relative proportions in the TRC have been observed over the years. Among males, one third of TRC were cancer of pharynx followed by cancers of the oral cavity & oesophagus.

It can be observed that, among Tobacco Related Cancers of the oral cavity in females was more than double compared to the proportion in males. This could be mainly due to the habit of chewing which is very common in females more so from the rural folk.

HOSPITAL CANCER REGISTRY
DEPT OF BIOSTATISTICS & CANCER RESEARCH (ANNUAL REPORT) 1995
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TOBACCO RELATED CANCERS
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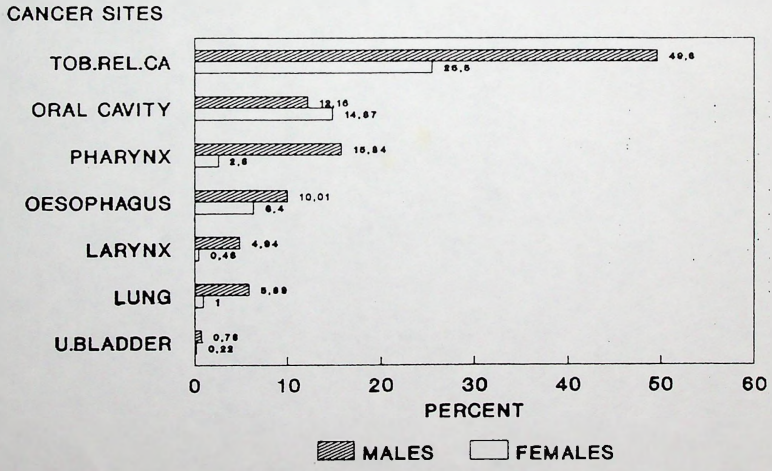

MALES=1575(49.6%): FEMALES=950(25.5%)

cancer incidence rate was observed in each registry. While in Barshi (rural) , on an average one out of 24 to 25 persons get cancer in their life time. While in Connecticut (USA) and in United kingdom (Oxford), on an average one out of 6 to 8 persons get cancer (0-64 years).

2.8 MOST COMMON FORMS OF CANCERS

The most common forms of cancers observed in men and women in Bangalore, Bombay, Madras, Delhi, Bhopal and Barshi areas are presented in Table 2.8.

TABLE 2.8 : MOST COMMON FORMS OF CANCERS (1989) - MALES

RANK	BANGALORE	BOMBAY	MADRAS	DELHI	BHOPAL	BARSHI
1.	Stomach (9.5)*	Trachea, Bronchus & Lung (14.6)	Stomach (16.5)	Trachea, Bronchus & Lung (11.9)*	Trachea, Bronchus & Lung (14.1)	Oesophagus (6.7)
2.	Oesophagus (9.4)	Oesophagus (11.5)	Trachea, Bronchus & Lung (13.5)	Larynx (8.6)	Tongue (13.2)	Penis (5.1)
3.	Trachea, Bronchus & Lung (8.6)	Larynx (8.8)	Oesophagus (10.2)	Tongue (7.7)	Mouth (10.4)	Rectum (4.7)
4.	Prostate (7.1)	Hypopharynx (8.2)	Mouth (7.3)	Oesophagus (6.4)	Hypopharynx (8.4)	Hypopharynx (3.5)
5.	Hypopharynx (5.9)	Stomach (7.0)	Hypopharynx (6.5)	Prostate (6.3)	Oesophagus (7.7)	Mouth (3.4)
6.	Tongue (4.7)	Prostate (6.9)	Larynx (5.5)	Uri Bladder (5.6)	Prostate (5.6)	Skin,other (2.7)
7.	Rectum (4.3)	Tongue (6.5)	Tongue (5.3)	Lymphoma (5.1)	Rectum (5.5)	Liver (2.6)
8.	Larynx (4.1)	Mouth (5.8)	Rectum (4.5)	Brain (3.4) Stomach (3.4)	Stomach (3.7)	Stomach (3.4)

FEMALES

RANK	BANGALORE	BOMBAY	MADRAS	DELHI	BHOPAL	BARSHI
1.	Cervix Uteri (26.4)*	Breast (26.1)	Cervix Uteri (43.5)	Cervix Uteri (30.1)*	Cervix Uteri (24.3)	Cervix Uteri (26.2)
2.	Breast (22.3)	Cervix Uteri (19.4)	Breast (24.6)	Breast (28.3)	Breast (21.9)	Breast (6.8)
3.	Mouth (11.1)	Oesophagus (6.2)	Mouth (8.2)	Ovary (8.7)	Mouth (6.8)	Bone (2.4)
4.	Oesophagus (10.2)	Ovary (7.0)	Oesophagus (7.7)	Gall Bladder (6.6)	Ovary (6.2)	Skin,other (2.3)
5.	Ovary (4.7)	Mouth (3.9)	Stomach (7.1)	Oesophagus (4.6)	Oesophagus (5.2) Gall Bladder (5.2)	Rectum (1.7)
6.	Stomach (4.3)	Trachea, Bronchus & Lung(3.7)	Ovary (6.0)	Brain (2.6)	Body Uterus (4.2)	Oesophagus (1.4) Lymphoma (1.4)
7.	Thyroid Gland (3.2)	Stomach (3.4)	Hypopharynx (2.7)	Body Uterus (2.5) Mouth (2.5)	Trachea, Bronchus & Lung (3.2)	
8.	Colon (2.3)	Rectum (2.6)	Rectum (2.6)	Stomach (2.4) Lymphoma (2.4)	Colon (2.1) Thyroid Gland (2.1)	

* Age-adjusted (world population) cancer incidence rate, per 100,000 persons.

2.9 SOME OBSERVATIONS ON SELECTED CANCER SITES

2.9.1 Lip, Oral Cavity and Pharynx (ICD.9 : 140-149)

Malignant tumours of the lip, oral cavity and pharynx are the most common site group of cancers in the Indian registries i.e., Bangalore, Bombay, Madras, Delhi, Bhopal and Barshi (Table 2.9.1).

The total incidence of the lip, oral cavity and pharynx cancers disguise very large differences in the individual sites in the Indian registries. The tongue (mainly base tongue), mouth, oropharynx and hypopharynx are the predominant sites in this group.

There is also a marked variation in the incidence of lip, oral cavity and pharynx cancer in different countries. Indian registries display much higher age adjusted and truncated rates than those reported by other registries in Cancer Incidence in Five Continents (Vol. V,1987). Although this grouping includes cancers of quite distinct etiology (e.g. cancers of the oral cavity, nasopharynx and hypopharynx). The global picture is dominated by the incidence of oral cancer in Southern Asia and of oral cavity plus nasopharynx cancer in South-Eastern Asia.

Oral cancer is one of the 10 most common cancers in the world. In India, Bangaladesh, Pakistan and Srilanka, it is the most common and accounts for about a third of all cancers. More than 100,000 new cases occur every year in south and South-East Asia, with poor prospect of survival (Bull. WHO, 1984).

TABLE 2.9.1 : LIP, ORAL CAVITY AND PHARYNX (ICD 9:140-149)

MALES*

ICD.9	SITE	BANGALORE	BOMBAY	MADRAS	DELHI	BHOPAL	BARSHI
140-149	**Lip, Oral Cavity & Pharynx**	**17.5**	**26.8**	**23.6**	**19.4**	**38.8**	**10.8**
140	Lip	0.4	0.3	0.6	0.5	0.2	0.0
141	Tongue	4.7	6.5	5.3	7.7	13.2	2.1
142	Salivary Glands	0.8	0.4	0.4	0.8	0.5	0.5
143-145	**Mouth**	**3.0**	**5.8**	**7.3**	**3.7**	**10.4**	**3.4**
146	Oropharynx	1.9	3.2	1.9	3.2	3.8	0.0
147	Nasopharynx	0.6	0.6	0.6	0.6	0.0	0.0
148	Hypopharynx	5.9	8.2	6.5	2.3	8.4	3.5
149	Pharynx Etc.	0.2	1.8	1.0	0.6	2.3	1.3

FEMALES*

ICD.9	SITE	BANGALORE	BOMBAY	MADRAS	DELHI	BHOPAL	BARSHI
140-149	**Lip, Oral Cavity & Pharynx**	**14.9**	**9.5**	**14.7**	**6.4**	**10.4**	**1.1**
140	Lip	0.1	0.2	0.3	0.3	0.0	0.0
141	Tongue	1.0	1.9	2.1	1.3	1.4	0.0
142	Salivary Glands	0.5	0.3	0.2	0.5	0.0	0.0
143-145	**Mouth**	**11.1**	**3.9**	**8.2**	**2.5**	**6.8**	**0.6**
146	Oropharynx	0.5	0.6	0.4	1.0	0.5	0.0
147	Nasopharynx	0.4	0.2	0.3	0.2	0.5	0.0
148	Hypopharynx	1.2	1.5	2.7	0.6	0.8	0.5
149	Pharynx Etc.	0.1	0.9	0.5	0.0	0.4	0.0

* Age-adjusted (world population) cancer incidence rate, per 100,000 persons.

Relative risk of oral cancer in people with various tobacco habits, as well as the frequency of those habits, based on retrospective case control studies in India and Srilanka are noteworthy. There is a wide variation in frequencies and risks in different regions, but certain conclusions stand out. Approximately, 90% of oral cancers in south and south-east Asia can be attributed to tobacco chewing and smoking habits (Bull. WHO, 1984).

Case-control studies conducted in different parts of India have demonstrated that cancers of the oral cavity and pharynx are associated to a wide variety of tobacco chewing (pan chewing and betel nut with tobacco, lime and other ingredients) and smoking habits prevalent among men and women. These associations are statistically significant. Although it is difficult to obtain precise estimates of the risk for oral cancer associated with specific substance, it is clear that almost all of the risk is due to smoking of tobacco and the chewing of quids of various kinds. Notani et al. (1989) estimated the attributable risks associated with these habits as 61% for oral cancer (81% for males, 36% for females) and 79% for cancers of the pharynx and larynx (90% for males, 30% for females).

The most obvious and efficacious measure of control for oral cancer in India would be the elimination of chewing and smoking habits. Intervention studies carried out in some parts of India show that leukoplakia, a possible precursor of oral cancer, does regress rapidly after cessation of betel chewing (Mehta et al., 1982). Education programmes which reduced the prevalence of chewing and smoking tobacco also seem to have had an effect in reducing rates of leukoplakia (Gupta et al., 1990).

TABLE 2.9.1b : COMPARISON OF LIFE TIME CUMULATIVE CANCER INCIDENCE RATES (0-64 YEARS), 1989.
LIP, ORAL CAVITY AND PHARYNX (ICD-9 ; 140-149)

REGISTRY	CUMULATIVE RISK (%)		ONE IN HOW MANY PEOPLE WILL GET CANCER IN THEIR LIFE TIME	
	MALE	FEMALES	MALE	FEMALE
BANGALORE	1.2	0.8	83	125
BOMBAY	1.8	0.6	56	167
MADRAS	1.6	1.1	62	91
DELHI	1.3	0.5	77	200
BHOPAL	2.8	1.0	36	100
BARSHI	0.9	0.1	111	1000

2.9.2 DIGESTIVE ORGANS AND PERITONEUM (ICD9 :150-159)

In the digestive system, the oesophagus and stomach are the most frequently affected sites in the Indian registries (Table 2.9.2).

TABLE 2.9.2 : DIGESTIVE ORGANS AND PERITONEUM (ICD 9:150-159) - 1989.

(a) MALES*

ICD.9	SITE	BANGALORE	BOMBAY	MADRAS	DELHI	BHOPAL	BARSHI
150-159	**Digestive Organs & Peritoneum**	**33.0**	**35.5**	**37.0**	**22.3**	**25.4**	**18.6**
150	Oesophagus	9.4	11.5	10.2	6.4	7.7	6.7
151	Stomach	9.5	7.0	16.5	3.4	3.7	1.2
152	Small Intestine	0.0	0.5	0.1	0.2	0.0	0.0
153	Colon	2.7	4.0	2.0	2.0	1.4	2.0
154	Rectum	4.3	3.9	4.5	3.0	5.5	4.0
155	Liver	3.2	3.5	1.9	2.2	2.1	2.6
156	Gall Baldder	0.5	1.6	0.3	1.9	2.6	0.0
157	Pancreas	1.7	2.5	1.4	2.3	2.4	0.0
158	Retroperitoneum	0.9	0.3	0.1	0.3	0.0	2.1
159	Other	0.8	0.7	0.0	0.6	0.0	0.0

* Age-adjusted (World Population) Incidence Rate, Per 100,000 Persons.

(b) FEMALES*

ICD.9	SITE	BANGALORE	BOMBAY	MADRAS	DELHI	BHOPAL	BARSHI
150-159	Digestive Organs & Peritoneum	22.8	23.9	20.2	20.6	15.5	5.5
150	Oesophagus	10.2	8.2	7.7	4.6	5.2	1.4
151	Stomach	4.3	3.4	7.1	2.4	1.1	1.3
152	Small Intestine	0.0	0.3	0.0	0.2	0.0	0.0
153	Colon	2.3	2.4	0.8	2.0	2.1	0.5
154	Rectum	2.2	2.6	2.6	1.8	0.0	1.7
155	Liver	1.0	1.8	0.6	1.1	1.1	0.0
156	Gall Bladder	0.8	2.3	0.6	6.6	5.2	0.0
157	Pancreas	1.0	1.8	0.7	1.3	0.8	0.6
158	Retroperitoneum	0.5	0.6	0.1	0.3	0.0	0.0
159	Other	0.5	0.5	0.0	0.3	0.0	0.0

* Age-adjusted (world Population) Incidence Rate, Per 100,000 Persons.

2.9.2.1 Cancer of the Oesophagus (ICD.9 : 150)

Oesophageal cancer is characterised by an extreme diversity of rates throughout the world. There are usually more cases among males then females (Table 2.9.2.1).

It is interesting to observe that the cancer of the oesophagus in India mainly occur in the persons who are 30 years and above and age-specific incidence rates vary between 1 and 75 per 100,000. In 1989, age-adjusted incidence rates of cancer of the oesophagus in males are Bangalore (9.4), Bombay (11.5), Madras (10.2), Delhi (6.4), Bhopal (7.7) and Barshi (6.7), While in females, the rates are lower than males, except Bangalore (10.2); in other centres rates are Bombay (8.2), Madras (7.7), Delhi (4.6), Bhopal (5.2) and Barshi (1.4).

One of the prominent epidemiologic characterstics of the oesophageal cancer is the great variability in sex ratios reported in different geographical regions of the world. The typical pattern of male preponderance has been noted by several registeries. The sex ratios in urban areas in India vary between (M/F = 0.9 : 1) and (M/F = 1.5 : 1). In Barshi rural population the sex ratio is (M/F = 5.6 : 1).

TABLE 2.9.2.1 : INTERNATIONAL COMPARISON OF AGE-ADJUSTED (AAR) AND TRUNCATED TR) (35-64 YEARS) INCIDENCE RATE PER 100,000 PERSONS.
OESOPHAGUS CANCER (ICD.9 : 150)
(a) MALES

YEAR STUDIED	REGISTRY	AAR*	TR*
1978-82	CHINA (SHANGHAI)	20.8	21.0
1978-82	SINGAPORE (CHINESE)	13.5	13.9
1978-81	JAPAN (MIYAGI)	13.3	14.5
1978-82	USA (CONNECTICUT) WHITE	5.1	6.2
	BLACK	24.0	47.8
1979-82	UK (OXFORD)	3.6	2.8
1977-81	FINLAND	3.7	3.4
1989	INDIA		
	BOMBAY	11.5	17.3
	MADRAS	10.2	19.6
	BANGALORE	9.4	14.3
	BHOPAL	7.7	13.4
	DELHI	6.4	10.7
	BARSHI	6.7	10.4

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YEAR STUDIED	REGISTRY	AAR*	TR*
1978-82	CHINA (SHANGHAI)	8.9	9.7
1978-82	SINGAPORE (CHINESE)	3.5	4.1
1978-81	JAPAN (MIYAGI)	3.1	2.5
1977-81	FINLAND	2.4	1.8
1979-82	UK (OXFORD)	2.9	3.6
1978-82	USA (CONNECTICUT) WHITE	1.5	1.9
	BLACK	6.0	11.8
1989	INDIA		
	BANGALORE	10.2	20.8
	BOMBAY	8.2	15.8
	MADRAS	7.7	16.1
	BHOPAL	5.2	11.1
	DELHI	4.6	10.0
	BARSHI	1.4	2.0

* World Population
Source : Cancer Incidence In Five Continents, Vol. V,1987. NCRP Data, 1989

In Bombay, where oesophageal cancer is almost as common as in men as in women, drinking of the local alcoholic brews and smoking of bidis & cigarettes are associated with particularly high risks in men, but chewing of tobacco quids, smoking and drinking explain only a small fraction of the incidence in women (Jussawalla & Deshpande, 1971). Notani et al. (1989) estimated that 34% of oesophageal cancer in India is related to tobacco use, although the percentages for males (50%) and females (13%) are very different.

2.9.2.2. Cancer of the Stomach (ICD.9 : 151)

In 1980, stomach cancer was estimated to be the single most common form of cancer in the world, accounting for some 670 000 new cases per year (10.5% of all cancers) (Parkin et al., 1988). It is probably now the second most common cancer, after lung cancer. The highest incidence rates occur in Japan (Males - 79.6; Females - 36.0 per 100,000) and lowest rates in Kuwait (Males - 3.7, Females - 1.6) (Table 2.9.2.2).

Age-adjusted incidence rates of stomach cancer in India are low. In 1989, the rates in men in Madras (16.5) is more than Bangalore (9.5), Bombay (7.0), Bhopal (3.7), Delhi (3.4) and Barshi (1.2). Thus stomach cancer, in men, in Madras is frequent where the incidence is almost 1.5 times than Bangalore, double that in Bombay and over three times as frequent as in Delhi and Bhopal. The female incidence rates are lower than males : Madras (7.1), Bangalore (4.3), Bombay (3.4), Delhi (2.4), Bhopal (1.1) and Barshi (1.3).

The incidence and mortality rates in males are approximately double those for females in both high-risk and low-risk countries.

The most remarkable feature of the epidemiology of gastric cancer is the universal decline in its incidence and mortality. The decline is about 2-4% per year, but there is a lot of variation between different countries. Rates are falling more rapidly for females than for males.

Christopher et al (1986) have indicated that, between 1950 and 1979, the Scandinavian countries , Switzerland and the USA exhibited the greatest percent decrease (65% - 73%) in their gastric cancer mortality rates. Western Euporean countries showed the next greatest percent decrease (59% - 62%), followed by Australia (56%). The countries that demonstrated the smallest percent change in gastric cancer mortality over the 29-year period were Japan and Italy (44%), and Northern Ireland (41%). The authors conclude that the major etiologic influences in gastric cancer are environmental rather than genetic.

Data from cancer registries indicate that the temporal changes in the incidence of gastric cancer in Norway (Munoz & Asvall, 1971) and Japan (Hanai et al., 1982) are due largely to the disappearance of the 'intestinal' type

of gastric cancer as opposed to the 'diffuse' type.

Case-control and cohort studies in a wide variety of populations have shown increased risk associated with more frequent use of starchy foods (such as corn, wheat, rice, potatoes, and beans), smoked, salted and fried foods, and a decreased risk associated with the more frequent intake of green leafy vegetables, citrus fruits and dairy products (Hirayama, 1980).

TABLE 2.9.2.2 : INTERNATIONAL COMPARISON OF AGE-ADJUSTED (AAR) AND TRUNCATED (TR) (35-64 YEARS) INCIDENCE RATE PER 100,000. STOMACH CANCER (ICD-9 : 151)

MALES

YEAR STUDIED	REGISTRY	AAR*	TR*
1978-81	JAPAN (MIYAGI)	79.6	111.8
1977-81	FINLAND	24.6	25.7
1979-82	UK (OXFORD)	20.2	22.5
1978-82	USA (CONNECTICUT) WHITE	10.8	11.5
	BLACK	19.4	22.0
1979-82	KUWAIT : KUWAITIS	3.7	4.1
1989	INDIA		
	MADRAS	16.5	32.6
	BANGALORE	9.5	16.3
	BOMBAY	7.0	9.5
	BHOPAL	3.7	8.5
	DELHI	3.4	6.2
	BARSHI	1.2	3.9

FEMALES

YEAR STUDIED	REGISTRY	AAR*	TR*
1978-81	JAPAN (MIYAGI)	36.0	50.5
1977-81	FINLAND	12.9	13.7
1979-82	UK (OXFORD)	7.8	6.8
1978-82	USA (CONNECTICUT) WHITE	4.3	4.5
	BLACK	9.1	11.3
1979-82	KUWAIT : KUWAITIS	1.6	2.0
1989	INDIA		
	MADRAS	7.1	17.4
	BANGALORE	4.3	8.4
	BOMBAY	3.4	6.1
	DELHI	2.4	5.0
	BHOPAL	1.1	3.0
	BARSHI	1.3	4.1

* World Population

Source : Cancer Incidence In Five Continents, Vol. V,1987. NCRP Data, 1989

2.9.3 RESPIRATORY AND INTRATHORACIC ORGANS (ICD 9 : 160-165)

In the respiratory and intrathoracic organs, cancers of the larynx and trachea, bronchus and lung are the most affected sites (Table 2.9.3).

TABLE 2.9.3a : RESPIRATORY AND INTRATHORACIC ORGANS (ICD 9:160-165) - 1989.
MALES*

ICD.9	SITE	BANGALORE	BOMBAY	MADRAS	DELHI	BHOPAL	BARSHI
160-165	**Respiratory & Intrathoracic**	**13.7**	**25.1**	**17.6**	**21.3**	**19.0**	**3.3**
160	Nasal Etc.	0.3	1.4	0.6	0.5	1.6	0.0
161	Larynx	4.1	8.8	5.5	8.6	2.9	1.3
162	Trachea, Bronchus & Lung	8.6	14.6	11.1	11.9	14.1	2.0
163	Pleura	0.6	0.2	0.2	0.2	0.4	0.0
164	Thymus etc.	0.1	0.1	0.2	0.1	0.0	0.0
165	Other	0.0	0.0	0.0	0.0	0.0	0.0

FEMALES*

ICD.9	SITE	BANGALORE	BOMBAY	MADRAS	DELHI	BHOPAL	BARSHI
160-165	**Respiratory & Intrathoracic**	**3.3**	**6.3**	**2.8**	**4.6**	**4.6**	**0.0**
160	Nasal etc.	0.4	1.0	0.8	0.4	0.4	0.0
161	Larynx	0.7	1.3	0.3	1.8	0.5	0.0
162	Trachea, Bronchus & Lung	1.6	3.7	1.7	2.2	3.2	0.0
163	Pleura	0.5	0.2	0.0	0.2	0.5	0.0
164	Thymus etc.	0.1	0.1	0.0	0.0	0.0	0.0
165	Other	0.0	0.0	0.0	0.0	0.0	0.0

* Age-adjusted (World Population) Incidence Rate, Per 100,000 Persons

2.9.3.1 Cancer of the Larynx (ICD.9 : 161)

The age-adjusted incidence rate of laryngeal cancer in Indian material is high in men than women. Among men, the highest incidence rates are in Bombay (8.8 per 100,000) and Delhi (8.6 per 100,000), during the period 1989.

TABLE 2.9.3.1 : INTERNATIONAL COMPARISON OF AGE-ADJUSTED (AAR) AND TRUNCATED (TR) (35-64 YEARS) INCIDENCE RATE PER 100,000.
LARYNX CANCER (ICD-9 : 161)
(a) MALES

YEAR STUDIED	REGISTRY	AAR*	TR*
1978	BRAZIL (SAO PAULO)	17.8	27.6
1978-82	USA (CONNECTICUT) BLACK	12.6	24.8
	WHITE	7.7	12.4
1977-81	FINLAND	4.5	7.1
1979-82	UK (OXFORD)	4.2	5.8
1978-82	SWEDEN	2.8	4.1
1989	INDIA		
	BOMBAY	8.8	15.6
	DELHI	8.6	19.7
	MADRAS	5.5	8.9
	BANGALORE	4.1	8.3
	BHOPAL	2.9	5.3
	BARSHI	1.3	4.1

(b) F E M A L E S

YEAR STUDIED	REGISTRY	AAR*	TR*
1978-82	USA (CONNECTICUT) BLACK	2.7	4.4
	WHITE	1.7	3.0
1978	BRAZIL (SAO PAULO)	1.3	2.8
1979-82	UK (OXFORD)	0.5	0.8
1977-81	FINLAND	0.3	0.7
1978-82	SWEDEN	0.3	0.7
1989	INDIA		
	DELHI	1.8	4.0
	BOMBAY	1.3	1.8
	BANGALORE	0.7	1.6
	BHOPAL	0.5	0.0
	MADRAS	0.3	0.5
	BARSHI	0.0	0.0

* World Population
Source : Cancer Incidence In Five Continents, Vol. V, 1987. NCRP Data, 1989

The rates in other centres are : Bangalore (4.1), Madras (5.5), Bhopal (2.9) and Barshi (1.3). While in females, laryngeal cancer age-adjusted incidence rates are very low in all the centres (vary between 0.0 and 1.8 per 100,000).

International comparisons are done in Table 2.9.3.1 for selected countries.The highest incidence rate of laryngeal cancer world wide have been reported from Sao Paulo (Brazil) in males (Males - 17.8 and Females- 1.3 per 100,000) and the lowest rate reported for European populatins in Sweden (Males - 2.8, Females - 0.3).

Jayant et al. (1977) estimated the proportion of cases of laryngeal cancer in Bombay that could be attributed to chewing tobacco quid and/or smoking. The attributable risk for these two exposures combined was 78%; 28% of the cases occurred in chewers who were nonsmokers, 38% in smokers who did not chew and 34% in cases who admitted to both habits. The smokers mostly smoked bidis and the chewers used pan with betel nut, tobacco and lime. Only 11% of the cases were nonchewers and nonsmokers compared to 46% of the controls.

2.9.3.2 Cancer of the Trachea, Bronchus & Lung (ICD.9 : 162)

Cancer of the lung is of epidemiological interest because of the wide spread geographical and racial variations observed and steadily increasing incidence and mortality noted in the West. This increase has so far been noticed particularly in men, but recently women have also begun to present a similar rising trend.

Age-adjusted and truncated incidence rates of lung cancer are much lower in India than the corresponding rates reported world wide by other countries in Cancer Incidence in Five Continents (Vol.V, 1987). Age-adjusted incidence is higher in the male population : Bombay (14.6), Bhopal (14.1), Delhi (11.9), Madras (11.1), and Bangalore (8.6). Lung cancer is in the first rank in Bombay, Delhi and Bhopal, but it is not in the first eight ranking sites in the Barshi. While in Indian women, incidence is low (ranges between 1.7 and 3.7 per 100,000).

The highest rates for cancer of the bronchus and trachea in people of European stock are 100.4 in males in western Scotland and 33.3 among white females in San Francisco (Bay Area); the lowest rates are found in Iceland in males (24.7) and in Doubs, France, in females (2.8), indicating a potential for prevention of 75% in males in western Scotland, and 92% in females in San Francisco (Tomatis et al., 1990). The overall incidence of the disease is much higher in the industrialised countries.

A large number of epidemiological studies in the West has shown that there is a progressive and absolute risk in its incidence which has occurred over the past few decades and that it is clearly linked to cigarette smoking and environmental pollution.

The association of cigarette smoking with lung cancer has now been universally accepted. The U.S. Surgeon General's Advisory Committee concluded that cigarette smoking is causally related to lung cancer in men and that its effect far outweighs all other probable etiological factors. The risk increases with the duration of smoking habit

and the number of cigarettes smoked daily. A heavy smoker (more than 50 cigarette per day) runs a 20 times higher risk of developing lung cancer, than a non- smoker. The increasing incidence of lung cancer in women in the West is clearly linked with the steep increase registered in cigarette smoking by women during the sixties.

Many specific occupations and occupational exposures have been associated with elavated risks for lung cancer, and in a number of cases the link has been clearly established to be causal. Clearly identified occupational lung carcinogens are asbestos, coal-tars and soots, arsenic and arsenic compounds, nickel compounds, mustard gas and radon. Increased risk for lung cancer have also been found to be causally associated with occupational exposure in aluminium production, in coal gasification and coal production, in iron and steel founding etc. (IARC, 1987).

TABLE 2.9.3.2 : INTERNATIONAL COMPARISON OF AGE-ADJUSTED (AAR) TRUNCATED (TR)(35-64 YEARS) INCIDENCE RATE PER 100,000. TRACHEA, BRONCHUS & LUNG (ICD.9 : 162)

M A L E S

YEAR STUDIED	REGISTRY	AAR*	TR*
1979-82	UK (WEST SCOTLAND)	100.4	120.7
1977-81	FINLAND	74.2	93.2
1979-82	UK (OXFORD)	68.8	68.1
1978-82	USA (BAY AREA) WHITE	65.8	84.0
1978-82	USA (CONNECTICUT) WHITE	64.3	81.1
	BLACK	89.8	140.1
1977-81	COLUMBIA (CALI)	19.5	25.5
1989	INDIA		
	BOMBAY	14.6	24.7
	BHOPAL	14.1	24.5
	DELHI	11.9	23.3
	MADRAS	11.1	23.2
	BANGALORE	8.6	13.2
	BARSHI	2.0	3.9

F E M A L E S

YEAR STUDIED	REGISTRY	AAR*	TR*
1978-82	USA (BAY AREA) WHITE	33.3	54.4
1979-82	UK (WEST SCOTLAND)	28.6	46.3
1978-82	USA (CONNECTICUT) WHITE	25.3	41.5
	BLACK	21.9	41.1
1979-82	UK (OXFORD)	19.5	25.6
1977-81	FINLAND	7.0	10.0
1972-76	COLUMBIA (CALI)	5.4	9.5
1989	INDIA		
	BOMBAY	3.7	5.3
	BHOPAL	3.2	6.3
	DELHI	2.2	4.5
	MADRAS	1.7	4.5
	BANGALORE	1.6	4.1
	BARSHI	0.0	0.0

* World Population

Source : Cancer Incidence In Five Continents, Vol. V,1987.

TABLE 2.10.1 : TRENDS IN AGE-ADJUSTED (WORLD POPULATION) CANCER INCIDENCE RATES

BANGALORE*

SEX : MALES YEAR : 1982-1989

ICD9	SITE	YEAR OF DIAGNOSIS 1982	1983	1984	1985	1986	1987	1988	1989
140	Lip	0.2	0.0	0.0	0.0	0.1	0.0	0.1	0.4
141	Tongue	4.5	4.0	3.0	2.6	2.8	4.5	2.9	4.7
142	Salivary Gland	0.4	0.4	0.0	0.3	0.4	0.5	0.7	0.8
143-145	Mouth	4.0	4.9	3.6	4.5	3.1	5.4	3.4	3.0
146	Oropharynx	2.2	2.0	2.3	1.3	1.9	1.9	2.5	1.9
147	Nasopharynx	0.9	0.4	0.7	0.7	0.4	0.3	0.2	0.6
148	Hypopharynx	4.9	6.0	6.6	6.0	5.2	7.5	7.3	5.9
149	Pharynx Uns	0.4	0.4	0.8	0.7	0.3	0.7	0.6	0.2
150	Oesophagus	8.4	6.3	8.2	7.3	7.6	11.1	9.9	9.4
151	Stomach	11.0	10.9	10.5	12.1	9.9	9.3	13.6	9.5
152	Small Intestine	0.0	0.2	0.0	0.1	0.4	0.0	0.2	0.0
153	Colon	2.0	2.0	2.4	2.6	2.4	2.1	2.6	2.7
154	Rectum	3.0	2.3	2.3	3.4	3.5	3.4	3.6	4.3
155	Liver	4.0	1.5	3.7	3.6	2.8	3.4	2.8	3.2
156	Gallbladder	0.0	0.3	0.2	0.3	0.7	0.7	0.4	0.5
157	Pancreas	0.7	1.2	0.7	0.7	0.8	1.4	2.3	1.7
158	Peritoneum	1.0	1.0	0.5	1.1	0.5	0.7	0.7	0.9
160	Nose Etc	0.2	0.2	0.5	0.8	0.6	0.9	0.6	0.3
161	Larynx	4.5	4.9	4.0	3.7	4.1	4.8	4.4	4.1
162	Lung	5.3	8.8	9.2	11.8	10.0	10.8	11.7	8.6
163	Pleura	0.7	0.4	0.2	0.5	0.5	0.3	0.5	0.6
164	Other Thoracic	0.4	0.2	0.2	0.2	0.1	0.2	0.1	0.1
170	Bone	1.0	1.6	1.1	1.1	0.5	0.5	1.3	1.3
171	Connective Tissue	1.5	1.2	1.3	0.8	0.3	1.6	0.6	0.6
172	Skin Melanoma	0.5	0.7	0.0	0.0	0.5	0.1	0.0	0.1
173	Skin Other	2.7	0.9	1.7	0.9	1.4	1.4	2.5	2.0
175	Breast	0.3	0.6	0.3	0.3	0.5	0.5	0.4	0.2
185	Prostate	4.1	3.2	4.2	5.6	5.0	5.5	4.9	7.1
186	Testis	0.7	0.3	0.9	0.7	1.0	0.7	0.3	0.6
187	Penis Etc	2.3	2.8	2.0	2.3	1.0	1.4	2.2	1.8
188	Bladder	3.3	4.5	2.9	2.8	3.0	3.1	3.3	2.7
189	Kidney	1.2	0.8	1.0	1.8	1.9	1.5	0.6	1.1
190	Eye	0.7	0.1	0.1	0.2	0.3	0.1	0.1	0.2
191-192	Brain-Ns	1.8	2.6	1.1	1.7	3.0	2.2	3.5	4.0
193	Thyroid Gland	0.9	0.4	0.4	1.1	1.7	0.6	1.2	0.9
194	Endocrine Other	0.2	0.4	0.1	0.0	0.0	0.1	0.0	0.1
201	Hodgkins Disease	1.5	1.4	1.0	1.4	1.6	1.5	1.2	2.4
200-202	Non-Hodg Lymphoma	3.1	3.1	3.4	2.9	3.2	1.7	4.2	3.1
203	Mult Myeloma	0.7	0.5	1.1	0.8	1.0	0.9	0.3	0.6
204	Leuk Lymphoid	0.9	0.7	1.1	1.0	1.2	0.8	1.2	1.6
205	Leuk Myeloid	1.0	1.0	1.2	0.8	1.0	1.5	0.9	2.3
206	Leuk Monocytic	0.0	0.0	0.0	0.2	0.0	0.0	0.0	0.1
207	Leuk Other	0.0	0.3	0.1	0.3	0.0	0.0	0.0	0.0
208	Leuk Uns	0.6	0.5	0.4	0.3	0.5	0.5	0.2	0.7
	Primary Unk	12.5	6.6	5.5	7.6	10.4	14.3	14.7	15.2
	ALL SITES	100.2	92.5	90.6	98.7	97.0	110.7	114.6	112.2

* Incidence Rate Per 100,000

TABLE 2.10.2 :TRENDS IN AGE-ADJUSTED (WORLD POPULATION) CANCER INCIDENCE RATES

BANGALORE*

SEX : FEMALES YEAR : 1982-1989

ICD9	SITE	YEAR OF DIAGNOSIS 1982	1983	1984	1985	1986	1987	1988	1989
140	Lip	0.1	0.1	0.3	0.1	0.1	0.1	0.2	0.1
141	Tongue	1.1	1.4	1.0	1.2	0.8	1.1	1.2	1.0
142	Salivary Gland	0.2	0.5	0.6	0.2	0.3	0.9	0.2	0.5
143-145	Mouth	13.4	9.6	10.2	9.2	10.4	8.9	11.2	11.1
146	Oropharynx	0.4	0.4	0.3	0.2	0.4	0.1	0.5	0.5
147	Nasopharynx	0.1	0.5	0.3	0.0	0.1	0.1	0.3	0.4
148	Hypopharynx	1.3	1.7	1.6	1.2	0.6	1.2	1.5	1.2
149	Pharynx Uns	0.3	0.4	0.0	0.6	0.5	0.2	0.3	0.1
150	Oesophagus	7.1	7.3	9.5	7.2	10.1	9.8	8.1	10.2
151	Stomach	6.0	6.0	5.7	7.0	4.7	5.2	6.3	4.3
152	Small Intestine	0.1	0.2	0.4	0.3	0.1	0.1	0.1	0.0
153	Colon	1.5	1.1	1.2	1.5	2.2	2.6	2.4	2.3
154	Rectum	2.6	1.9	2.8	2.5	3.2	3.0	3.6	2.2
155	Liver	1.4	1.2	0.6	0.8	0.9	1.1	1.5	1.0
156	Gallbladder	0.0	0.6	0.3	0.4	0.2	0.8	0.7	0.8
157	Pancreas	0.4	0.4	0.3	1.3	0.5	1.0	0.7	1.0
158	Peritoneum	1.6	0.7	0.7	0.1	0.7	0.2	0.7	0.5
160	Nose Etc	0.7	0.4	0.1	0.7	0.7	0.2	0.5	0.4
161	Larynx	1.3	0.8	0.6	0.9	0.7	0.6	0.5	0.7
162	LUNG	1.4	1.7	2.2	1.7	1.4	2.3	1.5	1.6
163	Pleura	0.4	0.4	0.4	0.4	0.3	0.3	0.2	0.5
164	Other Thoracic	0.1	0.0	0.0	0.1	0.0	0.1	0.1	0.1
170	Bone	1.2	0.4	1.3	0.2	0.6	0.7	0.8	0.9
171	Connective Tissue	1.1	0.7	0.9	0.7	0.8	1.0	0.5	0.3
172	Skin Melanoma	0.5	0.4	0.4	0.3	0.2	0.1	0.2	0.1
173	Skin Other	1.9	2.4	2.1	1.2	1.3	0.7	2.5	1.6
174	Breast	17.3	17.6	18.5	17.8	15.9	20.9	20.4	22.3
179	Uterus Uns	0.2	0.2	1.0	0.4	0.5	0.8	0.1	0.6
180	Cervix Uteri	35.6	33.7	31.0	29.5	28.7	32.4	32.2	26.4
181	Placenta	0.2	0.2	0.0	0.2	0.4	0.1	0.0	0.0
182	Corpus Uteri	1.8	2.2	1.6	1.0	1.3	2.0	0.9	2.0
183	Ovary etc	5.0	4.3	5.5	3.1	5.3	5.9	4.7	4.7
184	Other Fem Genital	2.3	1.2	1.2	0.8	1.5	1.5	1.9	1.4
188	Bladder	0.7	0.4	0.5	0.6	0.2	0.7	0.8	0.8
189	Kidney	1.7	0.9	0.4	0.6	0.8	1.1	0.5	0.4
190	Eye	0.3	0.2	0.0	0.2	0.1	0.2	0.4	0.0
191-192	Brain-Ns	1.2	1.0	1.1	1.6	1.4	1.8	1.3	1.7
193	Thyroid Gland	2.5	2.7	3.4	3.1	1.7	3.0	3.4	3.2
194	Endocrine Other	0.0	0.2	0.1	0.0	0.0	0.1	0.1	0.1
201	Hodgkins Disease	0.4	0.3	0.3	0.9	0.4	0.7	1.0	0.7
200-202	Non-hodg Lymphoma	1.4	1.6	1.7	1.0	2.5	2.0	1.3	2.1
203	Mult Myeloma	0.2	0.1	0.7	0.6	0.6	1.0	0.5	0.7
204	Leuk Lymphoid	0.5	0.3	0.5	0.8	0.6	0.4	0.5	0.6
205	Leuk Myeloid	0.9	1.0	0.9	1.4	1.3	1.5	2.1	2.0
206	Leuk Monocytic	0.2	0.0	0.0	0.0	0.0	0.0	0.0	0.0
207	Leuk Other	0.0	0.3	0.0	0.0	0.0	0.1	0.1	0.0
208	Leuk Uns	0.3	0.7	0.1	0.0	0.3	0.4	0.6	0.9
	Primary Unk	10.0	6.1	3.9	5.1	10.5	10.4	12.9	10.5
	ALL SITES	129.0	116.2	116.3	108.7	115.9	129.5	132.3	124.7

* Incidence Rate Per 100,000

TABLE 2.10.3 :TRENDS IN AGE-ADJUSTED (WORLD POPULATION) CANCER INCIDENCE RATES

BOMBAY*

SEX : MALES YEAR : 1982-1989

ICD9	SITE	YEAR OF DIAGNOSIS 1982	1983	1984	1985	1986	1987	1988	1989
140	Lip	0.3	0.4	0.3	0.3	0.4	0.3	0.2	0.3
141	Tongue	7.1	7.2	7.8	7.9	7.8	6.3	5.9	6.5
142	Salivary Gland	0.6	0.5	0.4	0.4	0.5	0.5	0.5	0.4
143-145	Mouth	5.7	5.9	5.0	6.9	5.9	5.6	6.1	5.8
146	Oropharynx	3.3	2.7	3.8	3.6	2.7	3.3	3.5	3.2
147	Nasopharynx	0.9	1.1	0.5	0.7	0.8	0.5	0.6	0.6
148	Hypopharynx	9.5	7.7	8.6	8.1	8.0	8.3	9.4	8.2
149	Pharynx Uns	2.6	2.3	1.6	2.4	2.6	2.1	1.8	1.8
150	Oesophagus	11.2	9.9	12.1	11.6	11.4	11.8	11.4	11.5
151	Stomach	7.4	7.4	7.1	7.3	7.9	6.8	7.7	7.0
152	Small Intestine	0.2	0.2	0.3	0.2	0.5	0.2	0.2	0.5
153	Colon	2.5	2.9	2.5	2.6	3.5	4.5	3.0	4.0
154	Rectum	4.0	3.1	3.5	3.2	2.9	3.2	3.3	3.9
155	Liver	3.8	3.3	3.3	3.3	3.7	3.2	3.5	3.5
156	Gallbladder	0.7	0.6	1.1	1.2	1.0	1.1	1.2	1.6
157	Pancreas	2.2	1.7	2.2	3.2	2.7	2.6	2.3	2.5
158	Peritoneum	0.5	0.1	0.2	0.3	0.3	0.4	0.6	0.3
160	Nose etc	1.1	0.8	1.1	1.0	0.9	1.1	0.7	1.4
161	Larynx	7.0	8.9	8.1	7.8	9.8	9.9	8.1	8.8
162	Lung	13.7	14.7	13.4	14.2	13.1	14.8	14.0	14.6
163	Pleura	0.1	0.0	0.1	0.3	0.5	0.5	0.5	0.2
164	Other Thoracic	0.1	0.0	0.1	0.1	0.1	0.2	0.1	0.1
170	Bone	0.9	0.8	0.9	0.9	0.9	0.9	0.8	0.8
171	Connective Tissue	1.0	1.2	1.8	1.1	1.4	1.3	1.3	1.5
172	Skin Melanoma	0.3	0.2	0.4	0.3	0.2	0.1	0.5	0.3
173	Skin Other	1.9	1.6	1.4	2.6	2.1	1.9	2.0	1.3
175	Breast	0.2	0.1	0.5	0.3	0.3	0.6	0.4	0.3
185	Prostate	5.4	5.7	6.9	8.3	6.1	7.3	8.2	6.9
186	Testis	0.8	1.0	1.1	0.9	1.1	1.0	0.9	0.9
187	Penis etc	2.2	1.7	2.1	1.7	2.2	2.0	2.0	1.6
188	Bladder	3.4	3.1	4.0	3.2	3.8	4.1	4.5	4.2
189	Kidney	1.1	1.5	1.5	1.1	1.5	1.5	1.6	1.4
190	Eye	0.2	0.5	0.2	0.3	0.2	0.3	0.1	0.4
191-192	Brain-Ns	1.8	1.8	2.8	2.7	2.0	2.6	2.8	3.1
193	Thyroid Gland	0.6	0.9	0.8	0.6	1.0	0.7	0.7	0.7
194	Endocrine Other	0.1	0.1	0.1	0.1	0.2	0.2	0.3	0.2
201	Hodgkins Disease	1.1	1.3	1.0	1.4	1.2	1.0	1.1	1.2
200-202	Non-hodg Lymphoma	2.6	3.4	3.3	4.1	3.6	4.4	3.1	4.0
203	Mult Myeloma	1.2	0.9	0.7	0.9	0.8	0.9	0.8	1.3
204	Leuk Lymphoid	1.7	1.1	2.2	1.7	1.5	1.4	1.7	1.6
205	Leuk Myeloid	1.5	1.4	2.1	1.9	1.9	1.7	1.7	1.9
206	Leuk Monocytic	0.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0
207	Leuk Other	0.0	0.1	0.0	0.0	0.0	0.1	0.1	0.2
208	Leuk Uns	0.4	0.5	0.6	0.5	0.5	0.6	0.4	0.3
	Primary Unk	6.6	6.8	6.8	8.5	8.9	9.0	10.0	9.7
	ALL SITES	119.9	116.5	123.9	129.5	128.5	130.4	129.6	130.4

* Incidence Rate Per 100,000

TABLE 2.10.4 :TRENDS IN AGE-ADJUSTED (WORLD POPULATION) CANCER INCIDENCE RATES
BOMBAY*
SEX : FEMALES YEAR : 1982-1989

ICD9	SITE	YEAR OF DIAGNOSIS 1982	1983	1984	1985	1986	1987	1988	1989
140	Lip	0.1	0.4	0.2	0.2	0.3	0.3	0.3	0.2
141	Tongue	2.9	2.4	2.0	2.5	3.2	2.5	2.2	1.9
142	Salivary Gland	0.7	0.3	0.4	0.3	0.5	0.3	0.3	0.3
143-145	Mouth	4.5	4.2	3.9	4.4	4.5	4.4	4.7	3.9
146	Oropharynx	0.5	0.7	0.3	1.0	0.6	0.7	0.6	0.6
147	Nasopharynx	0.5	0.4	0.2	0.2	0.3	0.1	0.3	0.2
148	Hypopharynx	2.1	1.3	2.0	2.6	1.9	1.8	2.2	1.5
149	Pharynx Uns	0.4	0.5	0.9	0.7	0.5	0.9	0.6	0.9
150	Oesophagus	8.4	7.4	8.4	8.9	8.3	8.8	8.0	8.2
151	Stomach	5.4	3.7	3.9	4.2	4.9	4.8	4.3	3.4
152	Small Intestine	0.5	0.3	0.3	0.2	0.2	0.2	0.3	0.3
153	Colon	2.3	2.7	2.8	2.5	2.4	2.8	2.7	2.4
154	Rectum	2.4	2.3	2.3	2.5	2.6	2.8	2.3	2.6
155	Liver	2.7	1.5	1.4	2.2	2.5	1.7	1.9	1.8
156	Gallbladder	1.0	1.6	1.4	1.9	1.5	2.0	2.1	2.3
157	Pancreas	1.4	1.3	1.2	1.9	1.1	2.0	1.9	1.8
158	Peritoneum	0.2	0.3	0.5	0.6	0.5	0.4	0.3	0.6
160	Nose Etc	0.8	0.6	1.0	0.9	0.9	0.7	0.3	1.0
161	Larynx	1.2	2.0	1.3	1.4	1.6	1.6	1.5	1.3
162	Lung	3.3	3.2	4.1	2.7	2.0	2.9	3.6	3.7
163	Pleura	0.1	0.0	0.0	0.3	0.4	0.1	0.2	0.2
164	Other Thoracic	0.1	0.0	0.0	0.1	0.1	0.0	0.1	0.1
170	Bone	0.7	0.8	0.9	0.6	0.8	0.6	0.6	0.7
171	Connective Tissue	1.0	0.8	0.7	1.1	0.7	0.6	0.9	0.9
172	Skin Melanoma	0.1	0.0	0.2	0.5	0.2	0.1	0.2	0.3
173	Skin Other	1.3	0.9	1.2	2.0	1.6	1.7	1.1	1.2
174	Breast	21.4	21.6	23.6	26.4	26.7	24.2	25.0	26.1
179	Uterus Uns	1.5	1.2	1.2	1.4	1.7	1.1	1.3	1.5
180	Cervix Uteri	18.5	18.5	19.6	19.3	19.9	19.1	21.0	19.4
181	Placenta	0.3	0.2	0.2	0.3	0.1	0.2	0.2	0.1
182	Corpus Uteri	2.1	2.2	2.1	2.0	2.7	2.4	2.2	2.2
183	Ovary etc	5.9	6.3	6.2	6.7	6.0	7.3	7.6	7.0
184	Other Fem Genital	1.6	1.2	1.4	1.1	1.2	1.7	1.6	1.7
188	Bladder	0.7	1.0	0.9	1.3	0.9	0.7	1.3	1.3
189	Kidney	0.5	0.7	0.7	0.8	0.7	0.6	0.7	0.8
190	Eye	0.2	0.3	0.1	0.1	0.1	0.3	0.4	0.2
191-192	Brain-Ns	1.3	1.2	1.5	1.7	1.6	2.3	1.7	2.3
193	Thyroid Gland	1.5	1.3	1.4	1.5	1.8	1.7	2.0	2.0
194	Endocrine Other	0.0	0.1	0.2	0.2	0.1	0.0	0.1	0.1
201	Hodgkins Disease	0.6	0.5	0.7	0.7	0.3	0.6	0.5	0.7
200-202	Non-hodg Lymphoma	1.8	2.0	2.4	2.0	2.3	2.8	2.6	3.0
203	Mult Myeloma	0.6	0.8	1.0	1.1	0.8	0.8	0.8	0.6
204	Leuk Lymphoid	1.0	0.7	0.8	0.9	1.3	0.9	1.1	1.1
205	Leuk Myeloid	1.4	1.3	1.7	1.4	1.4	1.5	1.4	1.3
206	Leuk Monocytic	0.1	0.0	0.0	0.1	0.0	0.0	0.0	0.0
207	Leuk Other	0.1	0.0	0.1	0.0	0.0	0.0	0.0	0.1
208	Leuk Uns	0.4	0.5	0.3	0.4	0.4	0.3	0.5	0.4
	Primary Unk	4.9	4.8	6.7	7.1	6.7	5.4	6.9	6.1
	ALL SITES	111.2	106.3	113.8	122.9	120.9	118.8	122.7	120.4

* Incidence Rate Per 100,000

TABLE 2.10.5 :TRENDS IN AGE-ADJUSTED (WORLD POPULATION) CANCER INCIDENCE RATES
MADRAS*
SEX : MALES YEAR : 1982-1989

ICD9	SITE	YEAR OF DIAGNOSIS							
		1982	1983	1984	1985	1986	1987	1988	1989
140	Lip	0.4	0.2	0.1	0.5	0.1	0.5	0.5	0.6
141	Tongue	3.8	3.5	4.0	5.5	5.0	5.1	8.2	5.3
142	Salivary Gland	0.3	0.8	0.7	0.7	0.4	0.7	0.9	0.4
143-145	Mouth	6.7	6.1	5.6	6.7	7.4	8.1	9.8	7.3
146	Oropharynx	1.8	1.7	1.4	1.1	2.0	2.2	2.9	1.9
147	Nasopharynx	0.7	0.6	0.9	0.8	0.8	0.4	1.4	0.6
148	Hypopharynx	3.7	5.4	4.2	3.8	5.9	6.6	7.8	6.5
149	Pharynx Uns	0.6	1.0	0.4	0.4	1.2	0.9	1.2	1.0
150	Oesophagus	6.3	6.1	7.6	7.7	7.2	9.5	10.4	10.2
151	Stomach	12.1	14.2	13.8	15.7	17.1	14.3	15.1	16.5
152	Small Intestine	0.3	0.5	0.2	0.1	0.0	0.2	0.2	0.1
153	Colon	1.5	2.1	0.7	1.7	1.7	1.3	1.9	2.0
154	Rectum	2.7	2.1	2.6	2.1	2.6	2.5	3.7	4.5
155	Liver	1.7	1.6	2.5	3.1	2.1	2.4	3.9	1.9
156	Gallbladder	0.1	0.4	0.3	0.4	0.3	0.9	0.5	0.3
157	Pancreas	1.0	1.0	1.1	0.9	1.2	1.5	1.0	1.4
158	Peritoneum	0.7	0.3	0.5	0.4	0.4	0.3	0.3	0.1
160	Nose Etc	0.6	1.1	0.7	0.7	1.2	0.6	1.6	0.6
161	Larynx	4.2	3.9	4.8	4.6	4.3	4.6	5.5	5.5
162	Lung	5.1	7.3	8.5	8.0	9.9	8.8	11.4	11.1
163	Pleura	0.0	0.1	0.0	0.2	0.1	0.1	0.4	0.2
164	Other Thoracic	0.0	0.1	0.0	0.1	0.2	0.1	0.0	0.2
170	Bone	0.9	1.1	1.0	0.7	0.1	0.7	1.4	0.9
171	Connective Tissue	0.6	1.1	1.1	0.6	0.9	0.9	1.5	1.0
172	Skin Melanoma	0.2	0.6	0.3	0.2	0.3	0.4	0.1	0.3
173	Skin Other	0.9	1.0	1.3	1.7	1.4	1.4	1.5	2.2
175	Breast	0.3	0.4	0.3	0.1	0.5	0.1	0.1	0.7
185	Prostate	2.8	2.1	1.3	1.5	3.1	2.6	2.9	3.6
186	Testis	0.6	0.3	0.5	0.9	0.8	0.5	0.7	1.1
187	Penis etc	2.9	3.7	3.0	1.9	2.5	2.6	4.0	2.8
188	Bladder	1.8	0.8	1.9	1.4	1.8	3.0	2.3	3.8
189	Kidney	1.7	0.7	0.6	0.9	1.7	1.5	0.4	0.9
190	Eye	0.5	0.4	0.1	0.3	0.6	0.4	0.9	0.3
191-192	Brain-Ns	1.3	2.3	2.8	1.7	2.1	2.4	2.7	1.8
193	Thyroid Gland	0.7	0.9	0.5	0.8	0.6	0.7	0.8	0.9
194	Endocrine Other	0.2	0.0	0.1	0.3	0.0	0.1	0.2	0.1
201	Hodgkins Disease	2.3	1.8	1.3	1.4	1.7	1.7	1.6	1.7
200-202	Non-hodg Lymphoma	2.3	1.8	2.0	3.2	2.7	3.4	3.5	3.9
203	Mult Myeloma	0.4	0.5	0.8	1.0	0.6	0.5	0.9	0.5
204	Leuk Lymphoid	1.2	1.0	1.3	1.4	1.1	1.0	1.4	1.5
205	Leuk Myeloid	1.4	0.9	1.1	1.1	1.2	1.4	0.9	1.4
206	Leuk Monocytic	0.3	0.0	0.0	0.0	0.0	0.0	0.0	0.2
207	Leuk Other	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
208	Leuk Uns	0.6	0.5	0.2	0.3	0.1	0.6	0.2	0.3
	Primary Unk	3.4	6.1	5.5	5.4	6.4	6.6	8.5	10.4
	ALL SITES	81.6	88.7	87.6	92.2	101.3	104.4	125.2	118.5

* Incidence Rate Per 100,000

TABLE 2.10.5 :TRENDS IN AGE-ADJUSTED (WORLD POPULATION) CANCER INCIDENCE RATES
MADRAS*
SEX : MALES YEAR : 1982-1989

ICD9	SITE	YEAR OF DIAGNOSIS 1982	1983	1984	1985	1986	1987	1988	1989
140	Lip	0.4	0.2	0.1	0.5	0.1	0.5	0.5	0.6
141	Tongue	3.8	3.5	4.0	5.5	5.0	5.1	8.2	5.3
142	Salivary Gland	0.3	0.8	0.7	0.7	0.4	0.7	0.9	0.4
143-145	Mouth	6.7	6.1	5.6	6.7	7.4	8.1	9.8	7.3
146	Oropharynx	1.8	1.7	1.4	1.1	2.0	2.2	2.9	1.9
147	Nasopharynx	0.7	0.6	0.9	0.8	0.8	0.4	1.4	0.6
148	Hypopharynx	3.7	5.4	4.2	3.8	5.9	6.6	7.8	6.5
149	Pharynx Uns	0.6	1.0	0.4	0.4	1.2	0.9	1.2	1.0
150	Oesophagus	6.3	6.1	7.6	7.7	7.2	9.5	10.4	10.2
151	Stomach	12.1	14.2	13.8	15.7	17.1	14.3	15.1	16.5
152	Small Intestine	0.3	0.5	0.2	0.1	0.0	0.2	0.2	0.1
153	Colon	1.5	2.1	0.7	1.7	1.7	1.3	1.9	2.0
154	Rectum	2.7	2.1	2.6	2.1	2.6	2.5	3.7	4.5
155	Liver	1.7	1.6	2.5	3.1	2.1	2.4	3.9	1.9
156	Gallbladder	0.1	0.4	0.3	0.4	0.3	0.9	0.5	0.3
157	Pancreas	1.0	1.0	1.1	0.9	1.2	1.5	1.0	1.4
158	Peritoneum	0.7	0.3	0.5	0.4	0.4	0.3	0.3	0.1
160	Nose Etc	0.6	1.1	0.7	0.7	1.2	0.6	1.6	0.6
161	Larynx	4.2	3.9	4.8	4.6	4.3	4.6	5.5	5.5
162	Lung	5.1	7.3	8.5	8.0	9.9	8.8	11.4	11.1
163	Pleura	0.0	0.1	0.0	0.2	0.1	0.1	0.4	0.2
164	Other Thoracic	0.0	0.1	0.0	0.1	0.2	0.1	0.0	0.2
170	Bone	0.9	1.1	1.0	0.7	0.1	0.7	1.4	0.9
171	Connective Tissue	0.6	1.1	1.1	0.6	0.9	0.9	1.5	1.0
172	Skin Melanoma	0.2	0.6	0.3	0.2	0.3	0.4	0.1	0.3
173	Skin Other	0.9	1.0	1.3	1.7	1.4	1.4	1.5	2.2
175	Breast	0.3	0.4	0.3	0.1	0.5	0.1	0.1	0.7
185	Prostate	2.8	2.1	1.3	1.5	3.1	2.6	2.9	3.6
186	Testis	0.6	0.3	0.5	0.9	0.8	0.5	0.7	1.1
187	Penis etc	2.9	3.7	3.0	1.9	2.5	2.6	4.0	2.8
188	Bladder	1.8	0.8	1.9	1.4	1.8	3.0	2.3	3.8
189	Kidney	1.7	0.7	0.6	0.9	1.7	1.5	0.4	0.9
190	Eye	0.5	0.4	0.1	0.3	0.6	0.4	0.9	0.3
191-192	Brain-Ns	1.3	2.3	2.8	1.7	2.1	2.4	2.7	1.8
193	Thyroid Gland	0.7	0.9	0.5	0.8	0.6	0.7	0.8	0.9
194	Endocrine Other	0.2	0.0	0.1	0.3	0.0	0.1	0.2	0.1
201	Hodgkins Disease	2.3	1.8	1.3	1.4	1.7	1.7	1.6	1.7
200-202	Non-hodg Lymphoma	2.3	1.8	2.0	3.2	2.7	3.4	3.5	3.9
203	Mult Myeloma	0.4	0.5	0.8	1.0	0.6	0.5	0.9	0.5
204	Leuk Lymphoid	1.2	1.0	1.3	1.4	1.1	1.0	1.4	1.5
205	Leuk Myeloid	1.4	0.9	1.1	1.1	1.2	1.4	0.9	1.4
206	Leuk Monocytic	0.3	0.0	0.0	0.0	0.0	0.0	0.0	0.2
207	Leuk Other	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
208	Leuk Uns	0.6	0.5	0.2	0.3	0.1	0.6	0.2	0.3
	Primary Unk	3.4	6.1	5.5	5.4	6.4	6.6	8.5	10.4
	ALL SITES	81.6	88.7	87.6	92.2	101.3	104.4	125.2	118.5

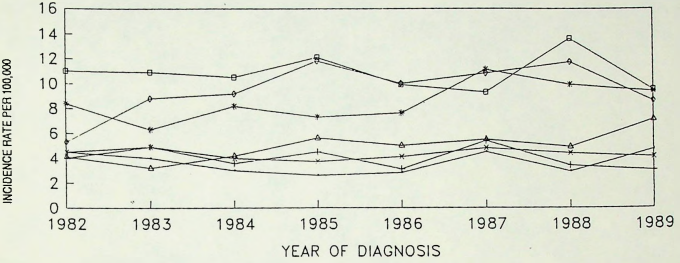
* Incidence Rate Per 100,000

TABLE 2.10.6 : TRENDS IN AGE-ADJUSTED (WORLD POPULATION) CANCER INCIDENCE RATES
MADRAS*
SEX : FEMALES YEAR : 1982-1989

ICD9	SITE	YEAR OF DIAGNOSIS 1982	1983	1984	1985	1986	1987	1988	1989
140	Lip	0.3	0.6	0.1	0.3	0.2	0.3	0.3	0.3
141	Tongue	1.7	1.5	1.1	1.8	1.1	1.6	1.2	2.1
142	Salivary Gland	0.2	0.4	0.5	0.4	0.4	0.9	0.4	0.2
143-145	Mouth	8.6	8.4	7.4	7.7	8.8	9.3	8.6	8.2
146	Oropharynx	0.8	0.3	0.3	0.3	0.7	0.4	0.5	0.4
147	Nasopharynx	0.2	0.3	0.4	0.4	0.4	0.3	0.3	0.3
148	Hypopharynx	1.1	1.8	1.4	2.5	2.2	1.8	2.8	2.7
149	Pharynx Uns	0.1	0.3	0.4	0.3	0.4	0.3	0.1	0.5
150	Oesophagus	3.3	5.8	5.9	5.6	7.6	6.3	7.2	7.7
151	Stomach	5.9	6.4	6.0	6.7	7.4	7.0	6.9	7.1
152	Small Intestine	0.1	0.2	0.1	0.2	0.1	0.1	0.0	0.0
153	Colon	0.5	1.5	1.9	1.4	1.2	1.6	1.3	0.8
154	Rectum	1.3	1.0	2.3	2.2	1.8	2.4	1.9	2.6
155	Liver	0.6	0.7	0.6	1.0	1.0	0.6	0.7	0.6
156	Gallbladder	0.2	0.4	0.6	0.5	0.5	0.5	0.2	0.6
157	Pancreas	0.3	0.3	0.4	0.5	0.7	1.5	0.8	0.7
158	Peritoneum	0.2	0.2	0.4	0.5	0.1	0.3	0.2	0.1
160	Nose Etc	0.3	0.4	0.9	0.1	0.7	0.6	1.0	0.8
161	Larynx	0.5	0.4	0.6	0.5	0.8	0.6	0.9	0.3
162	Lung	1.1	1.4	0.9	1.7	1.5	1.4	1.2	1.7
163	Pleura	0.0	0.0	0.1	0.2	0.0	0.0	0.1	0.0
164	Other Thoracic	0.1	0.0	0.0	0.1	0.0	0.0	0.0	0.0
170	Bone	0.7	0.7	1.0	0.8	0.6	0.4	0.5	0.6
171	Connective Tissue	0.9	0.8	0.8	0.5	0.6	0.8	1.1	0.7
172	Skin Melanoma	0.0	0.5	0.3	0.4	0.2	0.2	0.2	0.2
173	Skin Other	0.7	0.6	0.9	1.3	1.0	1.6	1.2	0.7
174	Breast	18.8	18.7	19.2	19.5	20.9	20.8	24.6	24.6
179	Uterus Uns	0.6	1.2	1.1	0.8	0.9	1.1	0.4	0.4
180	Cervix Uteri	41.6	44.8	43.3	48.5	52.6	46.2	41.5	43.5
181	Placenta	0.4	0.5	0.3	0.4	0.3	0.1	0.1	0.2
182	Corpus Uteri	1.4	1.0	1.6	1.8	1.5	2.4	2.7	1.9
183	Ovary etc	4.1	4.6	6.0	5.7	6.0	5.9	4.8	6.0
184	Other Fem Genital	1.8	2.0	2.1	2.1	1.8	3.1	1.8	2.0
188	Bladder	0.9	0.8	0.7	0.8	0.4	0.5	0.7	1.1
189	Kidney	0.4	1.3	0.5	0.6	0.1	0.6	0.4	0.7
190	Eye	0.4	0.3	0.3	0.2	0.6	0.4	0.1	0.6
191-192	Brain-Ns	0.8	1.1	1.6	1.0	0.7	1.7	1.0	0.8
193	Thyroid Gland	1.4	1.7	1.4	1.8	2.5	1.3	1.6	1.1
194	Endocrine Other	0.1	0.2	0.0	0.0	0.0	0.0	0.0	0.1
201	Hodgkins Disease	0.5	0.7	0.6	1.0	0.4	0.6	0.5	0.7
200-202	Non-hodg Lymphoma	1.0	1.2	0.8	1.3	1.8	0.9	1.7	1.8
203	Mult Myeloma	0.1	0.4	0.2	0.2	0.6	0.7	0.8	0.2
204	Leuk Lymphoid	0.3	0.5	0.5	0.9	0.7	0.7	0.7	0.5
205	Leuk Myeloid	0.3	0.6	0.8	1.1	1.2	1.1	0.7	0.9
206	Leuk Monocytic	0.1	0.2	0.1	0.0	0.0	0.0	0.0	0.2
207	Leuk Other	0.0	0.1	0.0	0.1	0.0	0.0	0.0	0.0
208	Leuk Uns	0.4	0.3	0.3	0.1	0.0	0.3	0.1	0.2
	Primary Unk	2.8	5.0	3.5	2.6	2.8	4.0	5.9	7.7
	ALL SITES	108.1	121.9	120.0	128.3	135.7	133.4	129.7	135.0

* Incidence Rate Per 100,000

TIME TRENDS IN AGE ADJUSTED INCIDENCE RATES OF CANCER
1982 - 1989
BANGALORE — MALES

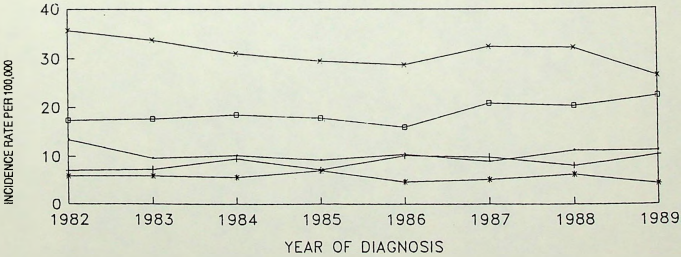


CANCER SITE

TONGUE — MOUTH — OESOPHAGUS — STOMACH

LARYNX — LUNG — PROSTATE

FEMALES



CANCER SITE

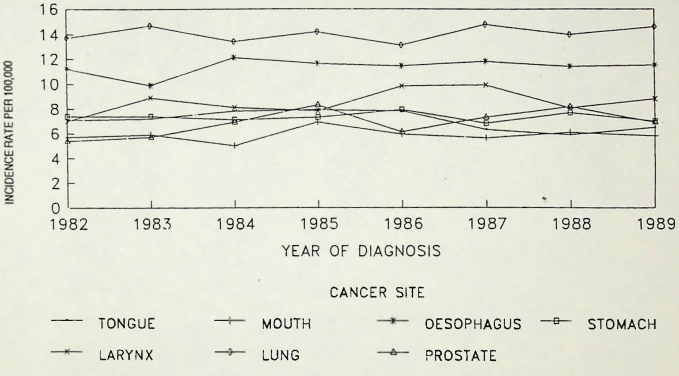
MOUTH — OESOPHAGUS — STOMACH

BREAST — UTERINE CERVIX

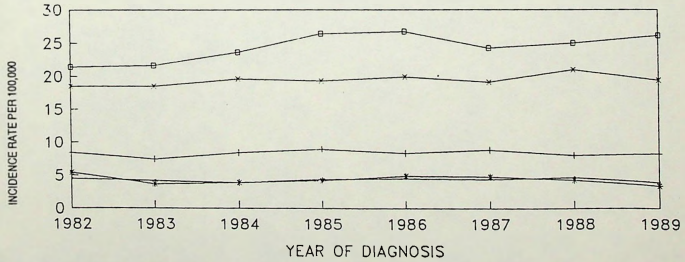
* WORLD POPULATION

SOURCE : NCRP DATA : 1982-1989

TIME TRENDS IN AGE ADJUSTED INCIDENCE RATES OF CANCER
1982 - 1989
BOMBAY — MALES



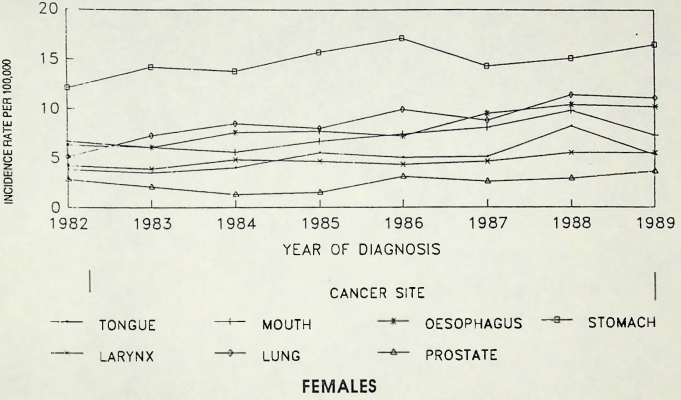
FEMALES



* WORLD POPULATION

SOURCE : NCRP DATA : 1982-1989

TIME TRENDS IN AGE ADJUSTED INCIDENCE RATES OF CANCER
1982 - 1989
MADRAS — MALES



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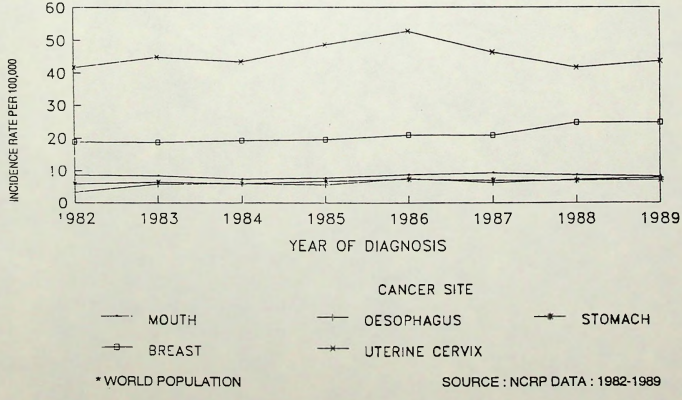

* WORLD POPULATION

SOURCE : NCRP DATA : 1982-1989

2.11 BURDEN OF TOBACCO RELATED CANCERS IN INDIA

NCRP has provided incidence rates of cancer in Bangalore, Bombay and Madras areas for eight years (1982-1989). Based on these figures, the burden of tobacco related cancers in India has been estimated.

TABLE 2.11 : BURDEN OF TOBACCO RELATED CANCERS IN INDIA, ESTIMATES FOR 1992 (AS ON JULY 1)

	MALES	FEMALES	TOTAL
Total Population (millions)*	450	412	862
Crude Rate Per 100,000	70	80	—
Number Of New Cancer Cases Per Year	315,000	329,600	644,600
New Cases Related To Tobacco Habits Per Year :			
Mouth	36,200	27,000	63,200
Pharynx & Larynx	49,200	10,600	59,800
Oesophagus	23,700	16,500	40,200
Lung	27,800	5,100	32,900
Others	15,000	7,200	22,000
Total - Tobacco Habits Related Cancers	151,900 (48.2%)	66,400 (20.1%)	218,300 (33.8%)

* As on July 1, 1992

Estimates are shown separately for males and females for commonly affected sites namely, mouth, pharynx & larynx, oesophagus and lung (Table 2.11). Some other sites related to smoking habits known from the experience of the west such as bladder, pancreas etc. are taken as others. Although stomach and uterine cervix cancers are appear to be associated with the bidi and cigarette smoking, but they are not taken into account. It is also possible that tobacco chewing and bidi smoking may show risks for cancers not studied so far. From these considerations, the present estimate of tobacco related cancers is a conservative one (Sanghvi, 1989).

In India, cancer morbidity cases related to tobacco habits, per year, are 151,900 (48.2%) in men and 66,400 (20.1%) in women with an overall estimate of 218,300 (33.8%) for the two sexes. Of 218,300, 74.7% cancers related to tobacco were found in mouth, pharynx & larynx and oesophagus; lung cancer accounted for only 15% of cases.

2.12 INCIDENT CASES OF CANCER BY YEAR 2001 A.D.

Incident cases of cancer by year 2001 A.D. (as on July 1) has been estimated as given in the Table 2.12. These estimates are based on averages of crude incidence rates for Bangalore, Bombay and Madras registries for the year 1989. India's population was projected, by sex, for the year 2001 A.D. (as on July 1), using 1981 and 1991 (provisional) censuses and applying the exponential rate of growth. The present estimates of cancer cases may be considered as a conservative one.

TABLE 2.12 : ESTIMATED NUMBER OF INCIDENT CANCER CASES FOR SELECTED SITES , ALL AGES, BY THE YEAR 2001 A.D. (AS ON JULY 1), IN INDIA *

SITE (ICD.9)	MALES	FEMALES	TOTAL
Lip, Oral Cavity (140-145)	39,000	31,000	70,000
Pharynx & Larynx (146-149,161)	53,000	14,000	67,000
Oesophagus (150)	31,000	26,000	57,000
Stomach (151)	35,000	16,000	51,000
Lung (162)	34,000	7,000	41,000
Breast (174)	—	80,000	80,000
Cervix Uteri (180)	—	100,000	100,000
Others	201,000	139,000	340,000
TOTAL	393,000	413,000	806,000

*Estimates are based on crude cancer incidence rates for Bangalore, Bombay, Madras and Delhi.
Source : NCRP Data, 1989.

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Relevance to Human Cancer of *N*-Nitroso Compounds,
Tobacco Smoke and Mycotoxins.
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LUNG CANCER AND THE CHANGING CIGARETTE

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Epidemiological studies have shown that the long-term smoker of low-yield cigarettes has a 20-50% lower risk of lung cancer than the smoker of high-yield cigarettes. This risk reduction is attributed to changes in the make-up of cigarettes and especially to the introduction of filter tips. Other changes relate to the use of tobaccos that produce lower smoke yields, including reconstituted and expanded tobaccos, as well as utilization of porous cigarette paper and perforated filter tips. New developments in the make-up of commercial cigarettes must be monitored in order to prevent unfavourable introductions. Although a smoke-free society should be the major public health goal, recent consumer statistics do not support this goal. Thus, a strong social case is made for further developments in the low-yield cigarette.

In 1961, Wynder and Day offered three postulates for the causation of noncommunicable diseases, including cancer:

(1) The greater and the more prolonged the exposure to the factor, the greater the risk of a population involved.

(2) The epidemiological pattern should be consistent with the distribution of the factor.

(3) Removal or reduction of the risk factors for a given population group should be followed by a reduction in the incidence of disease.

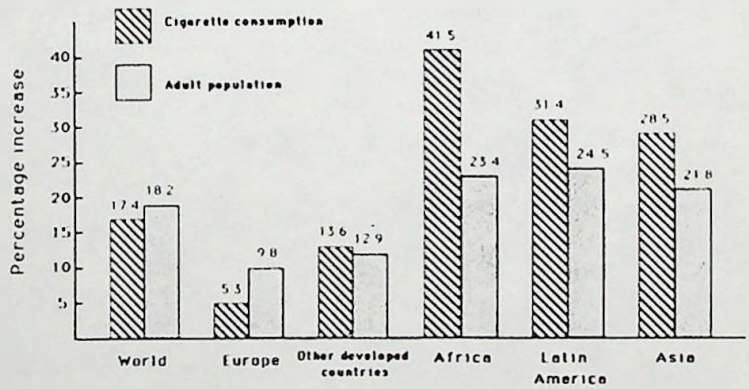
More than 100 epidemiological studies from various countries have demonstrated a dose-response relationship between the number of cigarettes smoked and the risk for cancer of the lung (IARC, 1986; US Department of Health and Human Services, 1989). Laboratory studies have substantiated these findings by documenting the dose-response relationship between exposure to cigarette smoke and tumours of the upper respiratory tract in hamsters (Dontenwill, 1974) and that between application of smoke condensate to the skin of mice and rabbits and tumour yield at the site of application (Wynder & Hoffmann, 1967). These findings clearly satisfy postulate (1) for a causative association between cigarette smoking and lung cancer.

Postulate (2) is sustained by the correlation between age at onset of cigarette smoking and depth of inhalation with risk for lung cancer. Further support is gleaned from the observation that, by comparison to cigarette smokers, primary cigar and pipe smokers have

a lower risk for cancer of the lung but the same risk for cancer of the oral cavity (US Department of Health and Human Services, 1989).

The observed decrease in lung cancer risk upon cessation of cigarette smoking supports postulate (3) for cancer causation. More importantly, it also has major public health implications. Independent of the length of smoking history, the risk for tobacco-related diseases diminishes further as the period of abstention from smoking increases (Table 1). Thus, the demand for a smoke-free society by the year 2000 (Koop, 1986) deserves the full support of the medical and scientific community. Unfortunately, the recent statistics on tobacco use do not support this goal. Between 1971-75 and 1979-81, the percentage increase in cigarette consumption in all parts of the world, except Europe, exceeded the increase in population (Fig. 1).

Figure 1. Change in apparent cigarette consumption and adult population size, by region; 1971-75 to 1979-81[a]



[a] From World Health Organization (1986)

These data on cigarette consumption reinforce the need for health education about the harmful effects of cigarette smoking and for the widest availability of smoking cessation programmes. However, these figures also show that a strong case can be made for less toxic cigarettes, since far too many people seemingly cannot or will not give up the smoking habit.

The changing cigarette — epidemiological observations

Since the early epidemiological studies on the association of cigarette smoking and lung cancer clearly showed a dose-response relationship, product modification was seen as one possible approach to reducing exposure (Wynder & Hoffmann, 1962). Changes in the design of cigarettes, most notably use of filter tips but also alterations of the composition of cigarettes, were implemented in several countries in the late 1950s and early 1960s. Since then, the yields of smoke condensate ('tar') and of nicotine in the smoke stream have fallen drastically. For example, between 1960 and 1984, sales-weighted average 'tar' delivery of cigarettes in the USA, the UK and the Federal Republic of Germany decreased from 26, 31 and 25 mg to 14.2, 13.7 and 12.8 mg, respectively, that is, a reduction of 45-50%. During

and nicotine values are based on standardized machine-smoking of cigarettes, and (ii) most smokers of low-yield cigarettes compensate for the reduced nicotine delivery by smoking more, by drawing puffs more frequently and more intensely, and by inhaling more deeply (Herning *et al.*, 1981; Haley *et al.*, 1985; Augustine *et al.*, 1989).

Epidemiological studies have also reported a reduction in the risks for cancers of the larynx and urinary bladder for long-term smokers of filter cigarettes (Wynder & Stellman, 1979; Vineis *et al.*, 1984; Wynder *et al.*, 1988).

In addition to comparing the cancer risks of smokers of plain and filter cigarettes, epidemiological studies have been concerned with the relative risk of smoking black cigarettes *versus* blended or bright cigarettes. It was found that smokers of cigarettes made exclusively of black tobaccos, such as those that are commonly smoked in France, North Africa and Cuba, are at higher risk for cancers of the lung, larynx and urinary bladder than are smokers of blended or bright cigarettes (Joly *et al.*, 1983; Vineis *et al.*, 1984, 1985; Benhamou *et al.*, 1985, 1987; DeStefani *et al.*, 1987).

The changing cigarettes — technical developments

The introduction of cigarettes with filter tips in North America and Europe around 1940 represents the first major change in the make-up of machine-made cigarettes. However, it was not until the first reports on smoking and lung cancer in the early 1950s that consumers demanded cigarettes with reduced 'tar'. In response, cigarettes with cellulose acetate filter tips were offered. These filter tips are usually 17-30-mm long and contain a few per cent of plasticizers such as glyceryl triacetate. In 1988, 96% of the cigarettes sold in the USA had filter tips; about half of them were 85-mm long and about one-third were 100-mm long (US Department of Agriculture, 1989). Similar developments were seen in other American countries, in Japan and in some parts of Europe, while in 1987 filter-tipped cigarettes in China accounted for only 26% and in the USSR, 27% (Anon., 1988).

The degree to which 'tar' and nicotine can be retained by conventional filter tips is limited to about 50%, primarily due to the fact that cigarette smokers will usually not accept a draw resistance above 140 mm (Kuhn & Klus, 1976). Apart from removing 'tar' and nicotine from the smoke, cellulose acetate can selectively remove up to 80% of certain hydrophilic, volatile smoke components, such as phenols and volatile *N*-nitrosamines (Wynder & Hoffmann, 1967; Brunnemann *et al.*, 1977).

The introduction of perforated filter tips around 1968 had a profound impact on the cigarette market (Norman, 1982). In general, such filter tips have one or more rows of perforation in the wrapper at the half-way point of the filter column. As a result, the smoke is diluted by air entering through the holes during puff-drawing without causing an increase in draw resistance. Enhancing the air dilution of the smoke stream by optimal perforation of the filter tip diminishes the velocity of the air that enters the burning cone. This, in turn, reduces the oxygen deficiency of certain zones in the burning cone, which results in the selective reduction of CO, nitrogen oxides and volatile aldehydes in these cigarettes (Newsome & Keith, 1965; Baker, 1984).

Even though cigarette length has increased from 70 mm to 85 mm, and even to 100 mm and 120 mm, the average weight of the tobacco in the typical US cigarette has decreased from 1300 mg in the 1940s to 750 mg in the 1980s (Norman, 1982). This is due mainly to

Table 3. Composition of a typical US blend for cigarettes[a]

Component	%
Flue-cured leaf	32
Burley leaf	20
Maryland leaf	2
Oriental leaf	10
Cut, rolled stems	6
Reconstituted sheet	22
Dip casing	4
Flavours/humectants	4

[a] From Perfetti (1987)

(Wynder & Hoffmann, 1962; Hoffmann *et al.*, 1980). Various processes have been tested for their efficacy by initially analysing the smoke of the modified cigarettes for 'tar', nicotine, CO, benzo[*a*]pyrene and tobacco-specific *N*-nitrosamines (TSNA). When this analytical profile showed a reduction in the smoke yields, determinations of volatile aldehydes, volatile *N*-nitrosamines, cyanide, phenols and catechol were made. Experimental cigarettes with significantly changed analytical smoke profiles were then designated for evaluation of the toxicity and tumorigenic potential of their smoke. Such bioassays were done with 'tars' as well as with smoke itself (Wynder & Hoffmann, 1967; Dontenwill, 1974), as summarized in Table 4. Several of the modifications described here have been incorporated in the design of present-day low-yield cigarettes. Modifications in cigarette make-up have also led to the selective reduction of certain smoke constituents and have specifically contributed towards lowering the toxic and tumorigenic potential of cigarette smoke. The decline of benzo[*a*]pyrene levels in the smoke of a leading US non-filter cigarette as measured over 1958-79 is one indicator of selective reduction of a carcinogen; while 'tar' and nicotine in the smoke of this cigarette were reduced by 31% and 39%, the reduction in benzo[*a*]pyrene was from 36 to 16 ng/cigarette, i.e., 56% (Hoffmann *et al.*, 1980).

In evaluating preventive strategies that involve product modification, it is important to monitor not only specific indicators but also the overall chemical composition of the smoke of commercial cigarettes. Use of nitrate-rich tobaccos and ribs increases the potential for higher smoke yields of TSNA (Brunnemann *et al.*, 1983). Consequently, low-yield cigarettes can deliver higher amounts of carcinogenic TSNA than some plain cigarettes, as was recently shown for some cigarettes in the Federal Republic of Germany by Fischer *et al.* (1989). Another concern is the addition of flavouring agents to the tobacco of low-yield cigarettes (LaVoie *et al.*, 1985). These few citations underscore how important it is that nonindustrial scientists monitor new developments in the make-up of cigarettes.

Outlook

Future research and development will probably bring about new features in the design of commercial cigarettes. Plans have been announced for the marketing of filter cigarettes made with tobaccos from which the bulk of the nicotine has been removed by supercritical extraction with CO_2 (Grubbs & Howell, 1987). This development is potentially beneficial

the utilization in present-day cigarettes of tobacco material with higher filling power, namely reconstituted tobacco, tobacco ribs and expanded tobacco. Reconstituted tobacco sheets are made from tobacco dust and fines and from opened ribs. They can be prepared by slurry or paper-like processes. Expanded tobacco is obtained by a freeze-drying process (Wynder & Hoffmann, 1967; Perfetti, 1987).

The composition of cigarette smoke and its toxicity and carcinogenic potency are also very much affected by the tobacco type(s) used. The composition of the tobacco filler in cigarettes in different countries is primarily the result of traditional usage and availability of tobacco types. In the USA, the Federal Republic of Germany and Scandinavia, blends of the four major tobacco types are used; in China, flue-cured tobacco is the dominant type for cigarettes; while cigarettes made exclusively from flue-cured tobaccos are preferred in the UK and Finland. A large segment of cigarette smokers in France, Italy, North Africa and several Central and South American countries prefer black tobaccos.

Bright tobaccos contain generally high levels of reducing sugars (15-20% of dry weight) and carbohydrates but relatively lower amounts of di- and tricarboxylic acids (< 4%) and nitrate (< 0.1%), while burley and black tobaccos are low in reducing sugars (< 2%), relatively high in di- and tricarboxylic acids (> 10%) and high in nitrate (> 1%); this is especially true for the ribs. Oriental and Maryland tobaccos are minor components of cigarette blends because of their specific smoke flavours. Their leaves contain moderate amounts of reducing sugars (10-15%) and of di- and tricarboxylic acids (< 10%), while their nitrate content is low (Neurath & Ehmke, 1964; Tso, 1972). The nicotine concentration of the leaves depends on the variety chosen; however, bright, oriental and Maryland tobaccos contain less nicotine (< 2%) than burley and black tobaccos (Tso, 1972).

The composition of a typical blend currently formulated for US cigarettes is shown in Table 3 (the composition of expanded tobaccos is described by Perfetti, 1987). Other changes in the make-up of commercial cigarettes include the use of cigarette paper of higher porosity as well as reduction of the circumference of some cigarettes (DeBardeleben *et al.*, 1978; Owens, 1978). Together, all of these changes have led to a gradual decrease in the sales-weighted 'tar' and nicotine yields in the smoke of commercial US cigarettes (Figure 2).

The changing cigarette — effect on tumorigenicity of smoke

As discussed earlier, smokers of low-yield cigarettes tend to compensate for the reduced delivery of nicotine and perhaps other smoke components; however, they do not compensate fully. The 20-50% reduction in risk for lung cancer of long-term cigarette smokers supports the concept that low-yield cigarettes have reduced carcinogenic potential. The IARC monograph on tobacco smoking states: 'no substantial cause (or cofactor) has so far been identified that offers a plausible explanation for the observed magnitude of the reduction of risk for lung cancer, other than changes in the cigarette design which include reduction in tar content.' (IARC, 1986).

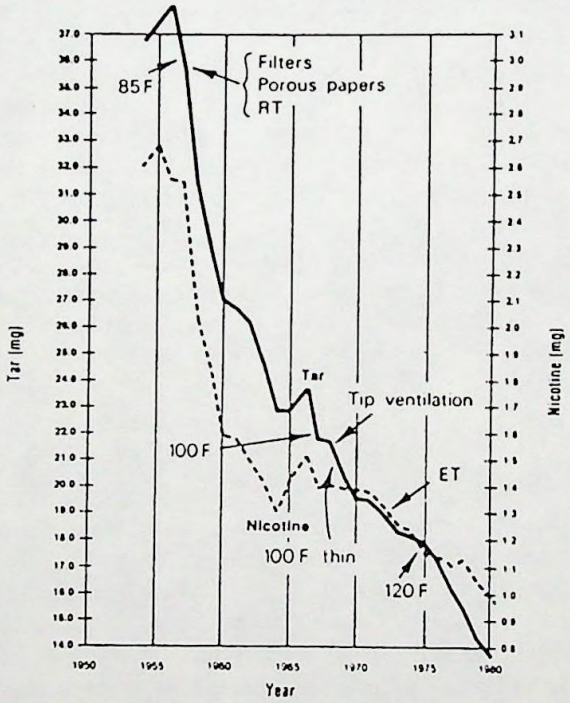
Whether other factors are indeed responsible for the reduced carcinogenic potential of the changed cigarette can at this time be evaluated only in laboratory studies. Concepts of 'less harmful' cigarettes have frequently been devised by investigators outside the industry

Table 2. Relative risk for lung cancer by type of cigarette smoked (filter *versus* nonfilter) in men

Reference	Type of study	Relative risk
Hawthorne & Fry (1978)	Cohort	0.8
Rimington (1981)	Cohort	0.7
Bross & Gibson (1968)	Case-control	0.6
Wynder *et al.* (1970)	Case-control	0.6
Dean *et al.* (1977)	Case-control	0.5
Wynder & Stellman (1979)	Case-control	0.6-0.9[a]
Lubin (1984)	Case-control	0.6[b]

[a] Depending on number of cigarettes smoked daily
[b] Men who smoked only filter cigarettes

Figure 2. US sales-weighted average tar and nicotine yields (adapted from Norman, 1982)[a]



[a] RT, reconstituted tobacco; ET, expanded tobacco; F, cigarettes with filter tips; numbers, lengths of filter cigarettes in millimetres. Arrows denote years in which specific changes were first introduced

in that it promises a selective reduction in the major habituating agent of tobacco and a precursor for carcinogenic TSNA. A recent attempt to market a modified cigarette that 'heats rather than burns tobacco' has not been accepted by consumers (R.J. Reynolds Tobacco Co., 1988).

Because large numbers of people continue to smoke cigarettes, development of less harmful cigarettes should not be rejected *per se*. One may agree with a recent editorial in the *New York Times* (Anon., 1989), which reads in part, 'Obviously, no smoking is better than smoking, but the best should not be the enemy of the good. There is a strong social case for encouraging manufacturers to develop safer cigarettes that will sell.'

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Table 4. Reductions in the biological activity of smoke from experimental cigarettes[a]

Method	Smoke constituents			Selective reduction in biological activity[b]		Remarks[c]
	'Tar'	Nicotine	Benzo[*a*]pyrene	Carcinogenicity	Tumour promotion	
Agricultural						
Tobacco type (bright–burley)[d]	+	+	+	+	+	Increase in TSNA
New cultivars	+	+	+	+	?	
Fertilization (nitrate)	+	+	+	+	?	Increase in TSNA
Tobacco processing						
Cut	±	±	±	±?	?	
Use of tobacco midribs	+	+	+	+ +	+ +	
Reconstituted tobacco sheets (RTS)[e]	+	+	+	+ +	±	Some RTS give high CO
RTS/paper process	+ +	+	+	+ +	±	
Expanded tobacco laminae	+	+ +	+	±?	±	
Expanded tobacco midribs	+	+ +	+	+ +	?	
Cigarette production						
Paper porosity	+	+	+	±	?	
Cellulose acetate filters	+	+	+	±	±	
Charcoal filters[f]	+	+	+	±	±	
Perforated filters	+ +	+ +	+ +	±	±	Smoker's compensation

[a] Adapted from Wynder & Hoffmann (1982). Methods known to be applied to commercial US cigarettes. Reductions: + +, > 50%; +, significant; ±?, questionable; ?, unknown

[b] Comparison of gram-to-gram 'tar' on mouse skin tests and/or smoke inhalation with hamsters

[c] TSNA, tobacco-specific *N*-nitrosamines

[d] Replacing bright with burley tobaccos

[e] Data given for RTS relate to those not made by the paper process

[f] Reductions in 'tar', nicotine, benzo[*a*]pyrene (and other nonvolatiles) and volatile *N*-nitrosamines are generally greater with cellulose acetate filters than with charcoal filters.

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Dimitrios Trichopoulos

Risk of Lung Cancer and Passive Smoking

6

Introduction ■

This Chapter concisely presents evidence indicating that exposure to environmental tobacco smoke (*ETS*), also termed involuntary or passive smoking, increases the risk of lung cancer, and can be considered as one of the causes of this disease. Several major reports of authoritative bodies that have addressed the question are available,[1–5] but this chapter is useful to clinicians, epidemiologists, and other health professionals who wish to familiarize themselves with the issues surrounding this important topic in modern public health.

Mainstream smoke (*MS*) is the tobacco smoke that is generated during a puff and is drawn through the butt end into the smoker's respiratory system. Sidestream smoke (*SS*) is emitted directly from the burning end of the cigarette, cigar or pipe. ETS is produced by smokers mostly in enclosed spaces and is inhaled by nonsmokers as well as by the smokers. ETS contains a vapor and a particulate phase and its main source is SS (about 80%), with exhaled MS, smoke that comes from the nonburning end but is not inhaled by the smoker, and smoke that diffuses through the paper wrapper of the cigarettes contributing the rest. Specifically, SS contributes almost all of the vapor phase of ETS and more than half of the particulate matter.[6,7]

Composition and Respiratory Deposition of Sidestream Smoke ■

At the time and point of generation, SS is characterized by higher concentrations of many of the definitely, probably or possibly carcinogenic compounds[8] found in MS, including benzene (5-fold), formaldehyde (2-fold), hydrazine (3-fold), butadiene (3-fold), N-nitrosamines (20-fold), aniline (30-fold), 2-napthylamine (30-fold), 4-aminobiphenyl (30-fold), benz[a]antracene (3-fold), benzo[a]pyrene (3-fold), and NNK (a tobacco-specific carcinogenic nitrosamine, 2-fold). SS also contains higher concentrations than MS of several toxic compounds, including carbon monoxide (3-fold), ammonia (4-fold), nicotine (3-fold) and particulate matter (tar, 1.5 fold). These data are abstracted from several references[1,2,5,7] and are based on the work of many investigators. The SS/MS ratios vary considerably, mostly because MS composition varies substantially by puff volume, filter characteristics and ventilation, and type of cigarette. By contrast, the variability of SS composition is limited and use of filtered, rather than unfiltered, cigarettes had little influence on the concentration of compounds in SS.[7] As might be expected from the relative concentrations of established and probable carcinogens in SS and MS, condensates of SS have demonstrated higher mouse skin tumorigenicity per unit weight than MS condensates.[9] Chemical characteriza-

tions of ETS, rather than SS, are limited, but the findings are essentially compatible with predictions based on SS composition.[5,7]

The different composition of SS and MS at the time and point of generation is caused by differences in temperature (lower in SS) pH (higher in SS) and oxygen concentration (substantially lower in SS). The rapid dilution of SS is accompanied by marked reduction in the concentration of all its constituents; however, about half of the tobacco in a cigarette is eventually consumed to form SS.[1]

Particles as SS are, originally, only slightly smaller than those as MS. Particles of MS, however, grow in size by coagulation, whereas particles of SS are rapidly diluted and their size distribution is shifted to smaller values. These changes are accompanied by changes in phase distribution of several constituents. Thus, nicotine exists mostly as particulate in MS, but mostly as gas in SS. The different particle size distribution and the different breathing patterns of smokers and nonsmokers explain the different deposition rates of MS and SS particles in the respiratory tract (more than 50% vs. about 10%, respectively). The deposited ETS particles, because of their small size, are likely to be found peripherally, rather than in the nasopharynx and the large conducting airways.[1,5]

Chemical Indicators of Environmental Tobacco Smoke ■

The difficulty in assessing exposure to mixtures is well recognized.[10,11] In assessing concurrent personal exposure to ETS, as distinct from actual absorption of ETS constituents, stationary measurements coupled with time-activity patterns of the subjects under consideration can be studied, or personal monitors can be used. Several factors can affect ETS concentrations, including the generation rate of the contaminants, the space volume, and the ventilation or air infiltration rate. Proximity of a subject to a smoker can also be a major determinant of exposure to passive smoking.

Several compounds have been measured as indicators of microenvironmental tobacco smoke pollution, including some of the established or probable carcinogens in ETS. N-nitrosamines and 4-aminobiphenyls are important in this respect because they are found in much higher concentrations in SS than in MS at the point of origin, they are generally considered as carcinogenic, and they are ETS-specific in the nonoccupational indoor environment.[5,7] However, these compounds cannot be measured easily, accurately and cost effectively, and thus fail to satisfy an important criterion for the selection of an appropriate ETS indicator. Among the many compounds that were used or suggested for use, nicotine has emerged as the most convenient indicator for the vapor phase constituents of ETS, whereas respirable suspended particulates (RSP, median mass diameter ≤ 2.5 μm) has become the indicator of choice for the particulate phase constituents of ETS. Although nicotine is specific to tobacco products, RSP are not and background levels must be accounted for before they can be utilized as a valid indicator of ETS particulate pollution. For both nicotine and RSP, indoor levels from less than 1 $\mu g/m^3$ to more than 1000 $\mu g/m^3$ have been reported, although usual nicotine values are below 15 $\mu g/m^3$ and usual RSP values below 50 $\mu g/m^3$.[5,7]

Static environmental measurements do not adequately reflect personal exposures. Modeling effective exposure as a function of several static measurements and the corresponding time-activity pattern represents an improvement, but personal monitors allow a better integration of the time-weighted individual exposures. However, personal monitors cannot account for interperson variations in ventilation rates, breathing patterns, and deposition factors. This limitation notwithstanding, studies using personal monitors have provided valuable data concerning exposure to airborne nicotine and RSP in the workplace,[12,13] and to RSP during a whole 24 hour day.[14]

Biomarkers of Environmental Tobacco Smoke Absorption ■

Biomarkers of exposure to ETS are good indicators of uptake and represent close correlates of effective individual exposure. Among the biomarkers proposed as indicators of ETS absorption, serum thiocyanate is not sufficiently specific, whereas the relatively short half-life of carboxyhemoglobin and nicotine (about 4 and 2 hours, respectively) limits their utility, unless attention is focused to a very recent exposure.

Cotinine, a major metabolite of nicotine, can be accurately measured in blood, saliva and urine in concentrations down to 1 ng/ml, is sufficiently specific for tobacco products, and has a half-life of about 24 hours, allowing its use as a biomarker of exposure to ETS over a period of about 48 hours. Cotinine has been extensively used for the validation of questionnaires assessing exposure to ETS[15,16] and in several surveys examining factors affecting the levels of this biomarker in biologic fluids.[15,17,18] These studies have demonstrated that self-reported exposure to ETS during the recent past is reasonably valid, and that 5-fold differences in

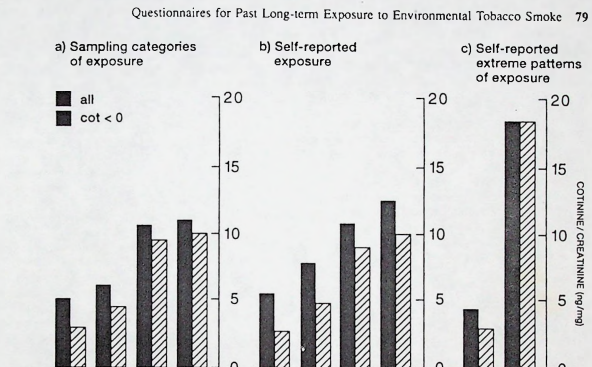

FIG. 6–1 Average cotinine/creatinine levels (ng/mg) for groups of nonsmoking women defined either by sampling categories of exposure or by self-reporting exposure to ETS from different sources during the four days preceding collection of a urine sample.[15]

levels of effective exposure to ETS are not unusual in everyday life (Fig. 6–1).

Cotinine studies suggest that exposure to ETS is equivalent to about 1% of exposure to active smoking. This, however, is only true with respect to cotinine and its parent compound nicotine, the concentration of which in SS is only 3 times higher than in MS (see p. 77). If, instead of nicotine a protein adduct, the 4-aminobiphenyl adduct of hemoglobin were used (4-ABP), exposure to ETS would have been estimated as close to 10% of that of active smokers, since the SS to MS ratio for 4-ABP is about 30 (see p. 77).[19,20] It is also relevant that the increase of urine mutagenicity after passive exposure to cigarette smoke is about 4% of the increase found in active smokers.[21] ETS is a mixture of more than 4000 compounds, variably related to each other and to their sources (MS or SS) and with different physicochemical properties and possibly interactive health effects. Therefore, concepts like "cigarette equivalent" and expressions in relation to active smoking are meaningful only with respect to single compounds and specific biomarkers.

Questionnaires for Past Long-term Exposure to Environmental Tobacco Smoke ■

For chronic diseases with long latencies like lung cancer, biomarkers and static environmental measurements are not directly useful, since they refer to the very recent past. As indicated (see p. 78), questionnaire-based, self-reported exposure to ETS correlates well with objective evidence of such exposure, as documented through cotinine in biologic fluids, and other biomarkers.[15–18] By contrast, questionnaire-derived information concerning long-term exposure to ETS is diffi-

cult to integrate over time and almost impossible to validate with an appropriate "gold standard." Nevertheless, the validity of self-reported exposure to ETS in the recent past argues in favor of the validity of questionnaire-assessed exposure to ETS over prolonged periods in the remote past.

Most studies concerning diseases of long latency, like cancer of the lung, have focused on risk comparisons between nonsmoking women married to husbands with different smoking habits. This is justifiable because[1,22–24]: (1) Among older people tobacco smoking has been more common in men than in women, particularly in traditional societies; (2) A smoking husband is the main source of passive smoking for an older woman, particularly for a housewife who is estimated to spend more than 80% of her time at her home; (3) Information concerning the smoking behavior of a spouse is usually more reliable than that concerning other relatives, friends and colleagues; (4) Nonsmokers married to smokers are likely to be more tolerant toward other sources of passive smoking; (5) Finally, since smokers tend to socialize with other smokers, and vice versa, the absolute difference of exposure to ETS between nonsmoking women married to smokers, rather than nonsmokers, tends to be amplified.

Tobacco smoking habits of cohabitants other than the spouse and recollection of ETS inhalation at work and other places outside the home have also been used, as secondary exposure variables, in some lung cancer studies. However, the irregular use of these variables and the possibility of inconsistent reporting of the corresponding data, limit the interpretability of the respective results.

Prediction of Lung Cancer Risk and Passive Smoking ■

Data from large analytic epidemiologic studies of the association between active smoking and lung cancer have consistently demonstrated dose-dependent relationships that extend to minimal exposure levels and have no apparent threshold.[25–28] The patterns that have been empirically demonstrated in four major studies are shown in Figure 6–2.[29] Doll and Peto[30,31] have argued that the true association between active smoking of the long-used high-tar cigarettes and lung cancer may be much stronger, with a relative risk for smokers of more than 1 pack of cigarettes per day exceeding 20. These authors also have pointed out that the unavoidable misclassification of exposure to the relevant carcinogenic compounds in MS at critical time periods, is bound to reduce the true slope of the regression of lung cancer relative risk on the amount of tobacco smoke reportedly consumed.[30,31] In any case, the epidemiologic evidence indicates that there is no safe level for tobacco smoking in relation to lung cancer risk. This is what should be expected from the known composition of MS, which contains several compounds with initiating carcinogenic potential and no demonstrable threshold.[8]

Since SS is qualitatively similar to MS and is readily absorbed in the body, an excess lung cancer risk from exposure to ETS should have been assumed even if there were no conclusive epidemiologic evidence. The situation is similar to what is known and assumed about the carcinogenic potential of ionizing radiation at various levels. High doses of ionizing radiation have been shown to cause cancer and, in the absence of a threshold, it is generally accepted that low doses from cosmic radiation or even diagnostic radiographs should cause some cases of cancer, even though this has never been empirically demonstrated in adult human beings. With respect to passive smoking a legitimate question is not whether it can cause lung cancer but whether the expected excess risk from long-term exposure to ETS is substantial enough to be empirically demonstrable with existing epidemiologic methods.

Extrapolations of the dose-response curves linking active smoking to lung cancer risk at the low ETS exposure levels, as assessed through nicotine absorption and continine excretion, generate relative risk estimates for passive smoking too low to be detected by conventional epidemiologic studies.[1,24,32,33] However, if urine mutagenicity or carcinogen-hemoglobin adducts are used as indicators of ETS exposure, higher relative risk levels for passive smoking are predicted.[20,21] Furthermore, exposure to ETS may start soon after birth, whereas active smoking usually starts in the teen-age years or later; since lung cancer risk is an exponential function of the duration of exposure,[30,31] the early exposure to ETS is likely to have disproportional risk implications.[24] In addition, the delayed clearance of nicotine among passive smokers, in comparison to active smokers, may lead to increased rate of formation of endogenous tobacco-specific nitrosamines with carcinogenic potential.[1,5,24,34] Finally, and perhaps more importantly, predictions of relative risk for lung cancer in association with passive smoking are based on models derived from studies of active smoking. In these studies the referent baseline group encompasses all smokers, including nonsmokers passively exposed to ETS. Therefore the baseline risk is regularly overestimated which leads to underestimation of relative risk values associated with active smoking, and similar underestimation of model-derived predictions of relative risk associated with passive smoking.[24,35] When the required adjustments are made the relative risk for lung

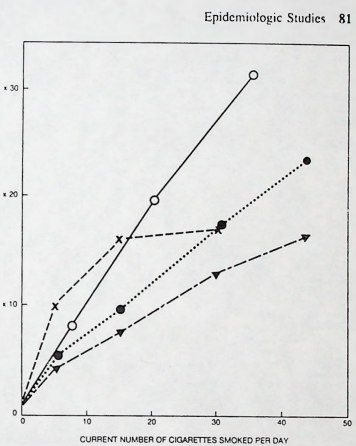

FIG. 6–2 Mortality ratios of deaths from lung cancer in men. Data from four large prospective studies.[25, 28]

cancer in association with passive smoking is substantially elevated and should be demonstrable in well designed epidemiologic studies.[24,35,36]

Epidemiologic Studies ■

At the time of this review (March 1994), 29 case-control studies and 4 cohort investigations have been reported in the literature.[37–73] Their findings are summarized in Table 6–1. The results have been abstracted from the original publications or from derivative calculations presented in earlier reports.[1,5,24,74]

In January 1981, Trichopoulos *et al.*[37] and Hirayama[40] reported simultaneously (within 2 days) and quite independently the results of the first two studies exploring the role of passive smoking in the etiology of lung cancer. One study[37] was of case-control design and was specifically undertaken in Greece to estimate the relative risk for lung cancer, other than adenocarcinoma or alveolar carcinoma, of nonsmoking women married to smokers, rather than nonsmokers. The other study[40] was based on women participating in a multipurpose cohort investigation in Japan. Both studies reported statistically significant and dose-dependent associations. The results of Garfinkel,[42] based on a cohort study by the American Cancer Society and published soon afterward were equivocal but not incompatible with a slight increase of lung cancer risk among persons exposed to ETS.

Between 1982 and 1994, 30 additional studies were published,[43–73] whereas Trichopoulos *et al.*[38,39] and Hirayama[41] reported additional results from their respective studies. Most studies were done in nonsmok-

Table 6–1
Epidemiologic Studies of Passive Smoking in Relation to Lung Cancer

Authors (year)	Reference Number	Cases (No.)	Controls (No.)	Relative Risk	90% Confidence Interval
Trichopoulos *et al.* (1981, 1983, 1984)	37, 38, 39	77	225	2.08	1.31–3.29
Hirayama (1981, 1984)	40, 41	200	Cohort	1.38	1.03–1.87
Garfinkel (1981)	42	153	Cohort	1.17	0.89–1.53
Chan and Fung (1982)*	43	84	139	0.75	0.48–1.19
Correa *et al.* (1983)	44	22	133	2.07	0.94–4.52
Buffler *et al.* (1984)*	45	41	196	0.81	0.39–1.66
Gillis *et al.* (1984), Hole *et al.* (1989)*	46, 47	14	Cohort	1.99	0.33–11.92
Kabat and Wynder (1984)	48	24	25	0.79	0.30–2.04
Garfinkel *et al.* (1985)	49	134	402	1.31	0.93–1.85
Wu *et al.* (1985)	50	29	62	1.20	0.65–2.23
Lam (1985)	51	60	144	2.51	1.49–4.23
Akiba *et al.* (1986)	52	94	270	1.50	1.00–2.50
Lee *et al.* (1986)	53	32	66	1.03	0.48–2.20
Koo *et al.* (1987)	54	86	136	1.55	0.98–2.44
Lam *et al.* (1987)	55	199	335	1.65	1.21–2.21
Pershagen *et al.* (1987)	56	67	347	1.20	0.75–1.92
Brownson *et al.* (1987)	57	19	47	1.52	0.49–4.79
Gao *et al.* (1987)	58	436	605	1.19	0.87–1.63
Humble *et al.* (1987)	59	20	162	2.20	0.90–5.50
Butler (1988)	60	8	Cohort	2.02	0.60–6.81
Geng *et al.* (1988)	61	54	93	2.16	1.21–3.84
Inoue and Hirayama (1988)	62	22	47	2.55	0.90–7.20
Kalada *et al.* (1988)	63	17	17	3.40	0.49–23.80
Shimizu *et al.* (1988)	64	90	163	1.08	0.70–1.68
Svensson *et al.* (1989)*	65	34	174	1.26	0.65–2.48
Wu-Williams and Samet (1990)	66	417	602	0.79	0.64–0.98
Kalandidi *et al.* (1990)	67	90	116	1.92	1.13–3.25
Janerich *et al.* (1990)	68	191	191	0.86	0.57–1.29
Sobue (1990)	69	144	731	1.13	0.83–1.54
Liu *et al.* (1991)*	70	54	202	0.77	0.35–1.68
Fontham *et al.* (1991, 1994)	16, 71	653	1253	1.29	1.08–1.55
Stockwell *et al.* (1992)	72	210	301	1.60	0.94–2.72
Brownson *et al.* (1992)	73	432	1402	1.80	1.21–2.69

*Primary ETS exposure indicator other than spousal smoking.

ing women and in most of them the principal exposure of interest was the smoking habits of the husband, i.e., the variable generally considered as the most valid indicator of long-term exposure to ETS. It is of interest that among the 6 studies that reported a point estimate of relative risk below 1 (inverse association), only 3 (50%) have used, as they should, spouse smoking habits as the principal exposure variable, whereas among the 27 studies that reported a point estimate of relative risk above 1 (positive association) the corresponding number was 25 (93%). In 12 of the positive studies there was clear evidence of a dose-response trend, whereas in no study was there evidence for substantial confounding by any of the co-variates that were examined, including age, socioeconomic status, occupation, and diet.[5,74]

Several meta-analyses of the available epidemiologic data at various points in time have been undertaken. Estimates of the relative risk for lung cancer contrasting individuals exposed to ETS (mostly women married to smokers) with individuals not so exposed (mostly women married to nonsmokers) were 1.34,[2] 1.30,[75] 1.44,[76] 1.35,[77] 1.17,[78] and 1.25.[5] All these estimates are significantly different from the null value of 1, even though in none of the respective analyses was dose-dependent trends accounted for (had they been the results would have deviated more clearly from the null value). There is no conclusive evidence that the relative risk linking ETS to lung cancer is different for adenocarcinoma and other histologic types,[5,16,57,71,74] although early reports[37,56] and studies in China[58,61,66,70] suggest that the relative risk may, perhaps, be slightly lower for adenocarcinoma.

Meta-analyses are of questionable value when applied to observational data generated under variable conditions through very different study designs. Nev-

ertheless, the fairly consistent overall pattern (Table 8–1), the identification of significant positive trends in almost half of the reasonably powerful studies, the robustness of the relative risk estimates to adjustments for several factors,[5,74] and the converging results generated by all cohort studies[41,42,47,60] and most case-control studies that were specifically undertaken to examine the ETS–lung cancer association[49,52,56,67,71–73] indicate that the overall association is not due to chance and is not confounded by any of the known risk factors for lung cancer.

The main objections raised against the causal interpretation are, allegedly, publication bias against studies showing no association between ETS and lung cancer, bias introduced in both cohort and case-control studies by misclassification of smokers or former smokers among the nonsmokers, and differential information bias in case-control studies.

Publication bias would be generated if papers reporting positive associations between ETS and lung cancer were more likely to be submitted and accepted for publication than papers reporting no such associations.[79] Selective publication could be a legitimate concern with respect to secondary indicators of exposure to ETS, for example, at work and from cohabitants other than the spouse, or when men, rather than women, represent the study base. For this reason this review, as well as several others, have focused on studies of women characterized according to their husbands' smoking habits.

Publication bias can be detected using a statistical technique in which relative risk estimates are plotted against an indicator of study power. In the absence of publication bias the relative risk estimates should be normally distributed around the true value, with decreasing variability with increasing study power. Deviations from the expected funnel-like plot can be interpreted as indications of selective publication. Using this procedure, Vandenbroucke[80] found no evidence of publication bias for studies based on women and evaluating the relative risk for lung cancer in relation to husbands' smoking habits. Wells[81] and Woodward and McMichael[82] have also examined this issue and have found no evidence for selective publication in the existing literature.

Misclassification of smokers and former smokers as nonsmokers can introduce bias in both case-control and cohort studies, since these persons are at increased risk for lung cancer and tend also to be married to, or live with, smokers.[83,84] The magnitude of this bias depends on the values of four necessary and sufficient parameters: the overall proportion of ever smokers, the proportion of misclassified ever smokers, the risk for lung cancer among those misclassified, and the aggregation of smokers. Using realistic values for these variables Wald *et al*[85] have estimated that about 15% of the excess lung cancer risk associated with passive smoking could indeed be attributed to this bias. Correction for misclassification of ever smokers among nonsmokers has been incorporated in several meta-analyses[2,5] but, as expected, had little effect. A point of interest is that those willing to invoke this bias in order to explain part of the reported excess risk for lung cancer among self-declared passive smokers, must also accept that active smoking increases substantially the risk for lung cancer. This is, of course, established, but has yet to be accepted by some tobacco smoking promoters. Finally, information bias could not exist in the early studies[37,40] and cannot account for the results of prospective cohort investigations.[40,42,47,60]

Environmental Tobacco Smoke as a Cause of Lung Cancer ■

Several criteria have been used by various authors in their efforts to operationalize the establishment of causality. To this reviewer, the criteria of causality can be reduced to just two: the relative risk gradient in relation to exposure, as generated by the collective epidemiologic evidence, and the biologic plausibility. On the one hand, causality should be seriously considered when there is a sharp relative risk gradient, even when etiology is not biologically plausible. On the other hand, a weak empirical association should be considered as causal only when the biologic evidence is overwhelming. The association of ETS with lung cancer falls into the second category. The collective epidemiologic evidence indicates that ETS is positively associated with the relative risk for lung cancer to a highly significant degree. Usually the relationship is dose-dependent and remains statistically significant even when bias and confounding are accounted for. Nevertheless, the association is weak, and the firm conclusion for causality is based, to a large extent, on the converging and overwhelming biologic evidence: the qualitative similarity of sidestream and mainstream smoke, their unquestionable no-threshold carcinogenicity, and the extraordinarily strong causal link of active smoking with lung cancer. Recent evidence that passive smoking is associated with epithelial possibly precancerous lesions of the lung in an autopsy study[86] and suggestive results linking exposure to ETS with canine lung cancer risk[87] provide additional, but hardly necessary, support for a causal link. The strength of the biologic evidence distinguishes lung cancer from other cancers and several nonrespiratory conditions that have also been fre-

quently associated with passive smoking (reviewed in[88]).

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Lung cancer and other diseases related to passive smoking: a large-scale cohort study

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In 1981, we demonstrated an elevated risk of lung cancer among nonsmoking wives of husbands who smoke; subsequently, there have been several studies on this topic. Seventeen out of the 22 studies published in 1989 showed elevated risks; in seven studies, the risks were statistically significant. The risks in 10 selected studies were mostly higher when husbands smoked more heavily, the average relative risks for lung cancer in nonsmoking women with nonsmoking husbands, light smoking husbands and heavy smoking husbands being 1.00, 1.41 and 2.38, respectively. In addition to lung cancer, our cohort study revealed significantly elevated risks for nasal sinus cancer, brain tumour, post-menopausal breast cancer and ischaemic heart disease in nonsmoking women with heavily smoking husbands as compared to those with nonsmoking husbands. These effects are due to carcinogens and other toxic substances, which are present in higher concentration in sidestream smoke than in mainstream smoke.

INTRODUCTION

Since our report on the effect of husbands' smoking on the lung cancer risk in nonsmoking wives (1), many studies have been conducted to examine the passive smoking-lung cancer hypothesis. The results of most of these studies were in line with our report, as reviewed by the US Surgeon-General (2) and others (3-7).

The purpose of this paper is to summarize the results of our study in Japan, with special reference to lung cancer and other selected causes of death the risk of which is elevated by passive smoking.

MATERIAL AND METHODS

In our large-scale cohort study in Japan, 9106 deaths were recorded among 91 450 nonsmoking wives whose husbands' smoking habits were known during the 16-year follow-up (1966-81). The risk of nonsmoking wives dying from lung cancer (n=260), ischaemic heart disease (n=494) and other selected causes of death was measured according to the extent of the husbands' smoking habit.

RESULTS

The results are summarized in Tables 1-4. Those diseases that showed a significant elevation in risk in nonsmoking wives with husbands who smoked 20 or more cigarettes daily are listed in Tables 1 and 2; associations with the extent of husbands' smoking (dose-response relationships) are shown in Tables 3 and 4.

Lung cancer: Out of 429 female lung cancer deaths that took place during the 16-year follow-up period, 303 were in nonsmokers. Of these women, 200 were from 91 450

Table 1

Relative risks of cancer of selected sites for nonsmoking wives with heavily smoking husbands (20 or more cigarettes daily). Risk for wives with nonsmoking husbands = 1.00. Cohort study, 1966-81, Japan*

Site of cancer	n	Relative risk	90% Confidence limits	One-tailed p
Brain tumour	34	4.78	1.62 - 14.11	0.008
Nasal sinus	28	3.29	1.36 - 7.96	0.013
Leukaemia	51	2.04	1.09 - 3.82	0.030
Lung	200	1.90	1.94 - 2.70	0.001
Breast	115	1.73	1.12 - 2.66	0.018
Malig. lymphoma	85	1.58	0.89 - 2.81	0.096
Liver	226	1.31	0.94 - 1.82	0.094
Bone	17	1.31	0.33 - 5.21	0.373
Cervix	273	1.28	0.95 - 1.74	0.089
Bile duct/Gallbladder	91	1.25	0.79 - 1.98	0.215
All sites	2705	1.21	1.10 - 1.32	0.000
Colon	142	1.11	0.77 - 1.61	0.318
Ovary	54	1.08	0.54 - 2.15	0.428
Urinary organs	49	1.03	0.50 - 1.91	0.468
Upper digestive tract	80	1.01	0.58 - 1.78	0.486
Rectum	112	1.01	0.64 - 1.60	0.484
Stomach	854	1.01	0.86 - 1.19	0.463
Pancreas	127	0.87	0.56 - 1.34	0.295

*Adjusted for husband's age by the Mantel-Haenzel method

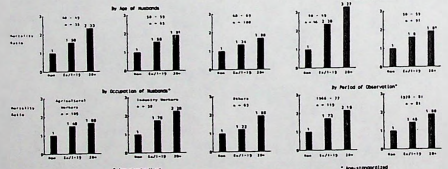


Fig. 1. Mortality ratios for lung cancer in nonsmoking wives by husband's smoking habit (prospective study, 1966-81, Japan)

nonsmoking wives whose husbands' smoking habits were known. The extent of the elevation in risk for lung cancer in nonsmoking wives was studied in relation to the smoking habits of the husbands.

The standardized mortality ratios for lung cancer in nonsmoking women were 1.00, 1.56, 1.42, 1.58 and 1.90 when their husbands were nonsmokers, ex-smokers, daily smokers of 10-14, 15-19 and 20 or more cigarettes per day,

Table 2

Relative risks of selected causes of death for nonsmoking wives with heavily smoking husbands (20 or more cigarettes daily). Risk for wives with nonsmoking husbands = 1.00. Cohort study, 1966-81, Japan*

Cause of death	n	Relative risk	90% Confidence limits	One-tailed p
Stomach ulcer	57	1.73	0.80 - 3.75	0.121
Subarachnoid haemorrhage	126	1.69	1.08 - 2.65	0.026
Emphysema	106	1.49	0.92 - 2.39	0.085
Suicide	200	1.46	1.07 - 1.63	0.019
Hypertensive disease	61	1.46	0.77 - 2.77	0.166
Ischaemic heart disease	494	1.31	1.06 - 1.63	0.019
Hypertensive heart disease	226	1.29	0.93 - 1.78	0.100
Cerebral haemorrhage	1179	1.25	1.08 - 1.43	0.036
Nephritis, nehprosis	128	1.27	0.83 - 1.93	0.399
Gastritis, enteritis	57	1.23	0.70 - 2.16	0.277
Diabetes	227	1.23	0.89 - 1.69	0.147
Cancer	2705	1.21	1.10 - 1.32	0.000
Ill-defined cerebrovascular disease	438	1.20	0.95 - 1.51	0.097
All sites	9106	1.19	1.13 - 1.26	0.000
Other heart disease	680	1.19	0.97 - 1.44	0.073
Pneumonia	258	1.15	0.84 - 1.59	0.232
Tuberculosis	100	1.15	0.71 - 1.86	0.321
Cholelithiasis	30	1.04	0.35 - 3.07	0.476
Arteriosclerosis	68	1.01	0.60 - 2.01	0.399
Cerebral thrombosis	992	1.00	0.85 - 1.17	0.493
Chronic rheumatic heart disease	106	0.86	0.55 - 1.34	0.286
Senility	164	0.81	0.53 - 1.24	0.204
Liver cirrhosis	180	0.75	0.52 - 1.08	0.094

*Adjusted for husband's age by the Mantel-Haenzel method

respectively (p for trend: 0.00178). A similar, significant dose-response relationship was observed by age and by occupation of husbands, by age of wives, and in each period of observation (Fig. 1), and also when other risk factors such as diet, prefecture and population density were adjusted for (Fig. 2) (8,9).

No other characteristic of the husbands or wives themselves, other than the amount of husbands' smoking, was found to elevate the risk of lung cancer in nonsmoking partners (Fig. 3).

Similar studies have been conducted in many countries. Most were case-control studies (10-27), and only a few were cohort studies (28,29). The results of most (17 out of 22 reported by 1989) were in line with the results of our study in Japan (Tables 5 and 6) (external consistency).

The earlier the age of marriage to husbands who smoked, higher was the risk for lung cancer in nonsmoking wives, suggesting the importance of duration of exposure to passive smoking (Fig. 4) (30). It was also observed that the risk for lung cancer in nonsmoking husbands was significantly higher when their wives were smokers rather than nonsmokers. Therefore, nonsmokers with a nonsmoking

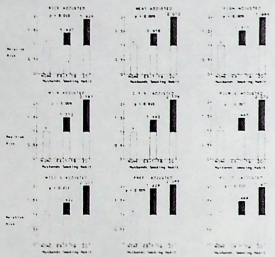


Fig. 2. Relative risk for lung cancer in nonsmoking wives by smoking habit of husbands. Comparison of 200 lung cancer cases and age-occupation matched controls. Observation by selected life style and demographic variables (prospective study, 1966-81, Japan)

spouse should be selected as the unit risk group in order to study the effect of exposure to tobacco smoke on lung cancer, either actively or passively (Fig. 5).

Other cancers: For most other sites, no significant association was observed between the risk in nonsmoking wives and the amount of

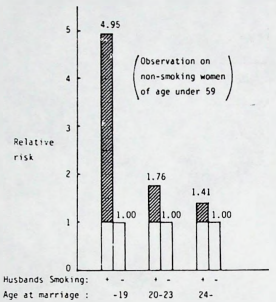


Fig. 4. Lung cancer risk in nonsmoking wives by husbands' smoking habit and by age at marriage (prospective study, 1966-81, Japan)

smoking of husbands. However, a significant elevation of risk for cancers of the paranasal sinuses, breast and brain, and leukaemia in nonsmoking wives was detected, according to the amount of the husband's smoking (Table 3).

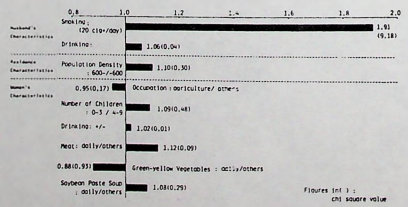


Fig. 3. Lung cancer mortality in nonsmoking women. Ratio by selected risk factors (prospective study, 1966-81, Japan)

The risk for breast cancer, although of borderline significance, when analysed by age groups of wife or standardized by occupation of husbands, revealed a significant dose-response relationship. At age 50-59 years when husbands smoked 1-19 and 20 or more cigarettes daily, the relative risk for mortality from breast cancer was 1.3 and 2.68, respectively (p for trend: 0.00969) (Fig. 6). The effect was independent of each of the other risk factors for wives, such as number of children (Fig. 7).

Other causes of death: Other causes of death in which the risk in nonsmoking wives is significantly associated with the amount of their husbands' smoking were ischaemic heart disease, subarachnoid haemorrhage, cerebral haemorrhage, suicide and all causes of death (Table 4).

DISCUSSION

The validity of interview-based information on exposure to passive smoking, on which the current study was based, was clearly demonstrated by recent IARC studies (31) that were conducted in 13 centres in 10 countries by measuring urinary cotinine levels.

For lung cancer, enough evidence to satisfy epidemiological criteria such as consistency

Table 3

Relative risks of cancers at selected sites for nonsmoking wives by husbands' smoking habits; dose-response relationship. Cohort study, 1966-81, Japan

Site of cancer	Husbands' smoking habit			Mantel-extension chi	One-tailed p
	Nonsmoker	1-19 daily	≥20 daily		
Lung	1.00	1.44	1.90	2.990	0.001
Nasal sinus	1.00[a]	2.28	3.29	2.064	0.019
Brain	1.00	4.01	4.78	2.069	0.019
Breast	1.00	1.12	1.73	1.795	0.036
Leukaemia	1.00[a]	1.79	2.04	2.009	0.022
All sites	1.00	1.11	1.21	3.143	0.000

[a]Including ex-smoking husbands

Table 4

Relative risks of selected causes of death for nonsmoking wives by husbands' smoking habits; dose-response relationship. Cohort study, 1966-81, Japan

Site of cancer	Husbands' smoking habit			Mantel-extension chi	One-tailed p
	Nonsmoker	1-19 daily	≥20 daily		
Cancer	1.00	1.11	1.21	3.143	0.000
Ischaemic heart disease	1.00	1.14	1.31	2.164	0.015
Subarachnoid haemorrhage	1.00	1.52	1.69	1.846	0.032
Cerebral haemorrhage	1.00	1.31	1.25	2.680	0.036
Suicide	1.00	1.34	1.46	2.030	0.021
All causes	1.00	1.15	1.19	5.449	0.000

Table 5

Relative risks for lung cancer among nonsmoking women, according to number of cigarettes smoked per day by their husbands

Author(s)	Ref. no.	Husbands' smoking status		
		Nonsmoker	Light	Heavy
Correa *et al.*	14	1.0	1.2	3.5
Trichopoulos *et al.*	26	1.0	2.4	3.4
Inoue *et al.*	19	1.0	1.2	3.4
Pershagen *et al.*	24	1.0	1.0	3.2
Akiba *et al.*	10	1.0	1.4	2.1
Wu *et al.*	27	1.0	1.2	2.0
Garfinkel *et al.*	16	1.0	1.1	2.0
Hirayamaª	8	1.0	1.4	1.9
Koo *et al.*	21	1.0	1.9	1.2
Garfinkelª	28	1.0	1.3	1.1

ªProspective study; all others are case-control studies.

Table 6

Relative risks (R) for lung cancer in women who had never smoked but had smoking husbands

Senior author	Ref. no.	Lung cancers	R	Senior author	Ref. no.	Lung cancers	R
Inoue	19	22	2.25	Garfinkel	16	134	1.31*
Geng	17	54	2.16**	Wu	27	<29	1.20
Trichopoulos	26	77	2.11**	Pershagen	24	67	1.20
Correa	14	22	2.07*	Gao	15	226	1.19
Lam	36	60	2.01**	Garfinkel	28	153	1.17
Humble	18	<28	1.80	Shimizu	25	90	1.10
Brownson	11	19	1.68	Gillis	29	8	1.00
Lam	22	199	1.65**	Lee	23	32	1.00
Koo	21	88	1.64	Kabat	20	24	0.79
Hirayama	1,8	183	1.63**	Buffler	12	41	0.78
Avika	10	94	1.50	Chan	13	84	0.75

*Significant only in trend analysis or in subjects validated as heavy smokers
**Significant at 95% confidence level in comparison of exposed and non-exposed subjects
Modified from ref. (7)

of association, specificity of association and dose-response relationship has already been accumulated in the literature to evaluate the risk of nonsmoking women with smoking husbands.

A different histological pattern of lung cancer in women than in men, e.g., predominance of adenocarcinoma, is considered to be due to the higher proportion of passive smoking-related cases in women than in men.

The results of our large-scale cohort study in Japan further showed an elevated risk for cancers of the nasal sinus, breast and brain and leukaemia in addition to lung cancer.

An elevation in risk for nasal sinus cancer, as in the case of lung cancer, is compatible with the existence of potent carcinogens in sidestream smoke, which is inhaled through the nose in even higher concentration than in mainstream smoke.

A significant elevation in risk due to passive smoking was reported for childhood brain tumours (32,33); a similar elevation related to passive smoking was also observed for adult brain tumours.

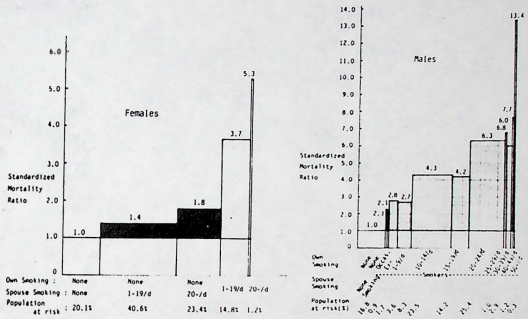


Fig. 5. Active and passive smoking and lung cancer mortality (prospective study, 1966-81, Japan)

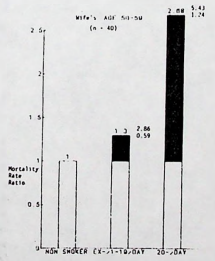
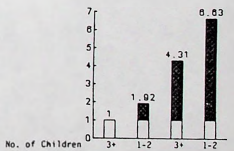


Fig. 6. Rate ratio for death from breast cancer in nonsmoking women by husbands' smoking habit



No. of children	Husband smoke: Others	Husband smoke: 20 or more/daily
1 - 2	1.92(0.61-6.04)	6.63(2.19-20.01)
3 or more	1.00	4.31(2.07-8.96)

Fig. 7. Relative risk for breast cancer (age 50-59) in nonsmoking women by number of children and by husbands' smoking habit

For breast cancer, the observed association is similar to that reported by Sandler *et al.*

(34). In our study, the association with the smoking habits of husbands was observed most strikingly in nonsmoking women at perimenopausal age, 50-59 years. The association was also observed to be independent of reproductive history. Epidemiological patterns of breast cancer are more or less similar to those of lung cancer (urban-rural relationship, international variation, increasing trend, etc.) may be due, at least partly, to the common association with passive smoking.

For leukaemia, in view of the recent report on the positive association between the disease and active smoking (35), intensive studies will be necessary to confirm the existence of an association with passive smoking as well.

The risks of ischaemic disease, subarachnoid haemorrhage, cerebral haemorrhage and suicide in nonsmoking wives were also significantly associated with their husbands' smoking habit. Most of these associations can be explained by the higher concentrations of carbon monoxide, nicotine and other toxic substances in sidestream smoke than in mainstream smoke. Further studies will also be necessary for these causes of death to clarify the mechanism of the association.

Meanwhile, in view of the enormous size of the population at risk, intensive efforts should be made to reduce the chances of exposure to passive smoking in our environment as low as possible in order to reduce the risk of these selected cancers and certain other diseases of vital importance.

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LUNG CANCER: POLITICAL MEASURES

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In countries where prolonged smoking of manufactured cigarettes is a widely established habit, it is responsible for about 90% of lung cancer. As lung cancer is usually incurable, even with expensive technology, the key to its control lies in prevention. World experience has shown the crucial need for government commitment, funding and action in controlling the epidemic of tobacco-related disease. It is recommended that each country establish a national council of 'tobacco or health' to coordinate a comprehensive tobacco control programme. This programme should incorporate data collection, including evaluation of specific anti-tobacco measures; legislative measures, including strong, rotating health warnings, limits on harmful substances, establishment of smoke-free areas, bans on any new forms of tobacco use, and a total ban on all direct or indirect promotion of tobacco products; health education campaigns; and taxation and price policies. The support and involvement of the medical profession is vital. Obstacles to success include the effect of advertising revenue in silencing the media, the inertia of governments and the medical profession, but most importantly the tobacco industry — the largest, wealthiest, most determined and strongest opposition to tobacco control worldwide.

In countries where tobacco smoking is an established habit, it is responsible for about 90% of lung cancer. As lung cancer is rarely curable, even with expensive technology, the key to reducing its frequency lies in prevention. While the prevalence of cigarette consumption is decreasing in industrialized countries, it is increasing in nonindustrialized countries which have fewer legislative controls and other measures that, in industrialized countries, limit the use of tobacco. Different countries are at very different points in the five-stage process of lung cancer prevention: epidemiology, social science, action, decrease in smoking prevalence and, finally, reduction in lung cancer mortality.

Science and epidemiology

Conclusive data on the hazards of tobacco exist on which preventive public health action can be based now, without waiting for further research. Continuing surveys on tobacco prevalence, mortality and morbidity related to tobacco use, attitudinal surveys and the economic impact of tobacco remain necessary, however, in order to assess the scope of the problem in each country, to illustrate the necessity of preventive measures and to evaluate the most effective of these measures.

Preventive measures

World experience has shown the crucial need for government commitment, funding and action in establishing a national programme to reduce the tobacco epidemic. It is important that all countries establish a national focal point to stimulate, support and coordinate anti-tobacco activities. The experience of such bodies is that it is not possible to cooperate with the tobacco industry, which is committed to the opposite goal — of increasing tobacco sales.

Ban on all tobacco promotion, advertising and sponsorship

Advertising conveys the message that smoking is associated with success, pleasure, relaxation, machoism, sports, freedom, beauty in nature, slimness, sophistication and sexuality. Castleden (1983), Charlton (1986) and Aitken *et al.* (1988) have shown that children are aware of and are influenced by tobacco advertising. Roemer (1986) reported that in 20 countries there was a total ban on advertising, in 17 there were strong partial bans, and in 21 there were moderate, partial bans. Partial bans have only partial effects and are frequently circumvented by ingenious, indirect advertising and sponsorship. A total ban allows children to grow up free from all commercial pressure to smoke and, as Bjartveit and Lund (1987) have shown in Norway, this leads to a decrease in the numbers of children who smoke.

Ban on sales to youth

Banning sales to young people may be good in principle, but in practice it is difficult to enforce. The countereffect is that, by suggesting that smoking is an adult activity, some youths, who wish to appear adult or daring, may even be encouraged to smoke. Saito (1987) reported that, in Japan, where persons under 20 years of age are not allowed to smoke, the adult rates of smoking are nevertheless established in the teenage years, indicating the ineffectiveness of that law.

Effective, rotating health warnings

Roemer (1986) noted that in 53 countries health warnings are required. Ramström (1980) in Sweden has shown that smokers read and are aware of informative, rotating warnings. In many countries, governments are moving from single, mild warnings, such as 'Smoking may harm your health', to tougher, rotating health warnings, such as: 'Smoking kills,' 'Smoking causes lung cancer,' 'Tobacco is addictive,' 'Smoking in pregnancy harms your baby,' 'Smoking causes heart disease,' and 'Quit smoking and feel healthier.'

Limits on harmful substances

Lowering the levels of tar in cigarettes can prevent about one-third of cases of lung cancer, although quitting can prevent more. A ceiling of about 10–15 mg tar per cigarette is a reasonable current aim. Smokers have an exaggerated perception of the benefits of low-tar cigarettes, however, so the tobacco industry should never be allowed to suggest that a lower tar cigarette is a 'safe' cigarette — especially since cigarettes kill even more people by other diseases than by lung cancer, and such evidence as is available on these other diseases suggests that differences in machine-measured tar delivery may involve little difference in risk.

Ban on new forms of tobacco

New forms of manufactured tobacco products are constantly being launched. Pre-emptive bans are true preventive health measures in that they avoid an additional range of cancers.

Smoke-free areas

Smoking is not only unpleasant to nonsmokers but may also give them cancer (IARC, 1986). In many countries, smoking has been banned in public areas, public transport, places of work (especially health premises), schools and government offices. Most people are nonsmokers; thus, the freedom of the majority to breathe clean air is an important consideration. Bans also help smokers: the creation of smoke-free areas encourages smokers to cut down or quit, thus helping them to make a decision in the best interest of their own health.

Price policy

Increasing taxes on cigarettes is a very effective way of reducing smoking without loss of revenue to governments. Most smokers give cost and health as the two main reasons for quitting. Lewit *et al.* (1981) and Warner (1984) reported that in the USA, for example, for every 10% increase in tax there is a 4% decrease in the number of smokers and a 14% decrease in the number of teenage smokers. The World Health Organization (1984) noted that 'Millions of lives could be saved if steep taxes were imposed on tobacco.' Grossman (1983) concluded that increasing taxes has a particularly beneficial effect upon young people and the poor, who have less money to spend and are therefore more likely to quit.

Health information and education

Health information and education form an important part of a comprehensive anti-tobacco programme, by educating both decision makers and the population to understand and accept legislative and other anti-tobacco measures. In contrast to the attractive 'Come and join us' images used by the tobacco industry, many health educators have traditionally used depressing, boring health statistics and finger-wagging 'Don't smoke' messages, which may encourage adults to quit but seem to have little effect in preventing young people from starting to smoke. Health education — especially that geared to youth — is now moving towards positive, healthy images.

Overcoming the obstacles

The media, the medical profession and politicians must be persuaded that smoking is harmful and that action is needed; yet these groups are often obstacles to tobacco control.

The media

Warner (1985) stated that 'Studies dating back to the 1930s provide evidence that the media's dependence on revenue from cigarette advertising has repeatedly led to suppression of smoking and health matters,' concluding 'It seems likely that there are more people who smoke today than there would be in an environment of responsible media coverage. The result is an avoidable excess burden of suffering and premature death. As

long as cigarette advertising remains legal and widespread, its influence on editorial coverage of smoking and health is likely to persist.'

As well as avoiding financial pressures that distort media coverage, it is important to avoid the pressure to regard tobacco-related issues as stale news. Simply saying that smoking causes cancer does not produce front-page headlines. Doctors involved with anti-tobacco programmes must learn to become public relations experts, to write press releases, to nurture journalists, to highlight newsworthy items and, perhaps most difficult of all, to drop their professional jargon and find lively ways of presenting complicated medical statistics accurately — roles for which we have received little training.

The health profession

Doctors are more often involved with cure than with prevention. Medical societies usually have little money in comparison with the wealth of the tobacco industry. Both individual doctors and medical societies are often reluctant to be involved in political issues or public confrontations with the well-groomed representatives of the tobacco industry. Tobacco is a health problem, but the resolution of this problem is political. Decisions on nationwide containment of tobacco use, for example by legislation, lie with governments not with hospitals. If doctors are in the business of prevention, however, they also are in the business of politics. Doctors who do not address the political dimensions of the tobacco epidemic cannot hope to contribute substantially to reducing the scope of this epidemic.

The support of medical organizations to national anti-tobacco efforts is essential: in giving health information to the public, in advising governments and in participating in anti-tobacco actions. Statements from international and national health organizations can have an influential effect by indicating solidarity on this issue. In Hong Kong, all 65 medical societies have agreed in writing that tobacco is harmful to health — a powerful statement of support. Medical meetings can be declared 'smoke-free meetings'. Individual doctors can set an example by not smoking, making their offices smoke-free, displaying posters, giving out pamphlets on how to quit, participating in anti-smoking efforts, refusing tobacco money and not buying shares in the tobacco industry.

Walking a more lively path, one finds organizations like 'BUGA-UP' (Billboard Utilising Graffitists Against Unhealthy Promotions), spawned in Australia, and 'DOC' (Doctors Ought to Care) in the USA. These groups comprise health professionals and others who have become weary of the inactivity of governments on this public health issue. Staging eye-catching 're-facing' of billboards, using catchy slogans, cheerfully disrupting tobacco-sponsored events and promotional displays with alternative messages and appearing dressed in skeleton suits, these groups certainly focus media and public attention on tobacco.

Governments and politicians

Governments are often worried about 'losing' immediate tax revenue, and politicians may have pressure put upon them by large tobacco companies. In fact, tobacco use drains the economy by medical and health costs, lost productivity, welfare costs, costs of fires and cost of the use of land that could be used to grow food.

The tobacco industry

The international tobacco industry is the largest, most determined and strongest opposition to tobacco control. It is organized globally, commands considerable political influence and continues to deny the main evidence about the health effects of tobacco. It has vast amounts of money to sponsor sport, the arts, academic institutions and many other organizations, and sponsorship of institutions makes them less likely to speak out against tobacco.

Nowadays, a country in which effective legislation is attempted can expect a coordinated and intensive confrontation with the international tobacco industry, and use of double standards. The international tobacco companies, although based in countries with long-established bans, strenuously fought Hong Kong's ban on tobacco advertising on television. The same companies are breaking the stated regulations of China by advertising cigarettes.

Sections of the US government have threatened trade sanctions against Hong Kong, Japan, the Republic of Korea, Taiwan and Thailand if those countries do not open their markets to the sale or advertising of US cigarettes. McNeil (1988) reported a comment of the Philip Morris tobacco company: 'The suspension of the tariffs in Japan and the recent opening of the market in Taiwan are the direct result of effective negotiations by the Office of the US Trade Representative [of the US government].' The political coercion of trade sanctions is noteworthy by an industry that so often speaks of freedom. The tobacco companies make no apology for this. Chan (1988) reported that a representative of the R.J. Reynolds company even said 'We expect such support [from the US government]. That's why we vote them in.'

A class action suit has been brought in the Philippines against US tobacco companies for failure to provide the same level of protection for Filipino children as that provided for children in their country of origin. If successful, this would result in a ban on television advertising, health warnings and enforcement of the same tar levels as in the same cigarettes sold in the USA. This case has implications for many developing countries.

Litigation is a more recent and interesting development in the 'tobacco war'. Ramström (1986) reported that compensation had been awarded for the harmful effects of passive smoking in causing lung cancer in Sweden; there has recently been a similar case in Australia; and headline-catching cases are now in progress in the USA (Eichenwald, 1988), which reverberate on tobacco shares on Wall Street. The number of such cases will undoubtedly increase over the next few decades and could possibly bring the tobacco industry to its knees financially.

A note of optimism

Is it possible to be optimistic about tobacco control? Worldwide, the health statistics give little comfort, and death and disability from tobacco will certainly increase over the next few decades. The behaviour of the tobacco industry gives no comfort either. But optimism stems from several points: data on health effects are slowly being collated — a crucial first step. While some countries have still taken virtually no action against tobacco, health concerns are mobilizing in many others. Remarkably similar battles are being fought all over the world. There is now sharing of international expertise in countering the tobacco

industry at the political and legislative level. Roemer (1986) reported that, by mid-1986, over 70 countries had enacted legislation to control smoking and many had strengthened existing legislation — a continuing process. An ancient Chinese saying goes: 'A journey of 10 000 miles begins with a single step.' The first steps in cancer reduction have already been taken, but there are many miles ahead.

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Relevance to Human Cancer of *N*-Nitroso Compounds, Tobacco Smoke and Mycotoxins.
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ANALYSIS AND PYROLYSIS OF SOME *N*-NITROSAMINO ACIDS IN TOBACCO AND TOBACCO SMOKE

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A new tobacco-specific nitrosamine, 4-(*N*-nitrosomethylamino)-4-(3-pyridyl)butyric acid (iso-NNAC), has been identified in tobacco, and its structure was confirmed by gas chromatography–mass spectrometry following enrichment of a tobacco extract. The levels of iso-NNAC ranged from 0.01 to 0.95 ppm. It does not induce DNA repair in primary rat hepatocytes and is inactive as a tumorigenic agent in strain A mice. In order to study the fate of nitrosamino acids during smoking, we spiked cigarettes with the following *N*-nitrosamino acids: iso-NNAC, 3-(nitrosomethylamino)propionic acid (NMPA), 4-(nitrosomethylamino)butyric acid (NMBA), *N*-nitrososarcosine (NSAR) and *N*-nitrosoproline (NPRO). NMPA and NMBA were partially transferred, unchanged, during smoking and partially formed the corresponding methyl esters, while pyrolysis of NSAR and NPRO resulted mainly in their decarboxylating products. This is the first time that the pyrosynthesis of methyl esters has been observed during smoking.

We have isolated and identified a new tobacco-specific nitrosamine (TSNA) and consider it a potential biomarker for exposure to TSNA. In addition, we studied the fate of certain nitrosamino acids during the burning of a cigarette in order to determine how they contribute to the formation of volatile nitrosamines and to the carcinogenic potential of cigarette smoke.

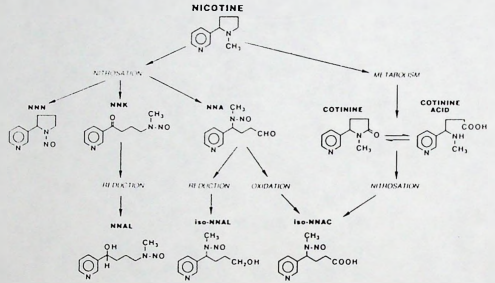
Tobacco-specific nitrosamines

Nitrosation of nicotine with sodium nitrite (Figure 1) *in vitro* gives rise to three TSNA: *N'*-nitrosonornicotine (NNN), 4-(nitrosomethylamino)-1-(3-pyridyl)-1-butanone (NNK) and 4-(nitrosomethylamino)-4-(3-pyridyl)butanol (NNA; Hecht *et al.*, 1978). Although NNA was found in neither tobacco nor tobacco smoke, its reduction product, 4-(nitrosomethylamino)-4-(3-pyridyl)-1-butanol (iso-NNAL), has been identified in dry and moist snuff together with the reduction product of NNK, 4-(nitrosomethylamino)-1-(3-pyridyl)-1-butanol (NNAL; Brunnemann *et al.*, 1987). The identification of iso-NNAL led to the hypothesis that 4-(*N*-nitrosomethylamino)-4-(3-pyridyl)butyric acid (iso-NNAC), an oxidation product of NNA, would be present in tobacco.

We developed an analytical procedure for the determination of iso-NNAC in tobacco, consisting of an aqueous extraction of tobacco and subsequent solvent partition with ethyl

acetate at pH 2 (nitrosamino acid fraction), pH 9 (TSNA fraction) and pH 4 (iso-NNAC fraction). The final fractions were methylated and analysed by gas chromatography-thermal energy analyser (GC-TEA; Djordjevic *et al.*, 1989). Table 1 presents the levels of iso-NNAC and other nitrosamino acids in different tobaccos. 3-(Nitrosomethylamino)propionic acid (NMPA) and *N*-nitrosoproline (NPRO) were the most abundant nitrosamino acids in all tobaccos analysed; 4-(nitrosomethylamino)butyric acid (NMBA) was present at lower levels, and iso-NNAC at concentrations of 0.01–0.95 ppm. The ranked order of abundance of the nitrosamino acids in tobacco was: NPRO > NMPA > NMBA > iso-NNAC.

Figure 1. Formation of tobacco-specific *N*-nitrosamines



In order to verify the structure of iso-NNAC, we analysed the enriched pH 4 fraction by capillary gas chromatography-mass spectrometry (GC–MS). The compound isolated from tobacco was confirmed as iso-NNAC. In order to study the biological activity of iso-NNAC, we employed the rat hepatocyte primary culture/DNA repair test (Djordjevic *et al.*, 1989; Williams *et al.*, 1989); in addition, iso-NNAC was bioassayed for lung adenomas in strain A/J female mice (Rivenson *et al.*, 1989). Iso-NNAC did not induce DNA repair in primary rat hepatocytes and, at 200 μmol/mouse, did not increase the rate of lung adenomas.

Pyrolysis studies

Carcinogenic volatile *N*-nitrosamines, such as *N*-nitrosodimethylamine and *N*-nitrosopyrrolidine, have been detected in tobacco and tobacco smoke. We postulated that they may be formed by decarboxylation of nitrosamino acids occurring in tobacco. We therefore selected NMPA, NMBA, *N*-nitrososarcosine (NSAR) and NPRO and applied 5 mg of each dissolved in 50 μl water to the tobacco column of 20 cigarettes. The cigarettes were then smoked under standard conditions and the smoke analysed by GC–TEA.

Table 1. Contents of nitrosamino acids in different tobacco products

Product type	Sample	Nitrosamino acids (μg/g dry weight)[a]				
		NMPA	NMBA	NPRO	iso-NNAC	Total
Chewing tobacco	KY 1S1	1.0	0.05	0.7	0.03	1.8
	A	0.6	0.03	0.2	0.02	0.8
Moist snuff	KY 1S3	4.6	0.40	6.6	0.13	11.8
	A	3.2	0.26	7.1	0.05	10.6
	E	11.0	0.12	4.5	0.21	15.8
Dry snuff	KY 1S2	13.1	1.54	15.4	0.95	31.0
	A	1.2	0.14	3.0	0.05	4.4
	B	4.5	0.46	8.1	0.21	13.3
Cigarette tobacco	KY 1R1	0.16	ND	0.59	0.01	0.76
	KY 1R4F	0.63	ND	0.57	0.01	1.21
	A	3.10	0.17	2.62	0.05	5.94

[a] Abbreviations: NMPA, 3-(nitrosomethylamino)propionic acid; NMBA, 4-(nitrosomethylamino)butyric acid; NPRO, *N*-nitrosoproline; ND, not detected.

NMPA did not yield its decarboxylation product but partially formed its methyl ester (Figure 2). This fraction was further enriched by rotary thin-layer chromatography, and subsequent GC-MS analysis confirmed the structural identity of the methyl ester of NMPA (Figure 3). In addition, we observed that some NMPA was carried over intact into the mainstream smoke. Pyrolysis of NMBA on a tobacco column also resulted in formation of the methyl ester, as confirmed by GC-MS. NMBA was also decarboxylated and was carried over into the smoke to some extent. NSAR was primarily decarboxylated to form *N*-nitrosodimethylamine. NPRO was decarboxylated to a large extent to form *N*-nitrosopyrrolidine, although some methylation and transfer into the smoke occurred. This is the first time that pyrosynthesis of methylesters has been observed during smoking.

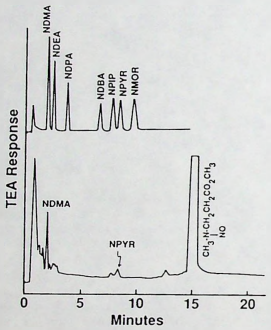
Interestingly, when iso-NNAC was pyrolysed on a tobacco column, it did not undergo decarboxylation but its condensation product was formed (0.07%); 0.9% of iso-NNAC was transferred unchanged into the mainstream smoke.

In order to study the mechanism of formation of these esters, we spiked cigarettes with 3-(*N*-nitrosoethylamino)propionic acid, which resulted in the formation of both the methyl and ethyl esters at a ratio of 2:1. Additional mechanistic studies with deuterated 3-(*N*-nitrosoethylamino)propionic acid are under way.

Future studies

Future studies will focus on the conditions leading to the endogenous formation of iso-NNAC and its analysis in urine. Iso-NNAC may serve as a biomarker for measuring exposure to TSNA and/or the extent of endogenous formation.

Figure 2. Gas chromatography–thermal energy analyser (TEA) traces of volatile *N*-nitrosamine reference mixture (top) and of pyrolysis fraction of 3-(*N*-nitrosomethylamino)propionic acid (bottom)[a]



[a] Abbreviations: NDMA, *N*-nitrosodimethylamine; NDEA, *N*-nitrosodiethylamine; NDPA, *N*-nitrosodipropylamine; NDBA, *N*-nitrosodibutylamine; NPIP, *N*-nitrosopiperidine; NPYR, *N*-nitrosopyrrolidine; NMOR, *N*-nitrosomorpholine

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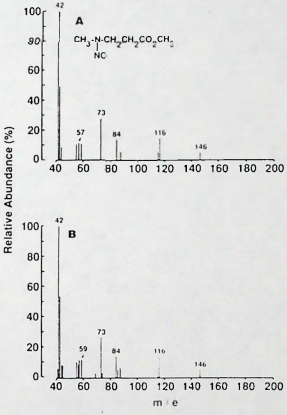
Figure 3. Mass spectra of the methyl ester of 3-(nitrosomethylamino)propionic acid: A, reference; B, isolated from tobacco smoke



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STUDIES IN TOBACCO CARCINOGENESIS

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The vapour phase of freshly generated cigarette mainstream smoke, of sidestream smoke and of environmental tobacco smoke was analysed for such tumorigenic agents as benzene, 1,3-butadiene and acrolein with a newly developed, highly sensitive gas chromatography–mass selective detection method. The major carcinogen in tobacco smoke, catechol, was studied in regard to its specific action on the metabolism of benzo[*a*]pyrene in mouse lung and mouse skin. The major tobacco-specific carcinogens in tobacco and its smoke are the nicotine-derived *N*-nitrosamines, *N'*-nitrosonornicotine and 4-(nitrosomethylamino)-1-(3-pyridyl)-1-butanone. A third nitrosamine that can be formed *in vitro* by nitrosation of nicotine is 1-(nitrosomethylamino)-1-(3-pyridyl)butylaldehyde. This aldehyde is not present in tobacco products, but its noncarcinogenic oxidation product, 4-(nitrosomethylamino)-1-(3-pyridyl)butyric acid, was found in tobacco and can be formed from the major nicotine metabolite, cotinine. It is also likely that this acid can be formed by endogenous reactions.

The objective of our studies in tobacco carcinogenesis lies in the elucidation of mechanisms of carcinogenesis and the determination of bioactive constituents in tobacco and tobacco smoke. This paper describes some of the chemical-analytical, biochemical and biological evaluations in progress.

Analysis of the vapour phase of tobacco smoke

The vapour phase of cigarette mainstream smoke and of sidestream smoke contains known tumorigenic agents (IARC, 1986). An analytical procedure was developed for the determination of selected gas-phase components in unaged smoke, utilizing cryofocusing capillary gas chromatography and mass selective detection. The latter was used in the selective ion monitoring mode, allowing us to scan for three selective ions, typical for each compound, during specific 'time windows'. Mainstream smoke was analysed *via* a ten-port gas sampling valve on a puff-by-puff basis. The concentrations of benzene and 1,3-butadiene increased only slightly with progressive numbers of puffs, except for cigarettes with charcoal-containing filter tips when volatiles that have been selectively retained in the filter from early puffs are released into the mainstream of later puffs. The mainstream smoke of one cigarette contains 6–73 µg benzene, 5–88 µg toluene, 16–70 µg 1,3-butadiene, 90–1060 µg isoprene and 8–260 µg acrolein. The sidestream smoke of one cigarette contains 350–650 µg benzene and 200–360 µg 1,3-butadiene. In the ambient air

of rooms polluted with tobacco smoke we found 7-36 µg/m3 benzene and 0.8-4.5 µg/m3 1,3-butadiene.

Effect of catechol on the metabolism of benzo[a]pyrene

Bioassays have revealed that catechol (1,2-dihydroxybenzene), a major phenolic constituent of tobacco smoke, is a potent carcinogen and a weak co-initiator with benzo[*a*]pyrene (BP). The mechanism underlying these biological phenomena is not known. *In vivo*, catechol alters the penetration of BP into mouse skin as well as its metabolism. Specifically, catechol suppresses secondary steps in the metabolism of BP, namely epoxidation of 7,8-dihydroxy-7,8-dihydro-BP (BP-7,8-diol) to 7,8-dihydroxy-9,10-epoxy-7,8,9,10-tetrahydro-BPs (BPDEs). Co-application of catechol with BP or with BP-7,8-diol also decreases the speed with which the hydrocarbons penetrate skin. When applied to mouse skin with the racemic BP-7,8-diol, catechol is as potent a cocarcinogen as it is with BP itself. However, we found differences in the effects of catechol on the extent of metabolic activation of racemic and enantiomeric BP-7,8-diols and also with regard to DNA binding. Catechol suppresses epoxidation of the moderately carcinogenic (+)-BP-7,8-diol to a greater extent than that of the more active (–) enantiomer. In the presence of catechol, less of the major adduct is formed between metabolites of the (+)-BP-7,8-diol and DNA, while the presence of the phenolic compound has no significant impact on formation of the major DNA adduct derived from the (–) enantiomer. Consequently, catechol affects the proportion of major adducts derived from (+)- and (–)-BP-7,8-diols in mouse skin.

Tobacco-specific N-nitrosamines

N-Nitrosation of nicotine *in vitro* leads to three tobacco-specific *N*-nitrosamines, *N'*-nitrosonornicotine (NNN), 4-(nitrosomethylamino)-1-(3-pyridyl)-1-butanone (NNK) and 4-(nitrosomethylamino)-4-(3-pyridyl)butylaldehyde (NNA; Figure 1). While tobacco and tobacco smoke contain significant amounts of the highly carcinogenic NNN and NNK, NNA has not been identified in any tobacco product. However, both the reduction product of NNA, 4-(nitrosomethylamino)-1-(3-pyridyl)-1-butanol (iso-NNAL; 66–2500 ng/g) and the oxidation product of NNA, 4-(nitrosomethylamino)-4-(3-pyridyl)butyric acid (iso-NNAC; 10–950 ng/g) have been identified in processed tobacco. This acid is not genotoxic, nor does it induce tumours in mice. Iso-NNAC is also formed *in vitro* from the major nicotine metabolite, cotinine. Biochemical studies in progress indicate that iso-NNAC may also be formed *in vivo* after *N*-nitrosation of cotinine and cotinine acid.

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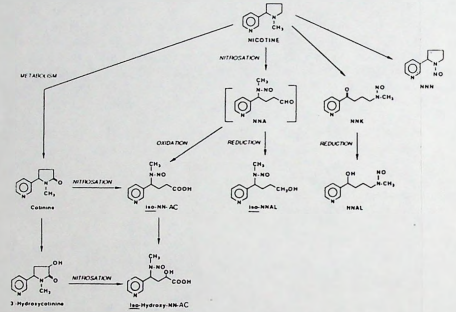
Reference

IARC (1986) *IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans*, Vol. 38, *Tobacco Smoking*, Lyon

Figure 1. *N*-Nitrosation products of nicotine[a]



[a] NNN, *N'*-nitrosonornicotine; NNA, 4-(nitrosomethylamino)-4-(3-pyridyl)butylaldehyde; NNK, 4-(nitrosomethylamino)-1-(3-pyridyl)-1-butanone; NNAC, 4-(nitrosomethylamino)-4-(3-pyridyl)-butyric acid; NNAL, 4-(nitrosomethylamino)-1-(3-pyridyl)-1-butanol

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CARCINOGENIC SUBSTANCES IN SOVIET TOBACCO PRODUCTS

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Chemical carcinogens were determined in mainstream smoke from nonfilter cigarettes produced and consumed in the USSR and in *nass*, a mixture of tobacco, lime, ash and cotton oil. Cigarettes contained high levels of tar (23–25 mg/cigarette) and nicotine (1.5–1.9 mg/cigarette) and, generally, a high content of polycyclic aromatic hydrocarbons, which are major epithelial carcinogens, *N*-nitrosamines, which are organ-specific carcinogens, and some carcinogenic metals, such as arsenic and chromium. *Nass* contained the tobacco-specific *N*-nitroso compounds, *N'*-nitrosonornicotine, *N'*-nitrosoanatabine, *N'*-nitrosoanabasine and 4-(*N*-nitrosomethylamino)-1-(3-pyridyl)-1-butanone, as well as volatile *N*-nitrosamines, but at levels lower than in other types of chewing tobacco and snuff. The low levels in *nass* are due to the short ageing process used, in contrast to commercially produced chewing tobacco and fine-cut snuff, which are highly processed products requiring long ageing and fermentation.

In the USSR, the proportion of filter cigarettes smoked increased from 0.3% in 1963 to 21.3% in 1982; however, 90% of the cigarettes consumed in this country fall within the category of 'high-tar' cigarettes (Zaridze *et al.*, 1986a). In some areas of the USSR, particularly in the central Asian republics, a smokeless tobacco product, *nass*, is widely used. Use of *nass* has been associated with a high incidence of oral cancer and a high prevalence of leukoplakia (Zaridze *et al.*, 1986b).

Carcinogens in cigarette smoke

Two types of nonfilter cigarettes were smoked according to ISO requirements (International Standards Organization, 1986) in a 20-port smoking machine (Borgwald). The concentration of polycyclic aromatic hydrocarbons was determined by spectroluminescence (Khesina *et al.*, 1983), metals by atomic emission spectroscopy (Westcott & Spincer, 1974; Jenkins, 1986), and carcinogenic nitrosamines by gas chromatography-thermal energy analysis (Brunnemann *et al.*, 1977; Adams *et al.*, 1983).

The cigarettes contained high levels of tar (23–25 mg/cigarette) and nicotine (1.5–1.9 mg/cigarette), and the smoke contained very high concentrations of some carcinogenic polycyclic aromatic hydrocarbons (Table 1). The concentrations of metals in Soviet

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TOBACCO-SPECIFIC NITROSAMINES IN COMMERCIAL CIGARETTES: POSSIBILITIES FOR REDUCING EXPOSURE

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Tobacco-specific nitrosamines (TSNA) are powerful carcinogens found in tobacco and tobacco smoke in relatively high concentrations. Tar delivery, which is generally accepted as an index for the carcinogenic potential of cigarette smoke, must be declared in most European countries. In this investigation of more than 170 types of commercial cigarettes from several European countries and the USA, no correlation was observed between tar delivery and mainstream smoke concentration of *N'*-nitrosonornicotine (NNN) and 4-(*N*-nitrosomethylamino)-1-(3-pyridyl)-1-butanone (NNK). Therefore, although crucial, tar delivery alone is not a sufficient index for the carcinogenic potential of cigarette smoke. It is proposed that TSNA concentrations be determined for characterization of the carcinogenic potential of cigarettes with low and ultra-low tar yields and that these be declared by an additional and adequate parameter. The mainstream smoke concentrations of NNN and NNK are given by the amounts of preformed compounds in tobacco, which is dependent on the nitrate content of the tobacco and the tobacco type. A further important determinant of the exposure of smokers to TSNA is the total volume drawn through a cigarette while smoking, which is dependent on puff volume and puff frequency and which directly influences TSNA transfer. Smokers inhale higher volumes when smoking low-nicotine cigarettes, so that low NNN:nicotine and NNK:nicotine ratios result in decreased exposure to TSNA. Reduction of exposure to TSNA can be achieved by selecting tobaccos with low levels of preformed TSNA (low nitrate content, small amounts of burley tobaccos and stems) and by manufacturing cigarettes with low NNN:nicotine and NNK:nicotine ratios.

Tobacco-specific nitrosamines (TSNA), which are powerful carcinogens, have been found in tobacco and tobacco smoke in relatively high concentrations (Hoffmann & Hecht, 1985). In order to reduce smokers' exposure to TSNA, we have investigated the main factors that influence their concentrations in mainstream smoke. Since tar delivery is generally accepted as an index of the carcinogenic potential of cigarette smoke, and must be declared in most European countries, this measure was compared with the amounts of TSNA, and especially *N'*-nitrosonornicotine (NNN) and 4-(*N*-nitrosomethylamino)-1-(3-pyridyl)-1-butanone (NNK), in cigarettes.

More than 170 types of commercial cigarettes from Austria, Belgium, Germany, France, Italy, Poland, Switzerland, the United Kingdom, the USA and the USSR were analysed for

TSNA in tobacco and in mainstream smoke as well as for nitrate in tobacco, by the methods of Spiegelhalder *et al.* (1989) and Fischer and Spiegelhalder (1989). The declared values of tar and nicotine were used. The results are presented in Table 1.

Tar delivery, which is widely considered to reflect the carcinogenic potential of cigarette smoke, did not correlate with the amounts of the strong carcinogens NNN and NNK in mainstream smoke (NNN: $r2 = 0.18$; NNK: $r2 = 0.14$). Furthermore, there was no correlation between nicotine and TSNA deliveries (NNN: $r2 = 0.13$; NNK: $r2 = 0.10$). Thus, the concentration of TSNA should also be determined and declared by an additional and adequate parameter (Fischer *et al.*, 1989a).

The mainstream smoke concentrations of NNN and NNK strongly depend on the amounts of preformed NNN and NNK in tobacco (Fischer *et al.*, 1989b). We saw a constant ratio between the two concentrations, which was not dependent on the level of nitrate in tobacco, except for NNK in nitrate-rich, dark tobacco cigarettes, nor on the nicotine level. Spiking the cigarettes with the nitrosamine precursors nicotine (at 10 mg/cigarette) and nitrate (at 4–20 mg/cigarette) prior to smoking did not significantly change the mainstream smoke concentrations of NNN and NNK (Fischer *et al.*, 1989b). These data indicate that NNN is not formed during smoking, and synthesis of NNK is very unlikely, at least for tobaccos with low nitrate levels. Thus, the NNN and NNK found in mainstream smoke is derived from preformed nitrosamines in the tobacco (Fischer *et al.*, 1989b).

The amount of preformed TSNA in tobacco is determined mainly by the nitrate level in the tobacco (Fischer *et al.*, 1989c), and this depends on the tobacco type, especially for NNK. The lowest TSNA concentrations were observed in oriental-type cigarettes, which contain little nitrate. In low-nitrate, Virginia-type cigarettes, the TSNA concentrations were also low, but NNK was present at the same or much higher concentrations than NNN, whereas in other cigarettes NNN levels exceeded NNK levels. The highest TSNA concentrations were found in cigarettes made of dark tobaccos, which are high in nitrate. In blended cigarettes, both high and low TSNA concentrations were found, correlating with the nitrate level of the tobacco composition.

A further important determinant of TSNA concentration in mainstream smoke is the total volume drawn through a cigarette while smoking, which is dependent on the puff volume and the puff frequency and which directly influences TSNA transfer (Fig. 1; Fischer *et al.*, 1989d). Since the smoker's interest is to maintain an adequate nicotine intake, smokers inhale higher volumes from low-nicotine cigarettes, resulting in higher intakes of TSNA and tar in relation to standard smoking conditions. Thus, with low ratios of NNN:nicotine and NNK:nicotine, the smoker's exposure to TSNA is decreased.

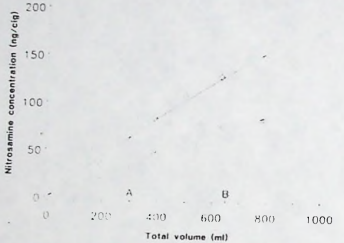
A reduction in the exposure of smokers to TSNA could be achieved by selecting cigarettes made of tobaccos with low concentrations of preformed TSNA, i.e., those with a low nitrate content, and containing little burley tobaccos and stems, and by manufacturing cigarettes with low ratios of NNN:nicotine and NNK:nicotine.

Table 1. Ranges of tar, nicotine, *N'*-nitrosonornicotine (NNN) and 4-(*N*-nitrosomethylamino)-1-(3-pyridyl)-1-butanone (NNK) deliveries in mainstream smoke (MS) as well as concentrations of preformed nitrosamines and nitrate in tobacco of commercial cigarettes from several European countries and the USA

Country	No. of samples	Tar (mg/cig min–max)	Nicotine (mg/cig min–max) MS	NNN (ng/cig) Tobacco (min–max)	NNN (ng/cig) MS (min–max)	NNK (ng/cig) Tobacco (min–max)	NNK (ng/cig) MS (min–max)	Nitrate (mg/cig; min–max)
Austria	5	9–15	0.7–0.9	42–172	306–1122	12–100	92–310	4.2–8.0
Belgium	7	13–16	1.0–1.3	38–203	504–1939	20–150	219–594	1.8–10.8
France	20	6–44	0.3–2.7	11–1000	120–6019	19–498	57–990	1.5–19.4
Germany	55	1–28	0.1–2.0	5–625	50–5316	ND–432	ND–1120	0.6–14.4
Italy	10	NA	NA	21–1353	632–12 454	8–1749	153–10 745	6.2–13.3
Poland	6	NA	NA	121–347	870–2760	38–105	140–450	4.4–12.8
Switzerland	3	12–15	0.9–1.2	121–226	1280–2208	69–124	450–554	6.4–7.8
United Kingdom	12	LT–MT	NA	17–123	140–1218	18–103	92–433	1.4–8.0
USA	20	NA	NA	54–197	993–1947	41–145	433–733	6.2–13.5
USSR	9	NA	NA	23–312	60–850	4–40	ND–150	1.7–9.1

NA, not available; ND, not detected (MS, < 4 ng/cigarette; tobacco, < 50 ng/cigarette); LT, low tar; MT, middle tar

Figure 1. Dependence of concentration of *N'*-nitrosonornicotine (NNN;◇) and 4-(*N*-nitrosomethylamino)-1-(3-pyridyl)-1-butanone (NNK, ○) in mainstream smoke on the total volume drawn through a low-tar, blended filter cigarette



A, approximate total volume for standard smoking conditions; B, approximate average inhalation volume for low-tar, low-nicotine cigarettes

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OCCURRENCE OF AND EXPOSURE TO *N*-NITROSO COMPOUNDS IN TOBACCO

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The concentrations of 21 *N*-nitroso compounds in smokeless tobaccos are presented. Tobacco-specific nitrosamines accounted for 70–90% of the total identified *N*-nitroso compounds. Daily exposure of smokeless tobacco users to preformed *N*-nitroso compounds may exceed 200 µg/day in certain populations.

We have identified 21 volatile, nonvolatile and tobacco-specific *N*-nitrosamines (TSNA) in smokeless tobacco products available commercially in 1987–88 (Tricker & Preussmann, 1988, 1989). Selected representative data are presented in Table 1. Currently, *N*-nitrosodimethylamine, *N*-nitrosoethylmethylamine, *N*-nitrosopiperidine and *N*-nitrosopyrrolidine are the most commonly found volatile nitrosamines; traces of *N*-nitrosodipropylamine and *N*-nitrosodibutylamine are present in heavily cured and/or fermented tobacco products. Trace levels of *N*-nitrosomorpholine are still found in some UK and Swedish oral tobacco products packed in waxed containers. The most commonly found nonvolatile *N*-nitrosamino acids and their derivatives are *N*-nitrosoproline, *N*-nitrosopipecolic acid, *N*-nitrosohydroxyproline, *N*-nitrososarcosine, 3-(*N*-nitroso-*N*-methylamino)propionic acid and 4-(*N*-nitroso-*N*-methylamino)butyric acid. Some heavily cured/fermented tobaccos, in particular *zarda* and some American moist snuffs (data not presented), were found to contain *N*-nitrosoazetidine 4-carboxylic acid (< 200 µg/kg) and *N*-nitrosothiazolidine 4-carboxylic acid (< 280 µg/kg). The presence of other nonvolatile *N*-nitrosamines, amenable to gas chromatography–thermal energy analysis only after methylation or silylation, were also found. TSNA are by far the most abundant *N*-nitroso compounds present in tobacco and usually account for 70–90% of the total. 4-(*N*-Nitrosomethylamino)-4-(3-pyridyl)-1-butanol (< 8100 µg/kg) has been detected in about 60% of all tobacco samples analysed (n = > 120), including various forms of smoking tobacco, indicating far greater exposure to this compound than previously reported (Hecht & Hoffmann, 1988).

In order to make a rough estimate of potential exposure to carcinogenic *N*-nitroso compounds, and in particular to 4-(*N*-nitrosomethylamino)-1-(3-pyridyl)-1-butanol and *N'*-nitrosonornicotine during use of smokeless tobacco, mean daily exposure to the identified *N*-nitroso compounds was estimated by multiplying the concentrations of individual compounds by the average amount of tobacco consumed by the tobacco-using population (Table 2). This method of calculating exposure is based on the assumption that

Table 1. *N*-Nitroso compounds in smokeless tobaccos (μg/kg)

N-Nitrosamine[a]	UK oral tobacco (5 samples)		Swedish moist snuff (5 samples)		Indian *zarda* (11 samples)		European nasal snuff (10 samples)	
	Mean	Range	Mean	Range	Mean	Range	Mean	Range
NDMA	37	6.0–82	1.5	1.0–2.5	11	2.0–31	20	2.0–82
NEMA	1.0	ND–2	ND		1.0	ND–2.0	1.6	ND–8.5
NPIP	20	2.5–40	ND		0.3	ND–2.0	3.8	ND–17
NPYR	120	64–190	5.0	4.5–6.0	100	6.0–69	44	1.5–13
NMOR	0.5	ND–1	1.0	ND–1.0	ND		ND	
NDELA	105	ND–220	19	8–31	9.5	ND–54	12	ND–42
NSAR	120	29–240	19	8–31	49	ND–350	21	ND–85
NPMA	3980	1360–8300	1340	1040–1820	2050	22–18 000	1620	490–4260
NBMA	640	62–1470	70	53–94	170	ND–2040	160	76–410
NAsCA	ND		ND		18	ND–140	ND	
NPRO	2260	330–4950	1100	630–1820	2850	280–18 000	3950	770–873
NPIC	540	83–1760	36	ND–130	260	ND–2040	80	ND–310
NTCA	6	ND–28	21	ND–69	48	ND–280	7.4	ND–46
NHPRO	330	92–610	140	ND–230	69	ND–190	98	46–27
iso-NNAL	65	ND–150	27	ND–80	1420	120–8100	360	ND–1590
NADINAT	3520	1980–4800	2640	1650–3250	16 030	780–99 100	3120	1030–7830
NNN	3960	1090–7630	3360	2100–4800	13 420	400–79 000	7840	2390–18 750
NNK	2800	400–8250	790	400–1040	4030	220–24 100	2430	580–6430
Total[b]	19 770	6130–36 450	9570	6220–12 500	40 530	1670–241 000	19 780	7190–42 530

[a] NDMA, *N*-nitrosodimethylamine; NEMA, *N*-nitrosoethylmethylamine; NPIP, *N*-nitrosopiperidine; NPYR, *N*-nitrosopyrrolidine; NMOR, *N*-nitrosomorpholine; NDELA, *N*-nitrosodiethanolamine; NSAR, *N*-nitrososarcosine; NPMA, *N*-nitrosopropylamine; NBMA, *N*-nitrosobutylmethylamine; NAsCA, *N*-nitrosoasparagine; NPRO, *N*-nitrosoproline; NPIC, 4-carboxy-*N*-nitrosopiperidine; NTCA, *N*-nitrosothiazolidine 4-carboxylic acid; NHPRO, *N*-nitrosohydroxyproline; iso-NNAL, 4-(*N*-nitrosomethylamino)-1-(3-pyridyl)-1-butanol; NADINAT, *N*'-nitrosoanabasine/*N*'-nitrosonornicotine; NNN, *N*'-nitrosonornicotine; NNK, 4-(*N*-nitrosomethylamino)-1-(3-pyridyl)-1-butanone.

[b] Total identified *N*-nitroso compounds.

ND, not detected; limits of detection: volatile nitrosamines, 0.1 μg/kg; nonvolatile nitrosamines, 1.0 μg/kg; tobacco-specific nitrosamines, 1.0 μg/kg tobacco

100% of TSNA are extracted from saliva. Österdahl and Slorach (1988) have shown that this is not true in Swedish snuff dippers, whose saliva contains higher levels of TSNA than can be accounted for by levels of preformed nitrosamines in tobacco. Thus, endogenous formation of TSNA in saliva (Österdahl & Slorach, 1988) and under simulated gastric conditions (Tricker *et al.*, 1988) probably results in higher exposure to TSNA than indicated in Table 2.

Table 2. Exposure to *N*-nitroso compounds from use of oral tobacco

Tobacco-using population	Use (g/day)	Daily nitrosamine exposure (μg/day)	
		Total	NNN/NNK[a]
Dry snuff (Europe)	2.0	39.6	20.5
Oral tobacco (UK)	4.5	89.0	30.4
Moist snuff (Sweden)	15.9	152.1	66.0
Zarda (India)	5.0	203.0	87.5

[a] NNN, *N*'-nitrosonornicotine; NNK, 4-(*N*-nitrosomethylamino)-1-(3-pyridyl)-1-butanone

We conclude that high levels of *N*-nitroso compounds present in smokeless tobaccos expose the consumer to a considerable exogenic burden of potentially carcinogenic compounds, and in particular TSNA.

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FEASIBILITY OF A PROSPECTIVE STUDY OF SMOKING AND MORTALITY IN QIDONG, CHINA

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Qidong is a rural county in eastern China with particularly good facilities for epidemiological research: cigarette use by adult males is widespread (70% now smoke), male lung cancer rates already appear to be rising, the population is stable and well served by a county-wide network of health care facilities, and systematic county-wide registration of all deaths has existed since the mid-1970s, causes currently being assigned according to the 9th International Classification of Diseases.

To help assess the feasibility of a prospective study of smoking and tobacco-related disease in rural China, we describe the current prevalence of smoking, the history of tobacco use, the age-specific mortality rates from lung cancer and the overall mortality rates from various broad groups of disease in one particular county, Qidong. Qidong is a low-lying, densely populated agricultural county located at the mouth of the Yangtze River, in Jiangsu province, just north of Shanghai municipality. There is little turnover of population: almost all the adults were born in the county and will probably continue living there. A central registry, with age, sex and ICD coding of the causes of all deaths in Qidong, is maintained by the Qidong Liver Cancer Institute. Direct information on tobacco consumption before 1949 is not available, although retrospective questioning of old people about their previous habits has been attempted. Since 1959, manufactured cigarette sales to the county as a whole have been recorded. The Qidong Statistics Bureau reported that the population of Qidong has about doubled, from 620 000 in 1950 to 1 130 000 in 1986; and that annual cigarette sales in 1950, 1960, 1970 and 1986 were 195, 378, 638 and 1294 million pieces, respectively (Table 1). The mean daily sales of manufactured cigarettes per person reached 3.15 in 1986, as against only 0.86 in 1950. Almost all of the cigarettes are consumed by men, so although no exactly representative survey of age- and sex-specific smoking habits is available, the consumption per adult male is probably well over 10/man per day.

All causes of death coded in ICD9 for 1987

A population-based registry system of all causes of death has been established in Qidong since 1974, although registration may have been seriously incomplete in the mid-1970s. In

1987, the causes were classified according to the 9th International Classification of Diseases (ICD 9), as recommended by the Health Ministry of China. The leading causes of death in Qidong in 1987 are given in Table 2. In classifying causes of death, particular attention is given to cancers, most of which are diagnosed at the county hospital, which is adjacent to the Qidong Liver Cancer Institute that houses the death registry.

Table 1. Trends in manufactured cigarette sales in Qidong

Year	Total sales of manufactured cigarettes (millions)	Annual sales per person	Daily sales per person
1949	97	160	0.44
1950	195	314	0.86
1951	243	382	1.05
1952	304	466	1.28
1953	338	492	1.35
1954	359	508	1.39
1955	376	528	1.45
1956	463	615	1.69
1957	392	509	1.40
1958	382	493	1.35
1959	381	480	1.32
1960	378	475	1.30
1961	153	191	0.52
1962	76	90	0.25
1963	195	224	0.61
1964	361	405	1.11
1965	611	668	1.83
1966	342	365	1.00
1967	388	407	1.11
1968	425	437	1.20
1969	607	608	1.67
1970	638	627	1.72
1971	656	637	1.74
1972	631	608	1.67
1973	664	634	1.74
1974	599	566	1.55
1975	747	700	1.92
1976	730	678	1.86
1977	708	654	1.79
1978	721	661	1.81
1979	680	621	1.70
1980	688	627	1.72
1981	778	706	1.93
1982	729	656	1.80
1983	1009	905	2.48
1984	920	822	2.25
1985	1092	973	2.67
1986	1294	1150	3.15

Table 2. Causes of death in 1987 in Qidong county, China, as recorded by the Qidong Liver Cancer Institute registry

Cause of death 9th ICD category	Age 0–34		Age 35–69		Age ≥ 70	
	M	F	M	F	M	F
011: Pulmonary tuberculosis	11	5	73	32	42	16
Rest of 001–138 (infectious and parasitic diseases	27	19	20	9	13	18
150: Cancer of oesophagus	0	0	32	12	36	21
151: Cancer of stomach	4	2	112	61	103	45
155: Cancer of liver	67	19	358	102	28	13
162: Cancer of lung	4	2	102	38	65	36
Rest of 140–230–4 (malignant neoplasms)	21	14	127	121	59	92
430–438: Stroke	4	3	120	111	319	417
410–414: Ischaemic heart disease	6	1	38	33	89	110
Rest of 390–439 (vascular diseases)	2	9	30	25	101	131
466, 490–3, 496: Bronchitis, emphysema, asthma	7	7	230	92	642	523
Rest of 460–519 (other respiratory diseases)	60	45	8	10	44	61
571: Cirrhosis	20	2	156	72	47	37
Rest of 520–579 (other digestive diseases)	13	12	48	36	77	88
Rest of 001–799 (other medical causes)	138	93	66	77	198	302
800–999: External causes	192	109	100	54	47	62
All causes	538	352	1620	886	1910	1972
(Rate per 100 000)	(147)	(97)	(943)	(501)	(9338)	(6036)

Age-specific mortality from lung cancer

During 1972–86, a total of 2572 deaths were attributed to lung cancer (although there is inevitably some under-registration, and, conversely, there is some possibility of confusion between primary and secondary disease, since many cases were diagnosed only by radiology and symptoms). During this period, the crude mortality rate attributed to lung cancer was 16/100 000 (22/100 000 males and 10/100 000 females).

The age-specific lung cancer mortality rates recorded in 1972–86 among females do not appear to be increasing. The age-specific rates for males were already higher than those for females in 1972–74, and the male rates increased significantly between 1972–74 and 1984–86.

Prevalence of smoking among male adults

A sampling survey on smoking prevalence was completed in 1987 among male peasants aged over 30 years: 70% are current smokers, 5% being heavy smokers (over 23 pieces/day) and 32% being light smokers (1–7 pieces/day); 69% of current and ex-smokers started to smoke before 24 years of age, the median age of starting being 22.

Manufactured cigarettes are the main type of tobacco used in Qidong. In 1987, the prevalence of cigarette smoking was 69% among adult males, while that of water-pipe smoking was 11%. Most water-pipe smokers, however, also smoke cigarettes.

Table 3, which is based only on retrospective recall of previous habits by adult males in 1987, suggests that the prevalence of smoking may have approximately doubled over the past few decades, but the limitations of such retrospective enquiries are obvious.

Table 3. Retrospective estimation of the prevalence of smoking in different periods in Qidong county, China

Year	No. of males interviewed at age over 15 years [a]	No. then smoking		
		Cigarette	Water pipe	Pipe
1987	694[b]	476 (69%)	74	0
1976	694[c]	447 (64%)	69	3
1966	566	420 (74%)	63	4
1958	426	245 (58%)	40	6
1949	293	154 (53%)	28	6
(1939)	(161)	(50) (31%)	(4)	(1)

[a] Estimated from those aged over 30 years at present
[b] Over age 30 in 1987
[c] Over age 19 in 1976 (and hence over age 30 in 1987)

Potential epidemiological enquiries

It has been estimated (Peto, 1987) that current Chinese smoking habits may eventually cause a total of about two million deaths a year from various neoplastic, vascular and respiratory diseases during the second quarter of the next century. This study indicates that lung cancer is already a common cause of death in Qidong (Table 2), and there has recently been a substantial further increase in cigarette consumption (Table 1). Male lung cancer death rates are increasing, and, even though liver cancer is particularly common in Qidong, lung cancer may eventually overtake it as a cause of death.

Qidong is in many ways a particularly suitable area for prospective, or other, field research on smoking and disease in rural China: (i) a county-wide network of health care has been in place since the early 1970s, and information on all causes of death is now collected routinely (Chen, 1987); (ii) these causes are already registered in such a way they could routinely be linked with personal identifiers; and (iii) there is a high prevalence of smoking, particularly of cigarettes. Qidong is, moreover, one of the 65 Chinese counties to which diet, life style and mortality rates were described extensively in a recent monograph (Chen *et al.*, 1990), and comparison of the characteristics of Qidong with those of other counties may be of further assistance in planning epidemiological studies.

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Table 3. Effect of dietary vitamin A status on urinary excretion of mutagens detected in the Ames *Salmonella*/microsome assay after metabolic activation

Strain	Treatment[a]	No. of revertants/plate[b]	
		Vitamin A-sufficient	Vitamin A-deficient
TA98	None	32 ± 1	28 ± 4
(SR = 30)	DMSO	32 ± 1	64 ± 4
	TE	39 ± 6	165 ± 11*
TA100	None	137 ± 8	122 ± 7
(SR = 100)	DMSO	134 ± 15	120 ± 2
	NNN	146 ± 14	459 ± 16*

[a] DMSO, dimethyl sulfoxide; TE, tobacco extract; NNN, *N'*-nitrosonornicotine.
[b] Mean ± SD of eight plates from two independent experiments; spontaneous revertants (SR) were not subtracted; viable cell count was 2×10^8 cells/ml.
* $p < 0.005$ as compared to DMSO controls.

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Relevance to Human Cancer of *N*-Nitroso Compounds, Tobacco Smoke and Mycotoxins.
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INHIBITION OF TOBACCO-SPECIFIC NITROSAMINE 4-(*N*-NITROSOMETHYLAMINO)-1-(3-PYRIDYL)-1-BUTANONE (NNK) TUMORIGENESIS WITH AROMATIC ISOTHIOCYANATES

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4-(*N*-Nitrosomethylamino)-1-(3-pyridyl)-1-butanone (NNK) is a potent tobacco-specific carcinogenic nitrosamine. At low doses, it induces primarily lung tumours in mice, hamsters and rats, regardless of the route of administration. Its unique organ specificity and potency suggest its possible role in the high incidence of lung cancer in smokers. The goal of this study was to find agents that would potentially prevent NNK tumorigenesis. Previous results led us to test phenethyl isothiocyanate (PEITC) on NNK tumorigenesis in a two-year bioassay in Fischer 344 rats. The NNK-treated group developed 80% lung tumour incidence, whereas NNK-treated rats fed PEITC diets had only 40% lung tumour incidence. Incidences in other organs were not affected by this treatment. We also tested PEITC in a 16-week, short-term bioassay against NNK-induced lung adenomas in A/J mice. Pretreatment of mice with PEITC by gavage at four daily doses of 5 μmol or 25 μmol reduced the formation of NNK-induced lung adenomas by 70% or 100%, respectively. Interestingly, benzyl isothiocyanate and phenyl isothiocyanate, the lower homologues of PEITC, were inactive in this bioassay. Using a protocol similar to that used in the bioassays, PEITC was shown to decrease DNA methylation by NNK in the lungs of rats and mice and suppress the metabolism of NNK by mouse lung microsomes. These results are consistent with the previous data suggesting that the inhibition of NNK-induced lung tumour formation by PEITC is a consequence of reduced DNA methylation caused by inhibition of NNK metabolism. As an extension of the structure-activity study, we also tested phenylpropyl and phenylbutyl isothiocyanate in the A/J mouse bioassay. These isothiocyanates were remarkably potent inhibitors of NNK-induced lung adenoma: at doses of 5 μmol, they completely inhibited lung adenoma formation caused by NNK treatment. These results provide a basis for future chemoprevention studies on lung cancer induction associated with exposure to NNK in tobacco smoke.

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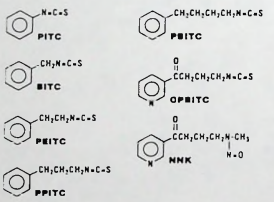
4-(*N*-Nitrosomethylamino)-1-(3-pyridyl)-1-butanone (NNK; Figure 1) is the most potent carcinogenic *N*-nitrosamine so far found in tobacco and tobacco smoke (Hecht & Hoffmann, 1988). The organ-specific effect of NNK in the induction of lung tumours in all species tested indicates its possible role in the development of lung cancer among smokers (IARC, 1985). Therefore, it would be of great importance to find compounds, either synthetic or dietary-related, that can counteract the carcinogenic action of NNK.

Our previous studies demonstrated that pretreatment of rats with a diet containing phenyl isothiocyanate (PITC), benzyl isothiocyanate (BITC) or phenethyl isothiocyanate (PEITC; Figure 1) resulted in reduced metabolic demethylation of NNK in hepatic microsomes as well as a decrease in hepatic DNA methylation by NNK (Chung *et al.*, 1985), suggesting that these aromatic isothiocyanates can potentially inhibit NNK carcinogenesis. In this study, we examined the effects of PEITC on NNK tumorigenesis in Fischer 344 rats and of PITC, BITC and PEITC on NNK tumorigenesis in A/J mice. We compared these results to their effects on NNK-induced DNA methylation in liver, lung and nasal cavity of rats and in lung of mice, all target tissues of NNK tumorigenesis. In a separate bioassay, we also evaluated phenylpropyl- and phenylbutylisothiocyanates (PPITC and PBITC), higher homologues of PEITC, and oxopyridylbutylisothiocyanate (OPBITC), an isothiocyanate related to NNK, for their effects on NNK tumorigenesis in A/J mice. Both PBITC and OPBITC are newly synthesized arylalkyl isothiocyanates.

Figure 1. Structures of isothiocyanates and of 4-(*N*-nitrosomethylamino)-1-(3-pyridyl)-1-butanone (NNK)[a]



[a] Abbreviations: PITC, phenyl isothiocyanate; BITC, benzyl isothiocyanate; PEITC, phenethyl isothiocyanate; PPITC, phenylpropyl isothiocyanate; PBITC, phenylbutyl isothiocyanate; OPBITC, oxopyridylbutylisothiocyanate

Table 1 shows the tumour incidences in lung, liver and nasal cavity of Fischer 344 rats after treatment with NNK, NNK plus PEITC or PEITC. The tumour incidences induced by NNK alone were within the range expected on the basis of the results of previous bioassays. Only 43% of rats fed a diet containing PEITC before and during NNK treatment developed lung tumours, whereas 80% did so in the group fed the control diet. The PEITC diet did not alter the incidences of tumours in the liver or nasal cavity induced by NNK.

Table 1. Incidences of lung, liver and nasal cavity tumours after treatment with NNK, NNK plus PEITC or PEITC[a]

Group no.	Treatment	No. of rats	No. of rats with tumours (%)									
			Lung			Liver			Nasal cavity			
			Adenoma	Carcinoma	Total	Adenoma	Carcinoma	Total	Benign[b]	Malignant[c]	Total
1	NNK	40	8	24	32 (80)	12	3	15 (38)	8	3	11 (28)
2	NNK plus PEITC	40	5	12[d]	17 (43)[e]	9	5	14 (35)	6	1	7 (18)
3	PEITC	20	0	0	0	4	2	6 (28)	0	1	1 (5)
4	Control	20	1	0	1 (15)	3	1	4 (20)	0	1	1 (5)

[a] NNK, 4-(*N*-nitrosomethylamino)-1-(3-pyridyl)-1-butanone; PEITC, phenethyl isothiocyanate. Male Fischer 344 rats, 8 weeks of age, were randomized into four groups; groups 2 and 3 were fed PEITC in the diet (3 μmol/g diet) *ad libitum* for 21 weeks, while groups 1 and 4 were given only NIH-07 diet. After the first week of feeding, NNK (1.76 mg/kg body weight) was administered to groups 1 and 2 by subcutaneous injection three times weekly for 20 weeks. The experiment was terminated after 104 weeks. Gross lesions and representative samples of all major organs were processed for microscopic examination.

[b] Squamous-cell papillomas, transitional-cell papillomas, polyps

[c] Squamous-cell carcinoma, transitional-cell carcinoma

[d] One animal had a squamous-cell carcinoma and 11 had adenocarcinomas

[e] $p < 0.05$ compared to NNK group

To determine the effects of PEITC on the formation of DNA adducts by NNK, we used experimental conditions analogous to those used in the bioassay. Table 2 shows the effects of two weeks' feeding of PEITC on DNA methylation by NNK in liver, lung and nasal mucosa of rats. The levels of 7-methylguanine in DNA of the liver and nasal mucosa of rats were not affected; in lung, however, the levels were reduced from 10.4 to 5.9 μmol/mol guanine, a reduction of nearly 50%.

In the A/J mouse bioassay, we examined the effects of PEITC and its homologues PITC and BITC on NNK-induced lung adenomas (Table 3). A single intraperitoneal administration of NNK at a dose of 10 μmol/mouse resulted in a 100% incidence of pul-

Table 2. DNA methylation in rats treated with 4-(*N*-nitrosomethylamino)-1-(3-pyridyl)-1-butanone (NNK) and fed control or phenethyl isothiocyanate (PEITC) diets[a]

Diet	7-Methylguanine (μmol/mol guanine)		
	Lung	Liver	Nasal mucosa
Control	10.4 ± 1.3[b]	20.6 ± 0.9[b]	21.5[c]
PEITC	5.9 ± 0.6[d]	22.8 ± 0.7	31.5

[a] Groups of six male Fischer 344 rats fed control or test diets containing 3 μmol/g of diet PEITC for 2 weeks. Beginning on day 11 of feeding, [^{3}H-CH$_3$]NNK was administered subcutaneously daily at a dose of 0.6 mg/kg body weight for four consecutive days. Four hours after the last NNK dosing, rats were sacrificed and tissue DNA was isolated for analysis of 7-methylguanine
[b] Mean ± SE for six rats
[c] Mean of two pooled preparations (two to three rats/pool)
[d] $p < 0.05$ compared to values in control group

Table 3. Effects of isothiocyanates on adenomas induced by 4-(*N*-nitrosomethylamino)-1-(3-pyridyl)-1-butanone (NNK)and on formation of of *O*6-methylguanine (*O*6-MeG) in lungs of A/J mice[a]

Group no.	Pretreatment[b]	Daily dose (μmol)	No. of mice	Mice with tumours (%)	No. of tumours/ mouse[c]	*O*6-MeG (μmol/mol guanine)[c]
1	None	-	30	100	10.7[1] ± 0.8	30.9[1] ± 5.9
2	PEITC	5	18	89	2.6[2] ± 0.4	3.9[2] ± 1.2
3	PEITC	25	20	30[d]	0.3[3] ± 0.1	ND[e]
4	BITC	5	20	100	7.6[1] ± 0.5	26.1[1] ± 6.7
5	PITC	5	20	100	9.5[1] ± 1.2	29.7[1] ± 4.4

[a] Groups of 20-30 female A/J mice, maintained on AIN-76A diet, were administered corn oil or isothiocyanates by gavage daily for four consecutive days. Two hours after the final gavaging, a single dose of NNK (10 μmol/mouse) was administered intraperitoneally. Sixteen weeks after NNK administration, mice were sacrificed and pulmonary adenomas were counted. For assay of *O*6-MeG, groups of five mice were administered corn oil or isothiocyanates by gavage for four consecutive days. Two hours after the final gavaging, NNK was administered intraperitoneally at a dose of 10 μmol/mouse. Mice were sacrificed 6 h after NNK administration. DNA was isolated from lung and hydrolysed in 0.1 N HCl for 60 min. *O*6-MeG was analysed by strong cation exchange high-performance liquid chromatography and fluorescence detection.
[b] PEITC, phenethyl isothiocyanate; BITC, benzyl isothiocyanate; PITC, phenyl isothiocyanate
[c] Mean ± SE; mean bearing different superscripts under each column are statistically different ($p < 0.05$) from one another as determined by analysis of variance followed by Newman-Keul's ranges test.
[d] Significantly ($p < 0.01$) less than that of group 1 as determined by the chi-square test.
[e] Not detected

monary adenomas, with a multiplicity of 10.7 tumours/mouse in only 16 weeks. The 5-μmol daily dose (20 μmol total) of PEITC did not significantly reduce the proportion of mice that developed pulmonary adenomas, but resulted in an approximately 70% reduction in tumour multiplicity. The 25-μmol daily dose (100 μmol total) of PEITC resulted in a 70% reduction in the percentage of mice that developed tumours and nearly complete inhibition of tumour multiplicity. However, pretreatment with BITC or PITC at 5 μmol/day resulted in no significant change in the percentage of mice that developed tumours or in tumour multiplicity. Both BITC and PITC proved too toxic to be tested at a daily dose of 25 μmol.

The effects of these isothiocyanates on NNK-induced *O*6-methylguanine (*O*6-MeG) in A/J mouse lung DNA were also investigated. The same dosing regimen as employed in the pulmonary adenoma assays was used. Six hours after NNK administration, the 5-μmol daily dose of PEITC had resulted in an 87% reduction in *O*6-MeG levels, while the 25-μmol daily dose gave undetectable levels. Neither BITC nor PITC pretreatment resulted in a significant reduction in *O*6-MeG levels. The effects of the isothiocyanates on NNK-induced *O*6-MeG formation are thus in good agreement with their effects on NNK lung tumorigenicity.

Our results indicate an upward trends in inhibitory potency as the alkyl chain length increases. To test this hypothesis, we assayed NNK using PPITC, PBITC, OPBITC, PITC, BITC and PEITC as inhibitors (Table 4). PPITC and PBITC exhibited remarkable inhibitory activities; both were considerably more potent than PEITC, and at a daily dose of 5 μmol for four days, they completely prevented the development of lung tumours by NNK. OPBITC was inactive. As in previous bioassays, PITC and BITC were inactive, whereas PEITC reduced lung adenoma multiplicity by 60-70%. The multiplicity and tumour incidences in the groups treated only with isothiocyanates were similar to those in a corn oil control group.

DNA methylation by NNK was reduced in the lungs of rats and mice administered PEITC; however, it was not affected in the liver and nasal cavity of rats fed PEITC or in the lungs of mice fed PITC and BITC. These effects are consistent with the effects of these isothiocyanates on tumorigenicity induced by NNK in the two species and clearly suggest that the protective effect of PEITC against NNK-induced lung tumours is due to its ability to inhibit DNA methylation by NNK. Since there is a parallel relation between NNK tumorigenicity and DNA methylation, ability to inhibit DNA methylation could be used as a means of screening potential inhibitors of NNK carcinogenicity.

These data represent the first demonstration of inhibition of NNK tumorigenesis by any compound (Morse *et al.*, 1989a,b). PEITC is a product of the hydrolysis of glucosinturtiin,which is commonly found in turnips and rutabagas (Tookey *et al.*, 1980). PPITC and PBITC are both synthetic compounds. The goals of our future studies are to develop inhibitors of higher efficacy by structure-activity studies and, ultimately, to test them in high-risk groups such as heavy smokers.

Table 4. Effects of isothiocyanates on pulmonary adenoma induction by 4-(*N*-nitrosomethylamino)-1-(3-pyridyl)-1-butanone (NNK) in A/J mice[a]

Treatment[b]	No. of mice	Weight (g; mean ± SE)	No. of tumours/ mouse (mean ± SE)[c]	Mice with tumours (%)
Corn oil + saline	29	24.2 ± 0.6	0.3[1] ± 0.1	31
Corn oil + NNK	39	21.9 ± 0.3	9.2[2] ± 0.5	100
PITC + NNK	30	23.4 ± 0.4	9.8[2] ± 0.9	100
BITC + NNK	29	22.1 ± 0.4	10.4[2] ± 0.7	100
PEITC + NNK	28	22.4 ± 0.3	3.3[3] ± 0.4	93
PPITC + NNK	30	22.0 ± 0.3	0.4[1] ± 0.1	37[d]
PBITC + NNK	28	22.2 ± 0.5	0.4[1] ± 0.1	32
OPBITC + NNK	28	23.1 ± 0.4	7.9[2] ± 1.0	96

[a] Groups of 20-40 A/J mice were administered corn oil or isothiocyanate (5 μmol/mouse per day) by gavage daily for four consecutive days. Two hours after the final dose of corn oil or inhibitor, a single dose of saline or NNK (10 μmol/mouse) in saline was administered intraperitoneally. Sixteen weeks after NNK administration, mice were sacrificed and pulmonary adenomas were counted

[b] PITC, phenyl isothiocyanate; BITC, benzyl isothiocyanate; PEITC, phenethyl isothiocyanate; PPITC, phenylpropyl isothiocyanate; PBITC, phenylbutyl isothiocyanate; OPBITC, oxyphenylbutyl isothiocyanate

[c] Means in this column that bear different superscripts are significantly different from one another as determined by analysis of variance followed by Newman-Keuls ranges test. Saline-treated groups and NNK-treated groups were tested separately.

[d] Significantly different from the appropriate control group as determined by the chi-square test

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MODULATION OF GENOTOXIC ACTIVITY OF TOBACCO SMOKE

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Tobacco smoke (TS) caused a three- to nine-fold increase in the frequency of *his*$^+$ revertants in *Salmonella typhimurium* TA98 but not in TA97a, TA100 or TA102. Activation by a post-mitochondrial fraction obtained from the liver of rats pretreated with Aroclor-1254 or methylcholanthrene was required; fractions from phenobarbital-pretreated or untreated rats had no effect. Vitamins A and E, but not ascorbic acid, inhibited the TS-induced mutagenesis by up to 63%, whereas glutathione and cysteine increased it slightly. Na_2SeO_3, but neither $CoCl_2$ nor caffeine, inhibited the mutagenic effect of TS by 46-56%. In Chinese hamster ovary cells, both Na_2SeO_3 and caffeine strongly potentiated the number of chromosomal aberrations induced by TS, while theophilline slightly reduced its clastogenic effect. Treatment of mice with TS for 60 min/day increased the frequency of micronuclei in polychromatic erythrocytes in bone marrow and in fetal liver and the number of NCE micronuclei in peripheral blood by four to five fold. Simultaneous treatment of mice with TS and Na_2SeO_3 reduced the clastogenic effect of TS. Ascorbic acid had no effect on clastogenicity but reduced toxicity as measured by body weight loss. Both Na_2SeO_3 and ascorbic acid suppressed the induction of TS-induced hyperplastic and metaplastic changes in bronchial mucosa but had no effect on the number of urethane-induced lung adenomas. Vitamins A and E and ascorbic acid may have a protective effect against the toxic and genotoxic activities of TS.

Chemoprevention of genotoxicity due to tobacco smoke (TS) might contribute to reducing the cancer risk linked to tobacco smoking. Thus, a better understanding of the role of modifiers in this process is needed.

Modulation in vitro *of TS-induced mutagenesis in bacteria*

We have seen previously a three- to nine-fold increase in mutation rate in *Salmonella typhimurium* TA98 but not in TA97a, TA100 or TA102 treated with TS (Balansky *et al.*, 1987, 1988). The addition of an exogenous metabolic activation system, obtained from the livers of Aroclor-1254 or methylcholanthrene pretreated rats was required; no activation was produced with liver from phenobarbital-pretreated or untreated rats. A dose-dependent

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inhibition of TS-induced mutagenesis up to 57-63% ($p < 0.05$) was seen in *S. typhimurium* TA98 treated with vitamins A or E (0.08-0.8 mg/plate) (Figure 1). Inhibition of 46-56% ($p < 0.05$) was observed when Na_2SeO_3 (25-100 μg/plate) was added to the top agar (Figure 1). Neither ascorbic acid (0.2-2.0 mg/plate), $CoCl_2$ (0.2-1.0 mg/plate) nor caffeine (0.2-0.8 mg/plate) influenced this process. However, the addition of glutathione (0.6-2.4 mg/plate) or cysteine (0.12-0.48 mg/plate) increased TS-induced mutagenesis slightly.

Figure 1. Dose-dependent inhibition of mutagenesis induced by tobacco smoke (TS; 240 cm3 in a 16-l glass chamber) in *Salmonella typhimurium* TA98 by Na_2SeO_3 and vitamins A and E; spontaneous mutation rate, 33-41 *his*$^+$ revertants per plate

Modulation in vitro *of TS-induced clastogenicity in Chinese hamster ovary cells*

Direct treatment of Chinese hamster ovary (CHO) cells with TS enhanced the number of metaphases that had chromosomal aberrations (breaks and exchanges). Treatment of CHO cells with Na_2SeO_3 (2.0-5.0 μg/ml) 2-4 h before or 18 h after exposure to TS increased the chromosome damaging effect of TS by 80.9-92.3% ($p < 0.05$). Similar treatments with caffeine (0.1-0.2 mg/ml) potentiated TS-induced clastogenicity by 97-141% ($p < 0.01$). In contrast, treatment of cells with theophilline (0.05-0.2 mg/ml) 4-15 h before exposure to TS caused a 31-53% ($p < 0.01$) decline in the frequency of TS-induced chromosomal aberrations.

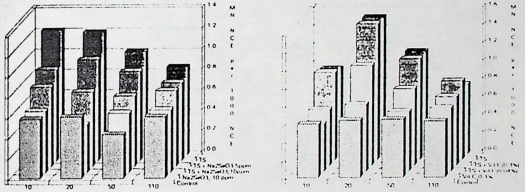
Modulation in vivo *of TS-induced clastogenicity in bone marrow, peripheral blood and fetal liver of mice*

Single or multiple treatment of BDF_1 (C57Bl x DBA_2) mice with TS (60 min/day) caused a dose-dependent, four- to five-fold increase in the number of polychromatic and NCE micronuclei in mouse bone marrow and peripheral blood, respectively (Balansky *et al.*, 1988). In addition, TS was shown to have transplacental clastogenic activity in fetal liver after single or multiple treatment of pregnant mice during the last third of gestation. Four months' treatment of mice with TS (60 min/day) did not change significantly the number of lung adenomas induced by urethane (1.0 g/kg). Ascorbic acid (0.04-0.3%) and Na_2SeO_3 (5-10 ppm) did not influence adenoma formation but suppressed TS-induced hyperplastic and metaplastic changes in bronchial mucosa. Simultaneous treatment of mice with

Na_2SeO_3 and TS decreased the number of NCE micronuclei as compared with that in mice given TS alone; ascorbic acid did not have a similar effect (Figure 2). Ascorbic acid slightly reduced the toxicity of TS, as measured by body weight loss.

Supplementation of the diet with vitamins A, and E and ascorbic acid might have a protective effect against the toxic and genotoxic activities of TS.

Figure 2. Numbers of micronuclei in the peripheral blood of mice treated with tobacco smoke (TS; 600 cm3 in a 14-L glass chamber, four exposures of 15 min each with 1-min intervals during which a total air change was made); Na_2SeO_3 and ascorbic acid were added to drinking-water starting ten days before the first TS exposure and continuing up to the end of the experiment.



Acknowledgements

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NATIONAL CANCER REGISTRY PROGRAMME - ICMR
CANCER PATTERNS IN BANGALORE - 1982-1989.

6. Tobacco Related Cancers (TRC)

Sites of cancer that have been attributed to use of tobacco include oral cavity, oropharynx, hypopharynx, pharynx, oesophagus, larynx, lung and urinary bladder. Accordingly, the number (#), proportion (%) of cancers of these sites relative to cancers of all sites, the Crude Rate (CR), Age Adjusted Incidence Rates (AAR) and Truncated Rate (TR) are indicated in Table 6.1. Cancers due to use of tobacco constitute 37.85% and 19% of all sites of cancers in males and females respectively.

Table 6.1
TOBACCO RELATED CANCERS

	Males	Females
#	3285	1856
%	37.8	19.0
CR	22.6	14.2
AAR	42.1	25.4
TR	75.5	52.1

Table 6.2 gives the number (#) and proportions (%) of individual specific sites of the TRC indicated above. The values given for the first proportion (%a) are relative to all sites of cancer and those of the second proportion (%b) are relative to all tobacco related sites. The most important of the tobacco related sites in males are lung, oesophagus and oral cavity which together account for over 60% (62.2%) of all tobacco related cancers. Among females 80% of the tobacco related cancers are those of cancers of the oral cavity and oesophagus.

Table 6.2
TOBACCO RELATED CANCERS (TRC) : 1982 - 1989
Numbers (#) & Proportions (%)

Site	Males			Females		
	#	%[a]	%[b]	#	%[a]	%[b]
Oral cavity	632	7.27	19.2	859	8.81	46.3
Oropharynx	157	1.81	4.8	24	0.25	1.3
Hypopharynx	466	5.36	14.2	95	0.97	5.1
Pharynx	43	0.49	1.3	25	0.26	1.3
Oesophagus	676	7.78	20.6	626	6.42	33.7
Larynx	329	3.78	10.0	56	0.57	3.0
Lung	737	8.48	22.4	129	1.32	7.0
U. Bladder	245	2.82	7.5	42	0.43	2.3
TRC **	3285	37.78	100.00	1856	19.03	100.00
All Sites	8694	100.00	100.00	9754	100.00	100.0

a *% of total numbers of all sites of cancers*

b *% of total numbers of all Tobacco Related Cancer Sites*

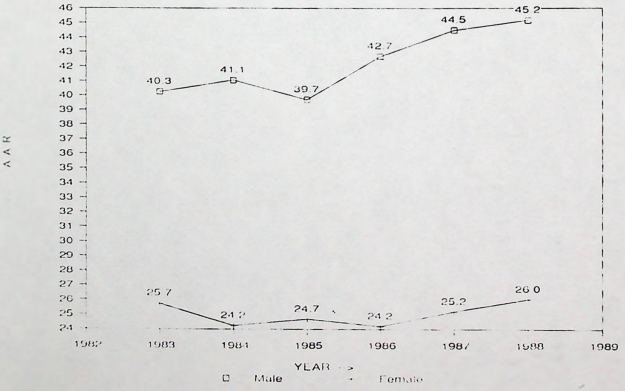
Trends Over Time

Table 6.3 gives the Age Adjusted Incidence Rates (AAR) and three year Moving Averages (MA) of tobacco related sites of cancer for different years. The same is graphically represented in Fig 6.1. There is a clear rising trend in the overall incidence of these cancers in males, whereas in females the rates are about the same over the years 1982 to 1989. The values of AAR for specific tobacco related sites is given in Tables 6.4 and 6.5

Table 6.3
TOBACCO RELATED CANCERS - TRENDS OVER TIME : 1982 - 1989
ALL SITES OF CANCER ASSOCIATED WTIH USE OF TOBACCO - MALES AND FEMALES
Table gives figures of AAR and 3 year Moving Averages (MA) of AAR

YEAR	1982	1983	1984	1985	1986	1987	1988	1989	1982-89
MALE	38.11	41.92	40.73	40.51	37.94	49.68	45.90	39.94	42.08
MA	40.3	41.1	39.7	42.7	44.5			45.2	
FEMALE	27.35	23.58	26.25	22.86	24.93	24.79	25.83	27.47	25.40
MA	25.7	24.2	24.7	24.2	25.2			26.0	

Fig. 6.1
TOBACCO RELATED CANCERS - TRENDS OVER TIME : 1982 - 1989
ALL SITES OF CANCER ASSOCIATED WTIH USE OF TOBACCO - MALES AND FEMALES
Figure shows line graphs of 3 year Moving Averages of AAR



TOBACCO RELATED CANCERS - TRENDS OVER TIME : 1982 - 1989

Table gives figures of AAR for different years

TABLE 6.4

SPECIFIC SITES OF CANCER ASSOCIATED WTIH USE OF TOBACCO - MALES

	1982	1983	1984	1985	1986	1987	1988	1989	1982-89
Oral Cavity	8.78	8.96	6.65	7.14	6.02	9.87	6.47	8.12	7.74
Oropharynx	2.24	2.02	2.29	1.29	1.85	2.06	2.46	1.90	2.01
Hypopharynx	4.87	6.04	6.68	5.95	5.23	7.41	7.25	5.86	6.19
Pharynx	0.37	0.36	0.78	0.71	0.40	0.69	0.64	0.24	0.53
Oesophagus	8.35	6.34	8.21	7.28	7.61	10.96	9.87	8.57	8.57
Larynx	4.47	4.93	4.03	3.68	4.08	4.81	4.34	4.04	4.29
Lung	5.47	8.77	9.17	11.67	9.78	10.75	11.44	8.57	9.53
U.Bladder	3.56	4.50	2.92	2.79	2.97	3.13	3.43	2.64	3.22
TRC Sites	38.11	41.92	40.73	40.51	37.94	49.68	45.90	39.94	42.08

TABLE 6.5

SPECIFIC SITES OF CANCER ASSOCIATED WTIH USE OF TOBACCO - FEMALES

	1982	1983	1984	1985	1986	1987	1988	1989	1982-89
Oral Cavity	14.66	10.98	11.54	10.57	11.27	9.88	12.51	12.31	11.69
Oropharynx	0.44	0.41	0.34	0.15	0.36	0.12	0.45	0.53	0.35
Hypopharynx	1.30	1.70	1.59	1.22	0.55	1.20	1.52	1.21	1.28
Pharynx	0.28	0.36	0.00	0.56	0.46	0.24	0.32	0.14	0.29
Oesophagus	7.25	7.27	9.52	7.16	10.02	9.74	8.18	10.18	8.73
Larynx	1.27	0.78	0.49	0.88	0.69	0.60	0.50	0.74	0.73
Lung	1.36	1.71	2.24	1.71	1.42	2.34	1.51	1.60	1.74
U. Bladder	0.79	0.37	0.53	0.61	0.16	0.67	0.84	0.76	0.59
TRC Sites	27.35	23.58	26.25	22.86	24.93	24.79	25.83	27.47	25.40

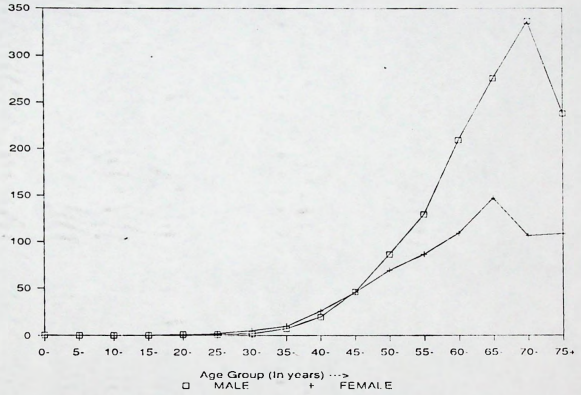
Age Specific Incidence Rates (ASR)

Table 6.6 gives values of age specific rates and the corresponding line graph is depicted in Fig 6.2. The curves on ASR show that as early as the age of 25 years in females and 30 years in males the curves start rising. Similar curves across religious groups show the lower rate of those cancers in Muslim women of all age groups though in terms of proportion of total cancers in Muslim females and males they are fairly comparable to that in Hindus.

Table 6.6
TOBACCO RELATED CANCERS - AGE SPECIFIC INCIDENCE RATE (ASR) : 1982 - 1989
ALL SITES OF CANCER ASSOCIATED WTIH USE OF TOBACCO - MALES AND FEMALES
Table gives figures of AST, Crude Rate (CR), AAR, Truncated RAte (TR) and number (#) of cases

AGE GROUP	MALE	FEMALE
0-4	0.5	0.2
5-9	0.0	0.1
10-14	0.0	0.0
15-19	0.1	0.3
20-24	0.9	0.8
25-29	1.0	2.1
30-34	1.5	5.1
35-39	7.1	9.7
40-44	19.5	25.7
45-49	46.2	45.8
50-54	86.3	69.2
55-59	129.1	86.6
60-64	209.3	108.9
65-69	275.5	146.6
70-74	336.5	106.2
75+	237.3	108.3
CR	22.58	14.19
AAR	42.08	25.40
TR	75.49	52.08
#	3285	1856

Fig 6.2
TOBACCO RELATED CANCERS - AGE SPECIFIC INCIDENCE RATES (ASR) 1982 - 1989
ALL SITES OF CANCER ASSOCIATED WTIH USE OF TOBACCO - MALES AND FEMALES



Religious Groups

The AAR of TRC combined and for specific sites by religious group is given in Table 6.7 and the age specific rates of TRC according to religious group is presented in Table 6.8. The overall AAR is lower in Muslims especially in women and for cancers of the oral cavity and oesophagus. However Muslim men have comparable and slightly higher rates of lung cancer than Hindu men. The curves of age specific incidence rates in males (Fig 6.3) are not very different in the three religious groups, but these are considerably lower in Muslim women compared to Hindu and Christian women.

Educational Status

Table 6.9 gives the number (#) and relative proportion (%) of cases according to known educational status. Table 6.9 (a) is for the tobacco related sites and 6.9 (b) is for all other sites. The proportion of illiterates among those who have tobacco related cancer sites is substantially greater than for all other sites of cancer in both males and females.

Table 6.7
TOBACCO RELATED CANCERS (TRC) : 1982 - 1989
AAR ACCORDING TO RELIGIOUS GROUPS

Site	Male			Female		
	Hindu	Muslim	Christian	Hindu	Muslim	Christian
Oral cavity	8.06	5.53	9.17	13.47	4.87	8.47
Oropharynx	2.04	2.00	1.40	0.37	0.12	0.61
Hypopharynx	6.48	5.42	4.85	1.47	0.80	0.51
Pharynx	0.48	0.85	0.37	0.35	0.10	0.17
Oesophagus	9.69	4.77	5.32	9.98	4.42	4.92
Larynx	4.26	3.77	5.58	0.89	0.26	0.00
Lung	9.42	10.24	10.39	1.66	1.94	2.42
U. Bladder	3.20	2.78	4.08	0.63	0.26	0.82
TRC	43.63	35.36	41.16	28.82	12.77	17.92
All Other Sites	64.37	42.34	59.27	103.23	59.22	102.94
All Sites	108.00	77.70	100.43	132.05	71.99	120.86

Table 6.8
TOBACCO RELATED CANCERS (TRC) : 1982 - 1989
ASR ACCORDING TO RELIGIOUS GROUPS

Age Group	MALE			FEMALE		
	Hindu	Muslim	Christian	Hindu	Muslim	Christian
0-4	0.1	0.0	0.0	0.1	0.4	0.0
5-9	0.1	0.0	0.0	0.0	0.4	0.0
10-14	0.1	0.0	0.0	0.0	0.0	0.0
15-19	0.4	0.4	0.0	0.2	0.5	0.0
20-24	1.4	0.4	0.0	0.9	1.0	0.0
25-29	1.3	1.0	1.0	2.5	0.5	0.0
30-34	3.3	3.0	5.1	5.5	2.2	3.0
35-39	8.7	2.7	7.5	11.3	3.3	8.6
40-44	23.1	26.8	13.6	28.7	14.6	17.5
45-49	56.4	46.5	41.4	53.4	19.4	25.3
50-54	94.3	72.6	78.8	78.3	48.1	23.7
55-59	158.9	140.7	127.5	98.5	43.9	57.9
60-64	204.6	162.5	146.8	121.5	59.8	84.6
65-69	265.8	234.5	357.8	165.5	49.7	152.3
70-74	292.7	224.8	199.2	120.8	65.5	51.5
75+	238.9	159.0	362.8	123.3	38.6	108.9
CR	23.49	19.02	21.21	16.09	7.27	9.60
AAR	43.63	35.34	41.16	28.82	12.77	17.92
TR	79.24	65.58	60.64	59.09	28.37	32.16
#	2624	420	212	1609	144	93

TOBACCO RELATED CANCERS - AGE SPECIFIC INCIDENCE RATES (ASR) 1982 - 1989

Fig. 6.3

RELIGIOUS GROUPS - MALES

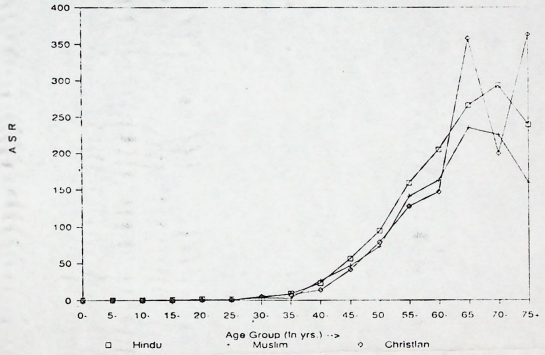


Fig. 6.4

RELIGIOUS GROUPS - FEMALES

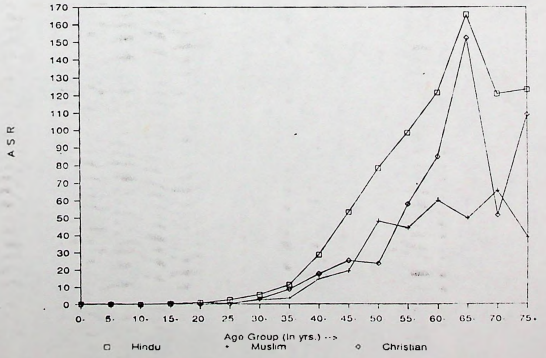


Table 6.9 (a)
Number (#) and Proportion (%) of ***TOBACCO RELATED CANCERS*** according to Educational Status

	Male		Female	
	#	%	#	%
Illiterate	806	24.54	1145	61.69
Literate	415	12.63	153	8.24
Primary	489	14.89	140	7.54
Middle	275	8.37	79	4.26
Secondary	552	16.80	91	4.90
Tec. Aft	67	2.04	10	0.54
College	163	4.96	18	0.97
Others	14	0.43	1	0.06
Unknown	504	15.34	219	11.80
Total	3285	100.00	1856	100.00

Table 6.9 (b)
Number and Proportion of all other sites according to Education

	Male		Female	
	#	%	#	%
Illiterate	800	14.79	3203	40.55
Literate	530	9.80	619	7.84
Primary	593	10.96	769	9.74
Middle	383	7.08	473	5.99
Secondary	865	15.99	944	11.95
Tec Aft	131	2.43	52	0.66
College	399	7.38	268	3.39
Others	44	0.81	17	0.22
Unknown	1664	30.76	1553	19.66
Total	5409	100.00	7898	100.00

...y records in eight treated patients with hypertension, but ...e individuals were selected for study because their indirect ...ssure readings seemed inappropriately high when ...nsidered against a general absence of target organ damage; ...e the same study a good correlation was observed between ...ra-arterial blood pressures and cuff pressures as obtained ...y the general practitioner or in the hospital setting in ...selected untreated subjects with hypertension. However, a ...ter study, which selected untreated subjects without clinical ...idence of target organ damage, did show mean waking ...ra-arterial pressures to be significantly less than mean ...patient blood pressures, by 18 mm Hg on average.[12] The ...ason for the discrepancy between cuff and ambulatory ...adings is not clear. These observations are important in the ...cision to treat subjects with mild or moderate hyperten- ...n. 20 of our 59 subjects fulfilled the conventional defi- ...ion of hypertension but their average ambulatory mean ...rterial pressure throughout the waking day was less than 108 ...m Hg (i.e., equivalent to 140/90 mm Hg) and even lower ...ring sleep when the average mean arterial pressure fell ...proximately 25% for waking levels.

Both the American hypertension detection and follow-up ...ogram[13] and the Australian therapeutic trial[17] showed the ...sult of treatment in reducing the morbidity and mortality ...mild hypertension. A noteworthy difference between these ...o trials was the smaller mortality from cardiovascular ...ease in the placebo group of the Australian study when ...mpared to either the "stepped care" or the "referred care" ...oup of the hypertension detection and follow-up program. ...was suggested[17] that the inclusion of some patients with ...nically detectable end organ damage in the American trial ...y have selected subjects with a higher degree of cardiovas- ...ular risk. The Australian subjects, interestingly, had a lower ...rterial mean arterial pressure (119 mm Hg) than our own ...bjects. One possibility, therefore, is that the better ...agnosis in both the placebo and treated groups of the ...ustralian study, and the lack of apparent benefit of therapy ...n patients under 50 years of age in both trials may have been ...e to a lower, perhaps even normal, ambulatory blood pres- ...re in a significant proportion of these individuals.

There is no doubt cuff pressures give a reasonable pre- ...ction of cardiovascular risk. We suggest, however, that the ...elationship between arterial pressure and subsequent cardio- ...vascular-morbid events might well be even greater if a more ...curate assessment of true arterial pressure and its daily fluc- ...tuations could be obtained on a wider scale than is possible ...ith present techniques.

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WILLIAM P. CASTELLI, THOMAS R. DAWBER, MANNING FEINLEIB, ROBERT J. GARRISON, PATRICIA M. MCNAMARA, WILLIAM B. KANNEL

Framingham Heart Study, National Heart, Lung, and Blood Institute, Framingham, Massachusetts; Biometries Research Branch, National Heart, Lung, and Blood Institute, Bethesda, Maryland; and Boston University Medical Center, Evans Research Foundation, Boston, Massachusetts, U.S.A.

Summary Long-term follow-up of the Framingham cohort for coronary heart disease (CHD) end-points has made it possible to test the hypothesis that those who smoke filter cigarettes are less likely to get clinical manifestations of CHD than those who smoke non-filter cigarettes. Men were classified at the 7th biennial examination (1963–64) according to whether they smoked filter or non-filter cigarettes. 58% of the cigarette-smoking men under age 55 at this examination smoked filter cigarettes. These men had slightly lower prior smoking exposure than smokers of non-filter cigarettes. Despite what seemed to be a favourable cigarette-smoking history, the filter-cigarette smokers did not have lower CHD incidence rates than non-filter smokers. This finding was unchanged even after multivariate logistic regression analysis to adjust for the slight differences in age, systolic blood pressure, and serum cholesterol between the two groups.

Introduction

THE introduction of low-tar and low-nicotine cigarettes was partly prompted by the finding that number of cigarettes smoked is positively related to subsequent disease. This dose-response relation suggested that cigarettes would be made less hazardous by removing, by filtration or other means, those substances responsible for the increased rates of cancer, pulmonary disease, and coronary heart disease (CHD). Of the more than 4000 chemical substances in cigarette smoke, nicotine and carbon monoxide are the most likely to be responsible for the cardiovascular consequences of smoking. Some studies show a parallel fall in nicotine and carbon monoxide in the low tar-low nicotine cigarettes whilst others show a rise in carbon monoxide dose with a fall in nicotine.

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The measurement of clinical disease end-points is the ultimate test of whether any alteration in the dose of noxious elements is beneficial. So far few large-scale studies have assessed CHD end-points. The very large American Cancer Society study[1] showed that low tar/nicotine smokers had a 20% lower rate of CHD mortality in 6 years than high tar/nicotine smokers. Three prospective surveys in Scotland[2] showed a slightly higher rate of ischaemic heart disease mortality among filter cigarette smokers. An English study, sponsored by the Tobacco Research Council, reported a 25% fall in risk of coronary heart disease in smokers of filter cigarettes.[3]

In our prospective survey reported here rates of CHD among Framingham Heart Study men were related to type of cigarette smoked (filter or non-filter). It also compares the smoking history of individuals who switched to filter cigarettes with those who continued to smoke regular cigarettes, and tests for the contribution of filter use to the prediction of CHD in multivariate analysis.

Methods

Framingham Heart Study Cohort participants have undergone physical examinations every 2 years since 1948.[4] Data presented here include those which were collected at the 1st examination and at the 7th to 14th examinations, inclusive. Details asked about cigarette-smoking history at the 1st examination included the number of cigarettes smoked daily and the duration (years) of cigarette smoking. The first time a question about filter cigarette use was asked was the 7th examination, which took place during the 2-year period starting in September, 1963. The most recent examination for which cigarette-smoking data is available is examination 12. At this follow-up questions were asked about filter use, frequency of cigarette use per day, maximum cigarette consumption per day for any 1-year period, and number of years previous cigarette smokers had not smoked. For this report the 7th examination was the baseline at which individuals were classified according to smoking habits. Thus, only those who underwent examination 7 are considered in the tables that present data from the 1st, 12th, or other follow-ups. Blood pressure, measured with the subject seated, and total serum cholesterol, measured by the Abell-Kendall method,[5] were recorded at the 7th biennial examination. These measurements, together with age in years, were used as independent variables in multivariate logistic regression analyses since they are consistent and powerful predictors of CHD risk. Regression coefficients (β_i) of the logistic function were calculated by maximum likelihood methods.[6] The standardised regression coefficients represent the relative strength of each independent variable in a given estimated equation as a predictor of the CHD end-point under consideration. The significance test associated with each coefficient indicates whether that variable contributes independent information, apart from that contributed by other variables in the equation, to the prediction of disease.

Diagnoses of clinically apparent CHD were made according to methods and criteria that have been described.[7] Only individuals who were free of pre-existing CHD at the 7th examination are considered in this report, and they were followed-up for the next 14 years (up to the 14th examination) for occurrence of new disease. The specific CHD end-points considered in this report are CHD death (both sudden and non-sudden death), myocardial infarction (MI) (all proven MI, whether fatal or not fatal), and total CHD (MI, coronary insufficiency, angina pectoris, and all CHD deaths).

Results

1605 men and 2132 women, aged 41–74 years, underwent the 7th biennial examination. Only the youngest women smoked cigarettes. Therefore no test of the hypothesis that filter and regular cigarettes differ in their relation with CHD was possible among women. The men were divided into a group who were above and a group who were below 55 y of age at examination 7, this age being approximately the midpoint of the age-range then. 60% of the younger group men smoked cigarettes at examination 7, and 58·0% of cigarette smokers smoked filter cigarettes (table I). Although fewer of the older men smoked cigarettes, a similar proportion of smokers (56·5%) used filters. In both groups nearly all men who smoked filter cigarettes continued to smoke carried on using filter cigarettes. More than half of the smokers of regular cigarettes (untipped) at examination 7 who were smoking cigarettes 10 years later were still smoking regular cigarettes. Other comparisons of exposure between the filter and regular cigarette groups are shown in tables II and III. Although a slightly higher proportion of filter smokers had stopped smoking cigarettes by examination 12 (table I) there were no significant differences between filter and non-filter smokers in duration of cessation of smoking among those who stopped smoking. Nor was there a difference in the number of cigarettes smoked

TABLE I—DISTRIBUTION OF SMOKING BEHAVIOUR OF MEN AT EXAMINATION 12 IN RELATION TO SMOKING HABITS AT EXAMINATION 7

Smoking status at exam 7	Smoking status at exam 12 (n = 1590)			
	Filter	Regular	Non-smoker	Non-examin.
Age <55 yr (n = 816)				
Filter (n = 295)	36·6%	1·4%	42·0%	20·0%
Regular (n = 214)	29·8%	22·0%	33·2%	15·0%
Non-smoker (n = 337)	2·1%	0·6%	86·1%	11·2%
Age ≥55 yr (n = 744)				
Filter (n = 178)	25·6%	2·9%	37·2%	34·3%
Regular (n = 137)	19·7%	11·0%	27·0%	42·3%
Non-smoker (n = 429)	0·2%	0·2%	67·7%	31·9%

*Plain or untipped.

TABLE II—SMOKING STATUS AT EXAM 12* FOR MEN BY AGE AND SMOKING STATUS AT EXAM 7.

Smoking status at exam 7	Smoking status at exam 12		
	No. of cigarettes smoked†	Maximum no. of cigarettes smoked†	No. of years non-smoking before exam 12‡
Age <55 yr			
Filter	23·9 (112)	30·5 (111)	5·4 (100)
Regular	24·6 (111)	30·2 (110)	5·0 (61)
Age ≥55 yr			
Filter	18·2 (51)	25·2 (51)	5·4 (53)
Regular	18·4 (42)	27·6 (42)	6·5 (28)

No. of observations in parentheses.
*Only those who underwent exam. 12 are included in these calculations.
†Smokers only
‡Quitters only

TABLE III—SMOKING STATUS* AT EXAM 1 FOR MEN BY AGE AT EXAM 7 AND TYPE OF CIGARETTE SMOKED AT EXAM 7

Smoking status at exam 7	Smoking status at exam 1		
	Percentage of men smoking at exam 1	Average no. of cigarettes smoked	Average duration of smoking†
Age <55 yr			
Filter (n = 295)	93·2	21·9	17·9
Regular (n = 214)	96·7	24·0	18·6
Age ≥55 yr			
Filter (n = 178)	89·9	19·4	29·7
Regular (n = 137)	94·9	23·1	30·5

TABLE IV—RATE PER 1000 AFTER 14 YEARS OF OBSERVATION FOR MI, CHD DEATH, AND TOTAL CHD FOR MEN BY AGE AND SMOKING STATUS AT EXAM 7*

	Age<55		Age ≥55+	
	Rate	No. of cases	Rate	No. of cases
MI				
Non-smoker	59	20	147	63
Regular smokers	112	24	146	20
Filter smokers	136	40	180	32
CHD death				
Non-smoker	27	9	101	43
Regular smokers	42	9	131	18
Filter	58	17	90	16
Total CHD				
Non-smokers	119	40	269	115
Regular smokers	236	44	285	39
Filter smokers	210	62	242	43

*Those with CHD at examination 7 are not included.

by those who continued to smoke, or the maximum number of cigarettes ever smoked over one year. Comparison of smoking behaviour at examination 1 reveals differences between filter and non-filter smokers (table III)—a higher proportion of non-filter smokers at examination 7 had smoked cigarettes at examination 1. Furthermore, those who smoked regular cigarettes at examination 7 and who smoked at examination 1 seemed to have done so longer and were smoking more cigarettes at examination 1 than participants who smoked filter cigarettes at examination 7.

Table IV shows the 14-year rates of occurrence per 1000 men for myocardial infarction, coronary heart disease (CHD) death, and total CHD by age and smoking status at the 7th examination. Among the younger men non-smokers had the lowest rates, and filter cigarette smokers the highest. No clear trend was observed among the older men. Differences in rates between non-smokers and smokers (filter and regular cigarettes combined) after adjustment for other risk factors were tested by multivariate logistic regression and are presented in table V, which shows a strong relation between cigarette smoking and CHD in middle-aged men. Although coefficients are also positive for the older men, none are statistically different from zero. It should be noted that among the older men smoking cigarettes at examination 7, less than one third continued to smoke cigarettes until examination 12 (table I). Also, those who continued to smoke reduced their daily consumption.

The hypothesis that MI, CHD death, or total CHD rates differ between men who smoked filter cigarettes and those who smoked regular cigarettes was tested by multiple logistic regression analyses (table VI) based on data for men who smoked at examination 7 but were free of pre-existing CHD. Thus, the positive standardised coefficients for the middle-aged men (<55 years group) indicate that filter cigarette smokers have higher rates of MI than smokers of untipped cigarettes, after considering any differences in total cholesterol, systolic blood pressure, and age. These coefficients parallel the difference in univariate rates presented in table IV. There are no statistically significant differences between filter use and MI, CHD death, or total CHD.

Discussion

Information about the timing of the "switch" to filter cigarettes in Framingham is not available but is assumed to have taken place fairly soon after the introduction of filter cigarettes in 1950. By 1964 filter cigarettes took 65% of the cigarette market.[8] A similar proportion was smoked by our subjects at examination 7, although differences would have been expected in view of the older age-structure of the Framingham sample compared with the general population.

The nicotine content of the cigarettes that were smoked by the subjects of this report can be inferred from sales-weighted average nicotine deliveries of filter and regular cigarettes for the U.S.[9] Between 1963 and 1977 (the period of follow-up covered in this report) the average nicotine delivery was 1·75 mg for regular cigarettes and 1·3 mg for filter cigarettes. Although the nicotine content of regular cigarettes remained fairly constant over the period, averages for filter cigarettes declined from about 1·4 mg to 1·1 mg in 1977. Most of this

TABLE V—STANDARDISED MULTIVARIATE LOGISTIC REGRESSION COEFFICIENTS AND t-VALUES FOR MEN WHO HAD NEW MI, CHD DEATH AND NEW CHD BETWEEN EXAMINATIONS 7 AND 14*

	Age <55 (n = 853)		Age ≥55 (n = 752)		All ages (n = 1605)	
Independent variable	Coefficient	*t*	Coefficient	*t*	Coefficient	*t*
New MI						
Total cholesterol	0·345	3·22	−0·014	−0·14	0·168	2·27
Systolic blood-pressure	0·303	2·80	0·293	3·05	0·299	4·16
Age (yr)	−0·049	−0·41	0·057	0·55	0·201	2·52
Cigarettes†	0·409	3·13	0·053	0·52	0·198	2·50
No. of cases	86		116		202	
CHD death						
Total cholesterol	0·324	2·12	0·054	0·46	0·175	1·84
Systolic blood-pressure	0·556	3·86	0·368	3·36	0·432	5·00
Age (yr)	0·545	1·87	0·035	0·29	0·407	3·95
Cigarettes†	0·376	1·91	0·092	0·77	0·186	1·82
No. of cases	36		79		115	
New CHD						
Total cholesterol	0·438	4·79	0·043	0·52	0·242	3·98
Systolic blood-pressure	0·340	3·85	0·299	3·67	0·322	5·37
Age (yr)	0·089	0·94	−0·002	−0·03	0·216	3·35
Cigarettes†	0·333	3·35	0·038	0·09	0·154	2·42
No. of cases	151		200		351	

*Those with CHD at examination 7 were excluded.
†Smokers were given a value of 1, and non-smokers a value of 0, for this variable.

TABLE VI—STANDARDISED MULTIVARIATE LOGISTIC REGRESSION COEFFICIENTS AND t VALUES FOR MEN WHO SMOKED CIGARETTES AT EXAM AND WHO HAD NEW MI, CHD DEATH AND NEW CHD BETWEEN THEN AND EXAMINATION 14*

Independent variable	Age <55 (n = 504)		Age ≥55 (n = 310)		All ages (n = 814)	
	Coefficient	t	Coefficient	t	Coefficient	t
New MI:						
Total cholesterol	0·261	2·08	0·100	0·63	0·190	1·94
Systolic blood-pressure	0·141	1·08	0·491	3·34	0·321	3·33
Age (yr)	−0·042	−0·31	−0·126	−0·77	0·020	0·20
Filter cigarettes†	0·120	0·87	0·116	0·72	0·116	1·12
No. of cases	64		50		114	
CHD deaths:						
Total cholesterol	0·419	2·40	0·313	1·67	0·367	2·95
Systolic blood-pressure	0·507	2·89	0·240	1·36	0·360	2·99
Age (yr)	0·402	1·85	−0·212	−1·08	0·289	2·14
Filter cigarettes†	0·143	0·66	−0·206	−1·11	−0·024	−0·17
No. of cases	26		33		59	
New CHD:						
Total cholesterol	0·370	3·38	0·109	0·82	0·270	3·22
Systolic blood-pressure	0·239	2·21	0·331	2·57	0·291	3·50
Age (yr)	0·066	0·58	−0·141	−1·04	0·048	0·56
Filter cigarettes†	0·021	0·19	−0·150	−1·14	−0·047	−0·55
No. of cases	106		79		185	

*Those with CHD at examination 7 were excluded.
†Filter cigarette smokers were given a value of 1, and regular cigarette smokers a value of 0, for this variable.

decline in average filter cigarette yield was probably due to the rapid increase in sales of "ultra" low tar-nicotine cigarettes.[10] Thus, the rapid change to filter cigarettes in the late 1950s and early 1960s and the apparent uniformity of cigarette nicotine content provide some assurance that the comparisons made in this report (despite the lack of specific brand information) between filter and regular cigarettes reflect true differences in exposure to nicotine. Data on the relative uniformity and differences in carbon monoxide exposure among filter and regular cigarette smokers are not available, but studies in England covering this period show no change in carbon monoxide delivery between filter and regular cigarettes. (Wald NJ, Coll R, personal communication).

Filter-cigarette smokers have consistently been shown to have a lower cancer mortality[1,11,12] than non-filter-cigarette smokers. This decrease has been attributed to the reduction in tar exposure, which is thought to be causally related to high cancer rates in cigarette smokers. However, the total impact of cigarette smoking on the health of individuals needs to be considered before drawing conclusions about the benefits of filter cigarettes. There is very little known, for example, about the specific constituents in tobacco smoke that might contribute to atherosclerosis or aggravate existing coronary or cardiovascular pathology. Only a dozen or so of the thousands of compounds in cigarette smoke have shown a possible connection with coronary heart disease, and only two, nicotine and carbon monoxide, have been looked at in any depth.

Nicotine acutely raises systolic blood pressure, heart rate, and cardiac output and causes cutaneous vasoconstriction,[13,14] probably by increasing catecholamine secretion.[15] It acts directly on the myocardium to produce positive chronotropic and inotropic cardiac muscle actions.[15] The rise in free fatty acids, also probably due to catecholamine stimulation,[16] may aggravate cardiac dysfunction[17] and contribute to the fatty cellular lesions of atherosclerosis.[18] Nicotine increases the diurnal secretion of cortisol,[19] which has been associated with myocardial infarction and with more frequent and complex ventricular arrhythmias.[20] Nicotine-stimulated catecholamine rele may increase platelet stickiness and aggregation.[21] Initiate formation, decreased fibrinolysis, decreased clotting tim change in the rate of initial clot formation, maximum de tensile strength, and clot retraction,[21] along with factors relating to platelet function, have been considered in work on the pathogenesis of atherosclerosis.[22]

Carbon monoxide has an affinity for haemoglobin that 245 times that of oxygen, so it can severely reduce oxyg delivery to the myocardium. This interference in oxyge transport is increased by the way carboxyhaemoglobin shi the oxyhaemoglobin dissociation curve to the left.[23] Carbo monoxide also combines with myoglobin thus impairing t diffusion of oxygen to mitochondria in heart muscle, and yi cytochrome oxidase, thus slowing oxidation at an enzymat level.[23] By decreasing left ventricular end-diastolic pressu left ventricular stroke index and cardiac index it has decidedly negative inotropic effect on the myocardium. patients with angina, carboxyhaemoglobin significan shortens exercise time and the product of systolic bloo pressure and rate (the double product) needed to produce ischaemic S-T segment depression is reduced. Carboxyhaemoglobin lowers the threshold for ventricul fibrillation in monkeys,[24] and exposure of rabbits to carbo monoxide results in prominent ultrastructural changes in t heart.[27] Carboxyhaemoglobin increases vessel wall hypo and permeability,[28] such increased permeability lipoproteins may promote atherosclerosis.[29] Wald reported a stronger association between carboxyhaemoglob and coronary heart disease than between smoking history a coronary heart disease.[30]

The present results indicate that nicotine lowering does have much effect on CHD risk in filter-cigarette smokers such results may be compatible with the growing suspici that carbon monoxide is probably one of the more harm constituents in tobacco smoke. Cigarettes which have a yield of tar and nicotine may not necessarily produce l yields of carbon monoxide. Indeed ordinary filter cigare without perforations in the filter lead to increased exposure carbon monoxide and higher levels

carboxyhaemoglobin,[31,32] while low tar and nicotine cigarettes with perforations in the filter have lower carbon monoxide yields.[32] Whether the ultra-low tar and nicotine cigarettes or the perforated filter will reduce CHD risk is not known. The most optimistic data, published by the Tobacco Research Council, suggest only about a 25% decrease in carbon monoxide exposure from such cigarettes.

The multivariate analysis is an attempt to "control" for other factors known to be strongly related to CHD but which may differ between filter and regular cigarette smokers, although other "confounding" variables, such as unmeasured lifestyle differences, may obscure the true relations between filter use and CHD. Furthermore, a substantial proportion of the older age-group had stopped smoking before the 7th biennial examination and therefore the power to detect differences in event rates between filter and regular cigarettes in this group is diminished. The high proportion of former smokers among the "non-smokers" makes the purity of the comparison between smoking and non-smoking men in the older age-group subject to some question. However, the comparison between filter and regular [illegible] is not influenced because it is an "internal" comparis[illegible] comprised of only men who are long-term cigarette smokers. Although the slightly higher rates of MI among filter cigarette smokers suggest a possible deleterious impact of filters, most of this difference results from higher rates very early in the follow-up period. It is not possible to resolve whether this is due to a "harvesting" effect of filter cigarettes or to selection of filter cigarettes by men who have had subclinical "warning" of CHD. The latter seems most unlikely because most of the men had been smoking filter cigarettes for a number of years before examination 7. The tendency for filter cigarette smokers at examination 7 to have a more favourable smoking history, although consistent with most other data, also suggests that these men should have more favourable CHD outcomes. Since they do not, more suspicion should be raised about potential benefit of filter cigarettes. The promise of the filter philosophy is that the toxins which cause degradation of lung function, cancer, and CHD can be identified and removed, leaving a "safe" cigarette. There is no evidence that the filter cigarettes of the 60s and early 70s conferred any protection from coronary heart disease for men in the Framingham Study.

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"Society, increasingly impressed with the seemingly unending achievements in medicine, has developed an almost insatiable appetite for health services and is now faced with the dilemma of decision as to the fraction of the nation's gross national product to be devoted to the enterprise we now call 'medical care' What is it that so seriously burdens the health care system? It is not those diseases which, thanks to successful research, can be prevented or cured—pernicious anaemia, tuberculosis, smallpox, pneumonia and many others. It is the management of those diseases which we cannot cure and, instead, the victims are offered expensive supportive but tempora y measures; among them I would include heart transplantation, the treatment of many forms of cancer, and most virus diseases for which we lack immunising procedures. I venture to predict that this half-way medical technology will increase its pseudo-curative offerings, that these will be demanded by an inadequately informed public, and that no health care system in the world will be able to afford them. Those who state that we now spend too much on research and who wish to deflect such funds into the health care system could not be more wrong! Our only hope is to seek with renewed vigour the ultimate understanding which will lead to rational preventive or curative treatments as successful as those we have gained for the infections and other diseases . . ."—Sir ANDREW WATT KAY, regius professor of surgery, University of Glasgow. Graduation speech, July 11, 1981.

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Mortality in relation to tar yield of cigarettes: a prospective study of four cohorts

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Abstract

Objective—To investigate relation between tar yield of manufactured cigarettes and mortality from smoking related diseases.

Design—Prospective epidemiological study of four cohorts of men studied between 1967 and 1982.

Setting—Combined data from British United Provident Association (BUPA) study (London), Whitehall study (London), Paisley-Renfrew study (Scotland), and United Kingdom heart disease prevention project (England and Wales).

Subjects—Of the 56 255 men aged over 35 who were included in the studies, 2742 deaths occurred among 12 400 smokers. Average follow up was 13 years.

Main outcome measures—Relative mortality from smoking related diseases according to tar yields of cigarettes smoked.

Results—Age adjusted mortality from smoking related diseases in smokers of filter cigarettes was 9% lower (95% confidence interval 1% to 17%) than in smokers of plain cigarettes (P=0·047). Mortality from smoking related diseases consistently decreased with decreasing tar yield. Relative mortality in cigarette smokers for a 15 mg decrease in tar yield per cigarette was 0·75 (0·52 to 1·09) for lung cancer, 0·77 (0·61 to 0·97) for coronary heart disease, 0·86 (0·50 to 1·50) for stroke, 0·78 (0·40 to 1·48) for chronic obstructive lung disease, 0·78 (0·65 to 0·93) for these smoking related diseases combined, and 0·77 (0·65 to 0·90) for all smoking related diseases.

Conclusion—About a quarter of deaths from lung cancer, coronary heart disease, and possibly other smoking related diseases would have been avoided by lowering tar yield from 30 mg per cigarette to 15 mg. Reducing cigarette tar yields in Britain has had a modest effect in reducing smoking related mortality.

Introduction

The average tar yield of cigarettes in Britain has steadily reduced from 32 mg per cigarette in 1965 to 14 mg in 1987.[1] Nicotine levels have also declined. However, because of compensation—cigarettes with lower tar yields being smoked more intensely—reduction in risk of smoking related diseases is likely to be less than expected from the reduction in tar yield. In addition, some other toxic components of cigarette smoke have not been reduced in the same proportion as tar.[2] It is therefore important to quantify the health effects of reduction in tar yield on mortality from smoking related diseases.

It is reasonably certain that lower tar yields are associated with reduced mortality from lung cancer.[3] The position is less clear with other smoking related diseases, particularly coronary heart disease.[4] We describe the results of the tar pooling project, in which data from four prospective studies were combined to investigate the effects of tar yield on smoking related diseases.

Subjects and methods

INDIVIDUAL STUDIES

We collected data on men from four prospective studies—the British United Provident Association (BUPA) study (London), the Whitehall study (London), the Paisley-Renfrew study (Scotland), and the United Kingdom heart disease prevention project (England and Wales). Table 1 shows details of the studies: the BUPA study recruited predominantly business and professional men who attended the BUPA Medical Centre in London for a comprehensive medical examination; the Whitehall study consisted of civil servants; the Paisley-Renfrew cohort was drawn from population registers of the relatively socially economically deprived towns of Renfrew and Paisley in the west of Scotland; and the men in the United Kingdom heart disease prevention project were middle aged industrial workers from the south of England, south Wales, the Midlands, and Manchester. These studies are described in more detail elsewhere.[5-8]

DEFINITION OF SMOKING CATEGORIES AND TAR CLASSES

Information on smoking was collected through self administered questionnaire completed on entry to the study. Men were classified into four categories: lifelong non-smokers, former smokers, smokers of manufactured cigarettes, and other smokers. Lifelong non-smokers had never regularly smoked tobacco

any form (more than one cigarette a day, or more than two cigars a week, or more than ¼ ounce of tobacco a week for as long as one year). Former smokers had previously smoked some form of tobacco but had given up completely. Smokers of manufactured cigarettes smoked only manufactured cigarettes at entry to the study. Men who smoked hand rolled cigarettes, cigars, or pipes were grouped as other smokers regardless of whether they also smoked manufactured cigarettes.

Smokers of manufactured cigarettes were further categorised according to whether the cigarettes were plain or filter. A tar yield was estimated for each smoker from the cigarette brand that was smoked the longest (was currently smoked in the BUPA study) using the tar yields published in *UK Smoking Statistics*.[7] The classification of tar yields was based on the values at entry to the study. Men for whom the number or tar yield of cigarettes smoked was not known were excluded. The analysis of relative mortality in smokers of plain and filter cigarettes was based on 14 327 men, and the analysis of mortality according to tar yield was based on 12 400 smokers.

DEFINITION OF CAUSES OF DEATH

Men from each cohort were flagged at the Office of Population Censuses and Surveys or the National Health Service Central Records (Scotland), which notified all deaths and causes of death. For this analysis, the causes of death were coded according to the *International Classification of Diseases, eighth revision (ICD-8)*. Lung cancer (ICD code 162), ischaemic heart disease (codes 410-414), chronic obstructive lung diseases (codes 491-492, 519), and stroke (codes 430-438) were grouped as "four major smoking related diseases." Twenty other diseases for which excess mortality in smokers was suggested by the International Agency for Research on Cancer to be partly or wholly attributable to smoking[8] were grouped as "other smoking related diseases." "All smoking related diseases" consisted of both the four major smoking related diseases and the 20 other smoking related diseases. Other causes of death were grouped as "the remaining causes."

STATISTICAL ANALYSIS

Relative risks were estimated with proportional hazards regression analysis to adjust for potential confounding factors such as age and the number of cigarettes smoked. For each relative risk, 95% confidence intervals were calculated, and intervals that excluded 1·00 were significant ($P < 0·05$).

Results

NUMBER OF SUBJECTS AND DEATHS

Table 2 shows the number of men in each study according to smoking habits. Of the total of 56 255 men, 38% were from the BUPA study, 34% from the Whitehall study, 12% from the Paisley-Renfrew study, and 16% from the heart disease prevention project. At entry to the studies, 11 794 (21%) of the men were lifelong non-smokers, 15 996 (28%) were former smokers, 14 327 (25%) were smokers of manufactured cigarettes, and 14 138 (25%) were other smokers. Of the smokers of manufactured cigarettes, 14 708 (82%) smoked filter cigarettes and 2619 (18%) smoked plain cigarettes. No data on smoking were available for 45 men.

There were 8251 deaths observed during an average of 13 years of follow up, of which 5995 were from smoking related causes.

RELATIVE MORTALITY ACCORDING TO FOUR MAJOR SMOKING CATEGORIES

Table 3 shows the number of deaths from specific

Table 1—Selected details of the four individual studies of the tar pooling project

	BUPA study	Whitehall study	Paisley-Renfrew study	Heart disease prevention project	Total
Subjects	Professional and business men	Civil servants	Residents	Factory workers	
Number	21 398	19 167	6581	9099	56 255
Age (years) at entry	35-64	36-78*	45-64	40-60	35-78
Period of recruitment	1975-82	1967-70	1972-6	1971-3	1967-82
Length of observation (years):					
Maximum	15·3	19·4	14·5	10·0	19·7
Mean	11·5	16·4	10·8	9·6	12·8
Total person years	245 443	314 702	71 243	87 604	718 992
Total deaths	1240	4730	1451	830	8251
Age standardised mortality†	6·4	14·0	15·0	10·1	11·5
Tar yield (mg/cigarette)‡:					
Mean	1·35	18·38	4·36	18·38	1·38
Median	16·0	24·2	19·9	22·6	20·5
% who smoked > 18 mg/day (%)	48	100	82	100	80

*All subjects were within age range 40-64.
†Deaths per 1000 person years standardised for age.
‡Information on tar yields could be determined for 12 400 of 14 372 smokers of manufactured cigarettes.

Table 2—Numbers of men in tar pooling project according to study and smoking status

	Lifelong non-smokers	Former smokers	Smokers of manufactured cigarettes: Plain	Smokers of manufactured cigarettes: Filter	Other smokers	Total
BUPA	6 365	6 586	262	3 666	4 519	21 398
Whitehall	3 110	5 275	1 216	4 458	5 108	19 167
Paisley-Renfrew	1 245	2 124	614	2 346	262	6 591
Heart disease prevention project	1 074	2 011	527	1 238	4 249	9 099
Total	11 794	15 996	2 619	11 708	14 138	56 255

Table 3—Relative mortality (95% confidence interval) of smokers compared with non-smokers from specific causes (adjusted for age and study)

Cause of death	No of deaths	Lifelong non-smokers	Former smokers	Smokers of manufactured cigarettes: Plain	Smokers of manufactured cigarettes: Filter	Other smokers
All causes	8251	1·0	1·23 (1·13 to 1·33)	2·34 (2·12 to 2·58)	2·23 (2·06 to 2·41)	1·68 (1·55 to 1·82)
Lung cancer	838	1·0	3·16 (1·94 to 5·14)	13·58 (8·31 to 22·18)	12·85 (8·08 to 20·43)	8·57 (5·37 to 13·68)
Ischaemic heart disease	2331	1·0	1·21 (1·06 to 1·38)	2·05 (1·73 to 2·42)	1·94 (1·70 to 2·21)	1·56 (1·36 to 1·78)
Stroke	489	1·0	1·00 (0·73 to 1·36)	1·98 (1·36 to 2·88)	1·62 (1·19 to 2·21)	1·17 (0·85 to 1·61)
Chronic obstructive lung disease	283	1·0	2·18 (1·16 to 4·09)	6·84 (3·55 to 13·16)	6·44 (3·55 to 11·71)	3·95 (2·13 to 7·35)
All smoking related diseases	1456	1·0	1·21 (1·00 to 1·46)	2·61 (2·07 to 3·30)	2·32 (1·92 to 2·79)	1·80 (1·49 to 2·18)
Remaining causes	2256	1·0	1·16 (1·02 to 1·33)	1·64 (1·35 to 1·99)	1·77 (1·54 to 2·02)	1·32 (1·14 to 1·52)
All major smoking related diseases*	4539	1·0	1·30 (1·16 to 1·45)	2·72 (2·38 to 3·11)	2·53 (2·26 to 2·83)	1·90 (1·69 to 2·13)
Other smoking related diseases†	5995	1·0	1·27 (1·15 to 1·40)	2·69 (2·39 to 3·02)	2·47 (2·25 to 2·72)	1·87 (1·70 to 2·06)

*Cancer, coronary heart disease, stroke, and chronic obstructive lung disease.
†Major smoking related diseases plus other smoking related diseases.

Table 4—*Relative mortality (95% confidence interval) of smokers of filter cigarettes compared with smokers of plain cigarettes from specific causes (adjusted for age, study, and number of cigarettes smoked a day)**

Cause of death	No of filter cigarettes smoked a day		
	1-10	11-20	>20
All causes	0·83 (0·68 to 1·00)	0·93 (0·83 to 1·05)	1·04 (0·90 to 1·21)
Lung cancer	0·99 (0·47 to 2·12)	1·01 (0·73 to 1·39)	0·87 (0·61 to 1·22)
Coronary heart disease	0·76 (0·56 to 1·03)	0·91 (0·75 to 1·11)	1·11 (0·94 to 1·46)
Stroke	1·06 (0·54 to 2·09)	0·74 (0·46 to 1·19)	0·77 (0·43 to 1·36)
Chronic obstructive lung disease	0·76 (0·33 to 1·76)	0·87 (0·77 to 1·45)	1·33 (0·61 to 2·92)
Other smoking related diseases	0·76 (0·48 to 1·19)	0·87 (0·66 to 1·15)	0·94 (0·66 to 1·33)
Remaining causes	0·87 (0·59 to 1·30)	1·03 (0·82 to 1·31)	1·32 (0·94 to 1·85)
Four major smoking related diseases†	0·83 (0·64 to 1·06)	0·91 (0·78 to 1·05)	1·00 (0·82 to 1·24)
All smoking related diseases†	0·81 (0·65 to 1·01)	0·90 (0·79 to 1·03)	0·98 (0·83 to 1·16)

*Smokers of manufactured cigarettes only.
†Lung cancer, coronary heart disease, stroke, and chronic obstructive lung disease.
‡Four major smoking related diseases plus other smoking related diseases.

causes and the mortality rates (adjusted for age and study) for the four smoking categories expressed relative to the lifelong non-smokers. In current smokers (of tobacco of any form) mortalities from all causes, lung cancer, ischaemic heart disease, stroke, chronic obstructive lung diseases, and the group of the 20 other smoking related diseases were significantly higher than those observed for lifelong non-smokers. Ischaemic heart disease and stroke showed an interaction with age. The relative risk of both diseases in cigarette smokers compared with lifelong non-smokers declined with increasing age: the risk of ischaemic heart disease was 2·66 (95% confidence interval 2·1 to 3·4) in those aged <50, 1·53 (1·3 to 1·8) in those aged 50-59, and 1·30 (1·1 to 1·6) in those aged 60 or more, while the risk of stroke was 2·2 (1·0 to 4·8), 1·46 (0·99 to 2·1), and 1·06 (0·7 to 1·6) in the three age groups.

RELATIVE MORTALITY IN PLAIN AND FILTER CIGARETTE SMOKERS

Table 4 shows the relative mortality rates (adjusted for age, study, and number of cigarettes smoked a day) in smokers of filter and plain cigarettes according to levels of cigarette consumption. Point estimates for mortality from each category of smoking related diseases were consistently lower in smokers of filter cigarettes than in smokers of plain cigarettes, but only the relative mortality for all smoking related diseases was significantly different (P=0·047).

RELATIVE MORTALITIES ACCORDING TO TAR YIELD

Table 5 shows the relative mortalities due to a decrease in tar yield of 15 mg per cigarette. In the American Cancer Society study low tar cigarettes were defined as having, on average, 17·6 mg of tar per cigarette and high tar cigarettes had, on average, 25·8 mg per cigarette.[1] In our study the mean difference in tar yield between high and low tar cigarettes was about 15 mg per cigarette. This ... express relative mortalities in terms of ... difference. There was a consistent trend ... mortality from smoking related diseases ... creasing tar yields; this was significant ... heart disease, four major smoking ... combined, all smoking related ... causes. The relative mortality from all ... diseases due to a decrease of 15 mg ... cigarette was 0·77 (0·65 to 0·90). The ... cancer mortality was not significant (0·... 1·09)) because of the relatively small ... from lung cancer (366). No trend ... mortality from causes not related to smoking

Table 5—*Relative mortality from specific causes due to decrease in tar yield of 15 mg per cigarette*

Causes of death	No of deaths	Relative mortality (95% confidence interval)	P value
All causes	2742	0·80 (0·70 to 0·92)	0·0014
Lung cancer	366	0·75 (0·52 to 1·09)	0·13
Coronary heart disease	917	0·77 (0·61 to 0·97)	0·026
Stroke	163	0·86 (0·50 to 1·50)	0·61
Chronic obstructive lung disease	127	0·78 (0·41 to 1·48)	0·45
Other smoking related diseases	486	0·73 (0·53 to 1·02)	0·060
Remaining causes	683	0·93 (0·70 to 1·23)	0·64
Four major smoking related diseases*	1573	0·78 (0·65 to 0·93)	0·0051
All smoking related diseases†	2059	0·77 (0·65 to 0·90)	0·0008

*Lung cancer, coronary heart disease, stroke, and chronic obstructive lung disease.
†Four major smoking related diseases plus other smoking related causes.

Discussion

Mortality from all smoking related ... lower in smokers of filter cigarettes ... smokers of plain cigarettes (95% confi... 1% to 17%). A decrease in tar yield of ... cigarette was associated with a 23% (... decrease in relative mortality. We found ... crease (48% decrease to 9% increase) ... mortality rate from lung cancer associated ... decrease in tar yield of 15 mg per cigarette ... consistent with other studies. In the 12 ... up of 120 000 male cigarette smokers aged ... same reduction in tar yield was associated ... reduction in mortality from lung cancer.[1]

A review of the evidence on lower tar ... and ischaemic heart disease concluded that ... one study (the largest, the American Cancer ... study), reductions in tar and nicotine yields ... effect on the risk of coronary disease.[2] ... accumulation of further data has clarified ... Two case control studies indicated a reduction ... lower tar yields.[12 29] Petitti and Friedman ... a 5 mg decrease in tar yield was associated ... decrease in risk of cardiovascular disease. ... showed that cigarette smokers with average ... 7·5 mg had a 10% lower risk of non-fatal ... infarction than smokers with average yields ... 13·3 mg.[2] Our findings have resolved the ... The relative mortality from ischaemic heart ... reduced by 23% (3% to 39%) by a reduction ... of 15 mg per cigarette.

The original uncertainty over the effects ... cigarettes on heart disease was ... findings. Firstly, in the early 1970s ... had higher carbon monoxide yields ... results of the Framingham study showed ... of filter cigarettes did not have a lower ... myocardial infarction than smokers of ... rettes.[30] During the 1960s and early 1970s ...

almost complete switch from plain to filter cigarettes, so that comparisons between plain and filter became less relevant. By the late 1970s most of the differences between smokers in tar yield reflected differences in filter cigarettes alone, and among filter cigarettes there was, and still is, a high correlation between yields of tar, nicotine, and carbon monoxide.

Data on the effect of tar yield on the risk of chronic obstructive lung diseases,[11 24] stroke, and other smoking related diseases are sparse. In our study death rates for these diseases were associated with tar yield, but the association was not significant. The position therefore remains uncertain.

POTENTIAL SOURCES OF BIAS

Two sources of bias may have underestimated the association between tar yield and mortality in our study. Firstly, smokers often do not identify their brand of cigarette with sufficient accuracy,[25] and brands with similar names can have different tar yields. Secondly, in the studies we used, tar yields were higher before entry into the study and in the earlier years of the subjects' smoking history. The studies recorded only the tar yields of cigarette smoked at entry to the study, yet the subsequent tendency was to switch to lower yield cigarettes. With the reduction in the average tar yield of cigarettes sold in Britain over the past two decades, the range of tar yields would also have become narrower. The range of death rates from smoking related diseases that were recorded were therefore incorrectly related to the range of tar yield on entry to the study rather than to the narrower range during follow up. This may be important since recent exposure to cigarette smoke is more relevant to risk.[26]

Confounding by social class did not seem to be a problem. Data from the Whitehall and the Renfrew-Paisley studies indicated that social class had little effect on the estimate of the effects of tar yield on mortality.

CONCLUSION

About a quarter of deaths from lung cancer, coronary heart disease, and possibly other smoking related diseases could be avoided by switching from higher tar cigarettes (30 mg/cigarette) to lower tar ones (15 mg/cigarette). This is consistent with studies of compensatory smoking; switching to cigarettes of half the tar yield reduces tar intake by about a quarter rather than a half.[2]

Key messages

- It is reasonably certain that smoking low tar cigarettes rather than high tar cigarettes reduces risk of lung cancer, but the position is less clear with other smoking related diseases, particularly coronary heart disease
- We used data from four large British cohort studies to investigate effect of lowering tar yield on smoking related diseases
- Mortality from smoking related diseases was reduced by about 23% for a reduction in tar yield of 15 mg per cigarette
- Mortality from ischaemic heart disease was also reduced by 23%, and mortality from lung cancer was reduced by 25%
- Britain's policy of reducing the tar yield of cigarettes has been associated with modest benefits, but these benefits are much less than that associated with stopping smoking completely

Our results indicate that the reduced tar yield of British cigarettes over recent decades has reduced mortality from smoking related diseases. The potential for further reductions in mortality from further tar yield reductions may be more limited. Very low tar cigarettes have not been widely accepted.[27] In Britain, in spite of the increasing number and advertising of low tar brands, the percentage of smokers who smoke cigarettes of tar yield below 10 mg per cigarette has remained small and has hardly changed since 1978.[1] Tar yields from British cigarettes are currently limited by regulation to 15 mg per cigarette, and this will fall to 12 mg per cigarette at the end of 1997. Future public health policy would be best directed mainly towards preventing cigarette smoking through public education, tobacco taxation, stricter legislation (including control over advertising of cigarettes), and measures that will discourage children and young adults from taking up the habit.

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Conflict of interest: None.

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7.19

Cigarette smoking, tar yields, and non-fatal myocardial infarction: 14 000 cases and 32 000 controls in the United Kingdom

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Abstract

Objectives—To assess the effects of cigarette smoking on the incidence of non-fatal myocardial infarction, and to compare tar in different types of manufactured cigarettes.

Methods—In the early 1990s responses to a postal questionnaire were obtained from 13 926 survivors of myocardial infarction (cases) recently discharged from hospitals in the United Kingdom and 32 389 of their relatives (controls). Blood had been obtained from cases soon after admission for the index myocardial infarction and was also sought from the controls. 4923 cases and 6880 controls were current smokers of manufactured cigarettes with known tar yields. Almost all tar yields were 7·9 or 12·15 mg/cigarette (mean 7·5 mg for low tar (< 10 mg) and 13·3 for medium tar (≥10 mg)). The cited risk ratios were standardised for age and sex and compared myocardial infarction rates in current cigarette smokers with those in non-smokers who had not smoked cigarettes regularly in the past 10 years.

Results—At ages 30-49 the rates of myocardial infarction in smokers were about five times those in non-smokers (as defined); at ages 50-59 they were three times those in non-smokers, and even at ages 60-79 they were twice as great as in non-smokers (risk ratio 6·3, 4·7, 3·1, 2·5, and 1·9 at 30-39, 40-49, 50-59, 60-69, 70-79 respectively; each 2P < 0·00001). After standardisation for age, sex, and amount smoked, the rate of non-fatal myocardial infarction was 10·4% (SD 5·4) higher in medium tar than in low tar cigarette smokers (2P = 0·06). This percentage was not significantly greater at ages 30-59 (16·6% (7·1)) than at 60-79 (1·0% (8·5)). In both age ranges the difference in risk between cigarette smokers and non-smokers was much larger than the difference between one type of cigarette and another (risk ratio 3·39 and 3·95 at ages 30-59 for smokers of similar numbers of low and of medium tar cigarettes, and risk ratio 2·35 and 2·37 at ages 60-79). Most possible confounding factors that could be tested for were similar in low and medium tar users, with no significant differences in blood lipid or albumin concentrations.

Conclusion—The present study indicates that the imminent change of tar yields in the European Union to comply with an upper limit of 12 mg/cigarette will not increase (and may somewhat decrease) the incidence of myocardial infarction, unless they indirectly help perpetuate tobacco use. Even low tar cigarettes still greatly increase rates of myocardial infarction, however, especially among people in their 30s, 40s, and 50s, and far more risk is avoided by not smoking than by changing from one type of cigarette to another.

Introduction

In countries such as the United Kingdom, where cigarettes have been used widely for several decades, tobacco now accounts for about 30% of all deaths in middle age, with lung cancer and coronary heart disease the most common fatal conditions.[1-3] Over the past few decades cigarettes have been altered in various ways, reducing the so called yields of tar and nicotine when smoked in a standard way by a machine. Typical British cigarettes had tar yields of 25-35 mg during the 1950s and 5-15 mg in 1990.[4] But, partly because the chief toxins in cigarette smoke are uncertain and partly because smokers may compensate for reduced yields (or other changes) by smoking cigarettes more actively,[5-10] the health effects of alterations in cigarette manufacture are unpredictable. Low tar cigarettes do cause substantial risks of cancer and heart disease, although the risk of lung cancer is less than with high tar cigarettes.[2,11-14] For heart disease, however, there remains uncertainty[10,15] about whether the rates have been decreased, increased, or not changed by alterations in cigarette composition over the past few decades. National heart disease mortality rates and trends are not informative because other factors cause such large differences in coronary heart disease between different populations and time periods. Instead, concurrent epidemiological comparisons within one population are needed.

But, although tobacco is a major cause of heart disease, particularly among young and middle aged adults, it is difficult for conventional prospective or retrospective studies to compare the risks from different types of cigarette. Only a narrow range of cigarette tar yields is concurrently available within one population, and the tar yields of cigarettes smoked by people in 1990 might correlate poorly with the tar yields smoked by these people years earlier. Hence, even large differences in risk between prolonged use of low, medium, and high tar cigarettes might produce only small differences in risk between current use of low and medium tar cigarettes. At younger ages the proportional difference in rates of coronary heart disease between smokers and non-smokers is particularly extreme, so any effect of cigarette type may also be extreme. Thus, to minimise the chances of a false negative result in a study of tar yields, the number of cases of myocardial infarction in middle aged cigarette smokers should be large—preferably several thousand—with at least as many controls. We achieved this by studying subjects from the United Kingdom who participated in the large ISIS (international studies of infarct survival) trials of the treatment of acute myocardial infarction,[16-20] by using postal questionnaires (copies available on request), rather than interviews, and by simplifying blood collection procedures.

Patients and methods

CASES AND CONTROLS

Cases were the survivors in the United Kingdom aged 30-79 from the ISIS-3 or ISIS-4 trials who completed an epidemiological questionnaire sent to them a few months after their infarction. Those who were asked to complete it were all the survivors from ISIS-3, but from ISIS-4 only the survivors aged 30-59 who on admission to hospital were reported to be cigarette smokers. Thus, although only cases from ISIS-3 can be used to compare smokers with non-smokers, the cases from ISIS-4 strengthen the analyses of tar yields among smokers aged 30-59. The ISIS-3 questionnaire asked the cases to identify all their brothers, sisters, and children aged at least 30 who were resident in the United Kingdom. A similar "control" questionnaire was then sent to such relatives, accompanied by a second copy, which the relatives, if married, were to ask their spouse to complete. One reminder was sent to cases and relatives who did not reply, and inconsistencies or omissions were queried once.

Of the 20 681 ISIS-3 patients in the United Kingdom, 19 065 who were not known to be dead were posted the case questionnaire, of whom 1346 were found to be dead and 13 960 (79% of presumed survivors) completed it. The control questionnaire was sent to 30 247 relatives of ISIS-3 cases, of whom 75 were found to be dead and 21 995 (73% of presumed survivors) and 14 245 of their spouses completed it. Patients with a history of stroke, gastrointestinal bleeding, or ulcer tended not to have been recruited into the ISIS-3 trial,[9] and so people with such conditions were not eligible as cases or controls. Of those who completed questionnaires, 2002 cases and 3851 controls were excluded because they were under 30, over 79, or of unknown age or because they had a self reported history of "definite stroke" or of "bleeding or ulcer in (or near) the stomach."

ISIS-4 patients in the United Kingdom aged 30-59 who were described at trial entry as current smokers were also sent the questionnaire. The response rate for such patients was similar in both trials. Any of these ISIS-4 patients whose questionnaire response indicated that they were not cigarette smokers at the time of their infarction were excluded. ISIS-4 (and, to some extent, ISIS-3) tended to exclude patients with shock or persistent hypotension,[9] but such exclusions should not bias the epidemiological analyses of tobacco use.

BLOOD SAMPLES

Blood was to be taken from patients in ISIS-3 immediately after randomisation but before the trial treatments and collected in a 10 ml vacutainer containing 0·12 ml preservative (15% potassium EDTA with aprotinin 0·34 mmol/l: Becton Dickinson). On returning their questionnaire, controls were sent an identical container for their general practitioner to collect blood. Case and control containers were sent by first class post to Oxford. Controls were sent one reminder about giving a sample. After a mean of two days in the post the blood was centrifuged, the packed cell volume was recorded, and the plasma and buffy coat were aliquoted for storage at −40°C. Blood arrived from 97% of ISIS-3 cases and 45% of controls, but breakages or haemolysis rendered 6% of these samples unusable. The present blood analyses involve only correlations of smoking with blood biochemistry results, and these analyses should not be materially biased by low response rates.

Plasma cotinine concentration was measured in controls who were current cigarette smokers, and in a 3% sample of controls who reported no current use of tobacco, by means of antibodies developed by Knight *et al* in a modification for plasma of the [illegible] radioimmunoassay.[9] Results with this [illegible] correlate closely with those with gas chromatog[illegible] Beckman CX-4 and CX-5 autoanalysers were used for measuring concentrations of cholesterol, albumin (both with Beckman reagents) and [illegible] proteins A_1 and B (with Immuno reagents). [illegible] for discoloration from haemolysis, an index [illegible] reading was subtracted from the final reading [illegible] from a large plasma pool were included in [illegible] analytical run, yielding coefficients of variation [illegible] for cholesterol and albumin and 4% for [illegible] proteins.

QUESTIONNAIRES

Information was sought on sex, age, [illegible] smoking, drinking, past health, and relations [illegible] were asked about their habits and history before their index myocardial infarction (because [illegible] heart attack may alter a patient's habits), [illegible] were asked about their present habits. [illegible] tions to cases often began, "Before your recent admission. . . ." Both cases and controls were [illegible] to list how many relatives of certain types [illegible] but only cases were to provide contact details; other respects case and control questionnaires were identical. The medical history section was [illegible] technical and recorded various conditions that might be associated with exclusion from the randomised trial (see above) or that might affect, or be affected by, smoking. After the question of whether they had ever smoked regularly (ie on most days for at least a year) the rest of the cigarette section was to be completed only by those who replied "yes." It dealt with the age at which the subject had first and last smoked regularly, whether any cigarettes had been smoked in the previous month, the number smoked per day when the subject had last smoked cigarettes regularly, and the way in which cigarettes were smoked. People were asked to tick against 137 detailed brand names the one or more which they last smoked, they usually smoked most often, or, if it was not on the list, to write one in. Cigarette packets (and, whenever possible, to enclose the packet or packets that brand with the questionnaire). For the few subjects who listed more than one brand, the average of the tar yields was taken. Ninety eight per cent of controls and 97% of cases who currently smoked only manufactured cigarettes with a known tar yield, and both reported using their current brand for, on average, the previous 10 or 11 years.

DEFINITIONS OF CIGARETTE SMOKING STATUS

Respondents were classified as current cigarette smokers (26% of the controls: those who had smoked cigarettes in the previous month, plus the few who failed to answer this yes/no question but gave positive evidence of current cigarette use); other tobacco users (3%: pipes, cigars, or smokeless tobacco in the previous year); or as not using tobacco (71%: all others). In table I these are further subdivided. Because of the possible confusion between those who were [illegible] smoking many years ago and those who never smoked, the main comparison group was defined as those smokers who had not used cigarettes regularly in the past 10 years.

ESTIMATED 1990 TAR YIELDS

The United Kingdom's government chemist conducts surveys of common cigarette brands, measuring tar, nicotine, and carbon monoxide yields, using [illegible] (R Waller, personal communication). During the [illegible] 1980s the annual decrease in sales weighted yields was about 2-3% for tar, 1-2% for nicotine, and 1% for carbon monoxide (J Rentoul, personal communication).[4] Most ISIS-3 cases replied in 1990 about [illegible]

before their myocardial infarction (mean date of infarction: February 1990), most controls replied in 1990-1 (mean: November 1990), and most ISIS-4 cases replied in 1992-3 (mean date of infarction: July 1992). To avoid secular trends in yields introducing minor biases, the mid-1990 survey results for each cigarette brand were used (R Waller, personal communication). If a brand was assayed only earlier or later than mid-1990, yields from the closest survey were extrapolated to mid-1990 by annual decreases of 2·5% in tar and 1·5% in nicotine.

RESURVEY OF CONTROLS A FEW YEARS LATER

To check reproducibility, about 2000 controls who originally returned both questionnaire and blood sample (and whose replies indicated no previous vascular disease) were sent the same questionnaire and blood kit again about 2-3 years later. To avoid over-sampling young controls, the random sample was stratified with respect to sex and age in groups of five years. Seventy per cent (1388/1996) returned the questionnaire, 95% (1324/1388) of whom gave blood.

STATISTICAL METHODS

The analyses are all unmatched—that is, they compare cases with all controls, not just with their own relatives—and for tar yield analyses among smokers the controls are as relevant to ISIS-4 as to ISIS-3 cases. All analyses of myocardial infarction rates were stratified either for sex and five year age group or for these factors and amount smoked (five categories; see below). Calculations of risk ratios—or, equivalently, relative risks—entailed unmatched stratified logistic regression (fitted by unconditional maximum likelihood), with one extra term included for each stratum. Risk ratios are often given with 95% confidence intervals. Two sided probability values (2P) are used.

Results

FREQUENCY DISTRIBUTIONS OF SMOKING HABITS

Table I shows the numbers of controls and cases in various categories of tobacco use subdivided by sex and by age. The age range of chief relevance to the tar yield analyses is 30-59, and among controls in this range 28% both of men and of women were current cigarette smokers, in close agreement with nationally representative, interviewer administered surveys in the early 1990s.[24] Twenty two per cent of these controls were current users of manufactured cigarettes only with known tar yields.

Figure 1 gives, for controls who currently used manufactured cigarettes only, the frequency distribution of (*a*) the reported number smoked per day and (*b*) the estimated 1990 tar yield. Self reported cigarette consumption was categorised as 1-9, exactly 10, 11-19, exactly 20, and ≥21 cigarettes a day; 85% reported smoking 10-30 cigarettes a day. The tar yields show a bimodal distribution, with commonest values 7-9 or 12-15 mg/cigarette. Tar yields of 10 mg were rare, which makes this a natural point of subdivision, unaffected by any slight differences in dates of case and control responses, to define two main categories: low tar (< 10 mg, mean 7·5 mg) and medium tar (≥ 10 mg, mean 13·3 mg). Medium tar is sometimes split into 10-12, 13, and ≥14 mg/cigarette. This definition of low tar is also used by the Department of Health (R Waller, personal communication).[1] Twenty five per cent of the smokers in figure 1b use low tar cigarettes, as in the nationally representative survey in 1990.[21] Almost all

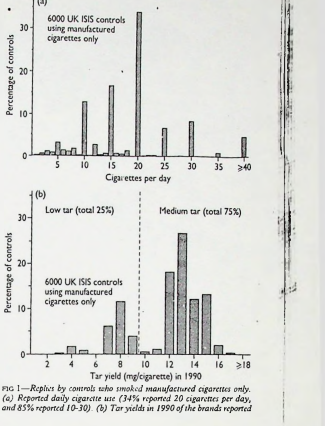
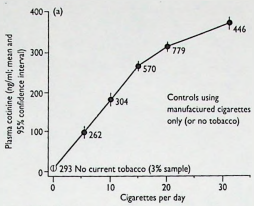


FIG 1—*Replies by controls who smoked manufactured cigarettes only. (a) Reported daily cigarette use (34% reported 20 cigarettes per day, and 85% reported 10-30). (b) Tar yields in 1990 of the brands reported*

TABLE I—*Tobacco use in cases and controls aged 30-79 with questionnaires returned*

		Current cigarette smoker					Other tobacco		Not using tobacco			
		Manufactured cigarettes and no other tobacco										
		Tar known	Tar unknown	Other cigarette users	% Now using any cigarettes	Smoking pipe or cigar but no cigarettes	Using smokeless tobacco only	Former regular cigarette smoker		Never regular cigarette smoker	Total*
								< 10 years ago	≥ 10 years ago		
Male		6880	162	1389	26	1031	71	3181	5502	14173	32389
Male	30-59	2184	35	958	28	676	40	1128	1785	4357	11163
Male	30-59	3264	60	153	28	11	1	1145	1385	6559	12578
Male	60-79	563	21	251	20	337	28	465	1506	906	4077
Male	60-79	869	46	27	21	7	2	443	826	2351	4571
Female		3453	65	1063	18	859	48	1311	2070	3098	11967
Female	30-59	1351	23	619	48	405	36	424	467	804	4119
Female	30-59	520	8	33	60	0	0	98	47	236	942
Female	60-79	858	16	382	27	450	20	537	1268	1171	4702
Female	60-79	724	18	29	35	4	2	252	288	887	2204
Female		1470	34	455	—	—	—	—	—	—	1959
Female	30-59	1117	29	430	—	—	—	—	—	—	1576
Female	60-79	353	5	25	—	—	—	—	—	—	383
Total*		11803	261	2907	—	1890	119	4492	7572	17271	46315

*Cases and non-users.



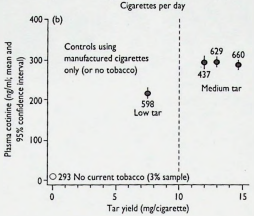


FIG 2—*Cotinine by cigarette smoking habit in controls. (a) Cotinine versus daily cigarette use. (b) Cotinine versus tar yield of reported brand. In the low and medium tar smokers whose blood samples were assayed, mean plasma cotinine concentrations were 217 and 292 ng/ml, mean cigarettes a day were 15·8 and 18·7, and mean yields per cigarette were 7·4 and 13·3 mg tar, 0·75 and 1·18 mg nicotine, and 8·4 and 15·0 mg carbon monoxide. Blood was taken on average of eight months after questionnaire, and in 12 out of 293 whose questionnaire had indicated no smoking cotinine concentration (mean 208 ng/ml) indicated current tobacco use*

TABLE II—*Non-fatal myocardial infarction: age-specific effect of cigarette use in people with no history of major neoplastic or vascular disease*

Age (years)	Current smoker of manufactured cigarettes only		Non-smoker with no regular cigarette use in past 10 years		Myocardial infarction*	
	Cases	Controls	Cases	Controls	Risk ratio (95% confidence interval)	Test statistic†
30-39	78	1784	35	4873	6·33 (4·22 to 9·51)	8·9
40-49	293	1497	190	4306	4·66 (3·82 to 5·69)	15·1
50-59	435	861	508	2701	3·10 (2·64 to 3·65)	13·7
30-59	806	4142	733	11880	3·85 (3·41 to 4·34)	22·1
60-69	416	653	707	2299	2·54 (2·16 to 2·98)	11·3
70-79	111	163	369	942	1·92 (1·45 to 2·54)	4·6
60-79	527	816	1076	3241	2·37 (2·06 to 2·72)	12·1

*Smoker v non-smoker rates standardised for age and sex.
†Number of standard deviations by which the logarithm of the risk ratio differs from zero.

used filtered brands (100% of the low tar group, 96% of the medium tar group), so filters accounted for little of the difference in yields between low and medium tar cigarettes in 1990.

RELATION BETWEEN QUESTIONNAIRE AND COTININE CONCENTRATIONS

Figure 2 shows the relation between plasma cotinine concentrations and (*a*) reported daily cigarette use and (*b*) tar yield for controls reporting use of manufactured cigarettes only or no current tobacco use. The mean cotinine concentration was very low in the self reported non-smokers, which helps validate both questionnaire and laboratory results. Among cigarette smokers there was a strong relation between cotinine concentration and the amount reported to be smoked, which again helps validate the questionnaire. The downward curvature in figure 2a suggests that those who smoke more cigarettes may absorb less nicotine from each one or that those reporting large numbers include disproportionately many who overreported, or both. Either way, self reported cigarette consumption provides only approximate information about the real doses of nicotine and of other substances.

In figure 2b the mean cotinine values were a third higher among the controls who smoked low tar cigarettes (low tar 217 ng/ml *v* medium tar 292 ng/ml). But the smokers of low tar cigarettes reported smoking 15·8 cigarettes a day compared with 18·7 a day for those in the medium tar group. After standardisation for age, sex, and area of residence, however, the mean plasma cotinine concentrations were still 19% higher with medium tar cigarettes. The difference in cotinine is still highly significant (2P < 0·00001), which helps validate the estimated difference of tar yield based on the questionnaire. But the difference is more extreme than the difference of over 50% in tar machine yield per cigarette measured by machine (0·75 *v* 1·18 mg). This may be partly because the underestimation of tar yields is imperfect, and partly because smokers of low yield cigarettes compensate by inhaling more smoke per cigarette. But, since this comparison predicts highly significant biochemical differences in blood taken months later (figure 2b), it supports validity.

CIGARETTE USE AND NON-FATAL MYOCARDIAL INFARCTION

When those using manufactured cigarettes only were compared with non-smokers who had never smoked cigarettes regularly in the past 10 years, controls of both cases those using any other type of tobacco, the relative risks for non-fatal myocardial infarction in people with no previous neoplastic or major vascular disease depended strongly on age (table II, fig 3). As is the case for mortality from coronary heart disease, the risk ratio comparing smokers with non-smokers was greater at younger ages, reinforcing the importance of the relevance of tar yields to be considered separately younger and older ages.

TAR YIELDS AND NON-FATAL MYOCARDIAL INFARCTION

Information about the relevance of tar yields from current users of manufactured cigarettes in these, much the most informative are the 800 aged 30-59, rather than the 3000 aged 60-79. This is because the numbers are larger but also because the risk ratio when smokers are compared with

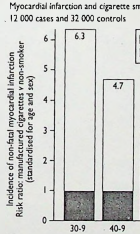


FIG 3—*Cigarettes and non-fatal myocardial infarction at d risk ratios at various ages. Results in people with no previous major neoplastic or vascular disease. Each risk ratio is stan sex and for quinquennium of age, and compares those who s tured cigarettes only with those who were not currently s tobacco and had not been regular cigarette smokers at any past 10 years. Risk ratio is given within each column. (Th recruited from ISIS-4 were cigarette smokers, this figure bein only from ISIS-3)*

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Comparison of myocardial infarction rates in current smokers of medium and low tar cigarettes

	No currently using manufactured cigarettes only, with known 1990 tar yield			Ratio of non-fatal myocardial infarction in smokers of medium tar v smokers of low tar cigarettes (with 95% confidence interval and significance)		
	"Cases" of infarction* ISIS-4	"Cases" of infarction* ISIS-3	Controls (no infarction)	Standardised for age and sex only	Standardised for age, sex, and amount smoked	Standardised for age, sex, and amount smoked: no previous disease†
...g 20-39: ...ow tar	274	359	1268	1·203 (1·061 to 1·364) 2P=0·004	1·166 (1·025 to 1·326) 2P>0·1	1·075 (0·900 to 1·283) 2P>0·1
...edium tar	1196	1512	4180			
...g 40-59: ...ow tar	—	438	433	1·046 (0·890 to 1·230) 2P>0·1	1·010 (0·856 to 1·191) 2P>0·1	1·010 (0·771 to 1·323) 2P>0·1
...edium tar	—	1144	999			
...g 60-79: ...ow tar	274	797	1701	1·142 (1·034 to 1·260) 2P=0·008	1·104 (0·998 to 1·222) 2P=0·06	1·055 (0·910 to 1·223) 2P>0·1
...edium tar	1196	2656	5179			

...ividual smoking low tar rather than medium tar cigarettes were similar in ISIS-4 and ISIS-3: after ...ustment for age, sex, and amount smoked, the odds ratio comparing the two tar yield categories in the two ...dies was 1·000 (SD 0·091).
...the comparison of the effects of different tar yields, inclusion of patients with some previous neoplastic or vascular ...ease may well produce no material bias and helps stabilise the estimates.

...Associations between smoking habits and blood lipid concentrations. Values are means (SE) ...ndardised for age, sex, and case-control status

	Cigarette use					
	Current smoker of manufactured cigarettes only (n=1256)	Non-smoker with no cigarette use in past 10 years (n=3183)	Significance	Cigarette tar yield		
...easurement				Low tar (n=295)	Medium tar (n=942)	Significance
...ol (mmol/l)	5·92 (0·03)	5·91 (0·02)	NS	6·01 (0·06)	6·02 (0·03)	NS
...poprotein A$_1$ (g/l)	1·273 (0·006)	1·288 (0·004)	2P>0·05	1·266 (0·013)	1·264 (0·007)	NS
...poprotein B (g/l)	1·194 (0·008)	1·165 (0·005)	2P>0·004	1·222 (0·016)	1·226 (0·009)	NS

...Reproducibility of smoking classification

	Response to original questionnaire				
	Currently using tobacco		Not using tobacco		
...se to repeat ...estion 2-3 years later	Manufactured cigarettes only	Other tobacco user	Former cigarette smoker		Never cigarette smoker
			<10 years	≥10 years	
...ufactured cigarettes only	99*	9	8	5	0
...r tobacco user	1	86	7	3	3
...r cigarette smoker:					
...ears	22	12	50	11	0
...ears	2	18	37	370	15
...cigarette smoker	4	9	2	24	591

...ercentages of these had known tar yield at both enquiries (65 classified as medium tar originally and medium tar ...ain then low, 8 as medium then low, 3 as low then medium).

smokers is more extreme in middle than in old age. As there was no significant difference between the tar yields of cases aged 30-59 in ISIS-3 and in ISIS-4 (table III), the groups were combined.

Table III provides age-sex standardised comparisons of non-fatal myocardial infarction in smokers of low tar versus smokers of medium tar cigarettes. Overall, there were only slight effects of the tar yield. The mean daily number of cigarettes smoked was slightly higher in the medium tar than in the low tar cigarette smokers (19·0 v 17·1). When standardised not just for age and sex but also for the daily number of cigarettes smoked, the incidence of myocardial infarction was 10·4% (SD 5·4) higher in medium than in low tar cigarette smokers (2P=0·06). This difference was non-significantly greater at ages 30-59 (16·6% (7·1) higher; 2P=0·02) than at 60-79 (1·0% (8·5) higher; 2P>0·1) (fig 4). As these two results are not significantly different from each other, they do not prove that tar yields are of greater proportional importance to the cardiotoxicity of cigarettes in middle than in old age, especially since the smoker versus non-smoker risk ratios are less extreme in old age. In both age ranges the difference between cigarette smokers and non-smokers was much larger than the difference between one type of cigarette and another: the risk ratios were 3·39 and 3·95 for smokers of similar numbers of low and of medium tar cigarettes at ages 30-59 and were 2·35 and 2·37 at ages 60-79. (Table III shows that results were similar when these comparisons were based on the smaller numbers of cigarette smokers with no reported history of neoplastic or major vascular disease.)

POTENTIAL CONFOUNDING FACTORS

Table IV relates smoking to blood lipid concentrations among ISIS-3 cases entering the trial within 0·4 hours of pain onset whose blood spent only one or two days in the post, and among one randomly chosen control per case (matched for age, sex, and days sample spent in the post). Apolipoprotein A$_1$ was 1·2% lower and apolipoprotein B 2·4% higher in smokers than in non-smokers, but these differences are too small to account for much of the excess risk among smokers.

There were no significant differences in blood lipid concentrations (or albumin concentration, data not shown) between smokers of low and of medium tar cigarettes, either overall or in those aged 30-59 (data not shown). For many factors there were likewise no significant differences between smokers of low and medium tar cigarettes. These include self reported height, weight, loneliness, depression, worry, insomnia, teenage acne, tea consumption, alcohol consumption, and whether living with a spouse. For a few factors, however, there were definite differences even after standardisation for age and sex. (Multivariate adjustment for these observed differences would make little difference, but these differences point to the possibility of others existing.) Those who smoked low tar cigarettes were, on average, almost six months older when they left full time education (mean leaving age 15·9 years for low tar group v 15·5 years for medium tar), were more likely to say that they had matured physically "later than average" (13·4% v 10·5%), had "softer hands than average" (14·4% v 11·0%), had been regular drinkers of coffee (75% v 67%), were older when they started to smoke (18·8 v 17·9 years old), and had changed to their current brand more recently (7·9 v 10·1 years previously). These suggest a general tendency for those who smoke medium tar cigarettes to include a slightly larger proportion of manual workers, and to have slightly less education. (Likewise, unpublished analyses by M Jarvis of the 1990 and 1992 general household surveys in the United Kingdom found significantly higher "indices of deprivation" in users of medium than of low tar cigarettes.)

REPRODUCIBILITY OF SMOKING CLASSIFICATION

A total of 1388 controls repeated the questionnaire a few years later, and table V compares their two replies. When subdivided three ways (manufactured cigarettes only; other tobacco or ex-cigarette smoker <10 years; remainder), 90% remained in the same category; of the 97 who smoked only manufactured cigarettes with tar known on both occasions, 89% had continued to smoke medium or low tar cigarettes as originally. Overall, there was a 5% shift towards the low tar category, in line with national trends, and the correlation coefficient between the two assessments of tar yield was 0·71.

Discussion

When cigarette smokers are compared with non-smokers the risk ratio for myocardial infarction is much more extreme in early adult life than in old age. The numbers contributing to figure 3 are unusually large (12 000 cases and 32 000 controls) and so the pattern of steadily increasing risk ratio with younger

age is particularly reliably demonstrated, as are the hazards at the extremes of the age range of 30-79. The risk ratio is twofold at ages 70-79, but it is almost fourfold at ages 30-59 (threefold at 50-59 but fivefold at 30-49). Even these large differences have probably been somewhat diluted by the misclassification of some smokers or non-smokers. Had it been possible, with no classification errors, to compare persistent cigarette smokers with lifelong non-smokers then the risk ratios would probably have been still more extreme than those in figure 3, and would have been at least fourfold at ages 30-59. As most of the excess risk associated with smoking is caused by smoking,[1,2] this fourfold risk ratio implies that about three quarters of the myocardial infarctions among cigarette smokers aged 30-59 were caused by tobacco (two thirds at ages 50-59, but four fifths at ages 30-49).

Any differences in the risk of heart disease between those who are smoking different types of cigarette must be much less extreme than the differences between smokers and non-smokers, so especially large studies are needed to assess them. Moreover, epidemiological studies that were undertaken when tar yields below 15 mg were still uncommon (N J Wald *et al*, unpublished data)[29-30] are of limited contemporary relevance in countries such as the United Kingdom where tar yields above 15 mg have already virtually disappeared (fig 1b) and where a European Union upper limit of 12 mg is soon to be enforced. As no other large recent studies are available, our current findings stand alone.

For tar yields the central finding is that after standardisation for age, sex, and number of cigarettes, the incidence of non-fatal myocardial infarction seemed to be about 10% greater with medium tar than with low tar cigarettes (95% confidence interval 0 to 22%, table III). Even if this 10% difference was highly statistically significant (which it is not: 2P=0·06) it would still not be epidemiologically secure. It is uncertain how much selective emphasis to put on the data at ages 30-59 as opposed to those at 60-79, how much selective emphasis to put on the data from people with no previous disease, and how much to emphasise

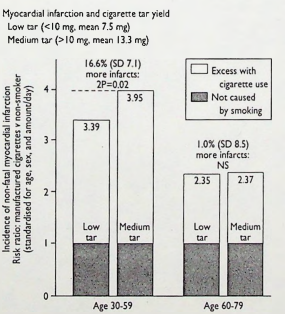

FIG 4—*Cigarette tar yields and risk of non-fatal myocardial infarction. Standardised for age, sex, and amount smoked, comparisons at ages 30-59 indicate that non-fatal myocardial infarction rates were 1·166 (SD 0·071) times as great among medium tar as among low tar cigarette smokers (2P=0·02; table III). The same standardised comparisons at ages 60-79 give 1·010 (0·085) (NS). These two estimates (1·166 and 1·010) are combined with the risk ratios of 3·85 and 2·37 for cigarette smokers versus non-smokers (fig 3) to yield the cited risk ratios for smokers of low and medium tar cigarettes: 3·39 and 3·95 at ages 30-59 and 2·35 and 2·37 at ages 60-79*

Key messages

- Non-fatal myocardial infarction rates [illegible] times as great among cigarette smokers as [illegible] non-smokers at ages 30-49, three fifths as [illegible] at ages 50-59, and twice as great at ages [illegible]
- Among cigarette smokers four [illegible] myocardial infarctions at ages 30-49 were caused by tobacco, two thirds at ages 50-59, and [illegible] ages 60-79
- The risks seem to be slightly greater [illegible] medium tar than with low tar cigarettes, but the difference is not definite
- Differences in risk between cigarette smokers and non-smokers are far greater than any differences in risk between one type of cigarette and another
- Far more myocardial infarctions could be avoided by not smoking than by changing from one type of cigarette to another

analyses that are standardised for the amount [illegible] (Those using low tar cigarettes reported [illegible] slightly fewer than those smoking medium tar cigarettes, and if lower daily consumption is a consequence of lower yields of tar, nicotine, and smoke components then it should not be standardised for.) Hence, table III reports several different comparisons of disease rates in smokers and non-smokers, with differences that are sometimes large, sometimes less than 10%. Also, there was a tendency for tar yields to be inversely related to education and to various other aspects of social class; it is difficult to see how some of these uncertainties can be resolved: large scale randomisation is impracticable, and even if the present study could have been much larger, thereby narrowing the confidence intervals, the possibility of confounding would remain.

Despite these uncertainties, however, the [illegible] results provide some reassurance to those in government or in industry who could direct decisions [illegible] cigarette tar yields to reduce cancer incidence. They indicate that such changes will not substantially increase the incidence of myocardial infarction, and may well decrease it. Thus, the limit of 12 mg/cigarette on tar yields that is now being introduced by the European Union should help limit the number of premature deaths from tobacco, unless governments or smokers come to regard reductions in tar yields as substitutes for the avoidance of cigarettes. In developed countries tobacco remains much the most important cause of premature death. This is particularly so for men, with tobacco now causing about a third of all deaths in middle aged men. But among women have been smoking cigarettes for some time (as, for example, in the United Kingdom or the United States) tobacco also already causes about 4% of all the deaths in middle aged women.[1]

For the general population, therefore, the important finding is not the slight and [illegible] difference in figure 4 between one type of cigarette and another but the large and definite difference in figure 3 between cigarette smokers and non-smokers, particularly in early middle age. Irrespective of whether low or medium tar cigarettes are used, three quarters of the smokers who have a heart attack in their 30s, 40s, or 50s need not have done so: more heart attacks could be prevented by [illegible] than by reducing cigarette tar yields.

The chief acknowledgment is to the patients

relatives who collaborated in this study, and to the medical and nursing staff from more than 100 hospitals in the United Kingdom listed in the ISIS reports.[1-20] We particularly thank Peter Froggatt, Cheryl Swann, and Robert Waller of the Independent Scientific Committee on Smoking and Health, Department of Health; Keith Darrall of the Laboratory of the Government Chemist; Martin Jarvis of the Imperial Cancer Research Fund; and Kuldip Bhamra, Vanessa Boag, Lee Buckingham, Mary Burton, Sarah Clark, Sarah Edwards, Sheila Foster, Heather Halls, Mavis King, Karen Kourellias, Christine Marsden, Gale Mead, Kevin Murphy, Martin Radley, and Karl Wallendszus of the Oxford Clinical Trial Service Unit and Epidemiological Studies Unit.

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A 28 year follow up of mortality among women who smoked during pregnancy

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Abstract

Objective—To investigate long term mortality among women who smoked during pregnancy and those who stopped smoking.

Design—A follow up of a geographically defined cohort from 1966 through to 1993.

Subjects—11 994 women in northern Finland expected to deliver in 1966, comprising 96% of all women giving birth in the area during that year. Smoking habits were recorded during pregnancy but not later.

Main outcome measure—Mortality by cause (571 deaths).

Results—The mortality ratio adjusted for age, place of residence, years of education and marital status was 2·3 (95% confidence interval 1·8 to 2·8) for the women who smoked during pregnancy and 1·6 (1·1 to 2·2) for those who stopped smoking before the second month of pregnancy, both compared with non-smokers. Among the smokers the relative mortality was higher for typical diseases related to tobacco intake, such as respiratory and oesophageal cancer and diseases of the cardiovascular and digestic organs and also for accidents and suicides.

Conclusion—The risk of premature death seems to be higher in women who smoke during pregnancy than in other women who smoke. This may be explained either by the low proportion of those who stop later and the high proportion of heavy smokers or by other characteristics of these subjects that increase the risk.

Introduction

The consequences for the child of maternal smoking during pregnancy have been well documented,[1] but less interest has been directed towards the mothers' prognosis. We analyse here 28 year mortality data on a geographically defined population of women who smoke during pregnancy; many background variables were recorded prospectively.

Methods

Population—The cohort consisted of 12 055 pregnant women (13 of them delivering twice) in the two most northern provinces in Finland, Oulu and Lapland, whose expected dates of delivery fell in 1966 and when the pregnancy resulted in a birth. The cohort covered 96% of all deliveries in the region in 1966.[2] The

Cigarette smoking, tar yields, and non-fatal myocardial infarction: 14 000 cases and 32 000 controls in the United Kingdom

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Abstract

Objectives—To assess the effects of cigarette smoking on the incidence of non-fatal myocardial infarction, and to compare tar in different types of manufactured cigarettes.

Methods—In the early 1990s responses to a postal questionnaire were obtained from 13 926 survivors of myocardial infarction (cases) recently discharged from hospitals in the United Kingdom and 32 389 of their relatives (controls). Blood had been obtained from cases soon after admission for the index myocardial infarction and was also sought from the controls: 4923 cases and 6880 controls were current smokers of manufactured cigarettes with known tar yields. Almost all tar yields were 7-9 or 12-15 mg/cigarette (mean 7·5 mg for low tar (< 10 mg) and 13·3 for medium tar (≥ 10 mg)). The cited risk ratios were standardised for age and sex and compared myocardial infarction rates in current cigarette smokers with those in non-smokers who had not smoked cigarettes regularly in the past 10 years.

Results—At ages 30-49 the rates of myocardial infarction in smokers were about five times those in non-smokers (as defined); at ages 50-59 they were three times those in non-smokers, and even at ages 60-79 they were twice as great as in non-smokers (risk ratio 6·3, 4·7, 3·1, 2·5, and 1·9 at 30-39, 40-49, 50-59, 60-69, 70-79 respectively; each $2P < 0{\cdot}00001$). After standardisation for age, sex, and amount smoked, the rate of non-fatal myocardial infarction was 10·4% (SD 5·4) higher in medium tar than in low tar cigarette smokers ($2P = 0{\cdot}06$). This percentage was not significantly greater at ages 30-59 (16·6% (7·1)) than at 60-79 (1·0% (8·5)). In both age ranges the difference in risk between cigarette smokers and non-smokers was much larger than the difference between one type of cigarette and another (risk ratio 3·39 and 3·95 at ages 30-59 for smokers of similar numbers of low and of medium tar cigarettes, and risk ratio 2·35 and 2·37 at ages 60-79). Most possible confounding factors that could be tested for were similar in low and medium tar users, with no significant differences in blood lipid or albumin concentrations.

Conclusion—The present study indicates that the imminent change of tar yields in the European Union to comply with an upper limit of 12 mg/cigarette will not increase (and may somewhat decrease) the incidence of myocardial infarction, unless they indirectly help perpetuate tobacco use. Even low tar cigarettes still greatly increase rates of myocardial infarction, however, especially among people in their 30s, 40s, and 50s; and far more risk is avoided by not smoking than by changing from one type of cigarette to another.

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Introduction

In countries such as the United Kingdom, where cigarettes have been used widely for several decades, tobacco now accounts for about 30% of all deaths in middle age, with lung cancer and coronary heart disease the most common fatal conditions.[1-3] Over the past few decades cigarettes have been altered in various ways, reducing the so called yields of tar and nicotine when smoked in a standard way by a machine. Typical British cigarettes had tar yields of 25-35 mg during the 1950s and 5-15 mg in 1990.[4] But, partly because the chief toxins in cigarette smoke are uncertain and partly because smokers may compensate for reduced yields (or other changes) by smoking cigarettes more actively,[5-10] the health effects of alterations in cigarette manufacture are unpredictable. Low tar cigarettes do cause substantial risks of cancer and heart disease, although the risk of lung cancer is less than with high tar cigarettes.[3 11-14] For heart disease, however, there remains uncertainty[15-17] about whether the rates have been decreased, increased, or not changed by alterations in cigarette composition over the past few decades. National heart disease mortality rates and trends are not informative because other factors cause such large differences in coronary heart disease between different populations and time periods. Instead, concurrent epidemiological comparisons within one population are needed.

But, although tobacco is a major cause of heart disease, particularly among young and middle aged adults, it is difficult for conventional prospective or retrospective studies to compare the risks from different types of cigarette. Only a narrow range of cigarette tar yields is concurrently available within one population, and the tar yields of cigarettes smoked by people in 1990 might correlate poorly with the tar yields smoked by these people years earlier. Hence, even large differences in risk between prolonged use of low, medium, and high tar cigarettes might produce only small differences in risk between current use of low and medium tar cigarettes. At younger ages the proportional difference in rates of coronary heart disease between smokers and non-smokers is particularly extreme, so any effect of cigarette type may also be extreme. Thus, to minimise the chances of a false negative result in a study of tar yields, the number of cases of myocardial infarction in middle aged cigarette smokers should be large—preferably several thousand—with at least as many controls. We achieved this by studying subjects from the United Kingdom who participated in the large ISIS (international studies of infarct survival) trials of the treatment of acute myocardial infarction,[18-20] by using postal questionnaires (copies available on request), rather than interviews, and by simplifying blood collection procedures.

aged 30-79 from the ISIS-3 or ISIS-4 trials who completed an epidemiological questionnaire sent to them a few months after their infarction. Those who were asked to complete it were all the survivors from ISIS-3, but from ISIS-4 only the survivors aged 30-59 who on admission to hospital were reported to be cigarette smokers. Thus, although only cases from ISIS-3 can be used to compare smokers with non-smokers, the cases from ISIS-4 strengthen the analyses of tar yields among smokers aged 30-59. The ISIS-3 questionnaire asked the cases to identify all their brothers, sisters, and children aged at least 30 who were resident in the United Kingdom. A similar "control" questionnaire was then sent to such relatives, accompanied by a second copy, which the relatives, if married, were to ask their spouse to complete. One reminder was sent to cases and relatives who did not reply, and inconsistencies or omissions were queried once.

Of the 20 681 ISIS-3 patients in the United Kingdom, 19 065 who were not known to be dead were posted the case questionnaire, of whom 1346 were found to be dead and 13 969 (79% of presumed survivors) completed it. The control questionnaire was sent to 30 247 relatives of ISIS-3 cases, of whom 75 were found to be dead and 21 995 (73% of presumed survivors) and 14 245 of their spouses completed it. Patients with a history of stroke, gastrointestinal bleeding, or ulcer tended not to have been recruited into the ISIS-3 trial,[4] and so people with such conditions were not eligible as cases or controls. Of those who completed questionnaires, 2002 cases and 3851 controls were excluded because they were under 30, over 79, or of unknown age or because they had a self reported history of "definite stroke" or of "bleeding or ulcer in (or near) the stomach."

ISIS-4 patients in the United Kingdom aged 30-59 who were described at trial entry as current smokers were also sent the questionnaire. The response rate for such patients was similar in both trials. Any of these ISIS-4 patients whose questionnaire response indicated that they were not cigarette smokers at the time of their infarction were excluded. ISIS-4 (and, to some extent, ISIS-3) tended to exclude patients with shock or persistent hypotension,[5] but such exclusions should not bias the epidemiological analyses of tobacco use.

BLOOD SAMPLES

Blood was to be taken from patients in ISIS-3 immediately after randomisation but before the trial treatments and collected in a 10 ml vacutainer containing 0·12 ml preservative (15% potassium EDTA with aprotinin 0·34 mmol/l: Becton Dickinson). On returning their questionnaire, controls were sent an identical container for their general practitioner to collect blood. Case and control containers were sent by first class post to Oxford. Controls were sent one reminder about giving a sample. After a mean of two days in the post the blood was centrifuged, the packed cell volume was recorded, and the plasma and buffy coat were aliquoted for storage at −40°C. Blood arrived from 97% of ISIS-3 cases and 45% of controls, but breakages or haemolysis rendered 6% of these samples unusable. The present blood analyses involve only correlations of smoking with blood biochemistry results, and these analyses should not be materially biased by low response rates.

Plasma cotinine concentration was measured in controls who were current cigarette smokers, and in a 3% sample of controls who reported no current use of tobacco, by means of antibodies developed by Knight Diagnostic Laboratories with gas chromatography. Beckman CX-4 and CX-5 autoanalysers were used for measuring concentrations of cholesterol and albumin (both with Beckman reagents) and apolipoproteins A_1 and B (with Immuno reagents). To correct for discoloration from haemolysis, an initial blank reading was subtracted from the final reading. Samples from a large plasma pool were included in each analytical run, yielding coefficients of variation of 2% for cholesterol and albumin and 4% for apolipoproteins.

QUESTIONNAIRES

Information was sought on sex, age, body size, smoking, drinking, past health, and relatives. Cases were asked about their habits and history just before their index myocardial infarction (because having a heart attack may alter a patient's habits), while controls were asked about their present habits. Hence, questions to cases often began, "Before your recent hospital admission. . . ." Both cases and controls were asked to list how many relatives of certain types they had, but only cases were to provide contact details. In other respects case and control questionnaires were identical. The medical history section was non-technical and recorded various conditions that might be associated with exclusion from the randomised trial (see above) or that might affect, or be affected by, smoking. After the question of whether they had "ever smoked regularly (ie on most days for at least a year)" the rest of the cigarette section was to be completed only by those who replied "yes." It dealt with the age at which the subject had first and last smoked regularly, whether any cigarettes had been smoked in the previous month, the number smoked per day when the subject had last smoked cigarettes regularly, and the way in which cigarettes were smoked. People were to tick against 137 detailed brand names the one that, when they last smoked, they usually smoked most of—or, if it was not on the list, to write out its exact name (and, whenever possible, to enclose the packaging of that brand with the questionnaire). For the few who listed more than one brand, the average of the yields was taken. Ninety eight per cent of controls and 98% of cases who currently smoked only manufactured cigarettes with a known tar yield, and both reported using their current brand for, on average, the past 10 or 11 years.

DEFINITIONS OF CIGARETTE SMOKING STATUS

Respondents were classified as current cigarette smokers (26% of the controls: those who had smoked cigarettes in the previous month, plus the few who failed to answer this yes/no question but gave other evidence of current cigarette use); other tobacco users (3%: pipes, cigars, or smokeless tobacco in the past year); or as not using tobacco (71%: all others). In table I these are further subdivided. Because of the possible confusion between those who stopped smoking many years ago and those who never smoked, the main comparison group was defined as non-smokers who had not used cigarettes regularly in the past 10 years.

ESTIMATED 1990 TAR YIELDS

The United Kingdom's government chemist conducts surveys of common cigarette brands, measuring tar, nicotine, and carbon monoxide yields, twice a year (R Waller, personal communication). During the late 1980s the annual decrease in sales weighted yields was about 2-3% for tar, 1-2% for nicotine, and zero for carbon monoxide (J Rentoul, personal communication).[4] Most ISIS-3 cases replied in 1990 about habits

replied in 1992–3 (mean date of infarction: July 1992). To avoid secular trends in yields introducing minor biases, the mid-1990 survey results for each cigarette brand were used (R Wallery personal communication). If a brand was assayed only earlier or later than mid-1990, yields from the closest survey were extrapolated to mid-1990 by annual decreases of 2·5% in tar and 1·5% in nicotine.

RESURVEY OF CONTROLS A FEW YEARS LATER

To check reproducibility, about 2000 controls who originally returned both questionnaire and blood sample (and whose replies indicated no previous vascular disease) were sent the same questionnaire and blood kit again about 2-3 years later. To avoid oversampling young controls, the random sample was stratified with respect to sex and age in groups of five years. Seventy per cent (1388/1996) returned the questionnaire, 95% (1324/1388) of whom gave blood.

STATISTICAL METHODS

The analyses are all unmatched—that is, they compare cases with all controls, not just with their own relatives—and for tar yield analyses among smokers the controls are as relevant to ISIS-4 as to ISIS-3 cases. All analyses of myocardial infarction rates were stratified either for sex and five year age group or for these factors and amount smoked (five categories; see below). Calculations of risk ratios—or, equivalently, relative risks—entailed unmatched stratified logistic regression (fitted by unconditional maximum likelihood), with one extra term included for each stratum. Risk ratios are often given with 95% confidence intervals. Two sided probability values (2P) are used.

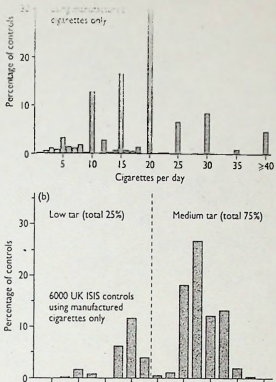

FIG 1—*Replies by controls who smoked manufactured cigarettes only. (a) Reported daily cigarette use (34% reported 20 cigarettes per day, and 85% reported 10-30). (b) Tar yields in 1990 of the brands reported*

Results

FREQUENCY DISTRIBUTIONS OF SMOKING HABITS

Table I shows the numbers of controls and cases in various categories of tobacco use subdivided by sex and by age. The age range of chief relevance to the tar yield analyses is 30-59, and among controls in this range 28% both of men and of women were current cigarette smokers, in close agreement with nationally representative, interviewer administered surveys in the early 1990s.[23] Twenty two per cent of these controls were current users of manufactured cigarettes only with known tar yields.

Figure 1 gives, for controls who currently used manufactured cigarettes only, the frequency distribution of (*a*) the reported number smoked per day and (*b*) the estimated 1990 tar yield. Self reported cigarette consumption was categorised as 1-9, exactly 10, 11-19, exactly 20, and ≥21 cigarettes a day; 85% reported smoking 10-30 cigarettes a day. The tar yields show a bimodal distribution, with commonest values 7-9 or 12-15 mg/cigarette. Tar yields of 10 mg were rare, which makes this a natural point of subdivision, unaffected by any slight differences in dates of case and control responses, to define two main categories: low tar (< 10 mg, mean 7·5 mg) and medium tar (≥ 10 mg, mean 13·3 mg). Medium tar is sometimes split into 10-12, 13, and ≥ 14 mg/cigarette. This definition of low tar is also used by the Department of Health (R Waller, personal communication).[4] Twenty five per cent of the smokers in figure 1b use low tar cigarettes, as in the nationally representative survey in 1990.[23] Almost all

BLE I—*Tobacco use in cases and controls aged 30-79 with questionnaires returned*

		Current cigarette smoker				Other tobacco		Not using tobacco			
		Manufactured cigarettes and no other tobacco		Other cigarette users	% Now using any cigarettes	Smoking pipe or cigar but no cigarettes	Using smokeless tobacco only	Former regular cigarette smoker		Never regular cigarette smoker	Total*
		Tar known	Tar unknown					< 10 years ago	≥ 10 years ago		
ontrols:		6880	162	1389	26	1031	71	3181	5502	14173	32389
Men	30-59	2184	35	955	28	676	40	1128	1765	4357	11163
Women	30-59	3264	60	153	28	11	1	1145	1385	6559	12578
Men	60-79	563	21	251	20	337	28	465	1506	906	4077
Women	60-79	869	46	27	21	7	2	443	826	2351	4571
SIS-3 cases:		3453	65	1063	38	859	48	1311	2070	3098	11967
Men	30-59	1351	23	619	48	405	26	424	467	804	4119
Women	30-59	520	8	33	60	0	0	98	47	236	942
Men	60-79	858	16	382	27	450	20	537	1268	1171	4702
Women	60-79	724	18	29	35	4	2	252	288	887	2204
SIS-4 cases:		1470	34	455	—	—	—	—	—	—	1959
Men	30-59	1117	29	430	—	—	—	—	—	—	1576
Women	30-59	353	5	25	—	—	—	—	—	—	383
otal		11503	261	2907	—	1890	119	4492	7572	17271	46315

Current users and non-users.

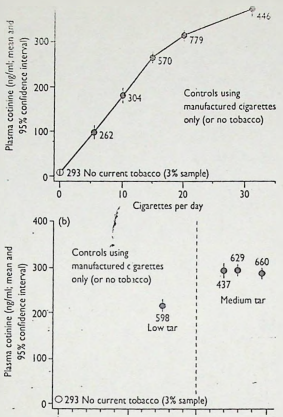

FIG 2—*Cotinine by cigarette smoking habit in controls. (a) Cotinine versus daily cigarette use. (b) Cotinine versus tar yield of reported brand. In the low and medium tar smokers whose blood samples were assayed, mean plasma cotinine concentrations were 217 and 292 ng/ml, mean cigarettes a day were 15·8 and 18·7, and mean yields per cigarette were 7·4 and 13·3 mg tar, 0·75 and 1·18 mg nicotine, and 8·4 and 15·0 mg carbon monoxide. Blood was taken on average of eight months after questionnaire, and in 12 out of 293 whose questionnaire had indicated no smoking cotinine concentration (mean 20·8 ng/ml) indicated current tobacco use*

TABLE II—*Non-fatal myocardial infarction: age-specific effect of cigarette use in people with no history of major neoplastic or vascular disease*

Age (years)	Current smoker of manufactured cigarettes only		Non-smoker with no regular cigarette use in past 10 years		Myocardial infarction*	
	Cases	Controls	Cases	Controls	Risk ratio (95% confidence interval)	Test statistic†
30-39	78	1784	35	4873	6·33 (4·22 to 9·51)	8·9
40-49	293	1497	190	4306	4·66 (3·82 to 5·69)	15·1
50-59	435	861	508	2701	3·10 (2·64 to 3·65)	13·7
30-59	806	4142	733	11880	3·85 (3·41 to 4·34)	22·1
60-69	416	653	707	2299	2·54 (2·16 to 2·98)	11·3
70-79	111	163	369	942	1·92 (1·45 to 2·54)	4·6
60-79	527	816	1076	3241	2·37 (2·06 to 2·72)	12·1

*Smoker v. non-smoker rates standardised for age and sex.
†Number of standard deviations by which the logarithm of the risk ratio differs from zero.

used filtered brands (100% bf the low tar group, 96% of the medium tar group), so filters accounted for little of the difference in yields between low and medium tar cigarettes in 1990.

RELATION BETWEEN QUESTIONNAIRE AND COTININE CONCENTRATIONS

Figure 2 shows the relation between plasma cotinine concentrations and (*a*) reported daily cigarette use and (*b*) tar yield for controls reporting use of manufactured cigarettes only or no current tobacco use. The mean cotinine concentration was very low in the self reported non-smokers, which helps validate both questionnaire and laboratory results. Among cigarette smokers there was a strong relation between cotinine concentration and the amount reported to be smoked, which again helps validate the questionnaire. The downward curvature in figure 2a suggests that those who smoke more cigarettes may absorb less nicotine from each one or that those reporting large numbers include disproportionately many who overreported, or both. Either way, self reported cigarette consumption provides only approximate information about the real doses of nicotine and of other substances.

third higher among the controls who smoked medium tar cigarettes (low tar 217 ng/ml v medium tar 292 ng/ml). But the smokers of low tar cigarettes reported smoking 15·8 cigarettes a day compared with 18·7 a day for those in the medium tar group. After standardisation for age, sex, and amount smoked, however, the mean plasma cotinine concentration was still 19% higher with medium tar cigarettes. This difference in cotinine is still highly significant ($2P < 0{\cdot}00001$), which helps validate the categorisation of tar yield based on the questionnaire. But it is less extreme than the difference of over 50% in the nicotine yield per cigarette measured by machine (0·75 mg and 1·18 mg). This may be partly because the categorisation of tar yields is imperfect, and partly because smokers of low yield cigarettes compensate by taking in more smoke per cigarette. But, since this categorisation predicts highly significant biochemical differences in blood taken months later (figure 2b), it has some validity.

CIGARETTE USE AND NON-FATAL MYOCARDIAL INFARCTION

When those using manufactured cigarettes only were compared with non-smokers who had not smoked cigarettes regularly in the past 10 years (excluding in both cases those using any other type of tobacco), the relative risks for non-fatal myocardial infarction in people with no previous neoplastic or major vascular disease depended strongly on age (table II, fig 3). As is the case for mortality from coronary heart disease,[12] the risk ratio comparing smokers with non-smokers was greater at younger ages, reinforcing the need for the relevance of tar yields to be considered separately at younger and older ages.

TAR YIELDS AND NON-FATAL MYOCARDIAL INFARCTION

Information about the relevance of tar yields comes from current users of manufactured cigarettes only. Of these, much the most informative are the 9000 aged 30-59, rather than the 3000 aged 60-79. This is not only because the numbers are larger but also because the risk ratio when smokers are compared with non-

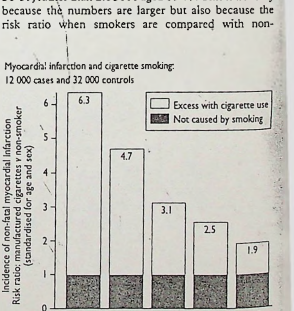

FIG 3—*Cigarettes and non-fatal myocardial infarction as a first event: risk ratios at various ages. Results in people with no previous history of major neoplastic or vascular disease. Each risk ratio is standardised for sex and for quinquennium of age, and compares those using manufactured cigarettes only with those who were not currently using any tobacco and had not been regular cigarette smokers at any time in the past 10 years. Risk ratio is given within each column. (As all cases recruited from ISIS-4 were cigarette smokers, this figure involves cases only from ISIS-3)*

TABLE IV—*Risk ratios for myocardial infarction in relation to current smoking of medium and low tar cigarettes*

	No currently using manufactured cigarettes only, with known 1990 tar yield			Ratio of non-fatal myocardial infarction in smokers of medium tar v smokers of low tar cigarettes (with 95% confidence interval and significance)		
	"Cases" of infarction* ISIS-4	"Cases" of infarction* ISIS-3	Controls (no infarction)	Standardised for age and sex only	Standardised for age, sex, and amount smoked	Standardised for age, sex, and amount smoked: no previous disease†
Age 30-59:						
Low tar	274	359	1268	1·203	1·166	1·075
Medium tar	1196	1512	4180	1·046 (1·016 to 1·364) 2P = 0·004	1·010 (1·025 to 1·326) 2P = 0·02	0·900 to 1·283) 2P > 0·1
Age 60-79:				1·046	1·010	1·010
Low tar	—	438	433	(0·890 to 1·230)	(0·856 to 1·191)	(0·771 to 1·323)
Medium tar	—	1144	999	2P > 0·1	2P > 0·1	2P > 0·1
All 30-79:				1·142	1·104	1·055
Low tar	274	797	1701	(1·034 to 1·260)	(0·998 to 1·222)	(0·910 to 1·223)
Medium tar	1196	2656	5179	2P = 0·008	2P = 0·06	2P > 0·1

*Proportions smoking low tar rather than medium tar cigarettes were similar in ISIS-4 and ISIS-3; after standardisation for age, sex, and amount smoked, the odds ratio comparing the two tar yield categories in the two studies was 1·000 (SD 0·091).

†For comparison of the effects of different tar yields, inclusion of patients with some previous neoplastic or vascular disease may well produce no material bias and helps stabilise the estimates.

TABLE V—*Associations between smoking habits and blood lipid concentrations. Values are means (SE) standardised for age, sex, and case-control status*

Lipid measurement	Cigarette use			Cigarette tar yield		
	Current smoker of manufactured cigarettes only (n=1256)	Non-smoker with no cigarette use in past 10 years (n=3183)	Significance	Low tar (n=295)	Medium tar (n=942)	Significance
Cholesterol (mmol/l)	5·92 (0·03)	5·91 (0·02)	NS	6·01 (0·06)	6·02 (0·03)	NS
Apolipoprotein A_1 (g/l)	1·273 (0·006)	1·288 (0·004)	2P = 0·05	1·266 (0·013)	1·264 (0·007)	NS
Apolipoprotein B (g/l)	1·194 (0·008)	1·165 (0·005)	2P = 0·004	1·222 (0·016)	1·226 (0·009)	NS

TABLE VI—*Reproducibility of smoking classification*

Response to repeat questionnaire 2-3 years later	Response to original questionnaire				
	Currently using tobacco		Not using tobacco		
	Manufactured cigarettes only	Other tobacco user	Former cigarette smoker: <10 years	Former cigarette smoker: ≥10 years	Never cigarette smoker
Manufactured cigarettes only	99*	9	8	5	0
Other tobacco user	1	86	7	3	3
Former cigarette smoker: <10 years	22	12	50	11	0
≥10 years	2	18	37	370	15
Never cigarette smoker	4	9	2	21	591

*Ninety seven of these had known tar yield at both enquiries (65 classified as medium tar originally and medium tar later, 21 as medium then low, 8 as medium then low, 3 as low then medium).

smokers is more extreme in middle than in old age. As there was no significant difference between the tar yields of cases aged 30-59 in ISIS-3 and in ISIS-4 (table III), the groups were combined.

Table III provides age-sex standardised comparisons of non-fatal myocardial infarction in smokers of low tar versus smokers of medium tar cigarettes. Overall, there were only slight effects of the tar yield. The mean daily number of cigarettes smoked was slightly higher in the medium tar than in the low tar cigarette smokers (19·0 *v* 17·1). When standardised not just for age and sex but also for the daily number of cigarettes smoked, the incidence of myocardial infarction was 10·4% (SD 5·4) higher in medium than in low tar cigarette smokers (2P = 0·06). This difference was non-significantly greater at ages 30-59 (16·6% (7·1) higher; 2P = 0·02) than at 60-79 (1·0% (8·5) higher; 2P > 0·1) (fig 4). As these two results are not significantly different from each other, they do not prove that tar yields are of greater proportional importance to the cardiotoxicity of cigarettes in middle than in old age, especially since the smoker versus non-smoker risk ratios are less extreme in old age. In both age ranges the difference between cigarette smokers and non-smokers was much larger than the difference between one type of cigarette and another: the risk ratios were 3·39 and 3·95 for smokers of similar numbers of low and of medium tar cigarettes at ages 30-59 and were 2·35 and 2·37 at ages 60-79. (Table III shows that results were similar when these comparisons were based on the smaller numbers of cigarette smokers with no reported history of neoplastic or major vascular disease.)

POTENTIAL CONFOUNDING FACTORS

Table IV relates smoking to blood lipid concentrations among ISIS-3 cases entering the trial within 0-4 hours of pain onset whose blood spent only one or two days in the post, and among one randomly chosen control per case (matched for age, sex, and days sample spent in the post). Apolipoprotein A_1 was 1·2% lower and apolipoprotein B 2·4% higher in smokers than in non-smokers, but these differences are too small to account for much of the excess risk among smokers.

There were no significant differences in blood lipid concentrations (or albumin concentration, data not shown) between smokers of low and of medium tar cigarettes, either overall or in those aged 30-59 (data not shown). For many factors there were likewise no significant differences between smokers of low and medium tar cigarettes. These include self reported height, weight, loneliness, depression, worry, insomnia, teenage acne, tea consumption, alcohol consumption, and whether living with a spouse. For a few factors, however, there were definite differences even after standardisation for age and sex. (Multivariate adjustment for these observed differences would make little difference, but these differences point to the possibility of others existing.) Those who smoked low tar cigarettes were, on average, almost six months older when they left full time education (mean leaving age 15·9 years for low tar group *v* 15·5 years for medium tar), were more likely to say that they had matured physically "later than average" (13·4% *v* 10·5%), had "softer hands than average" (14·4% *v* 11·0%), had been regular drinkers of coffee (75% *v* 67%), were older when they started to smoke (18·8 *v* 17·9 years old), and had changed to their current brand more recently (7·9 *v* 10·1 years previously). These suggest a general tendency for those who smoke medium tar cigarettes to include a slightly larger proportion of manual workers, and to have slightly less education. (Likewise, unpublished analyses by M Jarvis of the 1990 and 1992 general household surveys in the United Kingdom found significantly higher "indices of deprivation" in users of medium than of low tar cigarettes.)

REPRODUCIBILITY OF SMOKING CLASSIFICATION

A total of 1388 controls repeated the questionnaire a few years later, and table V compares their two replies. When subdivided three ways (manufactured cigarettes only; other tobacco or ex-cigarette smoker < 10 years; remainder), 90% remained in the same category; of the 97 who smoked only manufactured cigarettes with tar known on both occasions, 89% had continued to smoke medium or low tar cigarettes as originally. Overall, there was a 5% shift towards the low tar category, in line with national trends, and the correlation coefficient between the two assessments of tar yield was 0·71.

Discussion

When cigarette smokers are compared with non-smokers the risk ratio for myocardial infarction is much more extreme in early adult life than in old age. The numbers contributing to figure 3 are unusually large (12 000 cases and 32 000 controls) and so the pattern of steadily increasing risk ratio with younger

hazards at the extremes of the age range of 30-79. The risk ratio is twofold at ages 70-79, but it is almost fourfold at ages 30-59 (threefold at 50-59 but fivefold at 30-49). Even these large differences have probably been somewhat diluted by the misclassification of some smokers or non-smokers. Had it been possible, with no classification errors, to compare persistent cigarette smokers with lifelong non-smokers then the risk ratios would probably have been still more extreme than those in figure 3, and would have been at least fourfold at ages 30-59. As most of the excess risk associated with smoking is caused by smoking,[12] this fourfold risk ratio implies that about three quarters of the myocardial infarctions among cigarette smokers aged 30-59 were caused by tobacco (two thirds at ages 50-59, but four fifths at ages 30-49).

Any differences in the risk of heart disease between those who are smoking different types of cigarette must be much less extreme than the differences between smokers and non-smokers, so especially large studies are needed to assess them. Moreover, epidemiological studies that were undertaken when tar yields below 15 mg were still uncommon (N J Wald *et al*, unpublished data)[13-30] are of limited contemporary relevance in countries such as the United Kingdom where tar yields above 15 mg have already virtually disappeared (fig 1b) and where a European Union upper limit of 12 mg is soon to be enforced. As no other large recent studies are available, our current findings stand alone.

For tar yields the central finding is that after standardisation for age, sex, and number of cigarettes, the incidence of non-fatal myocardial infarction seemed to be about 10% greater with medium tar than with low tar cigarettes (95% confidence interval 0 to 22%, table III). Even if this 10% difference was highly statistically significant (which it is not: 2P=0·06) it would still not be epidemiologically secure. It is uncertain how much selective emphasis to put on the data at ages 30-59 as opposed to those at 60-79, how much selective emphasis to put on the data from people with no previous disease, and how much to emphasise

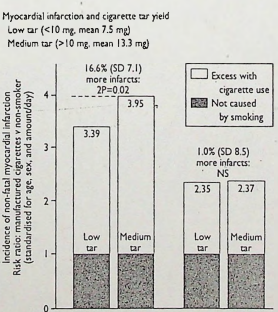

FIG 4—*Cigarette tar yields and risk of non-fatal myocardial infarction. Standardised for age, sex, and amount smoked, comparisons at ages 30-59 indicate that non-fatal myocardial infarction rates were 1·166 (SD 0·071) times as great among medium tar as among low tar cigarette smokers (2P=0·02; table III). The same standardised comparisons at ages 60-79 give 1·010 (0·085) (NS). These two estimates (1·166 and 1·010) are combined with the risk ratios of 3·85 and 2·37 for cigarette smokers versus non-smokers (fig 3) to yield the cited risk ratios for smokers of low and medium tar cigarettes: 3·39 and 3·95 at ages 30-59 and 2·35 and 2·37 at ages 60-79*

Key messages

- Non-fatal myocardial infarction rates are five times as great among cigarette smokers as among non-smokers at ages 30-49, three times as great at ages 50-59, and twice as great at ages 60-79
- Among cigarette smokers four fifths of myocardial infarctions at ages 30-49 were caused by tobacco, two thirds at ages 50-59, and half at ages 60-79
- The risks seem to be slightly greater with medium tar than with low tar cigarettes, but this difference is not definite
- Differences in risk between cigarette smokers and non-smokers are far greater than any differences in risk between one type of cigarette and another
- Far more myocardial infarctions could be avoided by not smoking than by changing from one type of cigarette to another

analyses that are standardised for the amount smoked. (Those using low tar cigarettes reported smoking slightly fewer than those smoking medium tar cigarettes, and if lower daily consumption is chiefly a consequence of lower yields of tar, nicotine, and other smoke components then it should not be standardised for.) Hence, table III reports several different comparisons of disease rates in smokers and in non-smokers, with differences that are sometimes more and sometimes less than 10%. Also, there was a slight tendency for tar yields to be inversely related to education and to various other aspects of social class. It is difficult to see how some of these uncertainties can be resolved: large scale randomisation is impracticable, and even if the present study could have been much larger, thereby narrowing the confidence intervals, the possibility of confounding would remain.

Despite these uncertainties, however, the present results provide some reassurance to those in government or in industry who could direct decreases in cigarette tar yields to reduce cancer incidence.[3 31-34] They indicate that such changes will not substantially increase the incidence of myocardial infarction and may well decrease it. Thus, the limit of 12 mg/cigarette on tar yields that is now being introduced in the European Union should help limit the number of premature deaths from tobacco, unless governments or smokers come to regard reductions in tar yield as substitutes for the avoidance of cigarettes, for in developed countries tobacco remains much the most important cause of premature death. This is particularly so for men, with tobacco now causing about a third of all deaths in middle aged men. But where women have been smoking cigarettes for some decades (as, for example, in the United Kingdom or the United States) tobacco also already causes about a quarter of all the deaths in middle aged women.[1]

For the general population, therefore, the most important finding is not the slight and uncertain difference in figure 4 between one type of cigarette and another but the large and definite difference in figure 3 between cigarette smokers and non-smokers, particularly in early middle age. Irrespective of whether low or medium tar cigarettes are used, about three quarters of the smokers who have a heart attack in their 30s, 40s, or 50s need not have done so, and far more heart attacks could be prevented by not smoking than by reducing cigarette tar yields.

The chief acknowledgment is to the patients and their

readership who collaborated in this study, and to the medical and nursing staff from more than 100 hospitals in the United Kingdom listed in the ISIS reports."[19] We particularly thank Peter Froggatt, Cheryl Swann, and Robert Waller of the Independent Scientific Committee on Smoking and Health, Department of Health; Keith Darrall of the Laboratory of the Government Chemist; Martin Jarvis of the Imperial Cancer Research Fund; and Kuldip Bhamra, Vanessa Boag, Lee Buckingham, Mary Burton, Sarah Clark, Sarah Edwards, Sheila Foster, Heather Halls, Mavis King, Karen Kourellias, Christine Marsden, Gale Mead, Kevin Murphy, Martin Radley, and Karl Wallendszus of the Oxford Clinical Trial Service Unit and Epidemiological Studies Unit.

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Conflict of interest: None.

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A 28 year follow up of mortality among women who smoked during pregnancy

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Abstract

Objective—To investigate long term mortality among women who smoked during pregnancy and those who stopped smoking.

Design—A follow up of a geographically defined cohort from 1966 through to 1993.

Subjects—11 994 women in northern Finland expected to deliver in 1966, comprising 96% of all women giving birth in the area during that year. Smoking habits were recorded during pregnancy but not later.

Main outcome measure—Mortality by cause (571 deaths).

Results—The mortality ratio adjusted for age, place of residence, years of education and marital status was 2·3 (95% confidence interval 1·8 to 2·8) for the women who smoked during pregnancy and 1·6 (1·1 to 2·2) for those who stopped smoking before the second month of pregnancy, both compared with non-smokers. Among the smokers the relative mortality was higher for typical diseases related to tobacco intake, such as respiratory and oesophageal cancer and diseases of the cardiovascular and digestic organs and also for accidents and suicides.

Conclusion—The risk of premature death seems to be higher in women who smoke during pregnancy than in other women who smoke. This may be explained either by the low proportion of those who stop later and the high proportion of heavy smokers or by other characteristics of these subjects that increase the risk.

Introduction

The consequences for the child of maternal smoking during pregnancy have been well documented,[1] but less interest has been directed towards the mothers' prognosis. We analyse here 28 year mortality data on a geographically defined population of women who smoke during pregnancy; many background variables were recorded prospectively.

Methods

Population—The cohort consisted of 12 055 pregnant women (13 of them delivering twice) in the two most northern provinces in Finland, Oulu and Lapland, whose expected dates of delivery fell in 1966 and when the pregnancy resulted in a birth. The cohort covered 96% of all deliveries in the region in 1966.[2] The

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7-20

ortality Attributable to igarette Smoking in China

g Lam, MD; Yao He, PhD; Lan Sun Li, MD; Liang Shou Li, MD; Shu Fang He, MD; Bao Qing Liang, MD

ext.—The few published prospective studies of smoking and mortality in have reported low relative risks, but the durations of follow-up were short. ective.—To assess the mortality of ever- and never-smokers in a cohort af- years of follow-up.

gn, Setting, and Subjects.—A cohort analytic study in a machinery factory n China, involving 1696 people aged 35 years or older (1124 men and 572 n) examined in May 1976.

n Outcome Measures.—All-cause and tobacco-associated mortality.

ults.—A total of 56% of the men and 12% of the women were ever-smokers seline. Through August 31, 1996, 218 persons (173 men and 45 women) had The relative risks (95% confidence intervals [CIs]) for ever smoking (after ad- for age, marital status, occupation, education, diastolic blood pressure, and ride and cholesterol levels) for deaths resulting from all causes, all cancer, ronary heart disease were, respectively, 2.42 (95% CI, 1.72-3.42), 2.50 (95% 1-4.43), and 3.61 (95% CI, 1.35-9.67) in men and 2.32 (95% CI, 1.18-4.56), 95% CI, 0.50-7.92), and 4.67 (95% CI, 0.78-27.8) in women.

nclusions.—Previous prospective studies of smoking-related mortality in tended to underestimate the risks, probably because of short durations of -up. We have demonstrated that smoking is a major cause of death in China, he risks are similar to those seen in the United States and the United King- Thus, about half of the 300 million smokers in China will eventually die of ng-related diseases if urgent tobacco-control measures are not instituted to st this growing epidemic.

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IDENCE OF the adverse health ef- g attributed to smoking derives ly from epidemiologic studies, par- rly prospective studies from the ed Kingdom and the United States, e the epidemic of tobacco-related ses reached its peak in the 1980s. ally, China is now the largest acco-producing country in the world, It has the most smokers—over 300 on.[1] Smoking prevalence in China increased rapidly in recent decades, compared with the West, China is only at the early stage of the epidemic. Data from a large case-control study in China estimated deaths from smoking at about 500 000 per year.[2]

Few prospective studies of smoking and mortality in China have been published; one recently appeared in a major international journal,[3] and several have appeared in Chinese journals.[4-7] All had a short duration of follow-up (4 to 13 years), and some were limited to men only.[4,5,7] One study compared tobacco-related mortality in Shanghai and the United States and concluded the risk of mortality in the Chinese was lower.[3] However, as the study from Shanghai only described the early stage of the Chinese epidemic[8] and as the risk estimates might have been underestimated, comparison of risk estimates from a developing nation in the early stage of the epidemic with those from a nation in the mature stage could be premature.

Our objective in this cohort study in Xi'an, China, was to examine the relationship between smoking and mortality in men and women after 20 years of follow-up.

METHODS

Subjects

From March to May 1976, a cross-sectional survey of risk factors and prevalence of coronary heart disease was carried out in a machinery factory in Xi'an by both the teaching hospital of the Fourth Military Medical University and the workers' hospital of the factory. All employees of the factory aged 35 years or older were included. A total of 1842 persons (1179 men and 663 women) were examined, accounting for 90% of workers (96% of those aged 40 years or older).

See also pp 1500 and 1531.

In early 1994, we began to review the records created at baseline and found that 1696 persons (1124 men and 572 women) had data on birth month and year, sex, marital status, education level, occupation, systolic and diastolic blood pressure, serum cholesterol and triglyceride levels, and smoking history (never, current, or ex-smoker; amount smoked daily; years of smoking). No baseline data were found for 146 subjects. We suspect their records were discarded because of incomplete data collection at baseline. These 146 subjects were not included in the present study.

Blood pressure measurement followed the 1974 Chinese national standards (take the measurement on the right arm, with the subject sitting, using a mercury sphygmomanometer; use the mean of 2 readings that must not differ by 4 mm Hg or more). Serum lipid analyses were performed on samples obtained after a 12-hour fast and were carried out in the laboratory of the teaching hospital. The Salkowski test ($Fe[SO_4]_3$) was used for total cholesterol, and the Hontzsch test

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Table 1.—Characteristics of 1124 Men and 572 Women in the Cohort at Baseline in 1976*

Characteristics	Men, No. (%)	Women, No. (%)
Age, mean (SD), y	45.4 (5.6)	43.3 (4.6)
Marital status		
Single	1 (0.1)	0 (0)
Married	1017 (90.5)	487 (85.1)
Divorced	21 (1.9)	8 (1.4)
Widowed	85 (7.6)	77 (13.5)
Occupation		
Technical	150 (13.3)	60 (10.5)
Cadre	409 (36.3)	86 (15.0)
Worker	566 (50.4)	426 (74.5)
Education, y		
0-3	34 (3.0)	78 (13.6)
4-6	258 (23.0)	220 (38.5)
7-9	470 (41.8)	150 (26.2)
9-12	210 (18.7)	87 (15.2)
≥13	152 (13.5)	37 (6.5)
Blood pressure, mm Hg		
Diastolic, mean (95% CI)†	83.2 (82.5-83.9)	82.1 (81.0-83.1)
Systolic, mean (95% CI)	125.2 (124.1-126.4)	126.3 (124.4-128.1)
Total cholesterol, mean, mmol/L (95% CI)	4.63 (4.58-4.69)	4.62 (4.55-4.69)
mg/dL	179	178
Triglycerides, mean, mmol/L (95% CI)	1.17 (1.12-1.20)	1.13 (1.09-1.17)
mg/dL	104	100
Smoking habit		
Current smoker	607 (54.0)	68 (11.9)
Ex-smoker	25 (2.2)	3 (0.5)
Ever-smoker (current and ex-smokers)	632 (56.2)	71 (12.4)

*Values are expressed as number (percent) unless otherwise indicated.
†CI indicates confidence interval.

(acetylacetone) was used for triglycerides.[7] Factory physicians classified only 7.2% of subjects, according to their work sites, as being exposed to factors that posed occupational hazards, such as chemicals like solvents, paints, and gases (3.7%) and physical factors such as noise (2.4%) and high temperature (1.1%). Because so few subjects were exposed, the contribution of occupational exposure to mortality could not be examined.

Vital status was assessed through August 31, 1996. Two senior physicians at the factory hospital were responsible for overseeing the follow-up. Interviewers were recruited from retired female cadres or technicians who had postsecondary education. Training sessions for ascertainment of vital status and pilot study testing of the interview instrument were carried out before the main fieldwork.

Vital status was traced from personnel files and union records. Face-to-face or telephone interviews were conducted with all accessible subjects. Those who were alive but had left Xi'an were traced by letters. Vital status was also confirmed through interviews of coworkers or relatives. If vital status was unknown, the last date the subject was known to be alive was recorded. For those who died after May 31, 1976, cause of death was obtained from medical records of the hospital or death certificates in the local police departments. This information was reviewed by 2 senior physicians of the Fourth Military Medical University teaching hospital and then coded according to the *International Classification of Diseases, Ninth Edition*.

The data were entered (double entry, once in Xi'an and once in Hong Kong) and managed by Foxbase 2.1 (Fox Holdings Inc, Perrysburg, Ohio). Only the baseline data from 1976 were used to examine the mortality of ever-smokers (including current and ex-smokers) compared with never-smokers. Kaplan-Meier survival analysis and log-rank tests were used to compare cumulative survival. The Cox regression model was used to estimate relative risk (RR) and 95% confidence interval (95% CI) after adjusting for potential confounders (age, marital status, occupation, education, diastolic blood pressure, and triglyceride and total cholesterol levels) for each sex separately. The date of death, the last date of known survival, or the last date of follow-up for those who were alive on that date (August 31, 1996) was used as the right censored date in the proportional hazards analysis as appropriate. The likelihood ratio test and the global χ^2 were used to test the Cox regression models. All statistical analyses were carried out using SPSS for Windows (6.1).[10]

RESULTS

The study entry date for all subjects was set as May 31, 1976. Through August 31, 1996, 1471 subjects (945 men and 526 women) were alive, and 218 (173 men and 45 women) had died. Seven (6 men and 1 woman) were lost to follow-up, and their last day at the factory was known date of survival was considered the censored date. The number of person-years of follow-up was 32 400, the mean duration was 19.1 years (range, 0.9-20.2 years).

Causes of death were assigned as university teaching hospitals or hospitals in the city hospital level or above for 201 deaths (84%); for 17 deaths (8%) cause of death were assigned at hospitals at the county level. Seventeen subjects (8%) died at home; the causes of death were determined from the diagnosis at the last hospital admission, and the underlying cause of death was recorded in the death certificate.

Demographic characteristics of the cohort at baseline in 1976 are shown in Table 1. The mean serum cholesterol concentrations for men (4.63 mmol/L [179 mg/dL]) and women (4.62 mmol/L [178 mg/dL]) were similar.

At baseline, 54% of the men and 11% of the women were current smokers. Because there were so few ex-smokers (28 persons only), they were grouped with current smokers as ever-smokers (56% in men and 12.4% in women). The prevalence of ever smoking 1 to 19 cigarettes per day and 20 cigarettes or more per day was 32.8% and 23.4% in men and 10.5% and 1.8% in women, respectively.

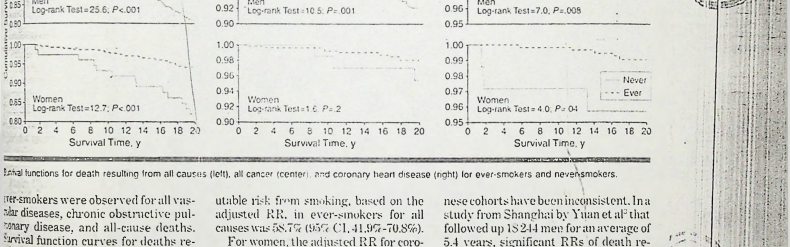
For male ever-smokers, the average amount smoked and duration of smoking was 14.5 (95% CI, 14.0-15.0) cigarettes per day and 25.1 (95% CI, 24.4-25.7) years, respectively. The female ever-smokers, on average, smoked 9.4 (95% CI, 8.3-10.5) cigarettes per day for 25.2 (95% CI, 23.5-26.8) years. The mean age for starting smoking in men was 22.0 years (95% CI, 21.6-22.4) and in women, 22.1 years (95% CI, 20.8-23.4). No association was found between the age for starting smoking and the amount smoked daily. The 25 male ex-smokers had stopped smoking, on average, 6.8 years (SD, 6.5 years) prior to the baseline study; the 3 female ex-smokers had stopped, on average, 3 years (SD, 1.7 years) prior.

Crude mortality rates in men for all cancer, coronary heart disease, cerebrovascular diseases, chronic obstructive pulmonary disease, and all causes were significantly higher in ever-smokers than in never-smokers (Table 2). There were 12 lung cancer and 8 stomach cancer deaths observed in ever-smokers, while no cases were observed in never-smokers. The RRs were indeterminable for these 2 cancers, but they were significant when 0.5 case was assumed to have occurred in never-smokers. In women, significant excess deaths

...e 2—Crude Mortality Rate (per 100,000 Person-Years) and Adjusted Relative Risk of Major Causes of Death by Smoking Status at Baseline*

Cause of Death (ICD-9 Code)	Men				Women			
	Never-Smokers, Rate (No. Who Died)	Ever-Smokers, Rate (No. Who Died)	P	RR (95% CI)†	Never-Smokers, Rate (No. Who Died)	Ever-Smokers, Rate (No. Who Died)	P	RR (95% CI)†
...ancer								
Lung (162)	0 (0)	102.0 (12)	.023‡	Undefined	40.7 (4)	75.5 (1)	.55	1.75 (0.17-18.1)
Stomach (151)	0 (0)	65.0 (5)	.047‡	Undefined	0 (0)	0 (0)	—	—
Liver (155)	73.5 (7)	76.5 (9)	.90	1.07 (0.40-2.91)	10.2 (1)	0 (0)	—	—
Esophagus (150)	21.0 (2)	55.0 (12)	.07	4.33 (0.93-19.9)	0 (0)	0 (0)	—	—
All cancers (140-208)	168.0 (16)	408.2 (48)	.002	2.50 (1.41-4.43)	101.8 (10)	228.4 (3)	.22	1.99 (0.50-7.92)
Vascular disease								
Coronary heart disease (410-414)	52.5 (5)	178.6 (21)	.01	3.61 (1.35-9.67)	61.1 (6)	286.4 (3)	.05	4.67 (0.78-27.8)
Stroke (430-438)	115.5 (11)	187.1 (22)	.17	1.54 (0.72-3.28)	61.1 (6)	152.9 (2)	.28	1.81 (0.31-10.6)
Vascular disease (390-459)	168.0 (16)	374.1 (44)	.005	2.29 (1.27-4.12)	142.6 (14)	452.8 (6)	.02	2.44 (0.83-7.18)
...ic obstructive pulmonary ...ease (490-496)	42.0 (4)	161.6 (19)	.01	4.05 (1.31-12.50)	20.4 (2)	152.9 (2)	.04	26.61 (2.08-339)
All causes	472.5 (45)	1088.4 (128)	<.001	2.42 (1.72-3.42)	325.9 (32)	981.1 (13)	<.001	2.32 (1.18-4.55)

...ding total person-years of follow-up: men who never smoked, 9523; men who ever smoked, 11 710; women who never smoked, 9820; and women who ever smoked, 1325.
...Deaths are classified according to International Classification of Diseases, Ninth Edition; RR, relative risk; CI, confidence interval; and ellipses, not applicable.
...RRs were adjusted for age, marital status, occupation, education, diastolic blood pressure, and triglyceride and total cholesterol levels.
...P value calculated after assuming that 0.5 case had occurred in the never-smokers.



...ival functions for death resulting from all causes (left), all cancer (center), and coronary heart disease (right) for ever-smokers and never-smokers.

...ver-smokers were observed for all vas-...ular diseases, chronic obstructive pul-...onary disease, and all-cause deaths. ...rvival function curves for deaths re-...ulting from all causes, all cancer, and ...oronary heart disease are shown (Fig-...re). With the exception of the category ...all cancer deaths" in women, all the ...g-rank tests were significant.

The adjusted RRs for ever-smoking ...om Cox regression analysis are shown ...n Table 2. No significant interactions ...ere observed between ever smoking ...nd the other 3 risk factors (total choles-...rol level, triglyceride level, and diastolic ...lood pressure), and all the Cox models ...ere statistically significant. For men, ...he adjusted RR for ever smoking for all ...ancer deaths was 2.50 (95% CI, 1.41-4.43) ...(P=.002); coronary heart disease deaths, ...3.61 (95% CI, 1.35-9.67) (P=.01); all vas-...ular disease deaths, 2.29 (95% CI, 1.27-...12) (P=.005); chronic obstructive pulmo-...ary disease deaths, 4.05 (95% CI, 1.31-...50) (P=.02); and all-cause deaths, 2.42 ...95% CI, 1.72-3.42) (P<.001). The attrib-utable risk from smoking, based on the adjusted RR, in ever-smokers for all causes was 58.7% (95% CI, 41.9%-70.8%).

For women, the adjusted RR for coronary heart disease deaths was 4.67 (95% CI, 0.78-27.75); for chronic obstructive pulmonary disease, 26.61 (95% CI, 2.08-339.82) (P=.009); and for all causes, 2.32 (95% CI, 1.18-4.56) (P<.001). The attributable risk from smoking for all-cause deaths was 56.9% (95% CI, 15.3%-78.1%). The 95% CIs for the risk estimates in women were wide because of the small number of deaths.

The population-attributable risks (for all the study subjects) for all causes of death, based on the formula [Pe(RR-1)/[1 + Pe(RR-1)] (where Pe is the proportion of ever-smokers and RR is the adjusted RR), were 41.4% (95% CI, 28.8%-57.6%) in men and 14.1% (95% CI, 2.2%-30.6%) in women.

COMMENT

Results from several prospective studies of the effect of smoking in Chinese cohorts have been inconsistent. In a study from Shanghai by Yuan et al[2] that followed up 18 244 men for an average of 5.4 years, significant RRs of death resulting from ever smoking (after adjusting for age and alcohol consumption) were found for all causes (1.4), all cancer (1.9), ischemic heart disease (2.0), and other heart diseases (2.4). These authors concluded that 21% of all deaths in the study subjects could be attributed to cigarette smoking, and the RR for total mortality (1.4) of Shanghai smokers vs never-smokers was lower than that in the United States (2.3).[3]

Our study provides further evidence that smoking is a major cause of death in China. Furthermore, our risk estimates for total mortality are higher than those from previous studies in China. For men, we calculated an RR of 2.42 (95% CI, 1.72-3.42), which is near that estimated for smokers in the United States (2.3) and the United Kingdom (2.0). In the United Kingdom, a 40-year follow-up study of male British physicians demon-

strated that during the period 1951 through 1971, death rates in cigarette smokers were about double those in nonsmokers throughout middle age; during the period 1971 through 1991, the corresponding difference was nearly triple.[11] In the United States, a study of 1 million US adults found that the RR of death in male smokers was 2.8 for those aged 35 to 69 years and about 2.0 in those aged 70 to 79 years.[2] Yuan et al[3] attributed their lower risk estimates to the later age for starting smoking in Shanghai (46% began smoking at age 25 years or older in Yuan's cohort, as compared with virtually no new smokers after age 25 years in the United States[2]; 32% of male smokers in our cohort started at age 25 years or older). But a cohort with a later age for starting smoking must be followed up for an even longer duration—until the true magnitude of risk can manifest. Studies with an insufficient length of follow-up may underestimate the risks of smoking on disease and death.

To examine the effect of the duration of follow-up on the risk estimates for total mortality, we repeated our analysis using different durations of follow-up. In men, the adjusted RR estimates for a follow-up duration of 5 years, 10 years, 15 years, and 20 years were 1.15 (95% CI, 0.49-2.71), 1.95 (95% CI, 1.10-3.45), 1.84 (95% CI, 1.22-2.76), and 2.42 (95% CI, 1.72-3.42), respectively. In women, the corresponding figures were 1.64 (95% CI, 0.27-10.09), 2.20 (95% CI, 0.70-6.90), 2.30 (95% CI, 0.93-5.66), and 2.32 (95% CI, 1.18-4.56). The results on crude RRs were similar (data not shown). Thus, as the duration of follow-up increased, the RRs also increased.

Based on an RR of 2 from a US cohort, Peto et al[2] estimated that about half of all young men who become regular cigarette smokers will eventually be killed by tobacco. Our risk estimate is in line with the estimate made by Peto et al,[2] so that at least half of the male smokers in China will eventually die of smoking-related causes.

Chinese women, though they smoke in smaller absolute numbers, will not be spared. A recent study from Shanghai by Gao et al[6] reported a significant excess in total mortality (RR, 1.19) in women smokers, but this risk could also be an underestimate because their duration of follow-up was only 5 years. Our RR was higher (2.32) and nearer to that from the US American Cancer Society cohort (2.15).[2] There was a long delay between the male and female epidemics in the United Kingdom and the United States, where smoking prevalence in females now approaches that in males.[2]

It should be noted that the risk estimates for active smoking are based on comparing smokers with nonsmokers as the reference, assuming that the latter are not exposed. However, nonsmokers who are exposed to environmental tobacco smoke have an increased risk of tobacco-related diseases such as lung cancer.[13] If many nonsmokers in the reference group were exposed to passive smoking, the RRs from active smoking would be underestimated. In China, previous case-control study of ischemic heart disease in never-smoking women showed that passive smoking at home was associated with coronary heart disease and that about one third of controls were exposed at work.[14] Hence, total mortality attributed to tobacco (including both active and passive smoking) could have been underestimated if the effect of passive smoking had not been taken into account in the present study or in other previous studies.

In conclusion, results from our study suggest that Chinese (particularly men who smoke like smokers in the West (particularly in the United States and United Kingdom) will die of smoking-related causes similar to their Western counterparts, although the relative importance of specific diseases may differ. Urgent and stringent tobacco-control measures are needed to prevent the growing epidemic in China and in other developing countries.

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ಪ್ರಬಂಧ- 8

ಬಾಯಿಯಂಬುಲಿಬೂ ಬಳ್ಳಿಗೆ ಸಾರುಗಳಬ್ಬಿಕೆ (Oral Submucous Fibrosis) ಎಂಬ ಶೀರ್ಷಿಕೆಯಲ್ಲಿ ಪ್ರಕಟಿತ ಲೇಖನವು ಸಾರಾಂಶ.

೦೨೦೦೮೨

Extracts from the article "ORAL SUBMUCOUS FIBROSIS" - by Soma Babu

Tobacco and vitamin deficiencies have also been incriminated as causes of Sub Mucous Fibrosis. Chewing of betel nuts and Areca nuts have now taken the attention of the workers all over the world working in this field.

OSF is an insidious disease which is progressing all over the country with the event of many newer eating habits including 'Pan Masalas, Gutkas and Kaporis with and without tobacco interspersed in them. Its further development should be arrested epidomiologically as well as clinically.

... When the detailed history was recorded, a significant observation made was that 9 out of 10 patients were habitual takers of different types of pan masalas available at least for one year, with 5 of them leven taking 'Gutkas'.

The Report may also highlight certain important aspects from the article written by Soma Babu, and others. The relevant extracts may be:

"A study was carried out to examine the comparative in vivo effects of pan masala / gutkha vis-a-vis betel quid chewing on buccal mucosal cytology in patients of oral submucous fibrosis(OSF). The nucleolated intermediate cells which constitute proliferating ratio of the cells in the buccal mucosa was

from Dr Ramesh Billimagga's file

significantly higher in all habitual chewers, more so in pan masala / gutkha consumers. The group which chewed pan masala / gutkha alone had developed OSF within 4 months to 4 years whereas betel quid induced OSF between 2 and 25 years. It, therefore, appears that habiutual chewing of pan masala / gutkha could induce OSF earlier than betelquid.

It is estimated that in India alone around two million cases of OSF exist.

In India, the use of betelquid can be traced back to more than 2000 years. In recent years, the traditional betelquid is gradually being replaced by a new product called 'Pan Masala / Gutkha'. Pan Masala contains all the ingredients of traditional betelquid except betel leaf, while gutkha contains tobacco in addition to other ingredients of pan masala.

The present study was carried out to compare the clinico-pathological features of OSF in subjects habituated to consumption of either betelquid and / or pan masala / gutkha.

In general, pan masala usage was seen predominantly in younger age group. The mean age of pan masala chewers with SE is 24.9 ± 0.87 years. They developed OSF after chewing for a mean duration of 2.7 ± 0.61 years, while betelquid chewers, who are older with a mean age of 34.3 ± 3.63 years had developed OSF after a mean duration of 8.6 ± 2.30 years of habitual chewing. The age analysis showed that 80% of pan masala and pan masala + betelquid chewers were below 30 years, whereas in betelquid group only 28% were below 30 years. The important observation is that pan masala alone or combined usage of pan masala and betelquid induced OSF changes in oral mucosa much earlier as compared to traditional betel quid chewing. The severity of restriction in the opening of the mouth i.e. inter incisal distance is almost same among all the habitual chewers but significantly reduced when compared to non-chewers.

Clinical and histological features observed in the present study showed that the habitual chewing of betelnut / tobacco / betelquid or pan masala / gutkha is associated with OSF. ...Since tobacco is one of the constituents of gutkha, its consumption probably results in OSF.

.....the addition of tobacco to betelquid increased the risk from 4 (without tobacco) to as much as 29 times with addition. ...the tissue collagen increased significantly in buccal mucosa biopsy samples obtained from patients who chewed betelnuts / pan masala and developed OSF.

It may be mentioned here that traditionally in India, adults only after marriage are consumers of betelquid. The children and unmarried persons by social customs refrain from such habits of chewing. However, during recent years with the advent of attractive, conveniently packed sachets and mass media advertisement, consumption of pan masala by younger people has considerably increased.

The group which chewed pan masala / gutkha and who had OSF, were consuming it for a period of 4 months to 4 years with a mean duration of 2.7 ± 0.61 years whereas habitual chewers of betelquid were between 2 to 25 years with a mean duration of 8.6 ± 2.30 years. This indicates that pan masala / gutkha chewing may induce OSF in a shorter period compared to betelquid chewing. The combined chewing of pan masala and betelquids also had a mean duration of 3.5 ± 0.62 years. .. Another possible reason for delayed effect of betelquid in the development of OSF compared to pan masala chewing could perhaps be due to composition of betelquid.... The average betelquid weighing 3.8 gms has 70% moisture, whereas the pan masala / gutkha sachet weighing 3.5 gms. has 7% moisture. The general impression among the habitual chewers is that, one who consumes 2 to 10 betelquids per day can conveniently and comfortably eat equal number of pan masala sachets. It appears that 3 to 4 gms quantity of either betelquid or pan masala can provide mouthful satisfaction for habitual chewers. Based on this observation and taking into account the moisture content, in the persons who consume one sachet of pan masala, the intake of active ingredients will be approximately 3 times higher than betelquid. Therefore, the induction of OSF is possibly more rapid with pan masala as compared to betelquid chewers.

It can be concluded that habitual chewing of pan masala / gutkha can induce OSF at a faster rate compared to conventional betelquid, the reasons being the absence of betel leaf and low moisture presence in the pan masala / gutkha.

antigens,[114-116] a similar association has been sought for OSF.

In an elegant study of 50 unrelated patients of Indian origin with OSF, Cannif *et al.*[117] showed increased frequencies of A10, B7, and DR3. It is of interest that in Indian populations HLA A10, B8, and DR3 occur in positive linkage disequilibrium.[118] The finding reported by Cannif *et al.*,[117] that A10 and DR3 were increased significantly in a group of patients with OSF, suggests the possibility that a haplotype encoding these antigens is associated with the susceptibility to OSF. It has been shown recently that particular haplotypes, rather than individual antigens, are associated with susceptibility to rheumatoid arthritis,[119] insulin-dependent diabetes mellitus,[119] and gold-induced nephropathy.[120] The defects in cellular immunity seen in OSF[21,23,83,87] are further suggestive of an autoimmune phenomenon. Moreover, the presence of autoantibodies against gastric cells, smooth muscle, and nuclei also has been documented.[121] Studies on serum from our laboratories also have shown elevated levels of immunoglobulins G and A.[106] A similar finding is seen in scleroderma, a disease resembling OSF histologically in that epithelial atrophy and dermal fibrosis are associated with a chronic inflammatory infiltrate and an increased frequency of HLA-DR3 and the haplotypic pair B8/DR3.[122,123]

Conclusions

From the data currently available on OSF, it appears quite clear that the disease is multifactorial, as is the case with oral cancer and most of its precursor lesions. It also appears that people in whom OSF develops have a genetic predisposition, which could render the oral mucosa more susceptible to chronic inflammatory changes in response to carcinogens. The latter definitely would include betel quid components including tobacco. As discussed earlier, betel nut extracts can stimulate collagen synthesis and fibroblast proliferation.[27,28] In addition, these extracts also can stabilize the collagen fibrils and render them resistant to enzymatic degradation. The role of genetic abnormalities apart from major histocompatibility complex (MHC) variability still needs to be defined for OSF. Also related to this is the role of viruses and their oncogenic potential. It appears that immune dysfunction is a common feature and could be related to any of the factors discussed so far. Based on these factors, we have suggested a possible model for the pathogenesis of OSF, as illustrated in Figure 4. The model is indeed speculative and needs to be completed. Research into genetic, viral, and immunologic aspects is ongoing in our laboratories. These, along with similar approaches elsewhere, should provide valuable information on this disease, which rapidly is becoming an excellent model for studying genetic–environmental–immunologic–nutritional interactions in disease pathogenesis.

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"ORAL SUBMUCOUS FIBROSIS"

—A NEW APPROACH TOWARDS ITS MANAGEMENT

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Submucous Fibrosis was first described by Schwartz[10] in 1952 as a clinical entity showing thickening of Oral Mucosa and restricted Mouth opening. He termed it as Atrophia idiopathica (tropica) Mucosae Oris but Joshi[7] in 1953 is credited to be the first person who described it and gave the present term. Though this disease is prevalent in Indian Sub-Continent, many cases have also been reported from all over the world. Pindborg[10,11,12] has defined it "as an insidious chronic disease affecting any part of oral cavity & sometimo tho Pharynx. Occasionaly preceeded by vesicle formation, always associated with fibrous bands and a Juxta epithelial inflammatory reaction followed by a fibro-elastic change of the lamina properia with epithelial atrophy leading to stiffness of the oral mucosa, trismus & inability to eat."

The most common initial symptom is the inability to eat spicy food and slight difficulty in mouth opening. Soon there is progression towards stiffness of oral mucosa and some even have difficulty in protruding the tongue. Referred pain to the ear & deafness due to obstruction of Eustachean tube were reported by Rao[14, 15] in 1962. On examination the patient had generalized stomatalities & Vesicle formation with ulceration. The mucosa is blanched opaque leather like showing typical fibrous bands which extend from the pharynx to retromolar area & pterygomand. raphae even extending to the lips involving the Palate as well. The involvement of mouth opening vary from few M. M. to several Cms. depending on the severity of the disease.

Etiology :

The exact etiology of this condition is still uncertain though many factors have been thought to be the causative agents, but it is widely accepted that Submucous Fibrosis is a collagen

What happens when person has OSF. OSF found in the stapled written sheets on pg. 4

disorder. Prolong Chronic irritation by chillies, tobacco, alcohol & betelnut is suspected to be the prime cause. Since the disease occures predominantly among the Indians, a possible allergen has been suspected in their common diet. Spices being an essential ingredient in Indian dishes, especially chillies & peppers, are supposed to be a chief or supporting etiologic factor. Sirsat & Khanolkar[19] has demonstrated changes similar to human Sub Mucous Fibrosis after painting rat palates for 8-28 weeks with a 2% concentrated capsaicin, the active irritant substance in chillies.

Tobbacco & Vitamin deficiencies have also been incriminated as causes of Sub Mucous Fibrosis. Chewing of betal nuts & Areca nuts have now taken the attention of the workers all over the world working in this field. Though the animal studies such as those involving the application of arecoline, the alkaloid isolated from Betelnuts, on the oral Mucosa of Rats have failed to yield positive results for Sub Mucous Fibrosis, so far.

Sub Mucous Fibrosis & Cancer of the Mouth

Sub Mucous Fibrosis of the oral cavity is considered to be a Precancerous lesion. The first report was mentioned by Pay Master[9] in 1956. In 1966, Pindborg and Sirsat[10, 12] reported a 9% epithelial atypia changes in 101 cases of Sub Mucous Fibrosis. The study by Kwan[17] found that 53.4% of patients with oral Malignancies had the betel nut chewing habit. Lab. tests to induce cancer by applying betel/tobacco quid on the ears of Swiss white mice failed to show a high incidence of cancer.

Histopathology :

In the early stages, fine fibrillar collagen seen dispersed in connective tissue along with marked oedema & presence of few inflammatory cells. In the advanced cases the oral epithelium is almost invariably extremely atrophic with complete loss of Retepegs. Epithelial atypia may also be present. The underlying connective tissue shows severe hyalinization with homogenisation of collagen bundles. Fibroblasts are markedly reduced in number and blood vessels are completely obliterated or narrowed. Some chronic inflammatory cells may be seen. The melanin containing cells in lamina propria become surrounded by dense collagen which explain the clinically observable loss of pigment.

Treatment :

This disorder has been treated by various workers on following lines of treatments with indifferent success.

1. Restriction of the habits
2. Local injections of fibrinolytic agents[3, 7, 8, 15, 18] (Collagenase, Trypsin, Hyaluronidase, Fibrinolysine)
3. Corticosteroids - locally/Systemically[2, 14]
4. Gold or high doses of vitimin A & E
5. Injections of Senotyphoid & large doses of Iodides[7]
6. Surgical splitting of Fibrous Bands[1, 2, 18]

B6	—	0.3 Mg
Nicotinamide	—	15.0 Mg
Ca. Pantothenate	—	1.0 Mg

& makes its use non-toxic and hepato-protective which is therapeutically extremely valuable.

The combination of iodine compound with Vit. B-complex is responsible for the stimulation of metabolic processes and enzymatic processes within the body (Oxygen reduction, transamination, etc) Moreover association with Vitimin B Complex potentiates the iodine action

Administration :- Treatment is initiated with Intramuscular Inj. of Smaller doses and continued with the larger doses of iodine (10,25 50,75 & 125 mg, in 2 ml ampoules) daily. The course of 5 injections is repeated after 7 days.

2. Placenta Extract (Inj Placentrex)

It is an aqueous extract of human placenta. It contains :

—Nucleotides : RNA, DNA, ATP

—Enzymes : Alkaline & acid phosphatase. Glutamic oxalo-acetic acid transaminase, glutamic acid Pyruvic acid transaminase,

—Vitimins ; Vit. E, B1, B2 B6, B12.
Pantothenic acid, nicotinic acid, biotin, PABA, Folic acid.

— Aminoacids

—Steroids : 17 Ketosteroids Cholastrian, Cholesterol.

Its action is essentially "BIOGENIC STIMULATION[13]", it is suggested that it stimulates the pituitary, adrenal cortex and regulates the metabolism of tissues. It is also proved to increase the vascularity of tissues. Its use is based on the new method of 'TISSUE THERAPY' introduced by Filatov in 1933, and later developed in 1953. His theory was that "Animal & vegetable tissues when severed from the parent body and exposed to conditions unfavourable, but not mortal to their existance undergo biological readjustment leading to development of substances in state of their survival to ensure their vitality biogenic stimulators. Such tissue" extracts when implanted into the body after resistances to pathogenic factor stimulates metabolic or regenerative process therapy favouring recovery[13]".

Administration: The region affected with Sub Mucous Fibrosis was divided into 5 regions. Each region was locally injected, if possible around fibrous bands presents, intramucously at the interval of 3 days for 15 days. Each time 2 Ml. of solution was deposited all round the specific region on both sides. This course can be repeated after a month if required.

3·5 Fluorouracil (FFU)[6,10] :

It is a fluorine substituted analog of uracil pyramidine derivative. Its

The present study shows the succesful treatment by the new approach. All the cases responded favourably. The minimum mouth opening achieved was 4 mm and maximum of 25mm. When the severity grades were assessed, it was found that in 3 cases with severe trismus mouth opening to the extent of 20-30mm was achieved. When the Mucosal colour, Burning sensation and Stomatitis were compared, it was found that in 90% of cases. Burning sensation and Stomatitis completely disappeared while the white patch decreased to a great extent.

The improvements seen in these cases compares favourably with the Studies done with other drugs including corticosteroids, though results with surgery were better than this study. But surgery was helpful in only very localised lesions, while Chemotherapy has to be resorted in generalised lesions. Its use (combination therapy) at the early stage cases of Submucous Fibrosis is without any doubt, though advanced cases have also shown considerable improvement.

Even though encouraging results were obtained with the drugs, it will be erroneous to say it to be a treatment of choice because the sample size being too small and duration of results does not guarantee it. It is felt that these procedures may be of greater value if they are followed up for a long time in a larger group of patients to keep the degree of trismus under arrest for a long time. The side effects of FFU and Piacentrex should be noted down in more details. The epidemiologic studies should be carried out in the main centres of dental research all round the country to establish the cause of Submucous Fibrosis even though to some extent, various preparations of Betelnuts, Arecanuts & Tobbacco available in the market can be incriminated.

2.8 SOME OBSERVATIONS ON SELECTED CANCER SITES

2.8.1 Lip, Oral Cavity and Pharynx (ICD.9 : 140-149)

Malignant tumours of the lip, oral cavity and pharynx are the most common site group of cancers in the three registries i.e., Bangalore, Bombay and Madras.

There is also a marked variation in the incidence of lip, oral cavity and pharynx cancer in different countries. Indian registries display much higher age adjusted and truncated rates than those reported by other registries in the Cancer Incidence in Five Continents (Vol. V,1987). Although this grouping includes cancers of quite distinct etiology (e.g. cancers of the oral cavity, nasopharynx and hypopharynx). The global picture is dominated by the incidence of oral cancer in Southern Asia and of oral cavity plus nasopharynx cancer in South-Eastern Asia.

Oral cancer is one of the 10 most common cancers in the world. In India, Bangaladesh, Pakistan and Srilanka, it is the most common and accounts for about a third of all cancers. More than 100,000 new cases occur every year in south and South-East Asia, with poor prospect of survival (Bull. WHO, 1984).

Epidemiological studies conducted in different parts of India have demonstrated that cancers of the oral cavity and pharynx are associated to a wide variety of tobacco chewing (pan chewing and betel nut with tobacco, lime and other ingredients) and smoking habits prevalent among men and women. These associations are statistically significant.

The total incidence of the lip, oral cavity and pharynx cancers disguise very large differences in the individual sites in the three Indian registries. The tongue (mainly base tongue), mouth and hypopharynx are the predominant sites in this group.

The relative risk of oral cancer in people with various tobacco habits, as well as the frequency of those habits, based on retrospective case control studies in India and Srilanka by Hirayama (1966) has made interesting observations. There is a wide variation in the frequencies and risks in different regions, but certain conclusions stand out. Approximately, 90% of oral cancers in south and south-east Asia can be attributed to tobacco chewing and smoking habits (Bull. WHO, 1984).

AVERAGE ANNUAL AGE-ADJUSTED (WORLD POPULATION) INCIDENCE RATE PER 100,000 (1982-1987) LIP, ORAL CAVITY AND PHARYNX (ICD 9:140-149)

		MALES			FEMALES		
ICD 9	SITE	BANGALORE	BOMBAY	MADRAS	BANGALORE	BOMBAY	MADRAS
140-149	Lip, Oral Cavity & Pharynx	16.1	27.2	19.7	12.9	10.4	13.0
140	Lip	0.1	0.3	0.3	0.1	0.2	0.3
141	Tongue	3.3	7.0	4.4	1.0	2.4	1.4
142	Salivary Glands	0.3	0.4	0.6	0.4	0.4	0.5
143-145	Mouth	4.0	5.5	6.6	3.4	4.1	8.0
146	Oropharynx	1.8	3.1	1.6	0.3	0.6	0.5
147	Nasopharynx	0.5	0.7	0.7	0.2	0.3	0.3
148	Hypopharynx	5.6	8.0	4.8	1.2	1.8	1.7
149	Pharynx etc.	0.5	2.2	0.7	0.3	0.6	0.3

COMPARISON OF LIFE TIME CUMULATIVE CANCER INCIDENCE RATES (0-74 YEARS) LIP, ORAL CAVITY AND PHARYNX (ICD-9 : 140-149)

	CUMULATIVE RISK (%)		ONE IN HOW MANY PEOPLE WILL GET CANCER IN THEIR LIFE TIME	
REGISTRY	MALE	FEMALE	MALE	FEMALE
BANGALORE	2.0	1.5	50	67
BOMBAY	3.3	1.3	30	77
MADRAS	2.4	1.5	42	67

Ref: Author/s, Year, Title of article/book, Journal name/Publishers of book, place,

ICD - Incident cases of cancer by most valid basis of diagnosis and site.

2.8.2 Cancer of the Oesophagus (ICD.9 : 150)

In the digestive system, the oesophagus is clearly the most frequently affected site in Bombay.

It is interesting to observe that the disease mainly occur in the persons who are 30 years and above and the ASR vary between 1 and 75 per 100,000.

One of the prominent epidemiologic characterstics of the oesophageal cancer is the great variability in sex ratios reported in different geographical regions of the world. The typical pattern of male preponderance has been noted by several registeries in Cancer incidence in Five Continents (Vol. V, 1987). But unlike as at other registries, Bombay presents high AAR together with a low sex ratio (M/F = 1.4 : 1). In Madras, sex ratio is lower (M/F = 1.3 : 1) than Bombay. While in Bangalore the sex ratio is almost equal to one (M/F = 0.96 : 1).

Although tobacco in its various forms is clearly associated with the disease; however, it does not provide an explanation for the sex ratio.

INTERNATIONAL COMPARISON OF AGE-ADJUSTED (AAR) WORLD POPULATION) AND TRUNCATED (TR) (WORLD POPULATION) (35-64 YEARS) INCIDENCE RATE PER 100,000

OESOPHAGUS CANCER (ICD.9 : 150)

MALES

YEAR STUDIED	REGISTRY		AAR	TR
1978-82	China (Shanghai)		20.8	21.0
1978-8	Singapore (Chinese)		13.5	13.9
1978-81	Japan (Miyagi)		13.3	14.5
1978-82	USA (Connecticut)	White	5.1	6.2
		Black	24.0	47.8
1979-82	UK (Oxford)		3.6	2.8
1977-81	Finland		3.7	3.4
1982-87	India			
	Bombay		10.8	16.8
	Bangalore		7.6	14.6
	Madras		7.2	14.3
1986-87	Bhopal $		8.8	16.1
1987	Delhi $		4.2	8.6

FEMALES

1978-82	China (Shanghai)		8.9	9.7
1978-82	Singapore (Chinese)		3.5	4.1
1978-81	Japan (Miyagi)		3.1	2.5
1977-81	Finland		2.4	1.8
1979-82	Uk (Oxford)		2.9	3.6
1978-82	USA (Connecticut)	White	1.5	1.9
		Black	6.0	11.8
1982-87	India			
	Bangalore		7.9	15.7
	Bombay		7.9	14.6
	Madras		5.5	2.3
1986-87	Bhopal $		5.3	9.1
1987	Delhi $		3.3	6.4

$ PROVISIONAL

SOURCE CANCER INCIDENCE IN FIVE CONTINENTS, VOL. V, 1987 NCRP DATA, 1982-1987

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INTERNATIONAL COMPARISON OF AGE-ADJUSTED (AAR) WORLD POPULATION) AND TRUNCATED (TR) (WORLD POPULATION) (35-64 YEARS) INCIDENCE RATE PER 100,000

OESOPHAGUS CANCER (ICD.9 : 150)

MALES

YEAR STUDIED	REGISTRY		AAR	TR
1978-82	China (Shanghai)		20.8	21.0
1978-8	Singapore (Chinese)		13 5	13.9
1978-81	Japan (Miyagi)		13.3	14.5
1978-82	USA (Connecticut)	White	5.1	6.2
		Black	24.0	47.8
1979-82	UK (Oxford)		3.6	2.8
1977-81	Finland		3.7	3.4
1982-87	India			
	Bombay		10.8	16.8
	Bangalore		7.6	14.6
	Madras		7.2	14.3
1986-87	Bhopal $		8.8	16.1
1987	Delhi $		4.2	8.6

FEMALES

1978-82	China (Shanghai)		8.9	9.7
1978-82	Singapore (Chinese)		3.5	4.1
1978-81	Japan (Miyagi)		3.1	2.5
1977-81	Finland		2.4	1.8
1979-82	Uk (Oxford)		2.9	3.6
1978-82	USA (Connecticut)	White	1.5	1.9
		Black	6.0	11.8
1982-87	India			
	Bangalore		7.9	15.7
	Bombay		7.9	14.6
	Madras		5.5	2.3
1986-87	Bhopal $		5.3	9.1
1987	Delhi $		3.3	6.4

$ PROVISIONAL

SOURCE : CANCER INCIDENCE IN FIVE CONTINENTS, VOL. V, 1987. NCRP DATA, 1982-1987

2.8.4 Cancer of the Larynx (ICD.9 : 161)

The age-adjusted incidence rate of laryngeal cancer in Indian material is high in men than women. Among men the highest incidence is in Bombay (rates vary between 6.7 & 8.4 per 100, 000 during the period 1982 through 1987). The AAR are low in Madras (rates vary between 3.7 & 4.6 per 100, 000) and Bangalore (rates vary between 3.1 & 4.9 per 100, 000). Among females, laryngeal cancer age-adjusted rates are very low in Bangalore (rates vary between 0.3 & 1.2 per 100, 000), Bombay (rates vary between 1.2 and 2.3 per 100,000) and Madras (rates vary between 0.4 & 0.7 per 100, 000).

International comparisons are done for selected countries. The highest incidence rate of laryngeal cancer world wide has been reported from Sao Paulo (Brazil) in males. (Males - 17.8 and Females - 1.3 per 100,000).

The ratio of laryngeal cancer to lung cancer incidence. In men, ordinarily ranging from 1:5 to 1:20, is 1:1.6 in Bombay, 1:2.2 in Bangalore and 1:1.8 in Madras.

The strong relation between tobacco use and laryngeal cancer has long been known. Much of the association seen for is demographic factors such as sex, race and geographic location is probably attributable to the effects of tobacco, alcohol and occupational exposure.

INTERNATIONAL COMPARISON OF AGE-ADJUSTED (AAR) (WORLD POPULATION) AND TRUNCATED (TR) (35-64 YEARS) (WORLD POPULATION) INCIDENCE RATE PER 100,000.

LARYNX CANCER (ICD-9 : 161)

MALES

YEAR STUDIED	REGISTRY		AAR	TR
1978	Brazil (Sao Paulo)		17.8	27.6
1978-82	USA (Connecticut)	Black	12.6	24.8
		White	7.7	12.4
1977-81	Finland		4.5	7.1
1979-82	UK (Oxford)		4.2	5.8
1982-87	India			
	Bombay		8.2	13.9
	Madras		4.3	7.4
	Bngalore		4.0	7.1
1986-87	Bhopal $		3.7	6.7
1987	Delhi $		5.7	11.0

FEMALES

YEAR STUDIED	REGISTRY		AAR	TR
1978-82	USA (Connecticut)	Black	2.7	4.4
		White	1.7	3.0
1978	Brazil (Sao Paulo)		1.3	2.8
1979-82	UK (Oxford)		0.5	0.8
1977-81	Finland		0.3	0.7
1982-87	India			
	Bombay		1.4	2.5
	Madras		0.5	1.2
	Bangalore		0.7	1.2
1987	Delhi $		0.6	1.4
1986-87	Bhopal $		0.0	0.0

$ PROVISIONAL

SOURCE : CANCER INCIDENCE IN FIVE CONTINENTS, VOL. V, 1987 NCRP DATA, 1982-87

2.8.5 Cancer of the Trachea, Bronchus and Lung (ICD.9 : 162)

Cancer of the lung is of epidemiological interest because of the wide spread geographical and racial variations observed and steadily increasing incidence and mortality noted in the West. This increase has so far been noticed particularly in men, but recently women have also begun to present a similar rising trend.

The AAR and TR of lung cancer are much lower in India than the corresponding rates reported by other countries in Cancer Incidence in Five Continents (Vol.V).

Lung cancer is one of the most common and lethal malignant tumours known. It occurs mainly in urban areas through out the industrialised world. In India, its incidence is higher in the male population (ranges between 10 and 13 per 100,000 in the three centres) than females. Among Indian women incidence is very low (ranges between 1 and 3 per 100,000). In white American males & females (USA-Connecticut), the incidence is 64.3 and 25.3 per 100,000. The male:female ratio thus works out to 2.5 :1. The overall incidence of the disease is much higher in the industrialised countries.

A large number of epidemiological studies in the West has shown that there is a progressive and absolute risk in its incidence which has occurred over the past few decades and that it is clearly linked to cigarette smoking and environmental pollution.

The association of cigarette smoking with lung cancer has now been universally accepted . The U.S. Surgeon General's Advisory Committee concluded that cigarette smoking is causally related to lung cancer in men and that its effect far outweighs all other probable etiological factors. The risk increases with the duration of smoking habit and the number of cigarettes smoked daily. A heavy smoker (more than 50 cigarette per day) runs a 20 times higher risk of developing lung cancer, than a non-smoker. The increasing incidence of lung cancer in women in the West is clearly linked with the steep increase registered in cigarette smoking by women during the sixties.

Atmospheric pollution from industry and automobile exhausts is also considered to be a significant etiological factor.

There are several studies in the West on industrial lung cancers arising in workers associated with certain occupations, such as :

(i) Asbestos miners and textile workers.

(ii) Manufacturers and handlers of arsenic - containing insecticides and those working as arsenic smelters.

(iii) Chromium refining workers and nickel & iron ore miners.

(iv) Uranium and Cobalt miners.

(v) Radon daughter products.

INTERNATIONAL COMPARISON OF AGE-ADJUSTED (AAR) (WORLD POPULATION) AND TRUNCATED (TR)(35-64 YEARS) (WORLD POPULATION) INCIDENCE RATE PER 100,000.

TRACHEA, BRONCHUS & LUNG (ICD 9 : 162)

YEAR STUDIED	REGISTRY		MALES		FEMALES	
			AAR	TR	AAR	TR
1979-82	UK (Oxford)		68.8	68.1	25.3	41.5
1977-81	Finland		74.2	93.2	21.9	41.1
1978-82	USA (Connecticut)	White	64.3	81.1	19.5	25.6
		Black	89.8	140.1	7.0	10.0
1977-81	Columbia (Cali)		19.5	25.5	5.4	9.5
1982-87	India					
	Bombay		13.3	21.4	2.9	4.6
	Bangalore		8.7	16.1	1.7	3.1
	Madras		7.7	17.2	1.3	2.9
1986-87	Bhopal $		10.3	19.0	1.9	3.0
1987	Delhi $		8.8	14.7	1.7	3.2

$ PROVISIONAL

SOURCE : CANCER INCIDENCE IN FIVE CONTINENTS VOL. V, 1987 NCRP DATA, 1982-1987

2.9 BURDEN OF TOBACCO RELATED CANCERS IN INDIA

NCRP has provided incidence of cancer in Bangalore, Bombay and Madras areas for the years 1982-1987. Based on these figures, the burden of tobacco related cancers in India has been estimated as given below in the table.

BURDEN OF TOBACCO RELATED CANCERS IN INDIA,ESTIMATES FOR 1990

	MALES	FEMALES	TOTAL
Total Population (millions)	430	410	840
Crude Rate per 100,000	70	80	75
Number of New Cancer cases per Year	301,000	328,000	629,000
New Cases Related to Tobacco Habits:			
Mouth	34,500	27,000	61,500
Pharynx & Larynx	47,000	10,400	57,400
Oesophagus	22,600	16,400	39,000
Lung	26,400	5,000	31,400
Others	14,500	7,200	21,700
TOTAL	145,000 (48%)	66,000 (20%)	211,000 (33%)

Estimates are shown separately for males and females for commonly affected sites namely, mouth, pharynx & larynx, oesophagus and lung. Some other sites related to smoking habits known from the experience of the west such as bladder, pancreas etc. are taken as others. Although stomach and uterine cervix cancers are appear to be associated with the bidi and cigarette smoking , but they are not taken into account. It is also possi ble that tobacco chewing and bidi smoking may show risks for cancers not studied so far. From these considerations, the present estimate of tobacco related cancers is a conservative one (Sanghvi, 1989).

In India, cancer morbidity related to tobacco is 48% in men and 20% in women with an overall estimate of 33% for the two sexes. 75% cancers related to tobacco were found in mouth, pharynx & larynx and oesophagus; lung cancer accounted for only 15% of cases.

2.10 Incident Cases of Cancer By Year 2000 A.D.

Incident cases of cancer by year 2000 A.D. has been estimated as given in the table. These estimates are based on weighted averages of crude incidence rates for Bangalore, Bombay and Madras registries. India's population was projected, by sex and age, for the year 2000 A.D., using 1971 and 1981 censuses and applying the linear rate of growth. The present estimates of cancer cases may be considered as a conservative one.

ESTIMATED NUMBER OF INCIDENT CANCER CASES FOR SELECTED SITES, ALL AGES, BY THE YEAR 2000 A.D., IN INDIA

SITE	(ICD.9)	MALES	FEMALES	TOTAL
Lip, Oral Cavity	(140-145)	45000	32000	77000
Pharynx & Larynx	(146-149,161)	60000	16000	76000
Oesophagus	(150)	30000	20000	50000
Stomach	(151)	33700	16000	49700
Lung	(162)	33700	8000	41700
Breast	(174)	—	72000	72000
Cervix Uteri	(180)	—	104000	104000
Others		172100	131200	303300
TOTAL		374500	399200	773300

ESTIMATES ARE BASED ON WEIGHTED AVERAGES OF CRUDE INCIDENCE RATES FOR BANGALORE, BOMBAY AND MADRAS SOURCE : NCRP DATA, 1982-1987.

HCR - Hospital cancer registry.

TABLE 4

ALL CANCER PATIENTS TYPE OF TREATMENT RECEIVED HCRs, 1987

Chandigarh		Dibrugarh		Trivandrum		Type of	Bangalore		Bombay		Madras	
Male %	Female %	Male %	Female %	Male %	Female %	Treatment	Male %	Female %	Male %	Female %	Male %	Female %
14.6	10.8	9.7	24.0	6.0	7.4	Surgery (S)	7.8	4.0	21 9	21.1	6.9	2.1
44.9	55.5	81.4	53.3	62.2	61.4	Radiotherapy (R)	36.2	61.6	44.1	48.6	71.9	71.1
18.9	13.2	3.7	12.4	8.0	8 5	(S) + (R)	4.9	3.9	9.7	7.3	6.1	2.1
5.5	4 5	2.6	5 0	5.1	2 9	Chemotherapy (C)	24 2	13.4	10.4	5.8	3.5	2.7
3.1	3.7	1.8	3.3	2.0	2.2	(S) + (C)	3.6	2.6	3.3	6.1	1.9	0.5
7.1	2.1	0.7	2.1	14.1	8.4	(R) + (C)	19.6	7.4	8.6	3.1	7.3	8.5
3.0	4.4	0.2	0.0	1.5	3.0	(S) + (R) + C)	2.6	2.1	1.1	2.8	1.6	6.5
2.8	5.5	0.0	0.0	1.1	6 2	Others	1.2	4.8	0.8	5.2	0.5	6.6
732	748	547	242	1245	1060	Total No. of Cases Trated	1133	1603	2852	2388	737	1181

Tobacco Related Head and Neck Cancers

Analysis of head and neck cancers (ICD 9: 140-149) in the hospital registries according to the 4th digit code of the ICD9 has a significant effect on the ranking of common cancers particularly in men. Pharynx comes out as a leading cancer site in men in five out of six registries (Table 5). This is in contrast to the 3-digit classification which shows oral cavity as a leading cancer site in three out of six registeries, pharynx in two and lung in one registry. The major reason for such a change is the shift of base tongue cancers from the oral cavity to the oropharynx where they really belong. Since base tongue is identifiable only by the 4th digit ICD9 code, such classification is needed if oral cavity and pharynx, aetiologically and biologically different, are to be distingulshed. Chewing tobacco causes oral cancer; bidi smoking is related to pharyngeal cancer.

Overall about 85-90% of oral and pharyngeal cancers are evaluated and more than 60% get cancer directed treatment. The proportion of patients treated is generally higher in general hospitals than in cancer centres; this is also reflected in the different categories of cancer spread.

Breast and Cervical Cancers :

Overall about 50% of breast cancer patients could be and were evaluated for cancer spread. Of these 40% received cancer directed treatment. In contrast almost 90% of cervical cancer patients could be and were evaluated and 60% wre treated. There are two major difference viz. (i) surgery is the first choice of traetment in breast cancer, (ii) surgical facilities are widely available outside reporting institutions so that breast cancer patients have often already had this before they come to reporting institutions; (iii) breast cancer is more common in upper socio-economic classes.

Pattern of treatment for breast and cervical cancer show a higher proportion of patients have been treated in general hospitals than in cancer centres in all the three categories (localised, regionally and distantly spread) of cancer spread. This proportion is highest for patients which localised cancers followed by regionally spraed cancers. Additional studies into patient noncompliance/compliance and of therapeutic facilities available outside reporting institutions are needed.

TABLE 5

LEADING CANCERS USING ICD 9 - 3-DIGIT AND 4-DIGIT CLASSIFICATION CODES –HCRs, Males-1987

3-DIGIT		REGISTRY	4-DIGIT	
General Hospital				
Lung	(9.9)	Chandigarh	Pharynx	(12.2)
Oral Cavity	(9.8)		Lung	(9.9)
Pharynx			Larynx	
Oesophagus	(7.3)		Oesophagus	(3.5)
Larynx			Brain	(5.7)
Pharynx	(26.1)	Dibrugarh	Pharynx	(32.9)
Oesophagus	(19.7)		Oesophagus	(19.7)
Oral Cavity	(12.9)		Oral Cavity	(6.2)
Lung	(14.9)		Lung	(4.9)
Larynx	(5.5)		Larynx	(4.2)
Stomach			Stomach	
Oral Cavity	(22.6)	Trivandrum	Oral Cavity	(20.3)
Lung	(12.4)		Lung	(12.4)
Pharynx	(8.5)		Pharynx	(10.8)
Oesaphagus	(5.9)		Oesaphagus	(5.9)
Brain	(4.2)		Brain	(4.2)
Cancer Centre				
Pharynx	(15.1)	Bangalore	Pharynx	(20.5)
Oral Cavity	(14.8)		Oesophagus	(11.4)
Oesophagus	(11.4)		Oral Cavity	(9.4)
Lung	(8.3)		Lung	(8.3)
Stomach	(5.3)		Stomach	(5.3)
Oral Cavity	(18.6)	Bombay	Pharynx	(18.5)
Pharynx	(11.8)		Oral Cavity	(11.9)
Oesophagus	(7.7)		Oesophagus	(7.7)
Lung	(6.9)		Lung	(6.9)
Larynx	(6.7)		Larynx	(6.7)
Oral Cavity	(21.5)	Madras	Pharynx	(17.0)
Pharynx	(11.6)		Oral Cavity	(16.1)
Oesophagus	(9.3)		Oesophagus	(9.3)
Stomach	(7.7)		Stomach	(7.7)
Lung	(5.4)		Lung	(5.4)

Regional Cancer Registry— Expansion of the Hosital Registry into a Network :

T
sp

Dibrugarh Hospital registry of Assam Medical College has taken initiative and provided additional data from the D.B. Barooah Cancer Institute at Guwahati. The data from these two sources in Assam complement each other. This is a welcome begining towards the development of a regional cancer registry composed of a group of registries ir different hospitals

Acknowledgements :

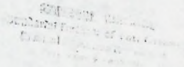
To registries, for cooperation and prompt despatch of data; Mr. M.D. Singh for statistical assistance; Ms. C Stewart for computer programme generation; Ms. V. Krishnan for correction of errors and generation of tables; M M. Gujarathi for typing assistance; messrs R. Keni and T Sable for circumstantial support.

Reference :

1 *National Cancer Registry report for 1986; Indian Council of Medical Research, New Delhi, 1989.*

7.23

A study of certain epidemiological factors on blood pressure distribution and prevalance of hypertension in a rural community of Pondicherry (S. India)



DISSERTATION SUBMITTED TO THE
UNIVERSITY OF MADRAS
IN PARTIAL FULFILMENT OF THE REQUIREMENTS
FOR
M.D. [Br. XV] COMMUNITY MEDICINE

NAME OF CANDIDATE : V. T. JAYAPRAKASH

MARCH 1986

No.1: TO STUDY CERTAIN EPIDEMIOLOGICAL FACTORS LIKE AGE, SEX , MARITAL STATUS, OCCUPATION , INCOME, HEIGHT, WEIGHT AND HABITS LIKE SMOKING AND DRINKING ALCOHOL ON BLOOD PRESSURE DISTRIBUTION.

No.2: TO ESTIMATE THE PREVALENCE OF HYPERTENSION AND TO STUDY THE EPIDEMIOLOGICAL FACTORS IN CASES OF HYPERTENSIVES THUS DETECTED .

Smoking and Blood Pressure:

Kannovan M. et al in 1959 conducted a blood pressure survey in Finland to study the relationship to study the relationship between, cigarette smoking, serum cholesterol and blood pressure . In this study it was observed that cigarette smoking varied inversely with the level of blood pressure. The level of blood pressure depended on the years of smoking.

Another study was conducted by Blackburn et al in Finland in 1960. The study population consisted of 1618 men aged 17-67 years. The level of smoking was divided into light less than 10 cig/day, Moderate 11-2o per day and High more than 20 per day. The study population included various categories. Amongst students and businessmen it was observed that smoking and blood pressure did not have any relationship. But on examination of data from broader studies of population , there was a tendency towards lower systolic and diastolic pressure in smokers. This was statistically significant in the three groups.

Goteberg's study in Sweden showed that the frequency of smoking and level of blood pressure showed a inversed relationship with each other.

Sive's study among Israeli men showed that smoking had a negative effect on the level of blood pressure. Gyntelberg's study in Copenhagen males aged 40-59 years showed that smokers had lower blood pressure levels than non-smokers. The level of smoking was divided into 3 categories - High more than 10 perday

Moderate 5-10 per day

Light less than 5 per day

The levels of blood pressure showed a decrease with increase in the frequency of smoking.

Poulter's study in an African tribe in 1980 showed that there was no apparent association between blood pressure and reported level of smoking.

Alcohol and Blood Pressure:

Goteberg's study revealed that there was a significant increase in the levels of blood pressure in case of drinkers compared to non-drinkers. The level of blood pressure increased with level of drinking.

In Gyntelberg's study it was observed that there was a significant increase in the levels of both systolic and diastolic blood pressure among drinkers. Also a statistically significant increase in both systolic and diastolic blood pressure was found with an increased alcohol consumption.

1594 male employees in Chicago People gas light and Coke Company, was studied for relationship

The study was conducted in the Jawaharlal Institute Rural Health Centre (JIRHC) Ramanathapuram from 1st October,1984 to 30th September,1985. This is situated at a distance of 15 Kms from Pondicherry the headquarters of the Union Territory of Pondicherry. The population of the state was 6,04,471 according to 1981 census.

The JIRHC caters to a population of 14,562 residing in fourteen villages (JIRHC, Annual report, 1983). The centre has got a good documentation system (Datta et al 1966). Details of the population of the 14 villages are given below:

Village	No. of Familes	Males	Females	Total
Ramanathapuram	283	635	684	1319
Thondamanatham	353	990	886	1876
Osudur	24	65	73	138
Pilliarkuppam	287	784	757	1541
Coodapakkam	768	2126	2106	4232
Konerikuppam	81	220	185	405
Karasur	169	430	410	840
Thuthipet	73	179	190	369
Agaram	85	258	228	486
Poraiyur	157	481	424	905
Olaivakkal	36	107	89	196
Sedarapet	414	1158	1097	2255

Total number of families - 2730
Males - 7433
Females - 7129

Study sample : The sampling unit was taken as ' family '. This was because

i) All the families in the study villages have been given folder numbers which could be conveniently used for choosing the study population by sampling.

ii) All the members in a family could be surveyed and any family history of hypertension could be studied.

It has been found in most Indian studies that incidence of hypertension was minimal before the age of 20 years (Padmavathi 1959, Ranganathan et al 1975). Therefore the study was restricted to persons 20 years and above.

Sample size: According to the prevalance studies conducted in rural areas of India, hypertension prevalence ranges from 0.17% (Padmavathi, 1959) to 8.1%. An average prevalence value of 4% was taken for calculating the sample size for the present study.

The sample size was calculated based on the formula $\frac{4PQ}{n} = 30\% \, P^2$ where 'P' was the prevalence rate.

An error of 30% was allowed on either side of the values.

Confidence limit was 95%.

Accordingly, the sample size was calculated as 1100. 100 more subjects were included for chances of drop outs. Hence 1200 subjects were required for the study.

Since the average family size in the study area is 5.3 and 52% of the total population are aged 20 years and above, to get the required study unit of 1200, 500 families were required to be selected.

The 500 families were chosen from all the families (2730) residing in the 14 villages giving proportionate representation to all the villages according to the number of families in the village. The study families were chosen from each of the villages by simple random sampling. The number of families chosen from each of the villages are given below.

Village	No. of families chosen
Ramanathapuram	52
Thondamanatham	65
Osudur	4
Pilliarkuppam	53
Coodapakkam	141
Konerikuppam	15
Karasur	31
Thuthipet	13
Agaram	14
Poraiyur	29
Olavaikkal	7
Sedarapet	76
Total no. of families	500

Data Collection: 1. House to house visit of the sampled families was made and each family member above 20 years in the family was contacted and data collected regarding name, age, sex, caste, marital status, income, habits like smoking and drinking alcohol, height, weight and blood pressure on a predesigned and pretested proforma (Annexure I). If any member / members in a particular family could not be contacted after three visits the particular family was eliminated from the sample and the family reiding next to it was taken into consideration.

The study was conducted in the morning hours between 6 AM to 12 Noon and in the evening hours between 4.30 PM to 7.00 PM.

2. The following procedures for recordi were followed for recording blood pressure , weight and height.

a) Recording of blood pressure: The blood pressure apparatus was checked every day for any leak in the mercury column or other problems in the apparatus. Blood pressure was recorded using a mercury sphygmomanometer with a 12.5 cm cuff with subject in a sitting position and the left arm slightly flexed at heart level (Dasgupta 1982). For this purpose a stool was carried to

every house. Before recording of blood pressure it was ensured that the subject was in a relaxed atmosphere. If the subject was engaged in any physical activity or smoking he was made to relax for 5-10 minutes and after filling up the history and identification data, blood pressure was recorded. Systolic blood pressure was taken as the pressure at which the ear distinguishes the first arterial sound. The point at which the arterial sound disappears (Korotkoff's phase 5) was taken as the diastolic blood pressure (TRS 628,1978). Three readings were taken at an interval of five minutes and the mean of the three values was taken.

A case was diagnosed as hypertensive if subject had systolic blood pressure 160 mmHg or more or diastolic blood pressure 95 mm Hg or more or both (TRS 628,1978). If the subject was diagnosed as hypertensive, details regarding family history, awareness and treatment details if any were obtained.

b. Recording of weight: This was recorded with subject in minimal clothes by bathroom scales weighing machine. The readings were taken to the nearest kilogram.

c. Recording of height: Height was recorded by means of a metal measuring tape, with the subject standing against the wall of the house. Readings were taken to the nearest centimetre.

3. Data on (a) smoking habits: Every individual was enquired about their smoking habits. If there was a positive history of smoking , details of regarding type of smoking and amount smoked per day was enquired.

Smokers were classified according to

i) number smoked per day.

Group I: Light ,Less than 5 per day

II: Moderate, 5-10 per day

III: High , More than 10 per day

(Gyntelberg 1962)

ii) type of smoking.

Group I: Beedi smokers

II: Cigarette smokers

III. Cigar smokers

(b) Drinking habits: If the subject was in the habit of taking alcohol, details regarding frequency of drinking and type (toddy, arrack, IMFL) and amount of drinking were enquired and the details classified according to

TABLE 1

DEMOGRAPHIC CHARACTERISTICS OF THE STUDY POPULATION

Demographic characters	Number (N=1262)	Percent
1. Age (in years)		
20 - 24	126	10.0
25 - 34	309	24.5
35 - 44	347	27.5
45 - 54	293	23.2
55 - 64	135	10.7
65 +	52	4.1
2. Sex		
Males	674	53.4
Females	588	46.6
3. Marital status		
Unmarried	135	10.7
Married	1055	82.8
Widowed/separated	82	6.5
4. Caste:		
Counders	699	55.3
Harijans	320	25.5
Others	243	19.2
5. Occupation		
Agriculture	515	40.8
Housewife	443	35.1
Farmer	137	10.9
Others	167	13.2
6. Education		
Illiterate	672	53.2
Read and Write & primary	382	30.3
Middle school and above	208	16.5
7. Percapita income per month		
Less than Rs.50	871	63.7
Rs.50 to 99	317	30.5
Rs.100 to 149	50	3.9
Rs.150 +	24	1.9

TABLE. 12

BLOOD PRESSURE DISTRIBUTION ACCORDING TO HEIGHT

Height in cms	No.	SBP Mean	SBP S.D.	DBP Mean	DBP S.D
130 +	65	121	11.0	75	7.4
140 +	286	124	11.4	78.	7.2
150 +	434	124	10.1	78	6.9
160 +	312	123	10.8	77	6.8
170 +	165	125	10.8	79	7.1

TABLE. 13

BLOOD PRESSURE DISTRIBUTION ACCORDING TO SMOKING HABITS AMONG MALES

Habit	No.	SBP Mean	SBP S.D	DBP Mean	DBP S.D
Smokers	203	125	11.1	79	6.7
Non-Smokers	471	125	11.4	79	6.4

Even with 3 standard deviation the Quetelet's index would remain at 0.25 indicating in the study sample that no one was over weight as per the index. This could be one of the reasons for the poor correlation of Quetelet's index with blood pressure.

Smoking habits: Table 13 shows blood pressure distribution according to smoking habits among males. None of the females in the study population gave history of smoking. Slight increase in the values of both systolic and diastolic blood pressure were seen among non smokers, but the difference in the means were found to be not statistically significant.

Table 14 shows blood pressure distribution according to frequency of smoking. The values of systolic and diastolic blood pressure show an uneven distribution and the values were not statistically significant.

Table 15 shows blood pressure distribution according to type of smoking. Most of the smokers were beedi smokers and only a small percentage of smokers (13%) were cigarette smokers.

Kanovan (1959) observed that smoking varied universely with blood pressure. Blackburn (1960) showed that the values of both systolic and diastolic blood pressure values were lower amongst smokers. Sive (1962) and Goteborg (1960) also showed an inverse relation with blood pressure amongst smokers.

TABLE 14

BLOOD PRESSURE DISTRIBUTION ACCORDING TO FREQUENCY OF SMOKING

Frequency	No.	SBP Mean	SBP S.D	DBP Mean	DBP S.D
Mild	60	125	10.8	79	6.3
Moderate	102	124	11.7	79	7.2
High	41	125	12.1	79	7.4

TABLE 15

BLOOD PRESSURE DISTRIBUTION ACCORDING TO TYPE OF SMOKING

Type	No.	SBP Mean	SBP S.D	DBP Mean	DBP S.D
Beedi	164	125	11.2	79	6.8
Cigarette	27	125	11.4	79	7.2
Cigar	12	124	11.9	79	6.9

TABLE 27

BLOOD PRESSURE DISTRIBUTION AMONG HYPERTENSIVES ACCORDING TO ALCOHOL DRINKING HABITS

Group	No	S B P		D B P	
		Mean	S.D	Mean	S.D
Drinkers	9	156	4.2	99	2.0
Non Drinkers	9	155	3.7	99	1.3

TABLE 28

BLOOD PRESSURE DISTRIBUTION IN HYPERTENSIVES ACCORDING TO AMOUNT OF ABSOLUTE ALCOHOL CONSUMPTION

Amount per year	No	S BP		D B P	
		Mean	S.D.	Mean	S.D
5000 +	4	155	2.5	99	1.8
10000 +	2	158	2.0	100	
20000 +	3	155	5.2	97	1.9

TABLE 29

BLOOD PRESSURE DISTRIBUTION IN HYPERTENSIVES ACCORDING TO SMOKING HABITS

Group	No	SBP		DBP	
		Mean	S.D.	Mean	S.D.
Non smokers	8	155	4.9	99	1.7
Smokers	10	156	3.5	99	1.6

absolute alcohol show an uneven distribution. The values are shown in Table 28.

Table 29 shows blood pressure distribution according to smoking habits. The values between smokers and non smokers was not statistically significant.

Awareness of hypertension: 6 persons (18%) were aware of being hypertensive. In this only 50% were taking regular treatment. The rest were on irregular patient. 27 persons (82%) who were not aware of being hypertensive, were found to be asymptomatic and pursued with their physical work though they were hypertensive.

Family history of hypertension: In the present study, there was no family history of hypertension among hypertensives. This could be because of the lack of knowledge of the hypertensives regarding blood pressure status of their parents or other relatives and may also be due to the small number of hypertensives in the study.

The present study was conducted in JIRHC, Ramanathapuram with the aim of studying certain epidemiological factors like age, sex, marital status, occupation, income, height, weight and habits like smoking and drinking alcohol on blood pressure distribution and to estimate the prevalence of hypertension and study the epidemiological factors in cases of hypertensives thus detected. Data was collected from 1262 persons above the age of 20 years by house visits.

Prevalence of hypertension: The prevalence of hypertension was estimated to be 2.6% . Prevalence of hypertension was slightly higher in males (2.7%) than males (2.5%) though the differences between the two proportions was not significant.

Epidemiological factors and blood pressure:

Age and Sex: The levels of both systolic and diastolic blood pressure increased with advancing age. A statistically significant positive correlation in males were found for both systolic blood pressure and diastolic blood pressure with age. In case of females, a statistically significant positive correlation was found only for systolic blood pressure.

Marital status: Unmarried individuals had lower systolic blood pressure and diastolic blood pressure compared to other groups (married group and widowed group). The values were statistically significant.

Occupation: House wives had significantly lower blood pressure values compared to other groups. The differences between the other groups were not statistically significant.

Income: Though values of blood pressure showed slight rise in the higher income group, the difference in the means were not significant.

Educational status: Educational status did not seem to have any apparent association with the levels of blood pressure. This may probably be because of the low level of education of the group studied.

Weight: There was a definite increase in the values of both systolic and diastolic blood pressure with increase in weight . A statistically significant positive correlation between weight and systolic blood pressure and diastolic blood pressure in case of males was observed. In case of females though a positive correlation was obtained, it was not found to be significant.

Height: Values of both systolic and diastolic blood pressure were least in the 130 to 139 cm group. This was significantly different from the other groups. The difference in the values between the other groups for both systolic blood pressure and diastolic blood pressure were uneven and not significant.

Quetelet's index: Though positive correlation was obtained between the quetelet's index and blood pressure the values were not significant.

Smoking: Both Systolic Blood Pressure and Diastolic Blood Pressure did not show any relation - ship between smokers and non smokers correlation coefficient values were not significant .

Drinking: Though slight differences were seen in the values of blood pressure between drinkers and non drinkers, the differences were not significant.

Epidemiological factors among Hypertensives:

The prevalence of hypertension increased with age in both the sexes. The increase in the levels were found to be statistically significant.

Mean blood pressure values did not show significant differences between the two sexes.

Mean values of blood pressure in hypertensives did not show significant differences with height, weight and habits like smoking and alcohol drinking.

Awareness of hypertension was found to be in 18% of the hypertensives . Of these 50% were on regular treatment and 50% were on irregular treatment.

No family history of hypertension was obtained in the hypertensive individuals which may be due to lack of knowledge, Also not more than one individual in a particular family was diagnosed as hypertensive.

7.24

Control of Tobacco-related Cancers and Other Diseases. International Symposium, 1990. Prakash C. Gupta, James E. Hamner, III and P.R. Murti, eds. Oxford University Press, Bombay, 1992.

Antitobacco campaign in Maharashtra, India: achievements and perspectives

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Recognizing that cancer is a preventable disease, the Government of Maharashtra, India, undertook an aggressive antitobacco campaign, consisting of health education programmes, slogans and billboards reminding nonusers of their right to a tobacco-free environment; a counter-campaign against cigarette advertisements was launched in Bombay City. Coupled with these activities, legislation was enacted making smoking in Government establishments and closed spaces in Maharashtra an offense.

INTRODUCTION

Most public health programmes of the Government of India are directed to communicable diseases such as malaria, tuberculosis and leprosy. The occurrence of certain diseases due to life style has now been recognized, and public health programmes are also being mounted against them. Lung cancer is one fatal but preventable life-style disease. The Government of the State of Maharashtra, India, thus initiated a campaign against smoking in 1986. The first reaction of smokers, mostly from urban upper-middle classes, was "We smoke because we like it. It is none of your concern. After all, it is we who would suffer, not you".

After experience of rejoinders of that type, an aggressive antitobacco campaign was launched in Maharashtra. This paper summarizes those activities and gives details of the legislation enacted against tobacco.

ANTITOBACCO MEASURES

Awareness of passive smoking: To counter indifferent attitudes of the kind illustrated above, the Public Health Department of the Government of Maharashtra adopted the slogan 'Your smoking is injurious to our health'. To support this line, a poster was designed depicting a half-smoked cigarette, with a man at one end and his wife and young daughter at the other end, coughing. This poster, which was displayed on the sides of buses, led to awareness of the hazards of sidestream smoke and of passive smoking. It was assumed that realization of the fact that smoking might be harmful to others in a family would at least incite people to keep away from children while smoking. Interestingly, nonsmokers began to use this slogan to counter the indifference of smokers. Youngsters reading this slogan aloud gave a clear but polite signal to nearby smokers either not to smoke or to move away. It also served to counter the rude antagonism of smokers towards antismoking activities.

In January 1987, the Tata Memorial Hospital, Bombay, and the Public Health Department of the Government of Maharashtra organized a two-day workshop on cancer in collaboration with the UICC, where a plan for a State cancer control programme was adopted. One of the strategies was to launch an aggressive anti-tobacco campaign. Perhaps

the only action that had been taken against tobacco use up to that time had been national legislation in 1975 that all cigarette packets and cigarette advertisements display a warning to the effect that 'Cigarette smoking is injurious to health'. Most manufacturers and advertisers ran the sentence, but preceded it with the words 'statutory warning'.

Smoking as a criminal offense: A move was made to make smoking in Maharashtra Government offices an offense. A proposal was initiated by the Public Health Department that resulted in billboards being put up in the corridors of the State Secretariat to the effect that 'Smoking is prohibited'. Predictably, however, this measure did not prove to be effective, indicating that an administrative order alone would be of no great value. A more powerful means of curbing smoking was found in certain provisions of the 'Bombay Police Act 1951', which read as follows: "Section 116: No person shall in any court, police station, police office, building occupied by Government or building occupied by any public body, smoke or spit in contravention of a notice by a competent authority in-charge of such places and affixed to such court, station, office or building. Section 117: Any person contravening the provisions of section 99 to 166 (both inclusive) on conviction, be punishable by fine which may extend to Rs. 100/-."

These provisions were explored to make smoking and spitting within Government offices a criminal offense. Applications were made to the Home Department and to the General Administration Department of the Government of Maharashtra. Finally, approval by the Minister of State for Health and the Health Minister was obtained, and orders were issued on 5 August 1987. A copy of the order is reproduced as Appendix.

The prohibition applies not only in built-up areas but the premises, including compounds. (i) The notice-boards, the colour scheme and the material to be displayed were specified; since these boards were put up right outside the gate, the campaign drew special attention. (ii) An antismoking environment was created by removing ashtrays from all Government offices in Maharashtra. (iii) Even cigarette and *bidi* kiosks within the premises of Government offices were closed down.

Within two days after these orders were issued, a small news item appeared opposing them. 'The workers in *bidi*-making units would march to the secretariat to protest', the news item stated. The march did not materialize; on the contrary, newspapers reported readers' satisfaction about the Governmental action. One letter read, "Why is it that Maharashtra Government is selfish? Why do they take care of their own employees? What about banning smoking in public spaces?"

Health education: Smoking can perhaps be prevented in Government offices by means of a Government order, but an intensive public education campaign is required to prevent people from smoking in public places. It was felt that, with a proper approach, such a campaign would incite a groundswell demanding legislation to restrict tobacco use, sales, advertisement and even cultivation.

'Wills' is a popular brand of cigarette manufactured by a leading firm, the India Tobacco Company, a subsidiary of British-American Tobacco. They advertise their product with attractive models and the slogan 'Made for each other', stating that the filter and tobacco are well matched. The antismoking advertisement used the same format but changed the content to imply that smoking and cancer are made for each other. A huge hoarding was erected at one of the busiest traffic roundabouts in Bombay (at Haji Ali) on the night of 31 December 1987, as a New Year's gift to the citizens of Bombay!

The Indian Tobacco Company, which was in the process of putting up its usual hoardings for 'Wills' in the same area, stopped the painting midway. Instead it put up the

hoarding of another of its brands, 'Bristol.' with the message 'I get what I want'. This was counteracted with an anti-advertisement slogan 'I get what I do not want — cancer'. Another manufacturer uses the slogan 'Taste the spirit of freedom'. To neutralize this, the visual content of the advertisement was changed to vultures and the caption to 'Taste the spirit of free doom'.

Several other slogans and hoardings were designed for the antismoking campaign. In an attempt to enlist the support and services of the women, one hoarding had 'Smoker stinks. Cigarette harms' on one side, and 'Be wise, live longer, choose a nonsmoker' on the other.

DISCUSSION

Maharashtra State is proud of its aggressive, blunt, outspoken and innovative antitobacco campaign. It has banned smoking and spitting in Government offices and made these acts a criminal offense. The orders are generally implemented properly, and many senior officers in Government departments in Bombay have stopped smoking in their offices. The penalty on conviction is a fine of only Rs. 100/- (US$ about 5); but the issue is one of criminal conviction. There may be a few violations, but the measure has created a fear of being convicted and a feeling of guilt about breaking the law. Furthermore, the environment for giving up tobacco use has become more congenial. We believe that this approach, with new slogans, new programmes and an aggressive antitobacco counter-campaign, has resulted in the creation of greater awareness of the harmful effects of tobacco and nonsmokers' right to have a tobacco-free environment. It is gratifying to note that other states in the country are undertaking similar measures.

Appendix

Cancer Control Programme Ban on smoking and spitting in Government/Semi-Government offices and institutions

GOVERNMENT OF MAHARASHTRA
Public Health Department
Resolution No. CNC 1086/CR 241/PH-6
Mantralaya, Bombay 400 032, dated 5 August, 1987

According to the estimates made by experts, there are 1.5 million cancer patients in the country at present. It is also estimated that 0.5 million new patients are added every year. Taking into consideration the increased longevity of the citizens in the country and at this rate, the number of cancer patients by 2000 AD is likely to have been tripled. According to the observations of the Indian Council of Medical Research, out of the total number of cancer patients, cancer could be prevented in respect of 40% totally. In respect of 30% cancer patients it can be cured if it is detected in early stages. For remaining 30% cancer patients, only long-term treatment/therapy can be given. Taking this position into consideration, the importance of preventive measures in Cancer Control Programme is self evident.

Among cancer patients, the number of patients, who are affected by cancer due to tobacco, is large. Smoking and tobacco-chewing not only cause cancer but also can cause respiratory and digestive system diseases. It is therefore necessary to prevent citizens from these diseases and to motivate them to refrain from smoking and tobacco-chewing. Government has, therefore, as an important preventive measure, decided to ban smoking and spitting in Government, Semi-Government, Zilla Parishads, Municipal Corporations, Municipal Council Offices and Institutions and Undertakings coming with in the purview of the State Government.

2. Bombay Police Act 1951 has the following provisions:

Section 116: No person shall, in any Court, Police Station, Police Office, Building occupied by the Government or by any public body, smoke or spit in contravention of a notice by a competent authority in-charge of such places and affixed to such Court, Station, Office or Building.

Section 117: Any person contravening the provisions of Section 99 to 116 (both inclusive) on conviction, be punishable by fine which may extend to Rs. 100/-.

3. Government directs that competent authorities in all Government, Semi-Government offices, Zilla Parishad, Municipal Council, Municipal Corporation Offices and Institutions, and Undertakings shall take recourse to the above provisions of Bombay Police Act, 1951 and should ban smoking and spitting. While implementing this, the accompanying guidelines should be followed. These orders shall come into effect immediately.

All Mantralaya Departments should instruct the Heads of Offices and Government Undertakings under their control to follow these orders.

By order and in the name of the Government of Maharashtra.

Sd/-
Arun Ghate
Section Officer

Accompaniment to Government Resolution, Public Health Department, No. CNC 1086/CR 241/PH-6, dated 5 August 1987.

Guidelines for ban on smoking and spitting

(1) In every room of the office or institution a Board having the following words may be displayed. *Smoking strictly prohibited* (Punishable under Section 116 and 117 of Bombay Police Act 1951). The size of the board should not be less than 15 x 45 cm.

(2) Similar boards should be displayed on the wall outside every room of the institution or office, if there is ample vacant space available, for example, Corridor, Out-patient Department, Meeting Hall. Such boards in Marathi and English as above should be displayed at a distance of every three metres.

(3) At every entrance of the building, a board of the minimum size of 60 cm x 75 cm should be displayed and the following words should be displayed in Marathi and English. *Smoking and Spitting strictly prohibited inside this building and compound.*

(4) A similar board of minimum size of 90 cm x 60 cm should be displayed at the entrance of the compound of the building.

(5) All these boards should be of permanent nature i.e. wooden, tin or of similar material. The ground colour of the board should be red and the words in white. If some period is likely to be taken for preparation of the permanent boards, temporarily, paper or card board boards should be displayed.

(6) The boards on the wall should be at a minimum height of 1.5 metre.

(7) If any ash-trays have been kept in any of the rooms or elsewhere in the institution or the office, they should be removed.

(8) If there are any *pan-bidi* vendors in the building or in the compound of the building, they should be moved outside the compound of the building.

7.25

Control of Tobacco-related Cancers and Other Diseases.
International Symposium, 1990. Prakash C. Gupta, James E. Hamner, III
and P.R. Murti, eds. Oxford University Press, Bombay, 1992.

Controlling cancer by suing tobacco companies: the potential for India in the light of the US experience

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Litigation on the liability presented by tobacco products is now widely recognized as providing unique opportunities for discouraging tobacco use by raising product prices and focusing public attention both on the misleading nature of tobacco promotions and the actual dangers of using the products. In view of the recent legal precedents from suits on motor accidents and the Bhopal gas tragedy, India has potentially the most promising legal environment for bringing such litigation.

INTRODUCTION

Lawsuits against tobacco companies are potentially powerful tools for controlling tobacco consumption. They have also proven — like most other such tools — to be difficult to wield and slow to produce results. Recent legal developments have made these cases easier to bring and more likely to win in the USA; Indian legal developments also suggest that such lawsuits, perhaps in a slightly different legal form, might also succeed.

POTENTIAL BENEFITS

The benefits sought from litigation on tobacco product liability include: (i) forcing the manufacturers to raise the price of tobacco products (to cover the expected cost of litigation and judgment), thus discouraging consumption; (ii) forcing the manufacturers to stop lying about the dangers of their products and, indeed, to 'volunteer' the truth about them; (iii) discrediting the industry in the legislative arena by releasing internal documents giving details of their disinformation campaign and their disregard of public health; and (iv) publicizing the dangers of tobacco use through media publicity attendant upon the filing and trial of such suits.

THE US EXPERIENCE

Difficulties that have arisen in bringing these suits in the USA include: (i) the willingness of the tobacco industry to spend endless amounts of money to intimidate plaintiffs and delay proceedings; (ii) the ability of the industry to evoke 'blame-the-victim' attitudes among judges and jurors by exaggerating the extent of both past and current public awareness of the dangers of tobacco use and by presenting a misleading picture of the amount of individual choice involved in the continued use of tobacco products; (iii) adverse judicial decisions resulting from judges' fears of a flood of litigation if the suits are permitted to proceed; and (iv) poor choice of plaintiffs in the first suits (weak etiological evidence and no effort to quit even after warnings received).

Recent, positive US legal developments have made each of these difficulties much less formidable. First, evidence about the knowledge and behaviour of the multinational tobacco companies, developed by plaintiffs and

lawyers at great expense for use in their trials, is now available cheaply from the Tobacco Products Liability Project. Also, five years of experience in fighting the tobacco companies have prepared the plaintiffs' bar for dealing effectively with the defendants' arguments and litigative devices. Cases against tobacco companies are now no more expensive to bring than other complex product liability cases.

Second, the decision on 5 January 1990 of the US Court of Appeals in Cipollone *vs.* Liggett Group, Inc. makes clear that juries will have to compare knowledge of the dangers of tobacco held by tobacco companies and by individual consumers at specific times in the past, rather than anachronistically evaluating earlier behaviour in the light of current levels of public knowledge. Furthermore, the 1988 US Surgeon-General's Report on Nicotine Addiction has helped change public consciousness on the amount of choice exercised by most long-time smokers.

Third, the fact that the first plaintiff's verdict in June 1988 in the Cipollone case did not lead to a flood of new cases has encouraged courts to begin decide tobacco-related cases consistently with the way they treat those on manufacturers of other dangerous products. Thus, the 5 January 1990 appellate decision in Cipollone, although it reversed the US$ 400 000 verdict and remanded the case for a new trial, for the first time allowed the plaintiff to use a risk-benefit analysis, which holds manufacturers liable whenever the risks of their products to consumers exceed the benefits. This holding, along with the court's strengthening of the 'failure-to-warn' and express warranty theories of action, opens up powerful legal theories for plaintiffs' attorneys.

Finally, plaintiffs' attorneys have learnt which cases to avoid.

The benefits achieved from tobacco litigation in the USA to date include: (i) at least a modest contribution to both snuff and cigarette price increases (which the industry explained were needed, in part, to cover litigation expenses); (ii) forcing the industry to adopt a defensive public relations posture of 'if you die from smoking, it was your own choice' — hardly the best way to sell cigarettes; (iii) releasing damaging internal documents which discredited the industry politically; and (iv) focusing public attention not just on statistics, but on the fact that real individuals die from tobacco use.

THE INDIAN POTENTIAL

The Indian legal situation is quite different from that of the USA, yet it appears to hold substantial possibilities for producing similar public health benefits from tobacco litigation. While product liability actions — and tort claims in general — have traditionally been rare, three recent legal developments in India have made it a potentially hospitable environment for litigation against multinational tobacco companies.

First, in two 1987 cases, the Indian Supreme Court articulated tort principles that were more liberal even than the risk-benefit test enunciated in the Cipollone case. Thus, in Gujarat State Road Transport Corporation *vs.* Ramanbhai Prabhatbhai, the court held for the first time that 'liability without fault' was 'a principle of social justice' in automobile accident cases. Then, in M.C. Mehta *vs.* Union of India, involving a pre-Bhopal release of toxic gases from a factory, the court articulated its willingness to go beyond the principles of liability applied in the United Kingdom and other foreign countries, and it illustrated this willingness by holding that: "If the enterprise is permitted to carry on a hazardous or inherently dangerous activity for its profit, the law must presume that such permission is conditional on the enterprise absorbing the cost of any accident arising on account of such hazardous or inherently dangerous activity, as an appropriate item of its overhead.

While the immediate application of this principle was to an industrial accident, the principle itself and the underlying reasoning were broad enough to encompass tobacco liability cases.

Particularly encouraging for our purposes is the paragraph of the Mehta opinion immediately following this discussion:

"We would also like to point out that the measure of compensation in the kind of cases referred to in the preceding paragraph must be correlated to the magnitude and capacity of the enterprise because such compensation must have a deterrent effect. The larger and more prosperous the enterprise, greater must be the amount of compensation payable by it for the harm caused on account of an accident in the carrying on of the hazardous or inherently dangerous activity by the enterprise."

Philip Morris and British American Tobacco are both very large and very prosperous!

Second, while India does not permit contingency fees (which, in the USA, recruit plaintiffs' attorneys by offering them part of the eventual recovery), the Indian Supreme Court has in recent years recognized a category of 'public interest litigation' in which it is willing to order defendants to compensate public interest plaintiffs for their expenses. This action, along with court rules which permit class actions, could facilitate injunctive actions against abusive industry practices, as well as perhaps carefully planned and respectably sponsored test cases in the product liability arena.

Finally, the political and legal ferment around the Bhopal disaster, focusing on the role of tort law both in deterring multinational corporations from dangerous practices and in providing compensation to large numbers of victims, appears to have produced a new receptivity among Indian judges, lawyers and politicians to the need for effective legal remedies for tortious acts injuring large numbers of people. I assume that in India, unlike the USA, the tobacco industry could not plausibly claim that everybody who uses tobacco products should know (and should have known for many years) of the attendant dangers; on the other hand, there is abundant evidence that Philip Morris and British American Tobacco should have known of these dangers for several decades. In this context, a public advocacy of tobacco product liability suits by respected Indian public health authorities could produce a positive public and judicial response.

Control of Tobacco-related Cancers and Other Diseases.
International Symposium, 1990. PRAKASH C. GUPTA, JAMES E. HAMNER, III AND P.R. MURTI, EDS. Oxford University Press, Bombay, 1992.

The public health practice of tobacco control

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Twenty-five years after the publication of the first US Surgeon-General's Report on the Health Consequences of Smoking, considerable progress against tobacco use has been observed in the USA. The public health practice of tobacco control has been refined during this period, and several essential elements in this practice may be identified: (i) surveillance systems, including behaviour process and disease outcomes to control tobacco have been established; (ii) disease impact estimates, i.e., smoking-attributable mortality, morbidity and economic costs, have provided potent information to policy makers and public health officials; (iii) policies that restrict smoking in public places and the excess of minors to tobacco have assisted in changing the social milieu supporting tobacco use in the USA; (iv) community planning and coalition-building have become mainstays in the complex task of tobacco controls; and (v) public information campaigns using several different media have been extremely effective in changing the public's perception of tobacco. Despite the significant progress against tobacco, and downward trends in its use, 50 million Americans continue to smoke.

INTRODUCTION

As a public health problem, tobacco use may not be unlike communicable disease, with which practitioners of public health have great familiarity. The public health practice of communicable disease control incorporates strategies for surveillance, case finding, clinical treatment, containment, immunization, public policy development and goal-setting. Many of these strategies can be applied to the control of chronic diseases, especially those caused by tobacco. Tobacco use is itself a disease of addiction, and it is responsible for 2.5 million deaths worldwide (1).

The 1964 Report of the Advisory Committee to the US Surgeon-General provided the scientific information needed to launch an effective, sustained public health campaign against tobacco (2). This campaign was described most recently in the Surgeon-General's 1989 Report, *Reducing the Health Consequences of Smoking — 25 Years of Progress* (3). Despite the notable successes of the last 25 years, tobacco use is still widespread in the USA.

Recently, tobacco prevention and control activities have focused on the individual states. It is within the states' jurisdiction to protect the public against environmental and infectious hazards.

This paper summarizes the progress made against tobacco use, outlines the essential elements of the public health practice of tobacco control, and describes the future directions of public health activities against tobacco use in the USA.

TWENTY-FIVE YEARS OF PROGRESS

The 1989 Surgeon-General's Report documents that knowledge of the health consequences of tobacco use has expanded dramatically since 1964; programmes and policies for controlling the hazards of tobacco use have

also proliferated. The conclusions of the report highlight important gains in preventing tobacco use and tobacco-related disease and emphasize areas of continuing concern. The conclusions are: (i) The prevalence of smoking among adults decreased from 40% in 1965 to 29% in 1987. Nearly half of all living adults who ever smoked have quit. (ii) Between 1964 and 1985, approximately three-quarters of a million smoking-related deaths were avoided or postponed as a result of decisions to quit smoking or not to start. Each of these avoided or postponed deaths represented an average gain in life expectancy of two decades. (iii) The prevalence of smoking remains higher among blacks, blue-collar workers and poorly educated people than in the overall population. The decline in smoking has been substantially slower among women than among men. (iv) Smoking begins primarily during childhood and adolescence. The age of initiation has fallen over time, particularly among females. Smoking among high school seniors levelled off from 1980 through 1987 after previous years of decline. (v) Smoking is responsible for more than one in every six deaths in the USA. Smoking remains the single most important preventable cause of death in our society (3).

The *per-caput* consumption of cigarettes in the USA is a sensitive measure of the remarkable change in smoking behaviour over the last few decades (Fig. 1). Significant events in the campaign against smoking included the first scientific reports on tobacco and its association with cancer, the release in 1964 of the Surgeon-General's Advisory Committee Report (2), the elimination of tobacco advertising from television (after the 'Fairness Doctrine' had mandated such effective anti-smoking television spots that the tobacco companies voluntarily agreed to accept the television advertising ban), the nonsmokers' rights movement (accompanied by the proliferation of clean indoor air policies), and the doubling of the Federal excise tax on cigarettes. Economic disasters such as the Great Depression of 1929-31 and World War II suppressed cigarette consumption because of decreased disposable consumer income. The current decline in *per-caput* consumption cannot be attributed to one event or even a series of identifiable events. Instead, it reflects a changing social milieu in which smoking is no longer seen as fashionable, healthful and safe. With this psychosocial change in attitudes towards tobacco use, the public health practice of tobacco control has evolved.

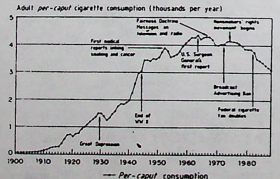

Fig. 1. Adult *per-caput* cigarette consumption and major smoking and health events, USA, 1900-85 (source: USDA, 1989)

ESSENTIAL ELEMENTS OF TOBACCO PREVENTION AND CONTROL

Surveillance: Surveillance of disease incidence and the prevalence of tobacco use is critical to assessing the severity of the public health problem and to evaluating changes in disease status resulting from control measures. Surveillance systems must be simple, informative, uniform and sensitive to changes in disease status. For tobacco use, the following surveillance items must be reported periodically:

Adult knowledge, beliefs and behaviour: This information indicates the coverage of public information and education campaigns and permits identification of subgroups that may need additional attention.

In the USA, national surveillance of adult smoking behaviour is accomplished through the National Health Interview Surveys (NHIS) and the Adult Use of Tobacco Surveys (AUTS). Data from the NHIS (4) show that smoking prevalence declined for both men and women between 1973 and 1985, with a steeper rate of decline for men (Fig. 2). It is predicted

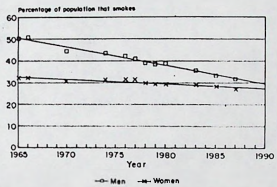

Fig. 2. Prevalence of smoking among adults 20 years old or older, USA, 1965-87 (source: ref. 3)

that by the late 1990s smoking will be more common among women than among men in the USA (5). Low educational status has been found to be the single most important predictor of slow change in current smoking prevalence (6). Thus, national goals should focus on reducing smoking among women (especially young women) and among all persons with low educational attainment.

The AUTS found (3) that knowledge of the health consequences of smoking increased significantly between 1964 and 1986 (Table 1). The data show that progress is being made with public awareness of the health consequences of smoking. Children and adolescents may need additional educational efforts, so that they also recognize the health hazards before experimenting with tobacco.

Adolescent knowledge, beliefs and behaviour: In the USA, about 90% of smokers begin to use tobacco before the age of 21 (3). Assessing knowledge, beliefs and behaviour among children and adolescents is a critical component of a tobacco-use surveillance system. Useful trend data have been provided by the National

Table 1

Percentage of US adults who believed 'smoking causes disease' 1964 and 1986[a]

Year and smoking status	Disease		
	Lung cancer	Heart disease	Lung disease
1964			
Smokers	53	32	42
Nonsmokers	74	41	55
1986			
Smokers	85	71	85
Nonsmokers	95	83	91

[a]Source: Office on Smoking and Health, adult use of tobacco surveys, 1964 and 1986

Institute on Drug Abuse High School Seniors' yearly survey (7). The prevalence of daily cigarette smoking among high-school seniors decreased from 29% in 1975 to 21% in 1980, after which it levelled off at 18-21% (Fig. 3). The prevalence of smoking among females has consistently exceeded that among males since 1977, although a part of this difference may be due to increased use of smokeless tobacco

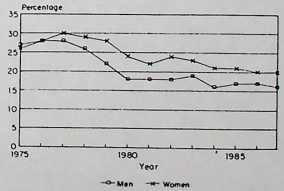

Fig. 3. Percentage of high-school seniors reporting daily cigarette smoking, USA, 1975-87 (source: ref. 7)

among young men over the last two decades (8). The age of initiation for smoking is decreasing (3), which indicates that national programmes should target young persons.

The tobacco-control process (policies, laws, programmes and educational programmes): In 1989, the Association of State and Territorial Health Officials (ASTHO) surveyed all state health departments about public health control activities within each state. These activities included developing tobacco or chronic disease coalitions, tobacco-control plans, surveillance systems, economic incentives and disincentives, clean indoor air policies, laws restricting minors' access to tobacco products, and others. States can use the results of this survey when comparing their activities with others, measuring the progress of programmes against tobacco and evaluating behavioural outcomes in different populations (9).

When national or state goals call for widespread policies, such as clean indoor air at all worksites, then surveillance systems should be established to follow the spread and coverage of these policies. Data can be obtained from sources such as business groups and unions. If schools are to be tobacco-free, then school boards may also wish to establish systems by which progress towards these goals can be measured. In 1989, the National School Boards Association found that 95% of school districts in the USA had a written policy on smoking in schools and that 17% of schools banned smoking on school premises or at school functions (10).

Problem assessment: The second element of tobacco control activities in the USA is problem assessment, which is a detailed analysis of current behaviour, tobacco consumption, current programme capabilities and the disease impact of smoking.

The disease impact measures used in the USA are both epidemiological and economic. The critical calculation in estimating disease impact is the attributable fraction formula:

$$\text{Smoking-attributable fraction} = \frac{p(RR-1)}{p(RR-1)+1}$$

where p is the prevalence of smoking and RR is the relative risk of death from a particular disease for smokers compared with 'never-smokers' (11). The relative risk for 14 smoking-associated conditions was reported in the Surgeon-General's 1989 Report (3). Using those values and current smoking prevalence data, it was estimated that 390 000 deaths were attributable to tobacco use each year in the USA (3).

Economic estimates have also been made of the direct costs of medical care and indirect losses due to disability and premature mortality. One estimate is approximately US$ 65 billion in smoking-attributable economic losses per year (12).

Each state has individualized its estimate of the impact of smoking-attributable disease by using software specifically designed for this purpose (13). Results were reported to each member of the US Congress by the Secretary of Health and Human Services, and results appeared in numerous local newsletters, state medical journals, and state tobacco reports (14). The data are often very useful to policy-makers who need to quantify the disease impact of smoking and compare it with other risks (15).

Policies and programmes: Interventions against tobacco must be multifaceted; no single intervention will be successful without scientifically-based public education and community-based activities, policies and legislative support. Interventions can be promoted through several channels (Table 2) and measured through several resources. If a particular goal is set — for instance, that all health care providers will advise their patients to quit smoking at every opportunity — then some form of monitoring of this activity must occur. Monitoring could take the form of public surveys or, for physicians, chart reviews.

In the USA, clean indoor air laws have become more widespread and stronger over the last several years (Fig. 4). Thus, a trend has begun that may help convince states to strengthen their laws as part of a larger national effort. However, the same trend is not true for laws restricting access to tobacco by minors. Very few states have even modestly strong enforcement of restrictions on the purchase of tobacco products by minors (Table 3). In future plans for improving tobacco-control activities, additional attention must be given to strengthening these restrictions and enforcing them.

Table 2

Examples of intervention activities

Health care system
- Motivate smokers to seek assistance for cessation from health care providers.
- Train physicians, dentists and pharmacists in cessation techniques.
- Expand cessation programmes and funding sources.

Worksites
- Promote changes in smoking behaviour at the worksite through presentations, posters and newsletters.
- Support worksite cessation programmes by offering self-help manuals, audiovisual activities and economic incentives.
- Develop smoke-free worksite policies.

Community organizations
- Present information about the health and economic consequences of tobacco use at organization meetings.
- Promote community cessation resources and self-help programmes of large organizations.
- Promote smoke-free meetings and events.

Schools
- Mandate tobacco prevention as part of the school curricula.
- Train teachers in prevention and cessation skills.
- Promote parental cessation through actions of children.
- Promote smoke-free policies for school buildings, sports events and other school activities.

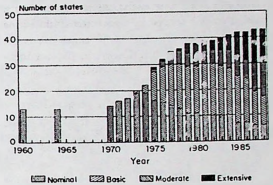

Fig. 4. Number of states with laws regulating smoking in public places, by year and type of law, USA, 1960-88

Table 3

Restriction imposed by laws on minors' access to cigarettes and other tobacco products

None	No restriction on sale of cigarettes or other tobacco products to minors
Nominal	Law banning sale of cigarettes to minors (minimum age requirement stated). In some places, the law applies to all tobacco products.
Basic	Statewide regulations for sale or distribution of tobacco products to minors (minimum age stated) with penalties of either a fine and/or imprisonment. Bans or restricts access to vending machines by minors
Moderate	Basic regulations that also require visible warning signs at points of sale about the illegality of the sale of tobacco products to minors. Requires a license to sell tobacco products that can be revoked or suspended for selling to minors.
Extensive	Moderate regulations with bans on free distribution of tobacco samples. Mandates enforcement and commits resources for enforcement through earmarked license fees

One effort that may inhibit young people from smoking is increasing the excise tax on

cigarettes (16). Currently, all states impose a tax on each package of cigarettes sold. These taxes range from 2 cents to 40 cents per pack, and they are generally lowest in the tobacco-producing states (17). Recently, portions of excise taxes have been earmarked by some states to fund tobacco-control programmes.

Public information campaigns: Figure 1 and Table 1 show that public information campaigns have considerable power. In the USA, media campaigns have been developed for specific groups (minorities, young women and children). Unfortunately, the tobacco industry has also targeted many of these same groups, and analysis of this targeting reveals disturbing and insidious marketing techniques (18).

Communications systems among various public health providers, advocacy groups and non-governmental organizations need to be developed and strengthened (19). These networks permit the rapid dissemination of information and exchange of ideas. Electronic bulletin boards and monthly newsletters have been developed in the USA to help these processes. Training constituency groups (in particular, health department personnel) in media relations is another component of successful public health communications campaigns. These groups can then disseminate to the public scientific information about tobacco-related disease and the need for tobacco-control programmes.

Social marketing is a technique for creating a market for a particular product or service (20). Social marketing can also create a milieu in which tobacco use is no longer the norm, thus facilitating change among users and discouraging young persons from beginning to use tobacco. Public information campaigns are the cornerstone of social marketing efforts.

Coalition building and community planning: Coalitions have become an integral part of tobacco-control activities in the USA. The further a coalition extends beyond the health community, the greater ownership the entire community exerts over tobacco-control initiatives. Coalitions may represent public health officials, health care providers, advocacy groups, voluntary organizations, business groups, religious groups, government officials, the insurance industry, the legal profession, the military, labour organizations, economists, educators, advertisers and communications specialists. Activities of coalitions include developing and implementing tobacco-control plans, public information programmes, and public and professional education programmes. Coalitions also sponsor research and evaluation. Among the 50 states and the District of Columbia, four states have no coalition, 25 states have modestly strong coalitions, 15 states have moderately strong coalitions, and 7 states have strong coalitions (21).

According to the ASTHO survey, nine states have separate public health plans for tobacco use, and 16 states address tobacco use as part of another programme plan (21). To assist states with tobacco-control plans, ASTHO analysed existing plans and published a guide for their development (9,22). The steps for developing a tobacco-control plan include the following: take advantage of national expertise; establish a coalition or advisory group; assess the tobacco problem; develop the mission, goals and objectives of the plan; analyse existing tobacco-control potentials; package and market the plan; and evaluate and revise the plan.

National objectives for the year 1990 included improved health status from the reduction of tobacco use, increased public and professional awareness, improved services and protection, and improved surveillance and evaluation (23). Evaluation methods for tobacco-control activities are still rather rudimentary. Evaluation is difficult because of the unique nature of the tobacco-use epidemic. First, outcomes change very slowly in response to extensive campaign efforts. For example, the prevalence of adult smoking is decreasing at only 0.6% per year in the USA (4); even after 25 years of change, only recently has the lung cancer mortality rate begun to level off among men (23). A 20-30-year lag period in the expression of chronic disease makes it difficult to measure the success achieved during the last 25 years of changing smoking behaviour in the USA.

Second, the rates of voluntary participation in cessation activities are low (80% of smokers quit on their own) (25), and rates for abstinence achieved through such programmes are low (26). Moreover, medical insurance does not, as a rule, cover payment for such programmes, and cessation programmes are often not appropriately designed for, nor accessible to, the most resistent populations. Thus, the proliferation of smoking cessation services may not be associated with widespread behavioural changes.

Third, behavioural change in response to policies, such as those restricting smoking in public places, is difficult to evaluate. In places where evaluation studies have been carried out (worksites), some policy changes have resulted in no change in overall cigarette consumption, some have been associated with a decrease in the daily consumption of cigarettes, and some have been associated with a decline in the prevalence of smoking (27). Yet, such policies contribute to an overall social norm of not smoking.

Finally, the tobacco industry has mounted a massive rear-guard action against restrictive policies on smoking and against economic interventions against the industry. About US$ 3.5 billion are spent yearly on tobacco advertising; tobacco is the second most common subject of advertising in the printed media and the most common in the outdoor (billboard) media (28). In addition, each state and nearly every local jurisdiction considering tobacco legislation is pressured by the powerful tobacco lobby. Grassroot efforts, including referenda, can be expensive and frustrating for groups not funded for and not trained in political processes.

THE FUTURE OF TOBACCO-USE PREVENTION AND CONTROL

Tobacco-control efforts in the USA will continue to encourage state and local activities. The American Stop Smoking Intervention Study for Cancer Prevention (ASSIST) will begin in 1993 (see paper by Glynn *et al.*, this volume). This multistate programme will coordinate, provide training for, and evaluate efforts to prevent and control tobacco use in 20 areas (entire states or large metropolitan areas) through 1998 (9).

California has achieved heretofore unimaginable funding levels for tobacco control through the passage of Proposition 99, a public initiative that increased the state excise tax on cigarettes, the revenues from which are directed, in part, to tobacco-related education. In the next few years, the question, 'If we had enough money, what could we do to prevent tobacco use?' may be answered in that State. About US$ 155 million have been earmarked for the health education component of the appropriations bill attached to this successful initiative. A substantial portion of these funds will be directed to a communications campaign that will be thoroughly evaluated (29).

In 1988, the governors of eight western states initiated the Rocky Mountain Tobacco-free Challenge, a regional effort intended to reduce the prevalence of tobacco use and of chronic diseases associated with it. The challenge will continue until the year 2000; key elements include increased community interest, strengthened interstate and intrastate collaboration, promotion of state activities for reducing tobacco use, and long-term evaluation of tobacco-related policies. Other regions of the country may adopt this innovative, competitive approach (30).

International cooperation has begun between the Office on Smoking and Health and the Pan American Health Organization (PAHO). In 1992, a joint report on smoking in the Americas will be produced by the PAHO and the US Surgeon-General. This report will highlight the changing tobacco-use environment in developing countries and emphasize the need to prevent chronic diseases associated with tobacco use. As tobacco use becomes less common in the industrialized world, it is becoming more of a problem in many non-industrialized countries (31).

CONCLUSIONS

Despite significant progress made against tobacco use, over 50 million Americans continue to smoke. The trend in tobacco use is downward in the USA, and several high risk groups, including young people, minorities, people with low educational attainment and pregnant women, have been targeted for future interventions. The public health practice of tobacco control continues to evolve, and methods for evaluating tobacco-control activities need further development. Public health efforts for controlling tobacco use differ somewhat from those used to control infectious diseases, but they incorporate several of the same principles. These principles involve scientific information, public policy, mass media, social marketing techniques and community-based programmes to affect change. No single intervention will stop the tobacco epidemic. Public health activities for controlling tobacco use need continual assessment and evaluation; as successful strategies emerge, they should be adapted to different cultural and social environments. Unfortunately, the chronic diseases resulting from the epidemic of tobacco use will be measurable for decades, both in developed and developing nations.

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Tobacco control in India: problems and solutions

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Tobacco control is a subject of worldwide importance. India is the third largest producer of tobacco in the world, and the tobacco industry in our country is labour intensive and provides employment to millions of people. It also earns the Government much revenue and foreign exchange. Tobacco in any form, however, is detrimental to health: about 13% of the estimated five million deaths in the adult population can be attributed to tobacco use. A conservative estimate of the annual health care costs attributable to tobacco-related diseases exceeds the revenue earned from tobacco by Rs. 6850 million (US$ 403 million). The Government of India has initiated several measures to tackle the problem. The Cigarette Act of 1975 stipulates that packets of cigarettes and cigarette advertisements display the statutory warning that cigarette smoking is injurious to health. Laws prohibit smoking in closed spaces such as cinemas, theatres, buses and on domestic flights. Tobacco advertisements are banned in state-controlled media. The National Cancer Control Programme launched in 1984, gave high priority to eliminating tobacco-related cancers. Unfortunately, these measures are yet to make a significant impact. A comprehensive programme is described with the aim of creating a tobacco-free society in the country during the next century.

INTRODUCTION

Tobacco appears to be as old as human civilization itself. Cultivation of the tobacco plant probably dates back 7000 years: tobacco seeds were discovered in archaeological excavations in Mexico and Peru, and the remains of permanent settlements built around 3500 showed that tobacco was an important article to the inhabitants (1).

Documented evidence of tobacco usage has been available since the end of the 15th century. In 1499, Indians on Margarita Island, off the coast of Venezuela, were observed chewing a green herb which was carried in a gourd around their necks. It was assumed that the green herb, known as tobacco, was chewed to quench thirst (2,3). Tobacco chewing appeared to be widespread in the late 1500s in parts of southern America (1); men in Veragua (presently Costa Rica) were also seen to be chewing a dried herb (2). Tobacco smoking was also popular in the 1500s: Columbus observed American Indians smoking thick bundles of twisted tobacco leaves wrapped in dried palm or maize leaves (4).

Inhaling of powdered tobacco (snuff) seems to have come into vogue much later. Snuff was prepared by grinding tobacco leaves into a powder with a block and pestle of rosewood (5). The Indians of Brazil were perhaps the first to use snuff. In Haiti, it was used as a medicine for cleaning nasal passages and as an analgesic; Mexican Indians were known to have used tobacco powder to heal burns and wounds by the year 1519 (3) and also inhaled powdered tobacco through a hollow Y-shaped piece of cone or pipe called *tobago* or *tobaca* (6).

TOBACCO PRODUCTION AND USAGE IN INDIA

Tobacco is now cultivated and consumed in various forms all over the world. India is one

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TOBACCO PRODUCTION AND USAGE IN INDIA

Tobacco is now cultivated and consumed in various forms all over the world. India is one

of the principal tobacco producing countries, ranking next to China and the USA. Tobacco is cultivated on an area of over 450 000 ha, with an annual production of 450-500 million kg, constituting 7.6% of total world production in 1987. The average yield per hectare increased from 750 kg in 1960-61 to 1199 kg in 1987-88 (7). Increases in the cultivated area, production and yield of tobacco leaf per hectare since 1949 are presented in Table 1. From 1967-68 onwards, the increase in the total area under this crop can be seen to be marginal; total production and average yield per hectare increased by about 2% *per annum*, which is due largely to better cultivation methods. When Indian yield is compared with that in Taiwan (2692 kg), Japan (2468 kg), Australia (2436 kg), Canada (2250 kg), the Republic of Korea (2210 kg), Pakistan (1774 kg) and Burma (1644 kg) (7), it is obvious that our productivity is likely to rise further. This implies increased availability of tobacco in India in the years to come.

Table 1

All-India compound growth rates (%) of area, production and yield of tobacco[a]

Period	Area $\times 10^3$	Production	Yield
1949-64	1.66	2.79	0.96
1967-85	0.05	2.15	2.11
1949-85	0.70	2.16	1.47

[a]Source: ref. (7)

Tobacco is used in various forms in India (see paper by Bhonsle *et al.*, this volume). Although there are no data on the extent of tobacco use on a national basis, reports from different parts of the country show that the prevalence rates vary from 62 to 82% among men and 15 to 67% in women (8). In a study supported by the Indian Council of Medical Research in Goa, 12% of school children were found to be tobacco users (see paper by Vaidya *et al.*, this volume); in Bangalore, Delhi, Diburgarh, and Ranchi, 56-64% of men over 20 years of age and 14-43% of women were tobacco users.

TOBACCO ECONOMICS IN INDIA

Tobacco production is a major industry in India. The current gross product value of manufactured tobacco is estimated to be of the order of Rs. 36 000 million (US$ 2117 million). Twelve companies with 20 factories manufacture cigarettes in India. In 1987, 75 420 million cigarettes, 51% of which were fil[illegible] tipped, were produced in India (7). The cigarette industry is capital-intensive in the organized sector, providing direct employment for about 20 000 people and indirect employement for hundreds of thousands of people.

The *bidi* industry, which is essentially a cottage industry, provides gainful employment for more than three million people, mostly in rural areas. Annual production of *bidis* is estimated to be over 550 000 million pieces. Tobacco is used not only for smoking, chewing in various forms (see paper by Bhonsle *et al.*, this volume) and as snuff, but also for making several chemicals (see paper by Chari and Rao, this volume).

The excise revenue earned from tobacco is second only to that from mineral oils, amounting to Rs. 15 515 million (US$ 916 milli[illegible]n 1986-87 (7). Tobacco products are an important source of foreign exchange earnings in India: during 1986-87, Rs. 1711 million (US$ 101 million) were earned through the export of unmanufactured tobacco and of manufactured tobacco products like *bidis*, cigarettes, chewing tobacco, snuff, *zarda* and scented tobacco. Interestingly, India also imports a limited amount of tobacco and tobacco products: in 1984-85, tobacco products worth Rs. 3.8 million (US$ 22 300) were imported (7).

NEED FOR TOBACCO CONTROL

In the past, tobacco use was considered by some to be beneficial. In the USA during the

19th and early 20th centuries, dental snuff was used to relieve toothache and neuralgia, to cure bleeding gums and scurvy, to preserve and whiten teeth and to prevent tooth decay (6).

The use of tobacco has, however, been controversial since the beginning. Tobacco was prohibited in Japan in 1590; and taxes on tobacco were increased by 4000% by King James VI of Scotland. In 1633, Sultan Murad IV of Turkey declared that the use of tobacco in any form was a capital offense. During 1613-45, the Czar of Russia prohibited the sale of tobacco. A major attitudinal change towards tobacco chewing arose from the germ theory of infection. In the USA, spitting on the floor and into brass cuspidors was considered a source of contamination and disease spread, and by the 1890s public outcry made tobacco chewing a socially unacceptable behaviour and it became unlawful in most public places (6). Anti-spitting laws were passed in New York and Philadelphia in 1896 and in Toronto, Canada, in 1904 (9).

In India, the earliest observation of the harmful effects of tobacco was made by Niblock (10), who observed in 1902 that cancer of the cheek accounted for almost one-third of all cancer admissions to a general hospital in the State of Madras (presently Tamil Nadu). He attributed this to the tobacco chewing habit, which was prevalent in that region. In 1933, a case-control study indicating a link between tobacco chewing and oral cancer was reported (11). Much later, several epidemiological studies carried out in the Mainpuri district of Uttar Pradesh demonstrated that the earlier the onset of tobacco chewing, the greater the risk for oral cancer (12). The association between tobacco use, oral cancer and precancer was also reported from this area (13-16). The carcinogenic potential of tobacco use has been described in other regions of India as well. For example, in the Bombay area, *bidi* smoking was found to carry risks for cancers of the oral cavity, pharynx and oesophagus (17,18). A dose-response relationship between smoking and lung cancer in India was also demonstrated (19). Data from the National Cancer Registry Project of the Indian Council of Medical Research (20) showed that 50% of all cancers in men and 20% of those among women are tobacco-related. Furthermore, the annual incidence of tobacco-related cancers was estimated to vary from 20 to 30 per 100 000 men and 12 to 14 per 100 000 women. Although the mortality rates from these cancers are very high, no effective cure is available, but these cancers can be prevented, simply by avoiding the use of tobacco.

It was estimated (21) that if a 20% reduction in the use of tobacco were to be achieved in 1985, as was envisaged, approximately 48 465 cancer cases could be prevented by 2000 AD. In terms of cost economics, the difference between the cost of treating these cancers and the cost of a primary prevention programme, i.e., the net savings, would be around Rs. 265 million (US$ 15.6 million). Further estimates indicate that the total annual costs for health care (diagnosis and treatment) for tobacco-related diseases (cancers, coronary heart disease and chronic bronchitis) exceed the tobacco revenue by Rs. 6850 millions (US$ 402.9 million). This is a very conservative estimate, as the cost of establishing essential health care facilities and the loss to the Gross National Product due to tobacco use (disability, fetal loss/underweight) are not included.

Other diseases commonly associated with tobacco use are chronic bronchitis, emphysema, ischaemic heart disease, chronic obstructive pulmonary disease and pulmonary tuberculosis. A cohort study showed that both *bidi* and cigarette smokers had a three-fold greater risk of developing coronary heart disease or myocardial infarct than nonsmokers (22).

The harmful effects of tobacco also include increased risk of low birthweight,

spontaneous abortion, stillbirth and neonatal deaths. An excess rate of stillbirths was observed among smokers (50 per 1000 births) compared to nonsmokers (17 per 1000 births), and babies born to mothers who smoked weighed on average 100-200 g less than babies born to mothers who did not smoke (23). In another study (24), children born to mothers who smoked weighed an average of 395 g less than those born to nonsmoking mothers (see paper by Krishnamurthy, this volume).

Numerous biochemical investigations on tobacco products also confirmed their harmful nature. For example, carcinogenic and cocarcinogenic polycyclic aromatic hydrocarbons were found in substantial amounts in *mishri*, which is applied to the teeth and gums, and in snuff used for inhalation (25). Nicotine, carbon monoxide, hydrogen cyanide, volatile phenols, polycyclic aromatic hydrocarbons, acrolein and acetaldehyde contribute to the toxicity/carcinogenicity of tobacco smoke (26). Betel quid also contains several carcinogenic substances (see paper by Hoffmann *et al.*, on smokeless tobacco, this volume). These findings indicate unequivocally that tobacco consumption in any form is a substantial health hazard.

It is estimated that at least 630 000 deaths among people aged 15 years and above in India are directly attributable to tobacco use; this forms 23% of the total deaths among men and 4% among women (8).

The tobacco industry spends Rs. 2682 (US$ 102) per ha, amounting to Rs. 1200 millions (US$ 70.6 million) *per annum* in curing the tobacco. The major share of this, which is on fuel, is Rs. 1598 (US$ 94) per ha, totalling Rs. 703 million (US$ 41.3 million) *per annum* (7). These figures indicate that since the tobacco industry requires considerable energy resources for curing, it is also responsible to some extent for deforestation in the country, which will lead to ecological imbalance in the years to come.

PROBLEMS AND POSSIBLE SOLUTIONS FOR TOBACCO CONTROL

Possible tobacco control measures can be split broadly into (i) sociobehavioural aspects; (ii) pharmacological and psychological aspects; (iii) economic losses and gains; and (iv) political will.

Sociobehavioural aspects: Every effort should be made to make tobacco use an antisocial habit, be it at home, at work, in public places or at social gatherings. Some state governments in India — for example, those of West Bengal, Tamil Nadu, Kerala, Karnataka, Maharashtra and Gujarat — have promulgated laws prohibiting smoking in enclosed areas, such as cinemas, buses, educational institutes and hospitals. Smoking is prohibited currently on all domestic flights of Indian Airlines. Any advertisement or even mention of tobacco is banned on the broadcasts of All-India Radio.

To achieve the aim of a tobacco-free society, environmental situations must be created in which nonsmokers are given preference over smokers. In order to achieve this, many gradual and carefully designed steps will have to be undertaken. For instance, antitobacco education, focused on young nonusers through an extensive, persuasive campaign would be an important step in that direction. Use of the mass media, voluntary agencies, women's organizations, educational institutions, religious organizations, shrines, no-tobacco days for users and traders, and messages from health-related institutions should be explored. Periodic cross-sectional assessment to measure the impact of such educational programmes would be essential in order to make the mid-course corrections.

Pharmacological and psychological aspects: Termination of nicotine ingestion, even after intake of small quantities (daily dose, 0.002 mg/kg body weight), produced behavioural patterns associated with aggressiveness,

regional languages, as a weekly serial with 28 episodes, by all of the 104 broadcasting stations, focusing on the rural community aged 10 years and over.

RESEARCH PRIORITIES

Operational research for antitobacco community education must be strengthened, and various agencies can be used for this purpose. A single approach will not be suitable for all population groups, but packages for different areas of the country could be devised and implemented. Research on tobacco usage would help in deciding the most effective method of community-based intervention.

A major hindrance to implementing antitobacco legislations is the fear of loss of employment and the revenue earned from tobacco. As described above, however, the amount spent on the treatment of tobacco-related diseases outweighs the gains due to tobacco revenue and export. The Indian Council of Medical Research is initiating studies on the cost of managing tobacco-related diseases, which will help in computing the tobacco economics for the country more accurately.

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hostility and irritability (28). Thus, nicotine acts as a reinforcing agent in tobacco smoking. The nicotine withdrawal syndrome, which includes sleep disturbances, changes in brain wave-pattern, fall in pulse rate and blood pressure, anxiety, nervousness and fatigue, contributes to the difficulty in giving up tobacco.

Counselling centres for quitting the tobacco habit, comprising psychological support to tobacco users, would be necessary. In some situations, the focus could be on mitigation rather than on elimination. People continue to smoke because of dependency due to cognitive helplessness: research must therefore be undertaken to find ways to satisfy their psychological and pharmacological needs. Non-smokers' rights in the face of the dangers of passive smoking are another important social issue. In a large proportion of people, initiation into alcohol and drug abuse starts after tobacco use (28).

Economic aspects: As discussed above, tobacco contributes to both the negative and positive aspects of the country's economy, but the losses to the economy far outweigh the gains. Unfortunately, this fact is still not well known and should be proven with sound data. While the gains are clear, in the form of employment generated by tobacco-related activities and revenue and foreign exchange earnings, the losses occur in the form of costs incurred in providing health care for people with tobacco-related diseases due to loss of productivity caused by decreased efficiency, disability and premature death. The use of wood in tobacco curing, resulting in environmental degradation and soil erosion, also has serious economic implications.

A conservative estimate, based on the impressions of a number of clinicians, of the cost of treatment of three major tobacco-related diseases, namely, cancers, heart diseases and bronchitis, is that it costs the government about Rs. 24 190 million (US$ 1422.8 million) annually, which is Rs. 6850 million (US$ 402.9 million) more than the revenue and foreign exchange provided by tobacco to the Government. As mentioned earlier, these estimates do not include the cost of diagnosis and treatment of other diseases and disorders or the cost of establishing health care facilities such as radiotherapy units and computerized tomography scanners.

Experience all over the world has shown that a gradual price rise is an effective means of reducing the smoking habit. Thus, a gradual increase in the prices of all tobacco products in the country would be the right approach.

Political will: A necessary ingredient for the success of any national programme is political and administrative support. Politicians and administrators must be convinced of the magnitude of tobacco-related problems, so that they will promulgate and strictly enforce any legislation directed towards tobacco control. Politicians can also act as leaders for anti-tobacco programmes, and this increases their chances of success. The political will can be stimulated by close interaction between scientists (health, agriculture, industry), politicians and administrators.

EFFORTS OF THE GOVERNMENT OF INDIA TOWARDS TOBACCO CONTROL

Realizing the magnitude of health problems associated with tobacco usage, the Government promulgated The Cigarette Act, 1975 (regulation of production, supply and distribution), which requires that all manufacturers or persons trading in cigarettes display prominently a statutory warning, 'Cigarette smoking is injurious to health', on all cartons and packets of cigarettes that are put on sale. This, however, made no significant dent in the smoking habit; because (i) the statutory warning is limited to cigarettes, which are consumed much less than *bidis*, which are cheaper and more harmful; and (ii) the printed warning can be read only by literates.

It has been suggested that, in view of the diverse forms of tobacco use, (i) the statutory warning be extended to other tobacco products; (ii) the warning be printed in local languages; and (iii) the warning made more effective by a pictorial depiction, for instance, in the form of a skull-and-crossed-bones. The printing of more direct messages like 'Tobacco can cause cancers and heart diseases' in local languages might also be useful. Printing the tar and nicotine levels on packets and cartons of all tobacco products and fixing the maximum permissible limits of these toxins for all tobacco products should also be made mandatory. High levels of taxation should be placed on high-tar, high-nicotine tobacco products. Both cigarettes and *bidis* should be required by law to have effective filters.

On the recommendations of the Luthra-Bisht Committee in 1984, a national cancer control programme was formulated, which gave impetus to the antitobacco cause. Noting that tobacco-related cancers account for about one-third of all cancers in the country, primary prevention of tobacco-related cancers constituted a major objective of this programme. Accordingly, the National Cancer Control Board and state cancer control boards have given high priority to antitobacco educational programmes for primary prevention of tobacco-related cancers. To date, 17 states and union territories in the country have constituted such cancer control boards.

Monitoring and controlling scenes that glamourize smoking in films, Doordarshan (television) programmes and road-side advertisements constitute another important control measure. As described earlier, a complete ban on tobacco advertisements in government media exists, and smoking is prohibited on domestic flights.

It is realized, however, that such governmental steps, although commendable, are not sufficient to make an impressionable dent on the tobacco habit of the community: it is necessary to have a comprehensive programme for tobacco control. The main planks of such a comprehensive programme should comprise tougher antitobacco legislation, a gradual price rise on tobacco, changes in agricultural practices to replace tobacco by other crops, finding alternative uses of tobacco, modifying tobacco products to make them less harmful and an aggressive health education campaign to wean people away from tobacco. Other steps that the Government should initiate urgently are: protection of nonsmokers in public places from passive smoking; banning tobacco advertisements in all public places; making it unlawful to sell tobacco items to people below the age of 18; sale of cigarettes and *bidis* in packets, as opposed to selling them singly; prohibition of the sale of tobacco in and around educational, health and religious institutions; and a ban on tobacco imports.

OPERATIONAL RESEARCH ON AN ANTITOBACCO PROGRAMME

The experience all over the world is that antitobacco education is an effective means of stopping or curtailing tobacco use. Although such efforts have to be targeted at users as well as nonusers of tobacco, the most profitable target group is the young nonuser. An intervention study by the Tata Institute of Fundamental Research, Bombay, showed that 9-17% of people stopped tobacco use and 20-49% reduced their habit substantially after five years of health education (27). The Indian Council of Medical Research initiated a multicentre study in Bangalore, Goa, Agra and Trivandrum, utilizing the existing health infrastructure. Workers at the Goa centre are also studying the use of school children as a means of changing tobacco habits in a community.

All-India Radio, in collaboration with the Indian Council of Medical Research, will soon initiate an educational programme on the hazards of tobacco, drugs and alcohol. This programme (Radio Date) will be broadcast in 17

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intervention and (v) intervention specially directed to high-risk populations.

Tobacco cessation clinics: Quitting the use of tobacco is complex and requires continuous support from various sources. Thus, tobacco cessation programmes should include health education, motivation and psychological, social, family and sometimes pharmacological support in order to bring attitudinal changes and modification of behaviour. Implementation of these programmes, therefore, must be multidisciplinary, involving clinicians, psychologists, sociologists and family support in a suitable environment. We envisage conducting tobacco cessation clinics incorporating the necessary infrastructure, especially for heavy tobacco users. The reasons for the high level of health awareness among some individuals may be applicable for primary prevention in others. We will therefore collect this information from a sample of the 100 000 individuals who registered themselves in the Kerala government scheme 'Cancer care for life'.

Chemoprevention: Chemoprevention is a major experimental activity for the control of oral cancer and precancer at the RCC, which is being conducted in collaboration with the British Columbia Cancer Research Centre, Vancouver, Canada. The main objective is to determine whether micronutrients can lower the risk of cancer by preventing or reverting the process of carcinogenesis. The feasibility of using micronucleated cells as intermediate endpoints is being evaluated. ß-carotene and vitamin A intake appear to result in higher rates of regression of leukoplakia among heavy chewers, smokers and alcohol users (6-8). The optimal doses, spacing and maintenance of these vitamins were also determined. Chemopreventive agents are believed to act even with the continued action of etiological factors; however, whether these agents really reduce the risk for cancer is yet to be determined from long-term follow-up studies. At this stage, the emphasis is on clinical trial; we hope to translate the experiences gained from these studies into a full-scale chemopreventive intervention trial.

Secondary prevention:

Use of primary health workers for early detection of oral cancer: Studies conducted in Sri Lanka (9) and in the Ernakulam district of Kerala (10) demonstrated that primary health care workers can be used in oral cancer detection programmes. A similar study is in progress in the northern part of Trivandrum district: primary health care workers in six primary health centres were trained by the RCC to identify people at risk and to examine their mouths to detect oral cancer and precancerous lesions. An area covered by primary health care workers in the southern part of the Trivandrum district has been selected as the control area. It is proposed to compare the numbers of oral cancer cases arriving from these two areas to evaluate whether early detection has been achieved in the study area.

Use of unemployed youths for early detection of cancers: Some 92 unemployed youths belonging to a community of 14 000 persons were informed about the seven warning signals of cancer and were briefly trained to examine the oral cavities of high-risk persons. These youths then screened 13 959 people from that community and identified 397 high-risk individuals. While examining the individuals, they also disseminated information on the seven warning signals. People who thought they might have cancer on the basis of these signals and people found by the unemployed youths to have a suspicious oral lesion were advised to consult physicians. Employing this method, nine cancers, of which four were buccal cancers, and 169 precancerous lesions and conditions were detected, vindicating the feasibility of using such young persons in oral cancer detection programmes.

Use of National Service Scheme volunteers: The National Service Scheme is a voluntary student organization which is involved in various

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Control of Tobacco-related Cancers and Other Diseases.
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Control strategies for tobacco-related cancers in Kerala, India

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Various cancer control activities undertaken by the Regional Cancer Centre, Trivandrum, Kerala, India, include a novel method of utilizing the services of National Service Scheme volunteers, primary health care workers, social workers and unemployed youth in both primary and secondary prevention of cancer. These approaches were found to be effective.

INTRODUCTION

Cancer control implies a broad spectrum of activities aimed at primary prevention, reduction in morbidity and mortality and rehabilitation. The basis for cancer control is research in basic sciences, cancer epidemiology, diagnostics, clinical oncology, social sciences, rehabilitation, health care organization and health delivery. Many countries have formulated cancer control policies consistent with their needs and priorities (1), and India is one of them (2). Tobacco-related cancers constitute 50-55% of cancers among men and 20-25% among women in India (3,4). Accordingly, in the National Cancer Control plan, primary prevention formed an important objective. In consonance with this objective, the State of Kerala on the south-western coast of India has formulated its own cancer control programmes (5). This paper gives an overview of the activities conducted by the Regional Cancer Centre (RCC), which is a major cancer treatment centre in the State.

CANCER IN KERALA

Data from the RCC show that every year 15 000 new cancer cases occur in the State (4). Of these, 17% among men and 11% among women are oral cancers. Other common cancers among men include cancers of the lung (11.5%), oesophagus (5.8%) and larynx and pharynx together (7%). Among women, the common cancers include those of the uterine cervix (25%) and breast (17%).

CONTROL STRATEGIES IN KERALA

To facilitate the planning of control strategies, the following data were collected: (i) the pattern of tobacco usage in the community; (ii) knowledge, attitude and perception of the general population; (iii) referral pattern; (iv) incidence rates of various cancers; (v) clinical extent of cancer at first presentation; and (vi) proportion of cases receiving radical treatment.

Several measures are being implemented in the State, but the major emphasis is on primary prevention, with an interdisciplinary approach utilizing health care delivery agencies and voluntary organizations. The various activities can be summarized as follows: Primary prevention involves surveys of tobacco use and of knowledge, attitude and perception, cancer registration, health education, tobacco cessation clinics, chemoprevention and legislation. Secondary prevention consists of utilization of primary health

workers, volunteers to the National Service Scheme and unemployed youth, cancer detection camps and peripheral centres for early detection of cancer. Tertiary prevention involves therapeutic intervention, surgical reconstruction, clinical trials, pain clinics and psychosocial surveys of morbidity.

Primary prevention:

Tobacco surveys: Information on the prevalence of tobacco use is important for planning control measures and was obtained from different parts of the State. For example, 13 000 people in the south were interviewed by health and social workers. These individuals represented a 10% sample of the 278 census enumeration blocks in each of which the entire population was enumerated for tobacco habits. In central Kerala, unemployed youth collected this information from 11 420 people; in Kottayam, all individuals over the age of 21 were screened by National Service Scheme volunteers with regard to their tobacco habits and alcohol consumption, as part of an oral cancer screening programme.

Tobacco smoking by itself or with chewing was common (46%) among men; only 9% were exclusively chewers. An overwhelming proportion (92%) of women in this group did not use tobacco. Compared to data available from other sources, these prevalences are rather different. Information on alcohol consumption was also collected from these individuals.

Surveys of knowledge, attitude and perception: Table 1 summarizes information collected on knowledge, awareness and perception about cancer among 600 individuals by hospital social workers. A high level of awareness was observed about cancer in general, about warning signals and about the risk factors for oral cancer. The knowledge of medical students was monitored in another survey, and such information is now being obtained from physicians and surgeons.

Table 1

Awareness about cancer among 600 individuals in Kera

Criteria	Percent
Heard about cancer	100
Aware about at least one or more risk factors for oral cancer	67
Aware about at least one or more risk factors for lung cancer	28
Aware about at least one or more of the seven warning signals of cancer	75
Aware about at least one or more common cancers	65

Cancer registration: Since 1982, a hospital based cancer registry has been functioning a the RCC, which is the only cancer treatmen centre in southern Kerala. Data from thi source is used to compute the minimal inci dence rates of different cancers in order t study their trends. Information on referra practices, the clinical extent of cancers at pres entation, treatment modalities and prognosis i also available from the registry.

Health education: Helping people to avoi tobacco use is accorded high priority in th cancer control programme. With that view various health educational programmes ar being undertaken at the Community Oncolog Centre of the RCC. Electronics and the pres are being used to disseminate in[illegible]matio about tobacco related-cancers to the publi Further, audiovisual programmes on canc are being shown during cancer detection camp in various parts of the state. School childre will be educated on the harmful effects o tobacco and will be used later to spread th messages. Suitable material to be included i the school curriculum is being developed. A part of self-help measures, pamphlets on exam ining one's own mouth are distributed perio ically, so that they will reach a large nun ber of households. The various health edu cation measures thus comprise (i) schoo based intervention, (ii) self-help strategies, (ii mass media approaches, (iv) community-base

developmental programmes in the community. The organization has different levels of leadership and implements many socially relevant schemes, such as teaching, hygiene and immunization, in the community. For the present purpose, volunteers were instructed about the seven warning signals of cancer and were also trained to conduct oral examinations. They have screened 4041 persons so far, and detected 15 oral cancers, 12 in clinical stages 1 and 2 and three in stages 3 and 4; they also found 92 precancerous lesions and conditions, which were confirmed by physicians. Thus, the strategy of using National Service Scheme volunteers was found to be fruitful, and they are now being used regularly in screening programmes in Kottayam.

Early detection centres and cancer detection campaigns: Two peripheral centres for early detection of cancer were established in Ernakulam and Palghat by the RCC in collaboration with the Kerala State Health Services Department. The main purpose of these peripheral units is to provide diagnostic services for cancers of the head and neck, breast and uterine cervix (11). The units also organize regular cancer detection campaigns in the community in order to examine high-risk individuals and to follow-up cases of precancer.

Tertiary prevention:

Tertiary prevention encompasses reconstruction, rehabilitation and pain control therapy. In order to provide optimal treatment and minimal loss of structure, a combined approach consisting of surgery, radiation and chemotheraphy is used for treating cancer at the RCC. Regular programmes propagate this approach to other centres in Kerala.

Clinical trials to assess the efficacy of multi-modal treatment of advanced tobacco-related cancers are in progress at the RCC. The cancer surgery division uses an indigenous reconstruction technique for oral and head-and-neck cancers. Pain relief management consistent with that recommended by the WHO global programme on cancer pain relief is part of the treatment protocol at the RCC, and this knowledge is disseminated to other centres in the State. Objective and subjective assessments of various pain relief methods are also being planned. Psychosocial surveys on morbidity of cancers of the head-and-neck, breast and cervix are being contemplated.

DISCUSSION

Kerala is a small state with a high literacy rate (65%), which is advantageous for raising the health consciousness of the people. As elsewhere in the country, tobacco use is deeply entrenched. In order to combat its health consequences, the RCC, in association with medical colleges in the State, the Health Services Department of Kerala Government, National Service Scheme volunteers, unemployed youth, general practitioners and various social organizations, has embarked on multifaceted cancer control activities. The active concern of the Government regarding the health consequences related to tobacco use and its supportive action are encouraging. For instance, the Government is contemplating measures to prevent tobacco from being available to children and to deter tobacco use in public places, educational institutions and Government offices. It is hoped that these attempts will produce the desired results in the near future.

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Efficacy of an anti-tobacco community education program in India

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In a study on 'Assessment of Efficacy of an Anti-Tobacco Community Education Program' on Kolar District of Karnataka, India, an experimental and two control areas were chosen based on comparable population, health, and socioeconomic parameters. The two main objectives were to prevent individuals from taking up the tobacco habit among those who currently did not smoke or chew tobacco, and to stop the tobacco habit in those who did smoke or chew tobacco. A baseline tobacco-habit survey of the population was followed by anti-tobacco education of the community in the experimental area only. Two years later, a repeat survey of the population was conducted, followed by a final survey after a further three years. Methods of health education of the community included screening of films, exhibits, and personal contact with a display of photographs of the harmful effects of tobacco. The results were evaluated through changes in prevalence rates, quitters' rates, and initiation rate. The final survey showed that in the experimental area, the decline in the prevalence rate in the combined sample compared with the baseline rates was 10.2 percent in males and 16.3 percent in females, with a corresponding quitter's rate of 26.5 percent in males and 36.7 percent in females. Among men, a higher proportion (30.2 percent) had given up chewing compared with smoking (20.4 percent). *Cancer Causes and Control* 1995, 6, 119-129

Key words: Anti-smoking education, India, program evaluation, tobacco control.

Introduction

Use of tobacco in various forms is widely prevalent in the Indian subcontinent, although exact figures of prevalence of the habit are available from only some areas.[1-3] In these studies, there is a wide variation from region to region in the prevalence and type of tobacco used (62 to 82 percent in males and 15 to 67 percent in females). The annual number of deaths in India attributed to tobacco use is estimated to be between 630,000 to one million.[3,4] The association between use of tobacco and the occurrence of oral cancer was reported over 60 years ago[5] and since then, the burden of tobacco-related cancers has been estimated[6-9] at 40 to 42 percent of all cancers among males and 15 to 20 percent of all cancers among females.

It is obvious, therefore, that education of the public,[10] including selected target populations, on the harmful effects of tobacco is of paramount importance. Few studies have been conducted in this part of the world in

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a systematic and evaluable way, so as to measure the impact of such an education program and also to examine whether this could be integrated into the general health scheme of the community. This study was conducted to assess the efficacy of such an anti-tobacco community-education program. It had two main objectives. The first was to prevent the uptake of the tobacco habit in persons who did not smoke or chew tobacco, and the second was to stop the tobacco habit in those who did smoke or chew tobacco—both objectives being achieved through health education of the community.

Materials and methods

An 'Anti-Tobacco Community Education Program' was conducted as a demonstration-cum-research study by Kidwai Memorial Institute of Oncology, Bangalore through funding from the Indian Council of Medical Research, New Delhi. It was carried out over a six-year period between February 1986 and March 1992. The work essentially involved a systematic survey of the population for the prevalence of the tobacco habit in three different areas. This was followed by intervention through anti-tobacco community education of one area, followed by two additional surveys in all three areas. The impact of the education was measured through tobacco-habit prevalence rates, the number and rates of persons who had quit the habit, and the rate of uptake of the habit by prior nonusers of tobacco.

Selection of place/areas for study

The study was conducted in one experimental and two control areas of Kolar District (population [pop] = 1.9 million [1981 Census]) in Karnataka State (pop = 37 million) of India. The district of Kolar was selected because of the proximity of the district to Bangalore. Three areas under the purview of the Primary Health Centers of Dibbur (pop = 60,447), Malur (pop = 64,202), and Gudibanda (pop = 46,878) comprising 117, 136, and 120 villages, respectively, were chosen on the basis of a fair degree of comparability of prevalence of the tobacco habit, availability of educational facilities, and socioeconomic infrastructure. Dibbur was chosen as the experimental area (ExA), and Malur and Gudibanda as control areas I (CoAI) and II (CoAII), respectively.

Plan of survey

The survey was carried out three times. The first survey was defined as the 'baseline survey' (BLS) and was carried out before undertaking any educational programs. The second survey was called 'first repeat survey' (FRS) and was done two years after education was imparted to the community covered by the ExA. The 'final survey' (FS) was made three years after the FRS. The actual survey was done in two sets of selected villages in the three areas. The first set referred to as 'panel sample' (PS) consisted of 10 villages in the ExA, five villages in CoAI, and 11 villages in CoAII. The population in these villages, comprising the PS in the experimental and control areas, was surveyed all three times during baseline, first repeat, and final surveys. The second set of villages referred to as the 'non-panel sample' (NPS) consisted of 47 villages in ExA, 32 villages in CoAI, and 34 villages in CoAII. These villages in the NPS were defined as those villages which were surveyed only once during any of the surveys mentioned above. Thus, of the 47 villages mentioned in the ExA, 19 were chosen for BLS, 14 for FRS, and another 14 for FS. Similarly, the number of villages chosen during the three surveys, respectively, for CoAI were 10, seven, and 15, and for CoAII were 17, eight, and nine. A stratified random-sampling method was used to select the villages. The above method of choosing one set of villages as PS and another set as NPS was done to ensure as much coverage of the population as was possible while at the same time to observe the impact of education on people in one set of villages. The results from the NPS also eliminates any bias that may be associated with the results in the PS from repeated tobacco surveys in the same population. This needs to be emphasized, since the PS was not exposed to any deliberate or planned intervention *vis-a-vis* the villages under the NPS.

The number of villages chosen in the combined sample (CS) (CS = PS + NPS) as well as for the panel and non-panel samples during each of the three surveys in the experimental and control areas with their respective population according to the 1981 census is shown in Table 1. However, the actual population of the different villages at the time of the survey was higher because of the period of time that elapsed between the conduct of the census in 1981 and the time when the surveys actually took place. The exact population at the time of each survey is indicated in the subsequent tables that give results of the survey.

Survey methodology

Three forms consisting of village appraisal, household information, and tobacco habit were completed by trained social investigators. The village appraisal form consisted of the basic characteristics of the village in terms of land available for cultivation, the literacy of the population, education, and health, as well as communication and transport facilities that were available. The household survey form was used to identify the household in the village, record income of the earning members, and number of persons in the house who

Table 1. Number of villages (Vil) and their total estimated population (1981 census) in the combined sample, panel sample, and non-panel sample during Baseline Survey (BLS), First Repeat Survey (FRS), and Final Survey (FS), India

	Experimental area				Control area (I)				Control area (II)			
	No. Vil	Population			No. Vil	Population			No. Vil	Population		
		Male	Female	Total		Male	Female	Total		Male	Female	Total
Combined sample												
BLS	29	5,097	5,116	10,213	15	4,341	4,126	8,467	28	4,667	4,594	9,261
FRS	24	2,246	2,281	4,527	12	1,905	1,875	3,780	19	1,773	1,758	3,531
FS	24	3,239	3,285	6,524	20	5,821	5,580	11,401	20	2,477	2,460	4,937
Panel sample												
BLS	10	1,228	1,249	2,477	5	862	851	1,713	11	1,397	1,367	2,764
FRS	10	1,228	1,249	2,477	5	862	851	1,713	11	1,397	1,367	2,764
FS	10	1,228	1,249	2,477	5	862	851	1,713	11	1,397	1,367	2,764
Non-panel sample												
BLS	16	3,869	3,867	7,736	10	3,479	3,275	6,754	17	3,270	3,227	6,497
FRS	14	1,018	1,032	2,050	7	1,043	1,024	2,067	8	376	391	767
FS	14	2,011	2,036	4,047	15	4,959	4,729	9,688	9	1,080	1,093	2,173
Total	47	6,898	6,935	13,833	32	9,481	9,028	18,509	34	4,726	4,711	9,437

smoked or chewed tobacco. The individual survey recorded details of the tobacco habit and level of awareness about the harmful effects of tobacco. Individuals of all ages were surveyed. Surveys took about five to six months to be completed. Information on the tobacco habit was elicited in-person by the social investigators.

Anti-tobacco education

Education on the harmful effects of tobacco was carried out in all the 117 villages (including 10 in the PS and 47 in the NPS) within the experimental area, but not in any of the villages in the control areas. Twenty-five junior health-workers of the Primary Health Center and three senior health-workers were involved in health education. Each junior health-worker would cover each village under his/her care once a week, and the senior health-worker once a month. Health education was imparted to individuals or small groups by the junior health-worker, whereas group discussions which were held once a month, were conducted usually in the presence of the senior health-worker. The intervention commenced soon after the completion of the baseline survey and lasted for about three years. The following health education materials were used to impart education:

- *Handbills*—Summary about harmful effects of tobacco on health. About 2,000 handbills were used. These were distributed by the health workers to households with literate persons;
- *Folders*—Brief explanation about tobacco-habit formation and misconceptions about tobacco messages. About 500 folders were distributed by the health workers to persons such as community leaders in the village;
- *Card* ($4'' \times 3''$) with photographs of advanced cancers of the oral cavity on both sides. A health-worker could carry this card easily in his/her pocket and use it during person-to-person contact in the community. Each health worker carried a card which was replaced whenever necessary with a fresh one. Approximately 100 cards were used;
- *Photo album* with 28 postcard-size photographs with appropriate captions and messages on harmful effects of tobacco and about cancer. Just as with the cards above, one photo album was used by each health-worker. In all, 40 photo albums were used;
- *Portable display boards* with messages about harmful effects of tobacco and photographs on cancer. Two sizes of boards one small ($15'' \times 12''$) and the other larger ($4' \times 3'$) were used for group discussions. Four sets of these boards were used;
- *Audio-visual aids* including 16 mm feature films—These consisted of two separate films (duration 10 minutes each) on smoking and the other on chewing in four languages (English, Kannada, Hindi, and Telugu);
  —the above also was prepared in the form of a video casette along with another video casette

titled 'Cancer is curable' with highlights on primary prevention of cancer, basic knowledge on its treatment and terminal care of cancer patients.

Films were screened at least twice during the period of intervention, in each of the 117 villages in the experimental area.

Statistical tables/methods

The findings of the study are expressed in quantitative terms in the following ways:

- *Prevalence rates:* The prevalence of the tobacco habit in the population as indicated by the number of users of tobacco (for at least six months' duration at the time of personal interview) per 100 persons (percent) in the population was calculated for the three surveys (BLS, FRS, and FS). The difference in the prevalence rates during the survey periods was observed;
- *Quitters' rates:* The number of persons among the tobacco users who had quit the use of tobacco (for at least six months' duration at the time of personal interview) was calculated for the surveys (FRS and FS) done subsequent to the intervention through health education of the community. The rates were calculated as number of quitters per 100 (percent) ever-users of tobacco in the population. This is the same as the 'quit ratio'[11] expressed for smokers;
- *Initiation rates:* The number of persons among the nonusers of tobacco who had taken up the tobacco habit within the past six months at the time of personal interview was calculated and the rates expressed as the number of these new habituates per 100 nonusers of tobacco in the population. This was calculated for persons between 10 to 24 years of age. The influence of age, as demonstrated by the age specific prevalence rates of tobacco users and age-specific quitters' rates, during the different surveys was also compared;
- An attempt was made to determine which among the health education materials used for intervention in the ExA had the most profound impact in motivating persons to quit the habit.

Each of the above was calculated for the populations in the villages selected for the combined sample and also separately for those villages in the PS and NPS.

In males, the rates also were calculated separately for chewing and smoking tobacco. Males who practiced chewing alone as well as those who practiced chewing and smoking were added in calculating the rates of chewers. Similarly, only smokers, and smokers who chewed tobacco were included in calculating the rates of smokers.

The survey results on type of tobacco use showed that over 99 percent of women, whether in ExA or either of the control areas, were tobacco chewers and the others were users of snuff. Thus, there were no smokers among women in any of the areas. Consequently, the results presented for females pertains exclusively to tobacco chewing.

Tests for statistical significance were calculated by computing chi-squares of observed and expected values in ExA compared with each of the control areas at the time of FRS and FS in relation to that of the BLS. This was done for the CS as well as for the panel and non-panel samples. The level of significance was examined by observing *P*-values of the chi-squares. Chi-squares and the level of statistical significance were calculated also for linear trend in the prevalence and initiation rates in the ExA for the three survey periods.[12]

Results

Prevalence rates

The population present at the time of the respective survey, the number of users of tobacco, and their prevalence rates (percent) in the population, in each of the surveys at the Experimental and two Control Areas are presented in Table 2. The proportions (percent) of differences in the rates between surveys are shown in Table 3.

Baseline prevalence rates. The prevalence rates in percent of tobacco users (Table 2a) during the BLS in the ExA is higher in both males and females compared with that in CoAI and CoAII. Females show a higher prevalence of tobacco use compared with males in experimental and control areas. Examination of the prevalence rates after stratifying according to villages of the PS and NPS did not show any marked difference.

Baseline prevalence of type of tobacco. Table 2b gives the respective prevalence rates of tobacco chewers and smokers among men in the experimental and control areas during each of the surveys. In the BLS itself, the type of tobacco habit of the population in the ExA and in the two control areas shows some variation. Thus, the ExA shows 16.4 percent of tobacco chewers compared with 7.7 percent and 8.4 percent chewers in CoAI and CoAII, respectively. Similarly, the ExA shows 17.7 percent of smokers compared with 21.0 percent and 21.7 percent in CoAI and CoAII, respectively.

Table 2(a). Population (Pop) and prevalence rates (PR), in percent (%), of tobacco users at the time of the three (BLS,[a] FRS,[b] FS[c]) surveys, India

	ExA[d]		CoAI[e]		CoAII[f]	
	Pop	PR (%)	Pop	PR (%)	Pop	PR (%)
Combined sample						
Males						
BLS	5,464	(30.9)	5,369	(27.0)	4,893	(29.1)
FRS	3,330	(19.6)	3,043	(26.0)	3,135	(30.3)
FS	3,454	(20.7)	6,290	(24.9)	4,169	(28.6)
Females						
BLS	5,236	(38.5)	4,905	(28.7)	4,677	(30.4)
FRS	3,212	(21.3)	2,889	(26.2)	3,014	(30.6)
FS	3,260	(22.2)	5,862	(25.8)	4,002	(29.8)
Panel sample						
Males						
BLS	1,413	(30.5)	1,600	(28.3)	1,285	(33.6)
FRS	1,462	(21.5)	1,505	(26.0)	1,469	(30.5)
FS	1,433	(17.4)	1,582	(28.3)	1,442	(32.7)
Females						
BLS	1,323	(40.1)	1,428	(24.6)	1,229	(36.7)
FRS	1,386	(21.6)	1,377	(22.7)	1,388	(33.7)
FS	1,361	(18.2)	1,425	(25.5)	1,417	(34.2)
Non-panel sample						
Males						
BLS	4,051	(31.1)	3,769	(26.5)	3,608	(27.5)
FRS	1,868	(18.1)	1,538	(26.2)	1,666	(30.1)
FS	2,021	(23.0)	4,708	(23.7)	2,727	(26.5)
Females						
BLS	3,913	(38.0)	3,477	(30.4)	3,448	(28.2)
FRS	1,826	(21.0)	1,512	(29.7)	1,626	(28.0)
FS	1,899	(25.0)	4,437	(25.9)	2,585	(26.9)

[a] BLS = baseline survey.
[b] FRS = first repeat survey.
[c] FS = final survey.
[d] ExA = experimental area.
[e] CoAI = control area I.
[f] CoAII = control area II.

Table 2(b). Prevalence rates (percent) of male tobacco-chewers (PRCh%) and male tobacco-smokers (PRSm%) at the time of the three (BLS,[a] FRS,[b] FS[c]) surveys, India

	PRCh%			PRSm%		
	ExA[d]	CoAI[e]	CoAII[f]	ExA[d]	CoAI[e]	CoAII[f]
Combined sample						
BLS	16.4	7.7	8.4	17.7	21.0	21.7
FRS	9.4	8.4	9.0	12.1	19.0	23.6
FS	10.8	6.5	8.4	12.0	19.8	22.5
Panel sample						
BLS	16.8	6.9	11.4	17.2	22.5	23.8
FRS	9.5	6.6	9.9	13.5	19.9	22.9
FS	8.1	7.1	11.4	11.1	23.1	24.9
Non-panel sample						
BLS	16.2	8.1	7.3	17.9	20.3	20.8
FRS	9.4	10.1	8.4	11.0	18.1	24.3
FS	12.8	6.2	6.8	12.5	18.7	21.2

[a] BLS = baseline survey.
[b] FRS = first repeat survey.
[c] FS = final survey.
[d] ExA = experimental area.
[e] CoAI = control area I.
[f] CoAII = control area II.

Prevalence rates following intervention. Table 2 also gives the prevalence rates of the tobacco habit during FRS and FS following health education of the community in the ExA. Table 3 indicates the proportion of reduction in prevalence rates of the tobacco habit between surveys. Comparison of results of FRS between the ExA and two control areas showed high statistical significance ($P < 0.0001$) in all samples.

The proportion of decline in prevalence rates between BLS and FS provides the overall picture of the effect of intervention in the ExA in contrast to nonintervention in the two control areas. The results were again highly significant ($P < 0.0001$).

The decline in the prevalence of chewing in males in the ExA was also statistically significant ($P < 0.0001$) for the results in all samples of the FRS and for that of CS and PS in the FS, but not significant in the NPS of CoAI ($P = 0.06$). Similarly, for smoking, the results of the PS in FRS were not significant ($P = 0.3$). Otherwise, all the remaining samples in both FRS

Table 3(a). Proportion (%) of reduction in prevalence rate of the tobacco habit between surveys (BLS,[a] FRS,[b] FS[c]), India

	Males			Females		
	ExA[d]	CoAI[e]	CoAII[f]	ExA[d]	CoAI[e]	CoAII[f]
Combined sample						
BLS-FRS	11.3	1.0	−1.2	17.2	2.5	−0.2
FRS-FS	−1.0	1.1	1.7	−0.9	0.4	0.8
BLS-FS	10.2	2.1	0.5	16.3	2.9	0.6
Panel sample						
BLS-FRS	9.0	2.3	3.1	18.5	1.9	3.0
FRS-FS	4.1	−2.3	−2.2	3.4	−2.3	−0.5
BLS-FS	13.1	0.0	0.9	21.9	−0.3	2.5
Non-panel sample						
BLS-FRS	13.0	0.3	−2.6	17.0	0.7	0.2
FRS-FS	−4.9	−2.5	3.6	−4.0	3.8	1.1
BLS-FS	8.1	2.8	1.0	13.0	4.5	1.3

[a] BLS = baseline survey.
[b] FRS = first repeat survey.
[c] FS = final survey.
[d] ExA = experimental area.
[e] CoAI = control area I.
[f] CoAII = control area II.

and FS showed a statistically significant ($P < 0.001$) decline in the prevalence rates of smoking.

Tests for a declining trend in prevalence rates in ExA from BLS to FS, indicated a statistically significant trend only for the PS in males when the tobacco habit was considered as a whole (chewing and smoking) ($P = 0.03$) and in the PS for male smokers ($P < 0.004$).

The prevalence rates of the FS also were compared with that of the FRS, and tests for statistical significance were carried out. Only the results of the PS showed a statistically significant decline during the FS compared with the FRS.

Age-specific prevalence rates. The baseline age-specific prevalence-rates of the tobacco habit for the population in the three areas did not show any variation among males. In females, the age-specific curves in the control areas were lower. In the ExA, in males and females, the curves of the FRS (to a larger extent) and that of FS (to a smaller extent) compared with that of BLS were at a lower level, indicating a decline in the prevalence rates in almost all age groups.

In the graphs for the PS, the age-specific rates in persons less than 30 years of age during the FS was lower than that seen in the FRS. Among males, the shift of the age-specific chewing rates was greater than the age-specific smoking rates. This effect was seen clearly during the FRS, but not as well demonstrated during the FS, except in the younger age groups of the PS. Curves of the age-specific prevalence rates of the tobacco-habit status during the three surveys showed little or no change in the two control areas in both genders.

Quitter's rates

Table 4a shows the number of habituates interviewed during the three surveys, the number who had quit the habit (for at least six months), and the rate (percent) of such quitters among ever-users of tobacco. The numbers and rate of persons who had quit ('quit ratio') the habit at the time of FRS was much higher in the ExA—where intervention through health education was given—compared with the control areas (in males, 26.5 percent in ExA *cf* 3.2 percent and 1.1 percent in CoAI and CoAII, respectively; and in females, 40.7 percent in ExA *cf* 2.4 percent and 0.2 percent in CoAI and CoAII, respectively). However, comparison of the quitters' rate between FRS and FS showed a decline in the quitters' rate in the ExA, although the actual quitters' rate itself was far higher than in the control areas. Stratification according to the PS and NPS gave a different picture of the difference in the quitters' rate between FRS and FS. The results of the PS showed an increase in the quitters' rate by 12.4 percent in males and 7.6 percent in females in the ExA, whereas there was a decline by 9.2 percent and 12.4 percent in the quitters' rate in males and females, respectively, in the NPS. A slight increase in the

Table 3(b). Proportion (%) of reduction in prevalence rate of the male tobacco-chewers and smokers between surveys (BLS,[a] FRS,[b] FS[c]), India

	Chewers			Smokers		
	ExA[d]	CoAI[e]	CoAII[f]	ExA[d]	CoAI[e]	CoAII[f]
Combined sample						
BLS-FRS	7.0	−0.7	−0.6	5.6	2.0	−1.9
FRS-FS	−1.4	1.9	0.6	0.1	−0.8	1.1
BLS-FS	5.6	1.2	0.0	5.7	1.2	−0.8
Panel sample						
BLS-FRS	7.3	0.3	1.5	3.7	2.6	0.9
FRS-FS	1.4	−0.5	−1.5	2.4	−3.2	−2.0
BLS-FS	8.7	−0.2	0.0	6.1	−0.6	−1.1
Non-panel sample						
BLS-FRS	6.8	−2.0	−1.1	6.9	2.2	−3.5
FRS-FS	−3.4	3.9	1.6	−1.5	−0.6	3.1
BLS-FS	3.4	1.9	0.5	5.4	1.6	−0.4

[a] BLS = baseline survey.
[b] FRS = first repeat survey.
[c] FS = final survey.
[d] ExA = experimental area.
[e] CoAI = control area I.
[f] CoAII = control area II.

Table 4(a). Number of tobacco habituates interviewed (HI), and the quitters' rate (QR) percent (%) at the time of the three (BLS,[a] FRS,[b] FS[c]) surveys, India

	ExA[d]		CoAI[e]		CoAII[f]	
	HI	QR (%)	HI	QR (%)	HI	QR (%)
Combined sample						
Males						
FRS	853	(26.5)	806	(3.2)	941	(1.1)
FS	946	(26.5)	1557	(1.1)	1,194	(1.1)
Females						
FRS	1,070	(40.7)	761	(2.4)	918	(0.2)
FS	1,042	(36.7)	1,469	(1.5)	1,165	(0.5)
Panel sample						
Males						
FRS	401	(26.9)	392	(3.6)	448	(2.0)
FS	395	(40.2)	461	(3.7)	478	(2.3)
Females						
FRS	482	(43.6)	315	(3.8)	363	(0.4)
FS	455	(51.2)	368	(6.0)	481	(0.8)
Non-panel sample						
Males						
FRS	452	(26.2)	414	(3.0)	493	(0.2)
FS	551	(17.0)	1,096	(0.0)	716	(0.3)
Females						
FRS	588	(38.0)	446	(1.0)	454	(0.0)
FS	587	(25.6)	1,101	(0.0)	684	(0.4)

[a] BLS = baseline survey.
[b] FRS = first repeat survey.
[c] FS = final survey.
[d] ExA = experimental area.
[e] CoAI = control area I.
[f] CoAII = control area II.

quitters' rate also was observed in the control areas in the PS but the reverse holds true for those villages in the NPS.

Tables 4b and 4c show the quitters' rate for males, among tobacco chewers and smokers, respectively. In the ExA, the rate of quitting the habit of chewing was higher than the rate of smokers quitting the habit.

Tests showed a very high degree of statistical

Table 4(b). Number of male tobacco-chewers interviewed (CI), and the quitters' rate (QR) percent (%) at the time of the three (BLS,[a] FRS,[b] FS[c]) surveys, India

	ExA[d]		CoAI[e]		CoAII[f]	
	CI	QR (%)	CI	QR (%)	CI	QR (%)
Combined sample						
FRS	463	(32.0)	260	(2.3)	286	(1.1)
FS	535	(30.2)	410	(1.2)	354	(1.1)
Panel sample						
FRS	211	(34.2)	101	(2.0)	146	(1.3)
FS	224	(48.2)	118	(4.2)	168	(2.4)
Non-panel sample						
FRS	252	(30.2)	159	(2.5)	140	(0.7)
FS	311	(17.4)	292	(0.0)	186	(0.0)

[a] BLS = baseline survey.
[b] FRS = first repeat survey.
[c] FS = final survey.
[d] ExA = experimental area.
[e] CoAI = control area I.
[f] CoAII = control area II.

Table 4(c). Number of male smokers interviewed (SI), and the quitters' rate (QR) percent (%) at the time of the three (BLS,[a] FRS,[b] FS[c]) surveys, India

	ExA[d]		CoAI[e]		CoAII[f]	
	SI	QR (%)	SI	QR (%)	SI	QR (%)
Combined sample						
FRS	495	(18.6)	597	(3.4)	746	(0.9)
FS	534	(20.4)	1,257	(1.0)	950	(1.2)
Panel sample						
FRS	244	(18.8)	312	(3.8)	342	(2.0)
FS	229	(28.8)	378	(3.4)	368	(2.4)
Non-panel sample						
FRS	251	(18.3)	285	(2.8)	404	(0.0)
FS	295	(14.6)	879	(0.0)	582	(0.3)

[a] BLS = baseline survey.
[b] FRS = first repeat survey.
[c] FS = final survey.
[d] ExA = experimental area.
[e] CoAI = control area I.
[f] CoAII = control area II.

significance ($P < 0.0001$) for the quitter's rate in the ExA compared with the two control areas, in all samples in either gender and for results during both FRS and FS.

The influence of age on quitting the habit was examined by generating graphs of age-specific quitters' rates during the FRS and FS, but the graphs did not show any variation with age group.

In order to determine whether the duration of the tobacco habit had any influence on quitting of the habit, the mean of the duration of the habit was calculated for quitters and also for those who had not quit the habit. This was not significantly different in the two groups.

Initiation rate

Table 5 gives the initiation rates of the tobacco habit during the survey periods in the three areas in the 10 to 24 year age-group since initiation is expected to be seen mainly in that age group. The baseline initiation rates among males were comparable in experimental and control areas, but were somewhat different among females. In the ExA, the initiation rate dropped in both males and females, but more in the latter, during the FRS, but increased in the control areas. During the FS, the initiation rate was higher than during the FRS among males in the two control areas and also in females in CoAI. Stratifying initiation rates into PS and NPS gave very small numbers for any

Table 5. Number of non users of tobacco (NT) in the 10-24 year age-group, and the initiation rate, percent (%), of tobacco (IRT) use, India

	ExA[a]		CoAI[b]		CoAII[c]	
	NT	IRT	NT	IRT	NT	IRT
Combined sample						
Males						
BLS	1,419	(0.2)	1,636	(0.2)	1,406	(0.1)
FRS	933	(0.0)	912	(0.8)	862	(0.7)
FS	1,068	(0.4)	2016	(0.8)	1,251	(1.7)
Females						
BLS	1,257	(1.6)	1,294	(0.6)	1,229	(1.4)
FRS	767	(0.1)	758	(1.1)	740	(4.7)
FS	902	(0.6)	1,623	(1.1)	1,033	(2.5)

[a] ExA = experimental area.
[b] CoAI = control area I.
[c] CoAII = control area II.

meaningful correlation. For the same reason of small numbers, age-specific initiation rates could not be calculated.

The initiation rates in the ExA showed a statistically significant decline in males ($P < 0.01$) and females ($P = 0.005$) during FRS. In the FS, males in CoAI did not show a statistically significant decline in the initiation rate ($P = 0.16$), but comparison with CoAII and the FS results in females showed a significant decline ($P < 0.005$).

Among males, the initiation rates of tobacco chewing and smoking were compared. In the ExA, during the FS the initiation rate of chewing was 0.2 percent and that of smoking 0.1 percent. In CoAI, the initiation rate of chewing was 0.1 percent compared with 0.3 percent for smoking. In CoAII, these were 0.4 percent and 0.9 percent for chewing and smoking respectively.

Impact of health education material used

The different types of health education materials used to impart messages about the harmful effects of tobacco have been mentioned above. Essentially, these consisted of three channels of communication. First, was the method which could be read by the literate population. The second was the audio-visual means which could be understood by almost all the persons who saw it. The last was interpersonnel communication, with the health worker actually explaining the contents of the messages and describing the photo albums and identity cards that they carried.

In order to assess the impact of the health education material in helping individuals to quit the habit, the proportion exposed to such material among the quitters was compared with the proportion exposed among non-quitters. There was no noticeable difference in this proportion in the first and last methods of communication listed above. However, in the audio-visual means of education, during the FRS, 68.6 percent of quitters had an opportunity to view the films on chewing and smoking compared with 57 percent of non-quitters of either gender. During the FS, 95.7 percent of quitters had viewed the films compared with 90 percent of non-quitters.

Discussion

With the initiation of several cancer-control programs in India under its National Cancer Control Program, knowledge of prevalence rates of tobacco usage, including the various types used, is becoming increasingly important. Unless these baseline rates of the population are known, the impact of any education programs cannot be assessed. The present study has shown ways of conducting tobacco-habit surveys in the population, the impact of education on the community, and methods of reporting such results.

Variation in the prevalence and type of tobacco used even within the same district of a state is seen in this study. The initial baseline prevalence-rates of the tobacco habit, showed that, in both genders, the rates were higher in the experimental than in either of the control areas. This was despite the fact that the experimental and control areas and the villages under them were chosen on a random basis. However, among males, when the type of habit was taken into account, the prevalence rate of tobacco chewing in the experimental area was almost twice that in the control areas, whereas the prevalence rate of smoking was marginally higher in the control areas compared with the experimental area.

The results of the FRS showed a decline in the prevalence rates by 11.3 percent in males and 17.2 percent in females in the experimental area. The proportion of persons who quit the habit was 26.5 percent in males and 40.7 percent in females. Among males, the decline by seven percent in the prevalence rates of chewers is marginally higher than the decline of 5.6 percent among smokers. However, the difference in the response of chewers and smokers towards giving up the habit is observed better if one looks at the proportion (32 percent) among chewers who have quit the habit compared with the proportion (18.6 percent) among smokers who have quit the habit. The former is almost twice that of the latter. Thus the effect of anti-tobacco education, as provided in the results of the FRS, is indeed considerable. Stratifying the results of the FRS into panel and non-panel samples does not show much difference.

If the results of the FRS in terms of response to the intervention were remarkable, the sustenance of the rate of decline in the habit appears missing from the findings of the FS. Nonetheless, on examination of the stratified sample, perceptible difference is seen between the panel and non-panel samples. The figures of the panel sample, do show a sustenance of the decline in the prevalence rates between FRS and FS as also a further increase in the proportion of people who have quit the habit between FRS and FS. However, this is not the case in the results of the non-panel sample.

Some reasons could be given for this difference in findings between the panel and non-panel samples. Even though the social investigators who worked on this program were not imparting any direct education to the community, their repeated visits to the villages under the panel sample probably would have added to the conscientiousness of the people and enhanced their response to the anti-tobacco education. Another reason could be because of the differences in educational,

socioeconomic, and cultural background among the villages coming under the purview of the panel sample on the one hand, and of the villages under the non-panel sample on the other. This factor probably could not be eliminated completely by random sampling of villages.

The results of the Anti-Tobacco Community Education Program indicate that there has been a substantial decline in the number of persons pursuing the habit as indicated by a drop in the tobacco prevalence-rates as well as in the proportion of persons who quit the habit. The response, as indicated by these two parameters, appears to be greater among women than men and among males who were tobacco chewers rather than smokers. The degree of the decline in the habit was considerable between the BLS and FRS, (regardless of whether the combined-sample results were observed or panel and non-panel sample results were seen) much less between the FRS and FS for the villages under the PS and no decline in the habit for the villages under the NPS. Any comparable decline in the habit as measured by these parameters was not observed in the control areas where no anti-tobacco education was given.

The influence of age was assessed by examining the age-specific prevalence and age-specific quitters' rates. There was a greater shift of the age-specific prevalence rates towards the lower side in the younger age group (<35 years) during the FS compared with the FRS, but no such perceptible change was seen between BLS and FRS in this age group. This suggests that persons below 35 years of age respond to the anti-tobacco education by quitting the habit rather slowly compared with the older age groups. The above effect of age was seen in both genders and for both chewing and smoking in males. It was more pronounced in the villages under the PS than in the NPS.

A third, quantitative, statistical indicator that was used to evaluate the impact of the program was the rate of initiation of the habit. Among males, the initiation rate was comparable during the BLS in experimental and control areas, but in the subsequent surveys, the increase in rates in the control areas was steep, whereas this was not the case in the ExA. In females, in the ExA, there was a decline in the initiation rate and, in both the control areas, an increase in the initiation rates. Thus, the anti-tobacco community education not only saw a decrease in the number of persons quitting the habit, but also saw a decline in the uptake of the habit. The reverse was true in the control areas where there was indeed an increase in the rate of uptake of the habit during the surveys following the BLS. A matter of concern about this indicator is not only the high rate of uptake of the tobacco habit in the control areas, but a probable increase in these rates with passage of time. The data indicate that the initiation rate (despite small numbers) of smoking among males within a period of six months was about 0.8 percent. This means that the incidence of smoking among males could be as high as 1.6 percent or 1600 per 100,000 which is over 10 times the estimated incidence of cancer in India.[8] Since anti-tobacco education of the community generally is not practiced routinely by the health workers, these figures easily would be applicable to the general rural population as a whole.

One of the outcomes of this study is to have a clear method of reporting results of tobacco surveys, in the form of prevalence rates, quitters' rates, and initiation rate. In this study, we used a minimum time-interval of six months to define the above rates, respectively, as to whether the person was a user of tobacco, a person who had quit, or a person who had taken up the habit during the interval. However, this time period could be taken as one year in future studies since that way it would be easier to calculate rates *per annum*, in keeping with incidence, prevalence, and mortality rates of cancer.

The package of health education material was prepared mainly to impart knowledge to change misconceptions and negative attitudes about the harmful effects of tobacco, through uniform and standardized health education. The materials utilized to educate literates were handbills and folders. The identification card and photo album were used for interpersonal education. The portable and exhibition panels and films on chewing and smoking were used to educate groups or large gatherings. Among all the educational devices used for the anti-tobacco community education program, the response appeared to be best in order of importance for film on the harmful effects of chewing and smoking, photo album, and identity card. The other items used for education also had some effect but perhaps not as marked, as indicated by the community's response.

Anti-tobacco education of the community in this study brought into focus the role of health workers in conducting such education. The points to be considered in this context include the concomitant healthcare program that health workers routinely carry out and the feasibility of their doing additional program on anti-tobacco education and cancer control. Further factors that determine effective education and successful response therefrom, include, the health workers' educational qualification and background, specific training received by them, their professional responsibility and commitment, and lastly, but most importantly, the skill with which they execute the work. However, the singlemost

important keystone towards the success of the program is almost entirely dependent on the interest, commitment, and motivation provided by the medical officer at the primary health center. As was done in this study, a built-in method of evaluating, at every step, the performance of health workers through details of visits, number of persons whom they have not only educated but also motivated, etc. is necessary.

Studies on the tobacco habit and the effect of education have been done earlier in different parts of this country,[13-15] but this is the first in the State of Karnataka. The strength of this study is in its case-control design with both experimental and control areas having an adequate sample size. The study has demonstrated that it is feasible to conduct anti-tobacco education programs through health workers and that there is substantial impact of such education on the community. The response of women is greater than that of men, and, among men, chewers seem to have responded better than smokers. The study also has brought into sharp focus the extremely high rate of initiation of the tobacco habit, calling for urgent action against this addictive habit at both levels concerning education and legislation.

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The Effects of Parental Divorce on Adult Tobacco and Alcohol Consumption*

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I use data from the 1977–1994 National Opinion Research Council General Social Survey to examine the impact of parental divorce on the alcohol and tobacco consumption of adult offspring. Divorce greatly increases the likelihood of being a smoker and, for men, a problem drinker. Parental remarriage completely offsets the effects of parental divorce on men's drinking but does not substantially affect cigarette use. Respondent socioeconomic characteristics accounted for a portion of the relationship between parental divorce and smoking but did not affect rates of problem drinking. Social control and psychosocial adjustment—two established explanations for the effects of parental divorce—could not adequately explain my findings.

INTRODUCTION

Cigarettes claim hundreds of thousands of lives annually. Tens of thousands more people die from alcohol-related accidents and diseases (see United States Bureau of the Census 1997). The associated medical costs are tremendous. For these reasons, it is important to understand the etiology of alcohol and tobacco use.

In this paper I examine the likelihood that the adult children of divorced parents will smoke and abuse alcohol. Previous researchers have established that parental divorce can have many lasting effects on the well-being of adult offspring, including marital instability (Amato 1996; Glenn and Kramer 1987; Kulka and Weingarten 1979; McLanahan and Bumpass 1988; Mueller and Pope 1977; Wolfinger 1996, 1997a,b) and poor psychological health (Amato 1991; Amato and Booth 1991; Cherlin, Chase-Lansdale, and McRae 1998; Kuh and Maclean 1990; Roy 1985; Schooler 1972). Broadly speaking, marital instability and poor psychological health are signs of maladjustment. Alcohol and tobacco use may well be two additional forms of maladjustment related to parental divorce.

I analyze data from the 1977–1994 General Social Survey (GSS) that are nationally representative. Further, my data allow differentiation between parental death and parental divorce, and contain detailed sociodemographic information. As such, they allow me to adjudicate among several competing theoretical explanations for the relationship between family of origin and offspring substance use.

THEORY

I expect parental divorce to increase alcohol and tobacco consumption in adult offspring for three reasons, outlined below, and derive hypotheses to be tested in a multivariate analysis.

Social Control

After a divorce almost every familial routine is disrupted (Wallerstein and Kelly 1980).

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Recently divorced mothers[2] often experience considerable emotional distress, thus debilitating their parenting skills (Dornbusch et al. 1985; Wallerstein and Kelly 1980). Moreover, single mothers are likely to be working and therefore less able to supervise children (McKeever and Wolfinger 1997). Visitation by absent fathers tends to be infrequent and when it does occur, it is often social in nature and not related to the more serious tasks of childrearing (Furstenberg and Nord 1985). For all of these reasons, I expect parental control to decrease in single-mother households.

In turn, lower levels of control afford children more opportunity to experiment with alcohol and cigarettes (Resnick et al. 1997; Kandel 1996), leading to an increased likelihood of substance use later in life. Adolescents are especially at risk as the chances of initiation into alcohol and tobacco use peaks at about age 18 (Kandel and Yamaguchi 1985).

According to the social control hypothesis, parental remarriage should largely offset the effects of parental divorce. In other words, the offspring of step-families should be no more likely to smoke and abuse alcohol than their counterparts from intact families. Although family structure is weaker in reconstituted families than in intact families (Cherlin 1978; Furstenberg and Cherlin 1991; Cherlin and Furstenberg 1994), I nevertheless expect to find stronger social control in step-parent families than in mother-only families. Whatever the family dynamics, a step-parent provides a second source of authority and discipline.

Socioeconomic Status

Socioeconomic status (SES) may affect the relationship between parental divorce and adult substance consumption in several ways. Low levels of education increase the likelihood of divorce (Bumpass, Martin, and Sweet 1991), so divorced parents as a whole comprise a disproportionately uneducated group. Due to their lower average level of education, divorced parents may be relatively permissive about smoking. In contrast, educated parents, even if divorced, are more likely to dissuade their children from smoking through both exhortation and example. The absence of cigarettes in the house substantially decreases the likelihood that offspring will smoke (Resnick et al. 1997).

In addition, levels of parental income may affect the children of divorce through downward residential mobility. McLanahan (1983) found that approximately 38 percent of single mothers moved within a year of getting divorced, more than twice the overall mobility rate. Moreover, single-mother families are much more likely to live in depressed areas than are intact families (McLanahan, Astone, and Marks 1991), and children living in depressed areas may have more opportunities to experiment with smoking and drinking than children raised in affluent neighborhoods. It is here that step-parenting impinges on the SES hypothesis: since step-parent families have incomes comparable to those of intact families (Bachrach 1983; Mason and Mauldon 1996), children with step-parents may be less likely to be exposed to as much drinking and cigarette-smoking as are children in single-mother families.

Finally, parental divorce may affect tobacco and alcohol consumption by reducing the socioeconomic attainment of offspring. Compared to people from intact families, the children of divorce complete fewer years of school (Blau and Duncan 1967; Krein 1986; Krein and Beller 1988; McLanahan 1985; McLanahan and Sandefur 1994) and do less well economically (Amato and Booth 1991; Amato and Keith 1991a; Mueller and Cooper 1986) as well as occupationally (Biblarz and Raftery 1993). This may affect their cigarette use, as smoking is strongly linked to both low education and low income (United States Bureau of the Census 1997). On the other hand, alcohol use increases with income (United States Bureau of the Census 1997).

Psychosocial Adjustment

A third theoretical perspective attributes the proclivity for alcohol and tobacco consumption to the social and psychological maladjustment that can result from parental divorce. There is little doubt that parental divorce often has profound social and psychological consequences for children (Hetherington 1993; Wallerstein and Kelly 1980).[3] The conflict accompanying divorce is especially traumatizing (Amato 1993; Amato and Keith 1991b; Emery 1982, 1988). Previous research shows that parental divorce and conflict can increase alcohol and tobacco consumption in teenagers (Ahlgren et al. 1982;

Baer et al. 1987; Johnson and Pandina 1991; Webb and Baer 1995). More generally, the children of divorce sometimes develop patterns of behavior that fit the classic sociological notion of deviance (Hetherington, Cox, and Cox 1985; Hetherington 1993; Wallerstein and Kelly 1980).

Unresolved, the troubles leading teenagers to drink and smoke may contribute to high rates of substance consumption in the adult children of divorce. Some psychosocial effects of parental divorce often persist into adulthood, including poor mental health (Amato 1991; Amato and Booth 1991; Cherlin et al. 1998; Kuh and Maclean 1990; Roy 1985; Schooler 1972) and difficulty in romantic relationships (Amato 1996; Amato and Rogers 1997; Silvestri 1992; Webster, Orbuch, and House 1995). Causality here could be reciprocal: if the adult children of divorce drink heavily, their social and psychological well-being may further deteriorate. If substance consumption in the children of divorce is related to poor psychosocial adjustment and difficulty in their own marriages, then variables measuring these factors should mediate the relationship between parental divorce and offspring substance consumption.

Across a variety of outcomes, children in step-families do no better than those reared by single mothers (Cherlin and Furstenberg 1994). According to the psychosocial adjustment hypothesis, step-parenting should increase the likelihood that the children of divorce will become smokers and problem drinkers, or, at best, will produce enough disruption to offset the beneficial effects of remarriage. Note that this prediction is the opposite of that resulting from the social control perspective.[4]

Why might remarriage not benefit children, despite the higher incomes typical of reconstituted families? Remarriage confuses traditional familial roles, yielding complicated and often problematic social dynamics (Cherlin 1978; Cherlin and Furstenberg 1994; Furstenberg and Cherlin 1991; but see MacDonald and DeMaris 1995). Girls have a particularly difficult time in step-families (Glenn and Kramer 1987; Hetherington 1993; Hetherington et al. 1985; McLanahan and Bumpass 1988), so women whose divorced parents remarried may experience especially high rates of alcohol and tobacco consumption.

PRIOR RESEARCH

Two prior studies of American adults show that parental divorce increases smoking but not alcohol consumption (DeFronzo and Pawlak 1993; Tucker et al. 1995). However, both studies have serious limitations. DeFronzo and Pawlak (1993) do not distinguish between divorcees and widows in spite of research showing that parental death does not have adverse effects on children (Acock and Kiecolt 1989; Amato 1988; Demo and Acock 1988; Wolfinger 1997a) or affects them much less severely than does divorce (McLanahan 1985, 1988; McLanahan and Sandefur 1994). Tucker et al. (1995) distinguish between death and divorce but use an exotic and unrepresentative data set: 1,528 high-IQ respondents born between 1904 and 1915, almost all white and middle-class, from Lewis Terman's longitudinal "genius" study. Perhaps even more important than the unrepresentative character of their data, however, is the fact that most of their respondents came of age during Prohibition. Kuh and Mclean (1990) find that parental divorce increase smoking and alcohol consumption, but they analyze a sample composed entirely of 36-year-old women. Moreover, their research was conducted in England, so their findings may not apply to Americans. Finally, Tennant and Bernardi (1988), using a clinical sample of 120 Australian alcoholics and drug addicts, found that a disproportionately high number of subjects came from broken homes.

METHODS

Data

My data comes from the General Social Survey (GSS) (Davis and Smith 1996), a national probability sample of English-speaking households within the continental United States conducted annually or biennially since 1972. I use data for the years 1977–1994, excluding the 1985 data (when questions on alcohol and smoking were not asked) and the Black oversamples in 1982 and 1987.[5] The smoking and alcohol items were not used in 1996 nor prior to 1977. With the exception of the 1994 survey, containing 2,904 respondents, approximately 1,500 people were interviewed in each cross-section analyzed in this study.

The GSS sampling unit is the household, with sample weights available to adjust for household size. Analyses using unweighted data produced results similar to those obtained with the weighted data, so I report the unweighted results.

The final sample size is 11,268: 6408 women and 4860 men. Cases with missing data were deleted listwise (except where noted).

Variables

I use two dependent variables, one to measure problem drinking and a second to measure smoking. The GSS measures smoking with a single question asking if the respondent currently smoked.[6] I created the problem-drinking variable by merging information from two items, the first asking if respondents drank and the second ascertaining whether drinkers ever felt that they drank more than they should.[7] This yielded a single dichotomous measure of problem drinking. More detailed information on alcohol consumption would be useful but is not available. My coding for all variables is shown in Appendix A.

My GSS data include two items that measure the structure of respondents' families of origin. Respondents were first queried about household composition at age 16. If respondents were not living with both biological parents, a second question ascertained the reason. My analysis is based on the 83 percent of GSS respondents who reported three varieties of family structure: intact two-parent families, mother-only families resulting from divorce or separation, and mother/step-father families resulting from divorce or separation.[8] Respondents reporting other living arrangements (e.g., with fathers or relatives) were omitted from the sample, as were those whose living arrangements at age 16 were the result of parental military service, incarceration, or death.[9] Unfortunately, the GSS does not permit identification of respondents born out of wedlock.

I recoded the family structure items as two dummy variables: respondent came from mother-only family and respondent came from mother/step-father family. The reference category was respondent from intact family. These variables are retrospective, while all others used are contemporaneous.

Cherlin and his colleagues (Cherlin et al. 1991, 1998) have shown that children's problems often begin before the divorce. Along similar lines, others (Amato, Loomis, and Booth 1995; Mechanic and Hansell 1989) contend that the conflict accompanying divorce (but sometimes also bedeviling intact marriages) is the primary source of children's woes. For these reasons, more detailed information on respondent family background would be useful. However, divorce appears to hurt children irrespective of conflict (Hanson 1993) or predivorce well-being (Cherlin et al. 1998). More generally, we can be certain that parental divorce is correlated with experiences inimical to children's well-being, even if levels of conflict and predivorce functioning cannot be directly measured.

Parental education may offset the effects of parental divorce. For respondents reared in intact families and step-families I use the higher level of education between the two parents. For respondents from mother-only families I use mothers' education. Data on parental income or occupational status are not available. An item that asks respondents to recall their families' economic well-being almost certainly fails to provide accurate recollections. Finally, to ascertain whether the effects of parental divorce on substance use are simply a product of diminished socioeconomic well-being I use two measures of respondent socioeconomic status, education[10] and occupational prestige (Hodge, Siegel, and Rossi prestige scores).[11]

I employ three measures of respondent psychosocial adjustment. The three measure "happiness," a belief that the world is a "fair place," and an assessment of whether people in general are "helpful." They allow me to see whether the problem drinking associated with parental divorce is concomitant with other symptoms of poor psychosocial adjustment. Along similar lines, respondent marital status may be related to alcohol consumption. Previous researchers have established that the children of divorce are disproportionately likely to end their own marriages (Amato 1996; Glenn and Kramer 1987; Kulka and Weingarten 1979; McLanahan and Bumpass 1988; Mueller and Pope 1977; Wolfinger 1996, 1997a,b). Could increased alcohol consumption among the children of divorce only follow in the wake of

a failed marriage? I test this notion with a dummy variable ascertaining whether or not respondents have ever been divorced.

The liability of cross-sectional data emerges most strongly in the psychosocial adjustment and marital status measures. It is impossible to know for sure whether respondent substance consumption causes or is caused by these variables. Nevertheless the variables will allow me to see whether adjustment and marital status play a role in the relationship between parental divorce and offspring substance use.

In all analyses I use four control variables. First, I adjust for survey year to capture period trends in alcohol and tobacco consumption. In recent years, for instance, far fewer people smoke (United States Bureau of the Census 1997). On the basis of lowess[12] plots (not shown), I model survey year as a continuous variable.[13] Second, I control for respondent birth cohort as recent cohorts contain many more people from divorced families (Bumpass and Sweet 1989).[14] Lowess plots (not shown) reveal a curvilinear relationship between birth cohort and smoking, while cohort has a monotonic but nonlinear impact on problem drinking. Accordingly I model the former relationship as a quadratic and the latter as a piecewise linear spline.[15] Based on preliminary analyses, I include an interaction between mother-only parenting and birth cohort in the equation predicting men's problem drinking. Third, I include a dummy variable to measure urbanicity, since parental divorce and initiation into substance use may vary according to whether a respondent was reared in a city. Fourth, and finally, I control for respondent race by contrasting blacks with all other respondents. Blacks are more likely to have grown up in divorced families (Bumpass 1984) and use alcohol and tobacco at different rates than other population groups (United States Bureau of the Census 1997).

Analysis

I examine the impact of parental divorce and remarriage on alcohol and tobacco consumption using bivariate probit models (Greene 1993:660–63). The probit specification is appropriate because my measures of smoking and problem drinking are both dichotomies. The bivariate probit allows two equations to be estimated simultaneously with correlated errors, assuming that the errors have a bivariate normal distribution with equal variances and means of 0. I assume that the errors will be correlated because the same unmeasured variables predict both smoking and problem drinking. With correlated errors, the bivariate probit produces more efficient estimates of coefficients and standard errors than could be achieved with separate probit equations.

I first examine the impact of family structure on the propensity to smoke and engage in problem drinking. Next I see whether the consequences of parental divorce persist while controlling for parental education and respondent socioeconomic well-being. I then add the variables measuring respondent psychological well-being, allowing me to ascertain whether the smoking and problem drinking resulting from parental divorce are associated with other symptoms of poor psychosocial adjustment. Finally, I introduce the variable measuring respondent divorce into the model to determine whether substance use is an artifact of the intergenerational transmission of divorce.

All analyses control for survey year, birth cohort, race, and urbanicity. Preliminary regressions with interaction terms revealed significant sex differences in the effects of parental divorce on substance consumption, so I conduct separate analyses for men and women. Models are estimated in Limdep.

RESULTS

Smoking

Table 1, Panel A shows bivariate probit estimates of the impact of parental divorce on men's substance consumption. For each of the five models I present two columns of coefficients. The left-hand column for each model shows the effects of parental divorce on the likelihood of being a smoker. The large and statistically significant coefficients in Model 1 indicate that both single-mother parenting and step-parenting increase the chances of smoking in men. Panel B displays results for women, which tell a similar story.

Probit coefficients are difficult to interpret so I compute predicted probabilities from regression standardization based on Model 1. The results are shown in the left-hand panel of Table 2. Forty-six percent of men whose parents divorced smoke compared to only 35 percent of those raised in intact families. Parental divorce therefore increases the risk of smoking by a little less than one third for men. Moreover, single-mother parenting and step-parenting produce the same risk of smoking. The results for women are slightly different. Thirty-six percent of women raised by single mothers smoke compared to 32 percent of those whose divorced parents remarried. In contrast, only 24 percent of women raised in intact families became smokers. Again, parental divorce produces about a one-third increase in the likelihood of becoming a smoker, but for women step-parenting slightly dampens this effect.

Table 2 provides evidence against the social control hypothesis: the presence of a step-parent, presumably a second agent of parental authority, reduces the likelihood of smoking only for women. Moreover, women reared in step-families still smoke at a much higher rate than do women from intact families. On the other hand, parental education accounts for a portion of the relationship between divorce and smoking. The coefficients for single-mother parenting and step-parenting decline somewhat from Model 1 to Model 2 (containing the variable for parental education) for both men and women (Table 1, Panels A and B respectively).

Respondent SES plays a large role in the relationship between parental divorce and the chances of smoking. The coefficients measuring family background decline considerably from Models 1 and 2 to Model 3 (containing the variables measuring respondent education and occupational prestige) for both men and women (Table 1, Panels A and B). In addition, the negative impact of parental education on smoking (Model 2) disappears when holding respondent education constant (Model 3). Parental education only affects offspring smoking indirectly, through the intergenerational transmission of socioeconomic attainment. However, except for women from step-families, the coefficients for the family background variables remain large and statistically significant in Model 3, indicating that the effects of family background on the propensity to smoke cannot be explained entirely by the reduced socioeconomic attainment often brought on by parental divorce.

My results offer little support for the psychosocial adjustment perspective, which states that substance consumption in the children of divorce is related to psychosocial maladjustment. Inclusion of the psychosocial adjustment variables (Model 4) did not affect the impact of parental divorce on cigarette use. Controlling for respondent marital status (Model 5) did not affect the results either.

Drinking

The second column for each model in Table 1, Panel A shows the effects of parental divorce on the likelihood that male offspring will become problem drinkers as adults. In Model 1, the positive and statistically significant coefficient indicates that single-mother parenting increases the odds of problem drinking in men. In contrast, the coefficient for step-parenting is much smaller and statistically insignificant. For men, step-parenting apparently repairs some of the damage done by parental divorce.

The story is quite different for women. According to Model 1 in Panel B of Table 1, neither single-mother parenting nor step-parenting increase the likelihood of becoming a problem drinker; both coefficients are small and insignificant.

I gauge the exact size of the effects of divorce on alcohol consumption from predicted probabilities obtained from a regression standardization (Table 2, Panel B). Men from intact families report sometimes drinking more than they should approximately 43 percent of the time. In contrast, 57 percent of men raised by single, divorced parents report problem drinking, an increase of just under one third. Men whose mothers remarried have the same level of problem drinking (43 percent) as men from intact families. On the other hand, for women step- and single-mother parenting result in levels of problem drinking similar to those of women from intact families. It is noteworthy, though, that step-parenting produces rates of problem drinking higher than either mother-only parenting or intact parenting. I will return to this point in the discussion.

My results do not support any of the three theoretical explanations for the relationship between parental divorce and offspring substance consumption. Step-parenting almost completely offset the effects of divorce, but if this were a product of social control, then step-parenting should also reduce the likelihood

TABLE 1. Panel A: Bivariate Probit Estimates of Men's Smoking and Problem Drinking on Family Structure of Origin

Variable	Model 1		Model 2	
	Smoking	Problem Drinking	Smoking	Problem Drinking
Parental Family Structure				
Divorced Single Mother	.29***	.67**	.25**	.71**
Divorced Mother and Step-father	.31**	.02	.29**	.02
Intact Family	—	—	—	—
Birth Cohort / Birth Cohort 1889–1910	.04***	.09***	.05***	.09***
Birth Cohort Squared / Birth Cohort 1911–1976	-.0004***	.02***	-.0004***	.02***
Birth Cohort 1911–1976*Divorced Single Mother	—	-.01*	—	-.01*
Parental Education	—	—	-.09***	.02
Parental Education Data Missing	—	—	.14	-.23
Respondent Education	—	—	—	—
Occupational Prestige	—	—	—	—
Occupational Prestige Data Missing	—	—	—	—
Psychosocial Adjustment				
Happiness	—	—	—	—
People are Helpful	—	—	—	—
The World is a Fair Place	—	—	—	—
Respondent is Divorced	—	—	—	—
Intercept	1.27***	.94*	1.28***	.96*
ρ	.28***		.29***	
Log Likelihood	-6085.05		-6067.26	

*p < .05; ** p < .01; ***p < .001 (2-tailed tests)
Source: General Social Survey, 1977–1994.
Notes: All models control for survey year, race, and urbanicity at age 16. N for all models is 4,860.

Model 3		Model 4		Model 5	
Smoking	Problem Drinking	Smoking	Problem Drinking	Smoking	Problem Drinking
.23**	.70**	.22**	.71**	.22**	.69**
.23*	.01	.22*	.01	.21*	-0.002
—	—	—	—	—	—
.06***	.09***	.06***	.09***	.05*	.09***
-.0006***	.02***	-.0006***	.02***	-.0005***	.02***
—	-.01*	—	-.01*	—	-.01*
.01	.03	.01	.03	.01	.03
-.02	-.25*	-.03	-.25*	-.03	-.25*
-.23***	.001	-.21***	.003	-.21***	.01
-.002	-.004*	-.001	-.004*	-.001	-.004*
-.35*	-.12	-.35*	-.12	-.32*	-.09
—	—	-.04	.02	-.03	.02
—	—	-.03	-.02	-.02	-.01
—	—	.07**	.01	.06**	-.003
—	—	—	—	.32***	.33***
1.02**	1.01*	1.05**	1.02*	1.25**	1.10*
.29***		.29***		.28***	
-5979.84		-5970.44		-5936.22	

that male offspring become smokers. However, this was not the case.

Also not supported by the data is the explanation concerning the low SES often associated with parental divorce. The introduction of controls for parental and respondent SES (Models 2 and 3, Table 1, Panels A) did not affect the relationship between parental divorce and problem drinking.

The psychosocial adjustment perspective states that the deviant ideation sometimes stemming from parental divorce can account for the propensity to be a problem drinker. This perspective is also not supported, as the controls for psychosocial adjustment (Model 4, Table 1, Panel A) failed to attenuate the impact of parental divorce on alcohol consumption. Moreover, the intergenerational transmission of divorce could not account for the relationship between family structure and men's alcohol consumption, although being divorced has a large and statistically significant impact on problem drinking (Model 5, Table 1).

The final noteworthy result concerns the negative interaction between birth cohort and mother-only parenting. This interaction indicates that the relationship between parental divorce and the propensity to become a problem drinker has weakened for men born since 1910. In other words, divorce does not, at least in this one respect, hurt children as much as it once did. This finding, consistent with earlier research (Amato and Keith 1991b; Wolfinger 1996), can probably be attributed to the normalization of divorce in contemporary America (see Whitehead 1997).

DISCUSSION AND CONCLUSION

My research shows that parental divorce increases the likelihood that adult offspring will be smokers and, for men, problem drinkers. Parental remarriage almost completely attenuates the impact of divorce on men's drinking but has little effect on the relationship between family background and cigarette use. I propose three mechanisms to explain the connection between family of origin and respondent substance consumption: (1) decreased social control in single-parent families; (2) the lower SES often associated with parental divorce; and (3) poor psychosocial adjustment in the children of divorce.

These three mechanisms were generally unsuccessful in explaining the results. Although the decreased socioeconomic attainment often brought on by parental divorce accounts for a portion of the relationship between parental divorce and smoking, it does not affect the impact of divorce on the proclivity to drink excessively. This result makes sense. The majority of educated Americans

TABLE 1. Panel B: Bivariate Probit Estimates of Women's Smoking and Problem Drinking on Family Structure of Origin

	Model 1		Model 2	
Variable	Smoking	Problem Drinking	Smoking	Problem Drinking
Parental Family Structure				
Divorced Single Mother	.35***	.11	.32***	−.08
Divorced Mother and Step-father	.23**	.05	.23**	.07
Intact Family	—	—	—	—
Birth Cohort / Birth Cohort 1889–1910	.05***	.08**	.05***	.08**
Birth Cohort Squared / Birth Cohort 1911–1976	−.0004***	.03***	−.0004***	.02***
Parental Education	—	—	−.09***	.06***
Parental Education Data Missing	—	—	.18	−.51**
Respondent Education	—	—	—	—
Occupational Prestige	—	—	—	—
Occupational Prestige Data Missing	—	—	—	—
Psychosocial Adjustment				
Happiness	—	—	—	—
People are Helpful	—	—	—	—
The World is a Fair Place	—	—	—	—
Respondent is Divorced	—	—	—	—
Intercept	.54	.29	.57	.29
ρ	.32***		.34***	
Log Likelihood	−6577.75		−6543.59	

*p < .05, ** p < .01; ***p < .001 (2-tailed tests)
Source: General Social Survey, 1977–1994.
Notes: All models control for survey year, race, and urbanicity at age 16. N for all models is 6,408.

	Model 3		Model 4		Model 5	
	Smoking	Problem Drinking	Smoking	Problem Drinking	Smoking	Problem Drinking
	.28***	−.07	.27***	−.06	.24***	−.09
	.15	.08	.14	.08	.12	−.05
	—	—	—	—	—	—
	.07***	.08**	.07***	.08**	.06***	.07**
	−.0006***	.02***	−.0006***	.02***	−.0005***	.02***
	.004	.06**	.01	.06**	.01	.06**
	.04	−.48**	.02	−.47**	.02	−.48**
	−.21***	.03	−.20***	02	−.20***	.03
	−.01**	−.002	−.01**	−.002	−.01**	−.002
	−.05	−.13	−.07	−.12	−.04	−.09
	—	—	−.05*	.04	−.05*	.04
	—	—	−.01	−.03	−.01	−.03
	—	—	.10***	.02	.10***	.02
	—	—	—	—	.33***	.34***
	.36	.43	.32	.29	.49	.37
	.35***		.35***		.34***	
	−6449.89		−6428.85		−6385.54	

perceive smoking as a serious health risk. In contrast, irrespective of social background most people drink at least occasionally (United States Bureau of the Census 1997).

Single-parenting and step-parenting produce almost identical increases in the risk of smoking. This is evidence against the social control argument: the presence of a step-parent, no matter how ineffectual a disciplinarian, should provide an additional agent of social control and thereby reduce initiation into smoking.

Female respondents from step-families report higher rates of problem drinking than women from either intact families or mother-only families. In contrast, step-parenting completely offset the large impact of parental divorce on men's problem drinking. These results are supported by Hetherington and her colleagues (1985; Hetherington 1993), who found that single-mother parenting was harder on boys than on girls. Conversely, step-parenting hurt girls but benefitted boys. That my results fit this pattern supports the claim that distinct antecedents of adult problem drinking originate in the family processes Hetherington and others describe (and not from an inherited predisposition towards alcoholism, a point I will return to).

Finally, my results do not support the psychosocial adjustment theory. The controls for psychosocial well-being did not attenuate the impact of parental divorce on either alcohol or tobacco consumption. Respondent marital status also could not explain the effects of parental divorce.

Due to the cross-sectional nature of the data it is impossible to ascertain whether these potentially intervening factors are actually anterior to offspring substance consumption. Panel data, with more refined measures of psychosocial adjustment, would permit a better test of the adjustment theory.

My results could also be affected by the fact that the GSS measures family structure at age 16. Some researchers (e.g., Allison and Furstenberg 1989; Amato 1996; McLanahan and Bumpass 1988; but see Stewart at al. 1997 and Wojtkiewicz 1993 for contrary findings) contend that the effects of a parental divorce may vary with its timing, although little consensus exists as to whether older or younger

TABLE 2. Predicted Percentages for the Liklihood of Being a Smoker or Problem Drinker as a Result of Parental Divorce

	Smoker		Problem Drinker	
Family Structure of Origin	Men	Women	Men	Women
Intact Family	35%	24	43%	24
Divorced Single Mother	46	36	57	21
Divorced Mother and Step-Father	46	32	43	26

Source: General Social Survey, 1977–1994.
Notes: Percentages are based on regression standardization, calculated from Model 1, Table 1. Percentages control for survey year, race, urbanicity at age 16, and birth cohort.

children fare better (Hetherington, Bridges, and Insabella 1998). Offspring in step-families at age 16 may have experienced parental divorce at any age prior to 16. In contrast, since two-thirds of divorcees eventually remarry (Cherlin and Furstenberg 1994), people in single-mother families at age 16 are more likely to have experienced parental divorce as teenagers. Unmeasured differences in divorce timing may therefore contribute to the differences in the effects of parental divorce based on family type. Finally, I should note that all children in step-parent families were first in mother-only families, if only for a short time. It is possible, perhaps, that the children of divorce often begin smoking before or soon after the breakup. Even if step-parenting helps children in some ways it may not be enough to keep them from smoking if they have already begun. For these reasons, I cannot arrive at a final decision about any of the three theoretical perspectives based only on differences between step-parenting and single-mother parenting.

Other limitations of my study stem from inadequate measures of alcohol consumption. First, the GSS measure of problem drinking is not optimal. Recent estimates show that only between seven percent and eight percent of the population fit DSM-IV criteria for alcohol abuse (Grant et al. 1994), so many GSS respondents who report sometimes drinking more than they should are not true abusers. However, there is no reason to think that the overestimation of problem drinking should depend on family background. A more serious limitation is the lack of data on problem drinking in respondents' families of origin. This raises the possibility that parental divorce is not the real story: alcohol problems may lead parents to divorce. The higher rates of problem drinking in the children of divorce may only reflect an inherited propensity for alcoholism.

Although it is impossible to know the exact role played by the genetic transmission of alcoholism, I am confident that it is not the only cause of dipsomania in the children of divorce. Step-parenting has such a great impact on problem drinking for both men and women that a large portion of the propensity for alcoholism must be the product of environmental and not genetic factors.[16]

The lack of information on parental alcoholism may be a limitation in explaining the findings but does not affect their implications. The children of divorce are clearly at high risk to become smokers and problem drinkers. This finding very clearly tells us where prevention efforts should be directed. This is an important issue in an age when more than half of first marriages end in divorce (Martin and Bumpass 1989).

Social scientists have documented many lasting effects of parental divorce. Most of these concern demographic or psychological outcomes. My study shows that parental divorce has serious consequences for the physiological well-being of offspring. Needless to say, this is cause for both concern and further research. Furthermore, on the basis of my findings, efforts at substance education and prevention should concentrate on the children of divorce.

APPENDIX A.
Coding of Variables for Multivariate Analyses

Variable	Coding
Birth Cohort	Continuous variable recoded as piecewise linear splines, with knot at 10 (for equation predicting problem drinking); continuous variable with squared term (for equation predicting smoking)
Education of Head of Respondent Parental Family	Continuous variable: 1 = not a high school graduate, 2 = high school graduate, 3 = junior college graduate, 4 = college graduate, 5 = post-graduate degree
Parental Education Data Missing	Coded 1 if data are missing, 0 otherwise
Number of Siblings	Coded 1 if only child, 0 otherwise

APPENDIX A.
Continued

Occupational Prestige (Hodge, Siegel, and Rossi scale)	Continuous variable, 100 point scale
Occupational Prestige Data Missing	Coded 1 if data are missing, 0 otherwise
Problem Drinking	Coded 1 if respondent feels s/he sometimes drinks more than s/he should, 0 otherwise
Race	Coded 1 if black, 0 if non-black
Respondent Family Structure at Age 16	Set of two dichotomous indicators, each coded 1 if family was: headed by a divorced single mother, remarried divorced mother; intact family is the reference category
Respondent Education	Continuous variable: 1 = not a high school graduate, high school graduate, 3 = junior college graduate, 4 = college graduate, 5 = post-graduate degree
Respondent Education Data Missing	Coded 1 if data are missing, 0 otherwise
Respondent Urbanicity at Age 16	Coded 0 if respondent lived in a city of 50,000 or more persons or in a suburb of a larger city, coded 1 if respondent lived in a town of under 50,000 persons or in a rural area
Smoking	Coded 0 if nonsmoker, 1 if smoker
Social Adjustment	Set of three items, each a 3 point Likert scale asking respondents whether they agree with items about happiness, a sense that the world is a fair place, and whether people in general are helpful
Survey Year	Continuous variable; the last two digits of the calendar year

NOTES

1. There is copious research examining the impact of parental divorce and conflict on adolescent alcohol and tobacco use. However, with the exception of the studies cited here none have taken a life course perspective by examining the effects of parental divorce on adult substance consumption. More generally, comparably little research has considered the long-term consequences of parental divorce (Furstenberg and Seltzer 1986; Chase-Lansdale and Hetherington 1990).
2. The vast majority—about 85 percent—of the children of divorce live with their mothers (Seltzer 1994).
3. Hetherington and Wallerstein note that the upheaval associated with divorce often subsides after a year or two. This is a misleading observation because many negative effects of parental divorce only become apparent in adulthood (see below).
4. In other respects, though, a lack of social control in the family of origin may exacerbate the maladjustment produced by parental conflict and divorce. In this sense, there is some overlap in the social control and psychosocial adjustment perspectives.
5. Although sampling design for the GSS has

undergone various changes over the years, one constant has been cluster sampling. This presents a problem for most statistical packages, which assume simple random sampling in the calculation of standard errors. Artificially inflated significance levels may result from standard errors derived from cluster-sampled data. To assess the bias induced by clustering, I conducted preliminary analyses using Huber-White standard errors (Huber 1967; White 1980; for overviews see Greene 1993; StataCorp 1995), making use of GSS data on primary sampling units in order to account for between-cluster variation. I did not use Huber standard errors in the analyses reported here because they are not available in the Limdep software package. The Huber standard errors yielded *t*-statistics similar to those produced by conventional methods, so I concluded that the clustering did not affect my results.

6. In 1977, 1978, 1980, 1983, and 1984 respondents who smoked were also asked if they smoked cigarettes (presumably as opposed to or in addition to cigars or pipes). The vast majority, ninety-three percent, smoked cigarettes. In other years respondents were not asked this question. To ascertain whether this omission is a source of bias I repeated all analyses a number of different ways: treating the seven percent of pipe or cigar smokers as nonsmokers, missing data, or lumping them in with those identified as cigarette smokers. The results were identical in all cases, so for the analyses reported here I used only the third solution.
7. The precise text of these items is: "Do you ever have occasion to use any alcoholic beverages such as liquor, wine, or beer, or are you a total abstainer?" and "Do you sometimes drink more than you think you should?"
8. It is not a concern that the GSS conflated separated and divorced parents. Bumpass et al. (1991) suggest that treating separations as divorces is not likely to be problematic.
9. Many researchers have shown that parental death does not have adverse effects on children (e.g., Acock and Kiecolt 1989; Amato 1988; Demo and Acock 1988) or affects them much less severely than does parental divorce (e.g., McLanahan 1985, 1988; McLanahan and Sandefur 1994).
10. I coded both parental and respondent education as continuous variables (see Appendix A). I repeated the analysis with dummy variables for education and obtained similar results.
11. I chose not to use respondent income as a variable because it is highly correlated with respondent marital status, another independent variable.
12. Lowess (Cleveland, Grosse and Shyu 1992) uses a moving window to calculate a local regression line for each data point. The result is a nonparametric, graphical depiction of the relationship between two variables. Lowess is therefore very useful for ascertaining functional form.
13. I tested interactions between survey year and the dummy variables measuring parental divorce, but they were insignificant and therefore omitted from the models presented here.
14. Respondent birth cohort is almost perfectly correlated with respondent age ($r = .97$), so any argument for using the latter in place of the former (or vice versa) is irrelevant.
15. Splines (Greene 1993) facilitate the modeling of nonlinear relationships by "cutting up" continuous variables into linear segments. The knots are the points at which these linear segments, the pieces of the spline, join.
16. It could be argued that the impact of stepparenting on men's problem drinking might only be a product of divorced mother's selection out of remarriage. In other words, if a divorced mother has a particularly grievous drinking problem, she might be less likely to remarry. It would then be the severity of her drinking problem that produces both her failure to remarry and her son's drinking problem. However, this scenario seems unlikely. Step-parenting *increased* by five percent the chances that female offspring would have drinking problems. This is strong evidence against the notion of selection out of remarriage on the grounds of parental alcoholism.

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US 1st Surgeon General's Report on Smoking & Health, 1964. & later reports demonstrate cigarette smoking as the foremost preventable cause of death in the USA esp. d/t Cardiovascular Diseases & Cancers (CDC 1987, US Dept Hlth & Human Services 1989, 1990.)

- Smoking cessation ↓ anxiety
  depressed
  heavy alcohol users
  poorer self assessed health
  heavily addicted smokers
  > 1 pack/day.
- smoking behaviour linked to heart attacks, hypertension, obesity.

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The Impact of Education and Heart Attack on Smoking Cessation Among Middle-Aged Adults*

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Considerable evidence supports the premise that higher levels of education lead to enhanced health, including protective health behaviors. This paper focuses on how education affects one health behavior known to lead to enhanced health: the cessation of smoking. In particular, the authors examine the extent to which education influences the decision by middle-aged adults to quit smoking following a heart attack, a potentially life-threatening health event. We first hypothesize that middle-aged adults with more formal education will stop smoking more readily than people with less formal education following the experience of a heart attack. Second, we ask what other factors might underlie and explain that hypothesized effect. Using longitudinal data, the authors track changes in individual smoking behaviors after a heart attack among preretirement-age Americans. We control for documented correlates of smoking and heart attack plus other factors associated with education, heart attack, and smoking that may also influence whether a person quits smoking. In addition to confirming evidence on the education-health association as well as the documented connection between heart attack and smoking cessation, this study provides a surprising twist on those links: Our results show that the move to quit smoking following the experience of a heart attack among middle-aged adults is significantly and dramatically moderated by their level of educational attainment.

Considerable evidence supports the premise that higher levels of education lead to enhanced health, including protective health behaviors, in both older and younger adults (Adler et al. 1994; Antonovsky 1967; Feinstein 1993; Feldman et al. 1989; Kitagawa and Hauser 1973; Ross and Wu 1995; Syme and Berkman 1976). This paper focuses more closely on how education affects one health behavior known to lead to enhanced health: the cessation of smoking. In particular, we examine the extent to which education influences the decision to quit smoking by middle-aged adults following a heart attack—a potentially life-threatening health event. Thus, we study one step in the process linking education and enhanced health in a highly selective group of middle-aged smokers. Specifically, these smokers may differ from younger smokers in several ways. They may represent a group of

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longer-termed and, thus, more heavily addicted or otherwise committed smokers who have successfully resisted decades of widely available information on the health dangers of cigarette smoking. Their unique characteristics may also contribute to their resisting current public health programs targeted to the smoking community at large or to younger smokers. This study aims to understand the role that higher levels of education may play in changing smoking behavior in the face of a health crisis.

Given the available literature, we hypothesize that middle-aged adults with more formal education will stop smoking more readily than middle-aged adults with less education following the experience of a heart attack. Second, we ask what other factors might underlie and explain such an effect. In exploring these issues, we bring together two voluminous bodies of literature that cross-cut such disciplines as sociology, psychology, medicine, economics, and epidemiology: one pertaining to the predictors of smoking cessation and the other to the relationship between education and health. Using longitudinal data, we track changes in individual smoking behavior after a heart attack while controlling for documented correlates of smoking and heart attack plus other factors associated with education, heart attack, and smoking that may also influence whether a person quits.

PREVIOUS RESEARCH

Previous studies dealing with smoking cessation as well as the links between education and health are wide and varied. Each area is summarized briefly below.

Smoking Cessation

The first Surgeon General's Report on Smoking and Health in 1964 as well as all subsequent reports from that office demonstrate that cigarette smoking is the foremost preventable cause of death in the United States and, in particular, those deaths resulting from cardiovascular diseases and cancers (Centers for Disease Control 1987; U.S. Department of Health and Human Services 1989, 1990). Although the 1990 Surgeon General's Report indicates that the proportion of smokers who stop smoking has increased consistently since 1964 (U.S. Department of Health and Human Services 1990), the reasons why some people quit and others continue to smoke are not entirely clear.

Education clearly plays a role in smoking cessation: The rates of quitting smoking since the 1964 Surgeon General's Report have consistently increased (and increased more rapidly over time) for those with more education. For example, although the overall quit rates have increased from 33 percent in 1965 to 44 percent in 1987, college graduates have quit at significantly higher rates than high-school graduates (U.S. Department of Health and Human Services 1990), suggesting that people with higher educational attainment may have better understood the risks of cigarette smoking and acted on the Surgeon General's recommendations.

Several other health as well as demographic, environmental, and psychosocial factors may also influence smoking behavior. Studies have shown that not smoking or quitting smoking is highest among older adults, people who are not married to other smokers, and workers not employed in manufacturing or day labor jobs (O'Loughlin et al. 1997; U.S. Department of Health and Human Services 1990; Wister 1996; Wray et al. 1996). In contrast, smoking cessation is lowest among people who are depressed (Anda, Williamson, and Escobedo 1990; Glassman, Helzer, and Covey 1990) or heavy alcohol users (Breslau et al. 1996; U.S. Department of Health and Human Services 1994). Smoking cessation may also be lower among individuals with poorer self-assessed health (Nevid, Javier, and Moulton 1996). More heavily addicted smokers—people who smoke more than one pack of cigarettes a day—are also less likely to quit (Marbella, Layde, and Remington 1995). In addition, studies have shown that smoking cessation may differ by gender, some indicating that women are more likely to quit smoking and others that men quit more often (Escobedo and Peddicord 1996; Jarvis 1995; Rogers, Nam, and Hummer 1995; U.S. Department of Health and Human Services 1989; Wenger 1995).

In general, although smokers perceive their health risks for cardiovascular diseases and cancer to be greater than those of nonsmokers, they also underestimate their health risks (Strecher, Kreuter, and Kobrin 1995). Nevertheless, higher proportions of smokers quit smoking once they experience a heart event compared to smokers who did not experience such an event (U.S. Department of Health and Human Services 1989). In addition, the proportion of those quitting following any heart event increases with the severity of the event (Baile et al. 1982). Given the well-established relationship between smoking and heart attack, smoking behavior may also be affected indirectly by modifiable risk factors associated with the experience of heart attacks or other heart-related conditions such as physical inactivity, high blood pressure, and obesity (Brownson et al. 1996; Bucher and Ragland 1995; Wenger 1995; Winkleby et al. 1996) as well as by enduring factors such as gender and race/ethnicity (Brownson et al. 1996; Nevid et al. 1996; Ransford 1986; Strecher et al. 1995).

Education and Health

Decades of studies have documented that higher levels of education are linked to a variety of measures of enhanced health, including protective-health behaviors such as weight management, regular exercise, and moderate drinking (Wray et al. 1996). Although the link between education and health is well-established across academic disciplines, the meaning of this association is open to debate (see Adler et al. 1994; Ettner 1996; Ross and Wu 1996). Four interpretations of the association are possible: two suggesting direct relationships between education and health (Grossman and Kaestner 1997), a third looking at an indirect relationship due to the existence of other factors that are associated with both education and health (Behrman 1997; Coburn and Pope 1974; Grossman and Kaestner 1997; Matthews et al. 1989; Ross and Wu 1995, 1996) and a fourth examining a conditional relationship that indicates that education and health outcomes are associated only under selected circumstances.

The third and fourth possibilities—which have received far less analytic attention than the other two primarily due to data constraints—serve as the basis for this study's conceptual framework. We begin by examining whether heart attack or education exerts direct effects on smoking cessation among middle-aged smokers as demonstrated in the literature for all smokers or, alternatively, whether they interact in some way to change smoking behavior. That is, perhaps educational attainment moderates the relationship between heart attack and smoking cessation so that the move to quit smoking varies across levels of education. In particular, it may be that higher levels of education produce more of the necessary knowledge, skills, and abilities that help a person to understand the link between cigarette smoking and heart attacks and, in turn, the advisability of quitting smoking following the experience of a heart attack.

We also consider the extent to which selected psychological, social environment, and resources consequences of education may mediate the process of quitting smoking. From a psychological perspective, acquiring higher levels of education in childhood and young adulthood may reinforce or augment cognitive ability in adulthood—particularly in the dimension knowledge-based intelligence (Perlmutter 1986) or product intelligence (Salthouse 1991, 1996). People who function at a higher cognitive level may be better able to use their educational resources to apply the ever-changing health data to their own lives (Kenkel 1991), thereby decreasing their propensity to smoke and, in turn, their risk for heart attack (Hamilton 1972; Ippolito 1979; Lewit, Coate, and Grossman 1981; Schneider, Klein, and Murphy 1981). Further, some smokers with higher levels of education and, relatedly, higher levels of cognitive ability may have been more positively influenced by evidence that 10 to 15 years of abstaining from smoking returns the all-cause mortality risks of past smokers to those of non-smokers and—perhaps more saliently—that even one year of abstention significantly reduces the risks of dying from various diseases (Samet 1992; U.S. Department of Health and Human Services 1990).

Another psychological factor that may explain a link among education, heart attack, and smoking cessation is a personality characteristic that predisposes people to invest in the future through "good" health behaviors in the present (Becker, Grossman, and Murphy 1991, 1994; Becker and Murphy 1988; Farrell and Fuchs 1982; Fuchs 1982; Grossman and Kaestner 1997; Kenkel 1991; Rakowski et al. 1987). People with higher levels of education are more likely than people with lower levels of education to engage in healthful behaviors overall, including never smoking (Matthews et al. 1989; Wagenknecht et al. 1990; Winkleby

et al. 1992), and thereby reducing their risk of many diseases (Antonovsky 1967; Diez-Roux et al. 1995; Wray et al. 1996). They may do so because they are more willing to plan or "invest" in the future rather than "consume" in the present. Thus, we speculate that differences in future orientation may explain the education-health association.

Alternatively, a social-environment perspective posits that educational levels may influence a person's choice of where to live or work that may differentially reinforce beneficial health behaviors or discourage harmful health behaviors through "social control" in the form of peer norms or values (Diez-Roux et al. 1995; Rogers et al. 1995; Ross and Wu 1995; Umberson 1987). As noted earlier, smoking cessation is reported to be highest among people whose spouse or other household members are nonsmokers (O'Loughlin et al. 1997; Wister 1996). Similarly, rates of smoking vary by job categories: Workers in professional or higher-status jobs are disproportionately nonsmokers compared to workers in lower-status jobs (Wray et al. 1996). Since less-educated people tend to marry other people with less education and work in jobs which require less education, it is possible that they are faced with disproportionately greater numbers of smokers in their immediate environment. The lower-status jobs may also include more physically demanding and repetitive tasks as well as less autonomy and flexibility, factors that may combine to increase job-related boredom and stress and, potentially, the likelihood of smoking to counter the boredom and stress. Thus, people with lower levels of education may be more likely to start or continue smoking not because of their levels of educational attainment per se but instead because of influences in their social environment which are related to educational level.

A similar logic applies to a resources perspective: Higher levels of education may yield better health through higher income and wealth that then purchase more health insurance or greater access to high-quality health-care (Grossman and Kaestner 1997; Patterson, Bengal, and White 1996; Schultz 1975; Welch 1977). Rather than advanced education linking directly to fewer heart attacks or to the cessation of smoking, it may be that the greater income or employer-provided health insurance associated with higher levels of education protect against heart attack or encourage a decision to quit smoking following a heart attack.

Whatever the true meaning of the education-health association, increased years of education are consistently found to be positively associated with many aspects of enhanced health in both younger and middle-aged adults. Whether education contributes directly, indirectly, or conditionally to enhanced health in the form of smoking cessation among a particular group of older smokers is the question that is the focus of this paper.

METHOD

Data

The lack of conclusive research on the process by which education changes health behaviors is due in part to the paucity of data sets containing appropriate longitudinal data to study this question. Ideally, such a data set would contain individual social, health, and economic characteristics as well as other individual and environmental factors which may influence making certain behaviors and decisions. The Health and Retirement Study (HRS), a large, nationally representative sample of preretirement-age Americans, is uniquely suited for exploring this study's issues for two primary reasons. First, the HRS is rich in information central to our interests, containing considerable sociodemographic, physical and emotional health, health behavior, functi work and retirement, income and ass health- and life-insurance data as well as measures on cognitive ability, future orientation, risk aversion, and subjective probabilities. Second, the HRS is a panel study that has collected three waves of data to date,[1] enabling us to explore a range of dynamic processes relating to health and economic decision-making among preretirement-age individuals.

Questions and Hypotheses

Based on our review of studies on smoking behavior and the health benefits of education, we expect that education will be an important—and perhaps even predominant—predictor of smoking cessation among middle-aged smokers. In addition, given the documented link between the experience of a heart attack

and smoking cessation, we anticipate that education will interact with the experience of a heart attack so that rates of smoking cessation will differ across educational levels. Because education is a proxy for knowledge, skills, and abilities developed over half a lifetime in the case of our HRS cohort, we also test whether selected psychological, social environment, and resources factors perceived as consequences of education might explain any of the effects of education or the interaction of education and heart attack on the decision to quit smoking. We anticipate that these education-related factors may be all the more important in decision-making for this particular group of middle-aged smokers. Because they are more likely to be highly addicted to cigarettes after many smoking years, their smoking behavior may also be influenced considerably more by each of the education-related factors to which they have been exposed for longer periods of time compared with their younger counterparts.

In this paper, we ask the following questions about middle-aged adults:

(1) Does education affect smoking cessation? Does the experience of a heart attack affect smoking cessation? Do education and the experience of a heart attack interact to affect smoking cessation such that people with more formal education are more likely to quit smoking following a heart attack than do people with less formal education?

(2) Is there any evidence for psychological, social environment, or resources factors explaining an education or an education-heart attack interaction effect on smoking cessation?

Based on our study questions and the extant literature, we test three primary hypotheses relating to smoking cessation among middle-aged adults:

(1) Smokers with higher levels of education are more likely to quit smoking than are smokers with lower levels of education.

(2) Smokers who have experienced a heart attack are more likely to quit smoking than smokers who have not experienced a heart attack.

(3) Smokers with higher levels of education are more likely to quit smoking than are smokers with lower levels of education following the experience of a heart attack.

Additional secondary hypotheses test six possible explanations for an education or education-heart attack effect on smoking cessation. Two hypotheses test whether psychological factors associated with education affect smoking behavior:

(4) Smokers with higher levels of cognitive ability are more likely to quit smoking than are smokers with lower levels of cognitive ability.

(5) Smokers who are more future-oriented are more likely to quit smoking than are smokers who are less future-oriented.

Similarly, two hypotheses test whether social-environment factors associated with education influence smoking behavior:

(6) Smokers who are not married to other smokers are more likely to quit smoking than are smokers married to other smokers.

(7) Smokers who do/did not work as a machine operator or laborer are more likely to quit smoking than are smokers who worked as a machine operator or laborer.

Finally, two hypotheses test the effects of resources factors associated with education on smoking behavior:

(8) Smokers who report greater net worth are more likely to quit smoking than are smokers who report lower net worth.

(9) Smokers who are covered by employer-provided health insurance are more likely to quit smoking than are smokers without employer-provided health insurance.

Samples

Although a large body of past research has consistently supported the strong negative association between higher levels of education and smoking, less conclusive evidence exists on a causal relationship between years of education and quitting smoking, particularly among middle-aged or older smokers (U.S. Department of Health and Human Services 1989, 1990). In order to isolate the effect of education on the process of modifying smoking behavior, we tracked the effects of education on smoking cessation following the experience of a heart attack between 1992 and 1994 (when the data for HRS Waves 1 and 2 were collected) among smokers age 51 to 61 in 1992.[2] Heart attack was chosen as an example of a major smoking-related health event that, if

diagnosed, can be reported with reasonable precision in surveys.

Two primary respondent groups were drawn for this study. First, a full sample included the 8,655 age-eligible respondents for whom we have unambiguous smoking history data in both 1992 and 1994 interviews. Among those respondents, 3,216 reported they had never smoked cigarettes or had smoked less than 100 cigarettes in their lives prior to 1992; 3,049 reported they had smoked in the past but had quit by 1992; and 2,391 reported they were current smokers in 1992 who had either continued to smoke or had quit smoking by 1994. The full sample provided us with data on the relationships between smoking history and various social, physical health, psychological, and economic characteristics and helped us to refine our major analytic models on smoking cessation. The second respondent group, which included the 2,391 people who reported they were current smokers in 1992 for whom we had matching 1994 data on smoking status, was the basis for our major analytic models.

Analysis Plan

We tested multivariate models using various subgroups of the full and smoking samples. First, exploratory models tested the effects of education and other hypothesized predictors on three dichotomous outcomes: never smoking among all middle-aged adults, quitting prior to 1992 among middle-aged adults who had smoked in the past but were not current smokers in 1992, and having experienced a heart attack between 1992 and 1994.[3] Findings from these analyses informed the design of our analyses on smoking cessation.

Second, the models that focused on our major analytic interest—smoking cessation between 1992 and 1994—were tested on the smokers sample only. Given the dichotomous outcome measure for this set of analyses as well, the models were tested using logistic regression.[4] In these primary analyses, we regressed smoking cessation between 1992 and 1994 on sequentially-entered blocks of variables that test the relative contributions of selected variables proposed to measure the education-smoking behavior relationships, and controlling for documented correlates of smoking cessation and heart attack.

The independent variables in our models of smoking cessation were restricted to:

(1) the measures of major analytic interest: education, incident heart attack, and an interaction term for education by heart attack;
(2) potential predictors that may explain the education-heart attack effect on smoking cessation, including selected psychological, social-environment, and resources factors;
(3) the primary correlates of smoking cessation: gender and measures of depressed or addictive personalities; and
(4) additional correlates of heart attack: race/ethnicity and specific measures of heart-related health.

Among the independent variables of major analytic interest, education is measured as the number of years of education completed by 1992 (0 to 17 years, with 17 representing post-baccalaureate education), centered on 12 years of education. The measure of incident heart attack indicates whether or not the respondent reports having experienced a heart attack between 1992 and 1994 (0 = no; 1 = yes). The interaction term, representing the dependency of education on heart attack, is measured as years of education multiplied by the experience of a heart attack (Jaccard, Turrisi, and Wan 1990).

The independent variables include six psychological, social-environment, and resources factors that may explain the effects of the interaction term on smoking cessation. These factors were also measured at baseline in 1992. Among the psychological factors, cognitive ability is a measure that combines the standardized total scores (Z-scores) from two cognitive performance tests available in the HRS—the immediate and delayed word recall tests as well as the WAIS-R word similarities test (0 to 54).[5] Future orientation is measured by whether or not the respondent reports a short-term financial planning horizon (a few months to one year) or a medium-term financial planning horizon (a few years), with a long-term planning horizon (more than five years) being the reference category.

The social environment factors include whether the respondent's spouse smokes (0 = no; 1 = yes) and whether the respondent worked as a machine operator or laborer (0 = yes; 1 = no). The resources factors include a measure of logged net worth (centered on the mean) and a dichotomous measure of whether the respondent is covered by employer-provided health insurance (0 = no; 1 = yes).

Finally, we include documented correlates of smoking cessation measured at baseline in 1992: gender (0 = male; 1 = female); heavy smoking measured as current cigarette dosage of greater than 25 per day (0 = no; 1 = yes); heavy drinking measured as currently drinking more than two alcoholic drinks per day (0 = no; 1 = yes); and the number of Center for Epidemiological Studies-Depression Scale (CES-D) depressive symptoms experienced most or all of the time in the past week (0 to 8), centered on the mean number of CES-D symptoms. Similarly, we include documented correlates of heart attack measured at baseline: two measures of race/ethnicity (1 = African American or 1 = Latino; 0 = White or other race/ethnicity as the reference category); diagnosis of high blood pressure in the past (0 = no; 1 = yes); obesity measured as greater than the third quartile of body mass index for the HRS respondents (0 = no; 1 = yes); irregular exercise measured as light exercise less than once a week (0 = no; 1 = yes); and two measures of self-assessed health status (1 = good or 1 = fair/poor health; 0 = excellent/very good as the reference category).

RESULTS

Correlates of Smoking History

Table 1 describes the characteristics of four subgroups of Americans age 51 to 61 in 1992, arrayed according to their smoking history in 1992 and 1994: (1) respondents who reported in both 1992 and 1994 that they had never smoked cigarettes; (2) those who reported in 1992 that they had smoked in the past but had quit prior to 1992; (3) those who reported they were current smokers in 1992 but were not smokers in 1994; and (4) respondents who reported they were current smokers in both 1992 and 1994. As expected, in general, middle-aged adults without any smoking history had fewer risk factors for heart disease and more characteristics associated with higher education than did smokers in 1992 or 1994. For example, never smokers are disproportionately female with higher levels of education and cognitive ability compared with their counterparts who report a smoking history. Never smokers also experienced significantly fewer heart attacks prior to 1992, fewer heart attacks between 1992 and 1994, have a lower history of high blood pressure, drink less heavily, and report better self-assessed health as well as fewer CES-D depressive symptoms than do smokers in 1992 or 1994. Never smokers are also less likely to be married to smokers or to work as machine operators or laborers and are more likely to report higher net worth than are recent smokers. Past smokers—smokers who quit smoking prior to 1992—are statistically similar to never smokers on many characteristics, including education, depressive symptoms, self-assessed health, cognitive ability, spousal smoking, employer-provided health insurance, and net worth. Three significant differences between those groups are worth noting. Compared with never smokers, past smokers are disproportionately men, people who experienced a heart attack before 1992, and people who reported they drink heavily. These differences are significant at the $p < .05$ level.

In contrast, current smokers in 1992 and 1994 are less well-educated, heavier drinkers, report higher levels of depressive symptoms, and test lower in cognitive ability than do never or past smokers in those years. Smokers in 1992 and 1994 are more likely to be married to other smokers and to report lower net worth than never or past smokers. Importantly, people who quit smoking between 1992 and 1994 also disproportionately report having experienced a heart attack during that same period.

Predictors of Never Smoking and Quitting Among Past Smokers

Tables 2 and 3 present results of exploratory analyses focusing on two of the smoking states illustrated in columns 1 and 2 of Table 1—never smoking and having quit smoking prior to 1992. The goal of each of these analyses is to gain some understanding of the role of education on pre-1992 smoking behavior while controlling on selected correlates of smoking in order to better design our major analytic models concerning smoking cessation between 1992 and 1994. As shown in Models 1 through 4 in each table, blocks of variables were entered sequentially: (1) demographic and status origin characteristics; (2) years of education; (3) measures of health behaviors

TABLE 1. Frequencies, Means, and Medians on Selected Characteristics of U.S. Adults Age 51–61, by Smoking History

Characteristics[a]	Never Smoked	Smoker Prior to 1992	Smoker in 1992 Quit by 1994	Smoker in 1992 and 1994
Psychosocial Risk Factors				
Female[b]	66.0	41.0	51.9	50.8
Race/Ethnicity[b]				
White	81.2	85.3	78.7	82.4
African American	9.4	8.4	12.8	10.4
Latino	6.4	4.9	5.8	5.3
Other	3.0	1.4	2.7	1.9
Father's Education (mean, 0–17)[b,c]	9.3	9.5	9.3	8.9
	3.8	3.9	3.8	3.8
Education (mean, 0–17)[b,c]	12.7	12.6	12.0	11.8
	3.0	3.0	2.8	2.9
Heart Attack Prior to 1992[b]	3.0	7.3	6.5	5.7
Heart Attack 1992–1994[b]	.9	2.5	9.4	2.2
High Blood Pressure[b]	35.7	42.9	40.3	33.8
Heavy Smoker in 1992[b]	—	—	19.8	30.1
Heavy Smoker Prior to 1992	—	39.6	—	—
Heavy Drinker[b]	1.5	5.3	6.6	10.2
Irregular Exerciser[b]	46.4	42.4	50.3	51.4
Obese[b]	24.0	27.4	25.4	16.6
Self-Reported Health[b]				
Excellent/Very Good	59.9	56.3	43.2	45.8
Good	24.8	26.2	28.7	28.4
Fair/Poor	15.3	17.6	28.1	25.8
CES-D Symptoms (mean, 0–8)[b,c]	.7	.7	1.0	1.0
	1.3	1.3	1.6	1.6
Psychological Factors				
Cognitive Ability (mean, 0–54)[b,c]	20.4	19.9	18.6	18.8
	6.7	6.6	6.3	6.8
Future Orientation[b]				
Short-Term Planner	25.7	25.4	27.7	32.1
Medium-Term Planner	35.6	33.7	38.5	31.5
Long-Term Planner	38.7	41.0	33.8	36.4
Social-Environment Factors				
Spouse Smokes[b]	11.1	12.9	28.5	31.1
Blue Collar Worker[b]	17.2	25.8	26.8	31.2
Resources Factors				
Net Worth (median)[b]	124,000	120,000	72,000	70,000
Employee Health Insurance[b]	74.6	76.4	71.6	64.9
N	3,216	3,049	402	1,989

[a] Values for all characteristics except "Heart Attack 1992–1994" are those reported at baseline in 1992.
[b] Values are significantly different across smoking history categories.
[c] Standard deviations are presented below means.

and lifestyle as well as physical and emotional health that may be associated with education; and (4) selected psychological, social environment, and resources consequences of education. For ease of interpretation, the tables present parameter estimates and t-statistics as well as odds ratios.

As shown in Table 2, certain enduring characteristics of individuals that may be seen as precursors to education are consistently associated with whether or not middle-aged adults ever smoked. For example, being female or Latino significantly increases the odds of never smoking in Model 1. These factors remain significant in Models 2–4 as well, even after education, health, lifestyle, and education consequences are introduced. Most central to our interest is that education is highly significant across Models 2–4, increasing the odds of never smoking by 5–8 percent for every additional year of education beyond high school. In other words, more highly educated people are less likely to have ever started smoking. In both Models 3 and 4, other behavioral, social-environment, and health factors such as being a heavy drinker, married to a smoker, or having experienced a heart attack prior to 1992 are also significantly associated with never smoking. Interestingly, greater numbers of CES-D depressive symptoms contribute significantly to decreased odds of never smoking. Model 4 also shows that working as a machine operator or laborer decreases the odds of never smoking while greater net worth increases the odds.

Table 3 presents data for middle-aged adults who ever smoked and contrasts those who quit prior to 1992 with those still smoking in 1992. Among the precursors of education shown in Model 1, being female or African American reduces the odds of past quitting. In contrast, higher levels of father's education (our measure of status origins) is positively associated with prior quitting. When education is introduced in Models 2–4, only being female remains consistently significant among the preprecursors. Education itself is significantly linked to past quitting as expected—those who are more highly educated are more likely to have quit smoking before 1992—but only in Models 2 and 3. Once the consequences of education are entered into Model 4, education itself loses significance. All of our health and lifestyle measures plus cognitive ability, net worth, and employee health insurance are also significantly associated with prior quitting and all in the direction we would expect from the literature. That is, higher levels of cognitive ability and net worth, having employer-provided health insurance coverage, or having been diagnosed with a previous heart attack or high blood pressure contribute positively to having quit smoking prior to 1992. In contrast, detrimental health behaviors such as irregular exercise or heavy drinking are negatively associated with prior quitting.

Predictors of Incident Heart Attack

Finally, Table 4 presents results of exploratory analyses focusing on the experience of an incident heart attack. In addition to trying to understand how education contributed to smoking behavior prior to 1992 (when the HRS started), we also wanted to understand how education might have influenced the experience of a heart attack between 1992 and 1994 (net of selected correlates of heart attack) in order to compare our findings on middle-aged adults with findings in the literature.

Surprisingly, neither education nor the consequences of education appear to play a role in the likelihood of an incident heart attack, counter to recent studies (Diez-Roux et al. 1995; Feinstein 1993; Feldman et al. 1989; Matthews et al. 1989). However, other findings shown in Table 4 demonstrate support for other existing literature. For example, being female or a heavy drinker significantly decreases the odds of experiencing a heart attack. In contrast, being a smoker in 1992, having been diagnosed with high blood pressure, and reporting higher levels of CES-D depressive symptoms increase the odds.

In sum, the three sets of exploratory analyses indicate that education is importantly linked to never starting smoking but only indirectly to stopping prior to 1992 and to the experience of an incident heart attack. The consequences of education—represented here as lifestyle and health status as well as psychological, social-environment, and resources factors—suppress the association between education itself and prior stopping. Other factors that are influential to both past smoking states include gender and race/ethnicity. In general, all of the potential predictors in these exploratory models except father's education are consistently associated with past smoking behavior. Fewer of the potential predictors in our models are significantly related to incident heart attack, but those that are generally support the literature and also are associated with educational level. Although the findings from the exploratory analyses are associational rather than causal, they provide us with useful information on which to base and interpret our models of smoking cessation between 1992 and 1994. The major analytic models that are described below combine all of the potential predictors of past smoking behavior and incident heart attack except father's education.

Predictors of Smoking Cessation Between 1992–1994

In this section, we describe the results of the multivariate analyses on those people we are most interested in, those represented in columns 3 and 4 of Table 1—the people who

TABLE 2. Logit Equations Showing Never Smoking Regressed on Education, Incident Heart Attack, and Selected Predictors Among U.S. Smokers Age 51–61, 1992 and 1994

Characteristics[a]	Model 1 Parameter Estimate	Model 1 Odds Ratio	Model 2 Parameter Estimate	Model 2 Odds Ratio	Model 3 Parameter Estimate	Model 3 Odds Ratio	Model 4 Parameter Estimate	Model 4 Odds Ratio
Intercept	−1.003*** (24.811)		−1.150*** (25.372)		−1.285*** (15.934)		−1.102*** (12.391)	
Female	.865*** (17.930)	2.375	.899*** (18.446)	2.457	.878*** (15.478)	2.405	.810*** (13.899)	2.247
African American[b]	−.120 (.227)	.980	.120 (.226)	1.020	.265* (2.535)	1.304	.214* (2.010)	1.239
Latino[b]	.280** (2.585)	1.323	.471*** (4.208)	1.601	.520*** (3.948)	1.682	.501** (3.749)	1.651
Father's Education	.011 (1.668)	1.011	−.012 (1.703)	.988	−.021*** (2.618)	1.063	−.020* (2.551)	.980
Education	—	—	.746*** (7.663)	1.077	−.010** (4.895)	.980	.051*** (4.040)	1.052
Cognitive Ability	—	—	—	—	.005 (.264)	1.005	.000 (.010)	1.000
Short-Term Planner[c]	—	—	—	—	−.027 (.398)	.973	.003 (.048)	1.003
Medium-Term Planner[c]	—	—	—	—	.070 (1.160)	1.072	.084 (1.381)	1.088
Blue Collar Worker	—	—	—	—	−.244** (3.189)	.783	−.225** (2.897)	.799
Net Worth	—	—	—	—	.1111*** (7.527)	1.117	.104*** (6.958)	1.109
Employee Health Insurance	—	—	—	—	.047 (.732)	1.048	.040 (.618)	1.041
Obese	—	—	—	—	—	—	.100 (1.557)	1.105
Irregular Exercise	—	—	—	—	—	—	.009 (.169)	1.009
Heavy Drinker	—	—	—	—	—	—	−1.279*** (6.945)	.278
Spouse Smokes	—	—	—	—	—	—	−.709*** (9.157)	.492
Heart Attack 1992–1994	—	—	—	—	—	—	−.541*** (3.683)	.582

TABLE 2. Continued

Characteristics[a]	Model 1 Parameter Estimate	Model 1 Odds Ratio	Model 2 Parameter Estimate	Model 2 Odds Ratio	Model 3 Parameter Est	Model 3 Odds Ratio	Model 4 Parameter Estimate	Model 4 Odds Ratio
High Blood Pressure	—	—	—	—	—	—	−.011 (.196)	.989
CES-D Symptoms	—	—	—	—	—	—	−.044* (1.990)	.957
Log Likelihood Ratio	373.857		398.487		453.522		642.876	
df	3		5		11		18	
p	.0001		.0001		.0001		.0001	
N	7,783		7,783		6,647		6,647	

* $p < .05$; ** $p < .01$; *** $p < .001$

Note: T-statistics are in parentheses.

[a] Values for all characteristics except "Heart Attack 1992–1994" are those reported at baseline in 1992.

[b] Reference category is white and other non-African American or Latino ethnicity.

[c] Reference category is long-term planner.

reported they were current smokers in 1992 and who had subsequently quit or continued smoking. The goal of these analyses is to discern the effects of education, heart attack, the interaction of education and heart attack as well as selected psychological, social-environment, and resources factors on smoking cessation between 1992 and 1994.

The four simple models in Table 5 demonstrate the effects of the following variables on smoking cessation by 1994: (1) heart attack alone; (2) education alone; (3) education and heart attack together; and, finally, (4) education, heart attack, and an interaction term of education with heart attack. Consistent with other studies, Model 1 demonstrates that the experience of a heart attack is a significant predictor of smoking cessation by 1994. In contrast, Model 2 shows that education alone is not. Heart attack's significant effects on quitting remain essentially the same when controlling for educational levels (Model 3). In this model, incident heart attack strongly and positively predicts smoking cessation, quadrupling the odds of quitting.

In order to explore the relationship among education, heart attack, and smoking cessation further, Model 4 introduces an interaction term for education and heart attack. Here, the interaction term is significant and positive, implying that for those who experienced a heart attack, each additional year of education beyond high school increases the odds of quitting smoking by 44 percent (from the interaction term) plus 622 percent (from the main effect for heart attack) for a total of 667 percent. In contrast, each additional year of education beyond high school increases the odds of quitting by less than 1 percent among those who did not experience a heart attack. Thus, education moderates the well-known heart attack and smoking cessation link, a finding illustrated graphically in Figure 1.

In this figure, we plot probability values and show that a high school or college education dramatically increases the probability of quitting smoking among people who experienced an incident heart attack compared with those who did not. As illustrated in the bottom curve, the probability of quitting smoking is remarkably low among those without an incident heart attack, with

TABLE 3. Logit Equations Showing Smoking Cessation Prior to 1992 Regressed on Education, Incident Heart Attack, and Selected Predictors Among U.S. Adults Age 51–61, 1992[1]

	Model 1		Model 2		Model 3		Model 4	
Characteristics[a]	Parameter Estimate	Odds Ratio	Parameter Estimate	Odds Ratio	Parameter Estimate	Odds Ratio	Parameter Estimate	Odds Ratio
Intercept	.653*** (14.390)		.502*** (10.247)		.457*** (4.985)		.617*** (5.848)	
Female	−.401*** (6.903)	.670	−.382*** (6.539)	.682	−.467*** (6.758)	.627	−.478*** (6.467)	.620
African American[b]	−.229* (2.185)	.796	−.185 (1.756)	.831	.086 (.664)	1.089	−.073 (.541)	.930
Latino[b]	.016 (.115)	1.016	.242 (1.685)	1.273	.308 (1.861)	1.361	.332 (1.943)	1.394
Father's Education	.034*** (4.379)	1.034	.003 (.388)	1.003	−.004 (.442)	.996	−.006 (.584)	.994
Education	—	—	.096*** (8.146)	1.101	.037* (2.434)	1.037	.024 (1.518)	1.024
Cognitive Ability	—	—	—	—	.052* (2.187)	1.053	.049* (1.986)	1.050
Short-Term Planner[c]	—	—	—	—	−.057 (.691)	.945	−.029 (.331)	.972
Medium-Term Planner[c]	—	—	—	—	.050 (.667)	1.051	.088 (1.126)	1.092
Blue Collar Worker	—	—	—	—	−.177* (2.127)	.838	−.129 (1.475)	.879
Net Worth	—	—	—	—	.123*** (7.450)	1.131	.126*** (7.371)	1.134
Employee Health Insurance	—	—	—	—	.170* (2.228)	1.186	.029*	1.192 (2.187)
Obese	—	—	—	—	—	—	.528*** (6.281)	1.695
Irregular Exercise	—	—	—	—	—	—	−.305*** (4.533)	.737
Heavy Drinker	—	—	—	—	—	—	−.603*** (4.589)	.547
Spouse Smokes	—	—	—	—	—	—	−1.184*** (14.567)	.306
Heart Attack 1992–1994	—	—	—	—	—	—	.345* (2.357)	1.412

TABLE 3. Continued

	Model 1		Model 2		Model 3		Model 4	
Characteristics[a]	Parameter Estimate	Odds Ratio	Parameter Estimate	Odds Ratio	Parameter Estimate	Odds Ratio	Parameter Estimate	Odds Ratio
High Blood Pressure	—	—	—	—	—	—	.332*** (4.614)	1.394
CES-D Symptoms	—	—	—	—	—	—	−.109*** (4.130)	.897
Log Likelihood Ratio	75.700		143.501		213.286		583.502	
df	4		5		11		18	
p	.0001		.0001		.0001		.0001	
N	4,902		4,902		4,180		4,180	

* $p < .05$; ** $p < .01$; *** $p < .001$

Note: T-statistics are in parentheses.

[a] Values for all characteristics except "Heart Attack 1992–1994" are those reported at baseline in 1992.

[b] Reference category is white and other non-African American or Latino ethnicity.

[c] Reference category is long-term planner.

higher levels of education increasing that probability only very modestly (from 14 to 16 percent). In stark contrast, among individuals who did experience a heart attack (top curve), higher levels of educational attainment clearly play a role in smoking cessation. Middle-aged adults with at least some high school education had a 30 percent probability of quitting if they had a heart attack, compared to a 53 percent probability for those who completed high school, 83 percent for those with a college education, and 88 percent for those with a postbaccalaureate education. People who never attended any high school and also experienced an incident heart attack were about as likely to quit smoking as those who did not experience a heart attack between 1992 and 1994.

Table 6 shows that introducing additional predictors of smoking cessation to Model 4 of Table 5 changes the story only slightly. In general, the additional predictors do not modify the powerful effect of education on the impact of heart attack on smoking cessation. Model 5 includes not only education, heart attack, and the interaction of education and heart attack but also the primary correlates of smoking cessation and heart attack. In Model 6, we add the potential explanations for an education and heart attack interaction. In those two models, heart attack remains a significant (and somewhat stronger) predictor of quitting, compared with Model 4. Education as a main effect continues to be nonsignificant. However, the effect of the interaction between education and heart attack remains significant and virtually unchanged in strength from its effect in the previous model without the primary correlates.

Among the correlates of smoking cessation, only being a heavy smoker, obesity, and the experience of heart attack are significant predictors: heavy smoking decreases the odds of quitting and being overweight or having a heart attack increases the odds, while all other factors are held constant. In addition, among the explanatory factors added in Model 6, medium- versus long-term financial planning significantly predicts smoking cessation, strongly and unexpectedly increasing the odds of smoking cessation.

TABLE 4. Logit Equations Showing Experience of Heart Attack 1992–1994 Regressed on Selected Risk Factors and Correlates of Education Among U.S. Adults Age 51–61, 1992 and 1994

	Model 1		Model 2		Model 3		Model 4	
Characteristics[a]	Parameter Estimate	Odds Ratio	Parameter Estimate	Odds Ratio	Parameter Estimate	Odds Ratio	Parameter Estimate	Odds Ratio
Intercept	−3.801***		−3.610***		−3.779***		5.161***	
	(29.377)		(26.903)		(13.804)		(11.827)	
Female	−1.223***	.294	−1.242***	.289	−1.225***	.294	−1.300***	.273
	(6.181)		(6.276)		(4.981)		(5.051)	
African American[b]	.112	1.118	−.011	.989	−.535	.586	−.511	.600
	(.381)		(.037)		(1.291)		(1.211)	
Latino[b]	−.284	.753	−.696	.498	−.692	.500	−.402	.669
	(.717)		(1.673)		(1.369)		(.798)	
Father's Education	−.076***	.927	−.034	.967	−.018	.983	−.020	.981
	(3.321)		(1.318)		(.584)		(.635)	
Education	—	—	−.126***	.881	−.050	.951	−.037	.964
			(4.206)		(1.342)		(.810)	
Cognitive Ability	—	—	—	—	−.028	.972	.027	1.028
					(.372)		(.354)	
Short-Term Planner[c]	—	—	—	—	.396	1.485	.275	1.316
					(1.531)		(1.042)	
Medium-Term Planner[c]	—	—	—	—	.210	1.233	.209	1.233
					(.844)		(.826)	
Blue Collar Worker	—	—	—	—	.283	1.327	.225	1.252
					(1.198)		(.942)	
Net Worth	—	—	—	—	−.119**	.888	−.041	.960
					(3.104)		(.978)	
Employee Health Insurance	—	—	—	—	−.192	.825	.057	1.058
					(.801)		(.225)	
Past Smoker	—	—	—	—	—	—	.633	1.884
							(1.872)	
Smoker in 1992	—	—	—	—	—	—	.972***	2.644
							(3.733)	
Heavy Smoker	—	—	—	—	—	—	.157	1.170
							(.508)	
Obese	—	—	—	—	—	—	.362	1.437
							(1.610)	
Irregular Exercise	—	—	—	—	—	—	.068	1.070
							(.325)	

TABLE 4. Continued

	Model 1		Model 2		Model 3		Model 4	
Characteristics[a]	Parameter Estimate	Odds Ratio	Parameter Estimate	Odds Ratio	Parameter Estimate	Odds Ratio	Parameter Estimate	Odds Ratio
Heavy Drinker	—	—	—	—	—	—	−1.031*	.357
							(2.000)	
Spouse Smokes	—	—	—	—	—	—	−.473	.623
							(1.655)	
High Blood Pressure	—	—	—	—	—	—	.662**	1.938
							(3.108)	
CES-D Symptoms	—	—	—	—	—	—	.291***	1.338
							(6.185)	
Log Likelihood Ratio	55.388		72.619		62.957		142.458	
df	4		5		11		20	
p	.0001		.0001		.0001		.0001	
N	7,771		7,771		6,637		6,637	

* $p < .05$; ** $p < .01$; *** $p < .001$

Note: T-statistics are in parentheses.

[a] Values for all characteristics are those reported at baseline in 1992.

[b] Reference category is white and other non-African American or Latino ethnicity.

[c] Reference category is long-term planner.

Finally, in Model 7, we add to our previous model a set of interaction terms representing the product of heart attack by each of the psychological, social-environment, and resources factors. We do this for two primary reasons. First, because each of these factors represents consequences of education, we wanted to test the relative effects of education and its consequences both separately and as interaction terms.[a] Second, we also wanted to test the effect of the heart attack-education interaction term after including all other education-related interaction terms. Model 7 indicates that, even with all of the interaction terms entered into the model, the results are scarcely altered, with one exception. Heart attack by education holds as the only significant interaction term, but the main effect for heart attack loses significance as well as considerable strength. Heavy cigarette dosage, obesity, and mid-term planning remain solid as other significant predictors.

DISCUSSION

This study's analyses of the effect of education on smoking cessation among middle-aged adults led to both expected and unexpected results, providing at least partial support for our primary and secondary hypotheses. Surprisingly, and counter to previous research (Douglas 1998; U.S. Department of Health and Human Services 1989) as well as one of our primary hypotheses, education alone was not a significant predictor of smoking cessation in middle-aged adults. In contrast, heart attack was significant, supporting both literature and one primary hypothesis. More importantly, the interaction of education and heart attack was a powerful and significant predictor of smoking cessation: Among smokers who experienced a heart attack, higher levels of education played a protective role by increasing the likelihood that they would quit smoking. Absent a heart attack, higher levels of education had virtually no effect on whether or not a person quit. Although this may seem contrary to the expectation that increas-

TABLE 5. Logit Equations Showing Smoking Cessation by 1994 Regressed on Education and Incident Heart Attack Between 1992–1994 Among U.S. Smokers Age 51–61 (N = 1,924)

Characteristics[a]	Model 1		Model 2		Model 3		Model 4	
	Parameter Estimate	Odds Ratio	Parameter Estimate	Odds Ratio	Parameter Estimate	Odds Ratio	Parameter Estimate	Odds Ratio
Intercept	−1.702*** (26.793)		−1.635*** (26.946)		−1.706*** (26.772)		−1.703*** (26.783)	
Heart Attack 1992–1994	1.590*** (5.821)	4.903	—	—	1.615*** (5.885)	5.027	1.827 (5.995)	6.218
Education	—	—	.016 (.703)	1.016	.023 (1.084)	1.026	.007 (.281)	1.007
Heart Attack x Education	—	—	—	—	—	—	.362** (2.632)	1.436
Log Likelihood Ratio	30.491		30.497		31.679		41.635	
df	1		1		2		3	
p	.0001		.0001		.0001		.0001	

* p < .05, ** p < .01, *** p < .001.
Note: T-statistics are in parentheses.
[a] Values for all characteristics except "Heart Attack 1992–1994" are those reported at baseline in 1992.

ing levels of formal education should lead to participating in more protective health behaviors (Fuchs 1982; Kenkel 1991), it may also reflect the fact that education had already exerted a major effect on smoking behavior before 1992 in our middle-aged adults by reducing the likelihood that a more highly educated person would have ever started smoking or would have remained a smoker until 1992.

The dramatic influence of higher levels of education following the experience of a heart attack suggests that more highly educated older smokers "learn" from their heart attacks and quit smoking. This result is particularly striking given the selection effect on smokers. As reported by other studies and our exploratory analyses, many people with higher levels of education had never smoked or, if they had smoked, had already quit by 1992, quite possibly in response to three decades worth of Surgeon General's reports, smoking-related health events, and family or workplace pressures. The highly-educated people who were still smokers in 1992 may have been longer-term smokers or more heavily addicted to cigarettes than were their counterparts who quit and, thus, may have found quitting under most circumstances to be especially difficult. Alternatively, they may have been exposed to other life events and risks or had different personality characteristics that impeded their quitting previously. Whatever their initial barriers to quitting, education apparently prevailed over addiction and other factors to impel the better-educated, middle-aged individuals to quit smoking once faced with a heart attack.

Second, we found partial support for only one of our six secondary hypotheses testing possible psychological, social-environment, and resources explanations for an education or education-heart attack effect on smoking cessation. In particular, one of the psychological factors, future orientation, helped us disentangle the effect of the heart attack-

FIGURE 1. Probability of Quitting Smoking by 1994, Given the Experience of a Heart Attack 1992–1994 in U.S. Adults Age 51–61 (Table 5, Model 4)

education interaction. Being a medium- versus long-term planner unexpectedly increased the odds of quitting smoking, counter to the idea that people who are more future-oriented should participate in more healthful and less addictive behaviors (Becker et al. 1991, 1994; Fuchs 1982). Preliminary analyses not presented here indicated that long-term planners were generally more highly educated and less likely to be smokers in the first place, compared with medium-term planners. However, long-term planners who were smokers in 1992 were also disproportionately heavy smokers, compared with short- and medium-term planners. It may be that the current smokers whose behaviors were analyzed in this study were affected by their future orientation differently than were past smokers. Their heavier cigarette dosage may have raised the "cost" of quitting to such an extent that their higher education or degree of future orientation became less protective. Alternatively, medium- versus long-term planning may reflect a more "realistic" tally of the costs and benefits associated with smoking cessation in older age. For example, middle-aged smokers may surmise that even though quitting considerably reduces the risks of heart attack, lung cancer, and other diseases within 5–15 years, the fact that these diseases are generally associated with older age may promote the belief that there is little eventual health benefit in stopping a presumably pleasurable habit in later life (Douglas 1983; U.S. Department of Health and Human Services 1990).

No evidence was found in our analyses to support the effects of cognitive ability nor the social-environment or resources factors associated with education that we posited might play a role in smoking cessation among middle-aged adults and help us to explain the heart attack by education interaction effect. Despite their nonsignificance, the inclusion of education consequences in our models—particularly in interaction terms—did lessen both significance and strength of the heart attack by education interaction. Perhaps other measures of psychological orientation, social environ-

TABLE 6. Logit Equations Showing Smoking Cessation Regressed on Education, Incident Heart Attack, Selected Predictors, and Interaction Terms Among U.S. Smokers Age 51–61, 1992 and 1994 (N = 1,924)

	Model 5		Model 6		Model 7	
Characteristics[a]	Parameter Estimate	Odds Ratio	Parameter Estimate	Odds Ratio	Parameter Estimate	Odds Ratio
Psychosocial Risk Factors						
Intercept	−1.676***		−2.280***		−2.231***	
	(11.669)		(6.515)		(6.219)	
Heart Attack 1992–1994	1.901***	6.692	1.900***	6.689	1.230	3.422
	(5.979)		(5.908)		(1.438)	
Education	.017	1.017	.007	1.007	.009	1.009
	(.658)		(.254)		(.317)	
Female	.021	1.021	−.004	.996	.006	.994
	(.157)		(.028)		(.040)	
African American[b]	.120	1.128	.199	1.220	.194	1.214
	(.584)		(.911)		(.885)	
Latino[b]	.333	1.396	.445	1.561	.449	1.567
	(1.213)		(1.593)		(1.597)	
Heavy Smoker	−.677***	.508	−.657***	.518	−.678***	.507
	(4.104)		(3.952)		(4.037)	
Heavy Drinker	−.198	.820	−.195	.823	−.188	.829
	(.799)		(.720)		(.749)	
CES-D Symptoms	.002	1.002	.014	1.014	.016	1.016
	(.036)		(.307)		(.361)	
High Blood Pressure	.168	1.183	.163	1.177	.155	1.167
	(1.205)		(1.166)		(1.101)	
Obese	.443**	1.557	.463**	1.589	.483**	1.620
	(2.844)		(2.953)		(3.072)	
Irregular Exercise	−.065	.937	−.088	.915	−.083	.920
	(.511)		(.691)		(.647)	
Good Health[c]	−.009	.999	.016	1.016	.011	1.011
	(.000)		(.101)		(.070)	
Fair/Poor Health[c]	−.064	.938	.027	1.027	.030	1.031
	(.355)				(.165)	
Explanations						
Cognitive Ability	—	—	−.056	.946	.063	.939
			(1.201)		(1.328)	
Short-Term Planner[d]	—	—	−.130	.878	−.164	.848
			(.766)		(.951)	
Medium-Term Planner[d]	—	—	.341*	1.406	.299*	1.349
			(2.288)		(1.969)	
Spouse Smokes	—	—	−.124	.875	−.124	.883
			(.951)		(.863)	

TABLE 6. Continued)

	Model 5		Model 6		Model 7	
Characteristics[a]	Parameter Estimate	Odds Ratio	Parameter Estimate	Odds Ratio	Parameter Estimate	Odds Ratio
Blue Collar Worker	—	—	−.162	.850	.175	.840
			(.996)		(1.042)	
Net Worth	—	—	.036	1.036	.033	1.034
			(1.351)		(1.210)	
Employee Health Insurance	—	—	.247	1.280	.246	1.278
			(1.608)		(1.554)	
Heart Attack x Education	.364**	1.439	.371**	1.449	.352*	1.422
	(2.671)		(2.672)		(2.182)	
Heart Attack x Cognitive Ability	—	—	—	—	.154	1.167
					(.682)	
Heart Attack x Short-Term Planner	—	—	—	—	1.029	2.799
					(1.113)	
Heart Attack x Medium-Term Planner	—	—	—	—	1.213	3.363
					(1.449)	
Heart Attack x Spouse Smokes	—	—	—	—	−.450	.638
					(.513)	
Heart Attack x Blue Collar Worker	—	—	—	—	−.155	.857
					(.208)	
Heart Attack x Net Worth	—	—	—	—	.054	1.055
					(.561)	
Heart Attack x Employee Health Insurance	—	—	—	—	.259	1.296
					(.369)	
Log Likelihood Ratio	77.741		96.515		99.717	
df	14		21		28	
p	.0001		.0001		.0001	

* $p<.05$; ** $p<.01$; *** $p<.00$

Note. *T*-statistics are in parentheses.

[a] Values for all characteristics except "Heart Attack 1992–1994" are those reported at baseline in 1992.

[b] Reference category is white and other non-African American or Latino ethnicity.

[c] Reference category is excellent health.

[d] Reference category is longterm planner.

ment, or resources would have proved more informative.

Finally, among the primary correlates of smoking cessation, heavy cigarette smoking in 1992 negatively influenced quitting by 1994. Since some people with higher levels of education continued to smoke despite widely-available information in the community on the dangers of cigarette smoking (Kunkel, 1991), factors other than health information must have driven decisions to quit or continue smoking. Our analyses pointed toward one such factor: The odds of smoking cessation decreased strongly among heavy smokers, demonstrating that the cost of quitting may be greater for more strongly addicted smokers, even after controlling for education and the experience of a heart attack. These results support other recent research (e.g., Marbella et al., 1995) also finding heavy smokers to be less likely to quit smoking.

In addition, being overweight strongly predicted smoking cessation, although physical activity did not, lending partial support to the notion that participation in some beneficial health behaviors should increase the likelihood of participating in other such behaviors (Matthews et al., 1989; Wagenknecht et al., 1990; Winkleby et al., 1992). In particular, middle-aged adults who are overweight may recognize the need to eliminate or control one risk factor for heart-related disease (smoking) but not others (exercise or weight manage-

ment), reasoning that smoking cessation may be a more critical predictor of enhanced health than either of the other health behaviors.

Additional factors identified in the literature as associated with education, heart attack, and smoking cessation (e.g., gender, race/ethnicity, heavy drinking, history of high blood pressure, self-assessed health status, and depressive symptoms) failed to reach significance in our models, whether or not we controlled for additional education-heart attack "explanations."

Certain attributes of the study's data set may have limited our ability to identify these or other potential predictors of smoking cessation. First, the HRS collects disease and health-condition data by self report. Although experience with heart attack in the past two years is likely to be remembered reasonably well by respondents and the HRS does ask what year the heart attack occurred, the data are only as good as the respondent's recall. Second, our measure of smoking cessation is static and indirect in that it is based on reports of current or past smoking behavior in 1992 and 1994. If a respondent stopped smoking between 1992 and 1994, the HRS does not ask when s/he quit. Thus, we cannot know whether a report of no longer smoking in 1994 means the person has quit for a day, a month, a year, or permanently. Neither can we know for certain that smoking cessation followed the heart attack in the case of those smokers who experienced incident heart attacks. Finally, we did not consider the influence of other long-term or more recent health problems other than high blood pressure on the decision to quit smoking. Clearly, smoking cessation is a complicated decision-making process that defies simple analysis or interpretation in our cohort of middle-aged adults.

CONCLUSION

This paper started by acknowledging the well-established positive association between higher levels of education and enhanced health, including protective health behaviors. Ultimately, our study results augmented the wealth of evidence from various academic disciplines in confirming that association. Higher levels of education do, in fact, play a role in one health-enhancing behavior, at least under some circumstances among preretirement-aged Americans. Our study also supported the documented connection between heart attack and smoking cessation. In addition, our study provided a surprising twist on those links: The move to quit smoking following the experience of a heart attack among middle-aged adults was significantly and dramatically moderated by their level of educational attainment. Among older smokers without an incident heart attack, the probability of quitting smoking was less than one in six. However, among older smokers who experienced a heart attack, only those with an education of at least high school or beyond changed their smoking behavior. Each additional year of educational attainment beyond high school dramatically raised the probability of quitting—from one in two for those with a high-school education to near certainty for those with postbaccalaureate education.

Although this study's focus on change in one health behavior following the experience of a potentially life-threatening health event was intentionally narrow, our analyses shed some light on the association between education and health. Our probe of education's effects on smoking cessation demonstrated that education alone did not always provide sufficient incentive to quit smoking among our group of older smokers. As noted, these smokers may be different from younger smokers in many ways, resulting in their being more resistant to decades of public health messages about the dangers of cigarette smoking. The higher levels of knowledge, skills, and abilities proxied by educational attainment furnished the necessary justification for quitting in such individuals only when they suffered the shock of a life-threatening health event. Future research could add to our understanding in this area by exploring education's effects on a wider range of health and economic outcomes at different points across the lifecourse, incorporating different moderating life events as well as other potential mediators of those outcomes.

NOTES

1. The public release data set for Wave 3 of the HRS is expected to be available in fall 1998.
2. In order to retain as many of the cases of incident heart attack as possible, all heart attacks between 1992 and 1994 were counted among respondents for whom these heart attacks represented first heart attacks as well as respondents for whom the heart attacks represented subsequent heart attacks.
3. The exploratory models focused on three dichotomous outcomes: never having smoked, quitting prior to 1992, and experiencing a heart attack between 1992 and 1994. These models were tested on four sequentially-entered blocks of variables (1) demographic and status origin characteristics; (2) level of education; (3) health status, health behaviors, and lifestyle variables; and (4) selected psychological, social environment, and resources factors. All of the variables except the measure of status origins—father's educational attainment—reached significance in most of the exploratory models. These variables were included in the final models predicting smoking cessation and are described in detail in the paper's text. Father's educational attainment was measured as the number of years the respondent reports his/her father completed, centered on 12 years of education.
4. Smoking cessation has been documented to be a dynamic process with alternating periods of quitting and relapse before permanent abstinence (U.S. Department of Health and Human Services 1990). While acknowledging that dynamic process, we are constrained in our analyses to using a static measure based on changes in self-reported smoking status at two points in time, 1992 and 1994.
5. We combine these scores in order to tap two dimensions of cognitive ability—fluid and crystallized abilities—that may influence a person's capacity for making informed decisions. Fluid ability measures processing capabilities that affect the ability to acquire new information. Often used in standardized cognitive screens for older adults, the word recall tests primarily (although not exclusively) assess fluid ability which may decline somewhat with aging. In contrast, crystallized ability measures the actual acquisition of that information in the form of knowledge-based abilities (e.g., verbal and abstract reasoning) which are closely tied to educational attainment, remaining stable or even increasing throughout the life course. Word similarities tests primarily measure crystallized ability.
6. Preliminary analyses that are not presented here demonstrated that a heart attack by cognitive ability interaction term (as a substitution for a heart attack by education interaction term) was a significant predictor of smoking cessation. That seemed a logical finding given that education and cognitive ability are often perceived as two sides of the same coin, that is, tapping into a similar concept. However, their moderate correlation ($r = 0.44$) suggests that they are still measuring different traits. Similar analyses were conducted substituting interaction terms comprised of heart attack by each of the other psychological, social-environment, and resources factors believed to be consequences of education. However, none of these other interaction terms proved to be significant predictors in the preliminary analyses.

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US 1st Surgeon General's Report on Smoking & Health, 1964, & later reports demonstrate cigarette smoking as the foremost preventable cause of death in the USA esp. d/t Cardiovascular Diseases & Cancers (CDC 1987, US Dept Hlth & Human Services 1989, 1990.)

- Smoking associated with
  - depressed
  - heavy alcohol users
  - poor self assessed health
  - heavily addicted smokers
    - > 1 pack/day.
- smoking behaviour linked to heart attacks, hypertension, obesity.

Smoking can also cause brittle bones

Researchers in the United States say they may have discovered why women who smoke are much more prone than non-smokers to develop brittle bones, or osteoporosis, in old age.

Scientists at the Argonne National Laboratory said the link between cigarettes and bone loss appears to be cadmium, a heavy metal found in trace concentrations in vegetables and tobacco. Pack-a-day smokers have blood levels of cadmium that average 15 times the levels in non-smokers or people who have quit.

Argonne biochemicists Maryka Bhattacharya and David Peterson fed mice a diet with elevated levels of cadmium, raising the concentration in their blood to a point comparable to that found in smokers.

They found the heightened levels of cadmium led to bone thinning in pregnant mice that had their ovaries removed. This operation on the mice cuts off their main source of the female reproductive hormone estrogen, making them physically comparable to post-menopausal women.

As the amount of cadmium in the diet of the mice was increased, the amount of bone loss increased proportionately, the scientist found, but only in the two groups of females lacking estrogen.

Osteoporosis, or brittle-bone disease, is one of the most common perils of humans in old age, affecting typically, post menopausal, small-boned, white women who have smoked. As the bones are stripped of calcium, they become thin and brittle, breaking readily, leading to repeated fractures, especially of the hip, wrist and ankle and crushing of backbones leading to a condition known as Dowager's Hump.

"Because the amount of cadmium introduced into the blood stream through feeding produced blood cadmium levels similar to those found in the blood of smokers", Bhattacharya said.

Bhattacharya said in an interview to UPI that cadmium levels are heightened in smokers because lung tissue absorbs cadmium from tobacco smoke much more effectively than the digestive tract absorbs from vegetables.

But she said the first clues that cadmium might be a factor in osteoporosis actually came from a tragedy that involved ingested, not inhaled, cadmium.

Japanese researchers found that post-menopausal women living in a town downstream from lead and zinc mines had very high incidence of osteoporosis. They suspected the high levels of cadmium in the stream's water and their diet were responsible for the women's brittle bones, but the Argonne study provides the first direct evidence that cadmium was to blame.

The fact that post-menopausal women and female mice in pregnancy or with their ovaries removed show the cadmium effect most strongly indicates that estrogen is also involved in the effects of cadmium on the bones, Battacharya said. But she does not yet know how.

Exercise, calcium supplements, and the hormone estrogen are typically prescribed to prevent bone loss in women prone to osteoporosis. Studies described elsewhere in the United States showed sodium fluoride may also help strengthen thinning bones in the spine.

Meanwhile, a group of researchers from the West Valley Medical Center in Los Angeles studied 38 women to see how their production of a key substance involved in dilating blood vessels was affected in they smoked and took birth control pills. They found evidence offering one possible explanation for why women who smoke and use oral contraceptive pills may have an increased risk for heart disease.

The key substance, known as prostacyclin, which doctors believe may help prevent heart attack and other cardiac disorders, was lowest in women who took the pills and who had smoked for at least five years, the researchers found.

These women were compared to those who took birth control pills but did not smoke, those who smoked but did not take the pill and those who did neither.

The analysis, led by Dr. Gil Mileikowsky, suggests decreased prostacyclin production is the cause of increased cardiovascular risk. Because prostacycline also decreases the formation of blood clots. Meleikowsky cautions that lower levels of the substance pave the way for dangerous blood clot formation.

These clots can circulate throughout blood vessels and land in the lungs, thus creating pulmonary embolisms", he said.

Embolisms diminish the capacity of the lung to function and supply the body with oxygen.

The study suggests steroids contained in birth control pills may work in tandem with substances in tobacco to dramatically lower prostacyclin levels.

— Deccan Herald (Bangalore)

Smokeless Tobacco and Oral Cancer: A cause for concern?

Minni Sood

Advertisements for smokeless tobacco imply that the habit is less harmful than smoking. Unfortunately this impression is common among the public and even among health professionals.

It is instructive to consider data available from India, where more than 48% of cancers are found in the oral cavity. This high incidence of oral cancer has led a number of researchers to look for factors that might account for the observed morbidity. In a series of extensive epidemologic studies, Pindborg and co-workers followed 50,000 Indians for five years and a group of 30,000 for 10 years. They concluded that oral cancer and oral precancerous lesions (leukoplakia) occurred almost solely among those who had tobacco habits of one type or another. The use of tobacco in various forms, such as in cigarettes, cigars, and for chewing, is widespread in India, with between 47% and 73% of the population indulging in the habit, compared with approximately 36% in the U.S. High incidence of oral cancer in India is not a reflection of a unique susceptibility or a more pernicious lesion, but simply of the very high prevalence of tobacco use.

It is well known that in India, as in many parts of South-east Asia, chewing tobacco is mixed with a variety of other substances, the most common additive being the nut of the betel palm, betel leaf, and slaked lime.

Further evidence that points to tobacco as a major etiological factor in the development of oral lesions and emphasises the greater risk of chewing over smoking comes from studies in both India and U.S. These reports have calculated the relative risk for tobacco use, a factor that indicates the greater risk of developing cancer for a tobacco user compared with a non-user. The Indian data suggest that the relative risk of developing oral cancer is 2.82 for smoker and 5.98 for chewers. The study by Winn et. al. of female smokers and snuff dippers on the south east U.S. showed that the relative risk of developing cancer of the gums and buccal mucosa is 4.6 for smokers and from 13 to 48 for snuff dippers, depending on how long the user had indulged in the habit. (fig. 1). Thus both the American and Indian studies point to a greater risk of developing oral cancer among users of snuff and chewing tobacco than among smokers, despite the differences in the way smoke-less tobacco is used in the two populations.

Unfortunately, both the general public and health professionals are largely unaware of these risks. There is a great need of health education. The dental profession can play a leading role in such programmes by promoting an awareness of the cancer risks from smokeless tobacco, by discouraging its uses, and by vigilance in detecting early mucosal lesions among those who persist with the habit. ■

Smokeless Tobacco is not Safe

Smokeless tobacco (snuff for example) does not carry the health hazard warning that cigarettes do, but it should. It's tobacco just the same and is habit forming. The nicotine in it lifts you up first... then lets you down. That high-low effect on your nervous system sets you up for a continued need. That's what the ads are really doing — trying to get you hooked!

But that's all. Habitual use of snuff and chewing of tobacco means there are other health hazards also. The habitual users of smokeless tobacco lose their ability to smell and the sense of taste. Hence they need more salt and sugar in their food, both of which are unhealthy if used in excess. They also face dental problems, such as receding gums and greater wear and tear of tooth enamel. These lead to both decay and bad breath. Like most tobacco users they too develop discoloured teeth.

Smokeless tobacco plays worse havoc inside our body. If the person is in the habit of chewing tobacco, it irritates the delicate mucosa of his mouth and over the course of years he developes a white patch. This white patch generally occurs at a place where the quid is kept. The white patch is known as leukoplakia.

This leukoplakia is a very peculiar thing. Nearly 95% of cancers in the mouth start with this patch. If a person stops using tobacco, this leukoplakia does disappear but it takes years. But once it disappears, there is no danger of getting cancer.

— Consumer Confrontation

PH-7.

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Dietary factors in oral leukoplakia and submucous fibrosis in a population-based case control study in Gujarat, India

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OBJECTIVES: To investigate the relationship of specific nutrients and food items with oral precancerous lesions among tobacco users.
DESIGN: A population-based case-control study.
SETTING: Villages in Palitana taluk of Bhavnagar district, Gujarat, India.
SUBJECTS AND METHODS: An interviewer-administered food frequency questionnaire, developed and validated for this population, was used to estimate nutrient intake in blinded, house-to-house interviews. Among 5018 male tobacco users, 318 were diagnosed as cases. An equal number of controls matched on age (±5 years), sex, village, and use of tobacco were selected.
MAIN OUTCOME MEASURES: Odds ratios (OR) from multiple logistic regression analysis controlling for relevant variables (type of tobacco use and economic status).
RESULTS: A protective effect of fibre was observed for both oral submucous fibrosis (OSF) and leukoplakia, with 10% reduction in risk per g day^{-1} ($P < 0.05$). Ascorbic acid appeared to be protective against leukoplakia with the halving of risk in the two highest quartiles of intake (*versus* the lowest quartile: OR = 0.46 and 0.44, respectively; $P < 0.10$). A protective effect of tomato consumption was observed in leukoplakia and a suggestion of a protective effect of wheat in OSF.
CONCLUSION: In addition to tobacco use, intake of specific nutrients may have a role in the development of oral precancerous lesions.

Keywords: India; oral neoplasms; precancerous conditions; nutrition; diet; β-carotene; zinc; iron; ascorbic acid; submucous fibrosis; leukoplakia; tobacco chewing; smoking

Introduction

Oral cancer is the sixth commonest cancer in the world (Parkin *et al*, 1993). Its incidence is particularly high in India, some other countries in Asia, and certain places in the Western hemisphere, e.g., parts of France and Brazil. In the Western hemisphere, smoking and alcohol drinking are major risk factors, whereas in India, the chewing of tobacco products, in addition to smoking in various forms, is primarily responsible for the high incidence. The WHO have estimated that 90% of oral cancers in India among men are attributable to the chewing and smoking of tobacco (WHO, 1984).

Nutritional risk factors have also been implicated in cancers of the oral cavity. A number of studies have indicated that the consumption of various vegetables and fruits reduces risk. These relationships may be independent of other risk factors and show a dose-response (Marshall *et al*, 1982; Winn *et al*, 1984; Franco *et al*, 1989). However, there is considerable potential for confounding, and this may be difficult or impossible to control in most epidemiologic studies on the subject (Marshall and Boyle, 1996).

Oral cancer is often preceded by oral precancerous lesions and conditions (Pindborg, 1980). Conversely, the relative risk of individuals with oral precancerous lesions developing oral cancer has been demonstrated to be very high, even after controlling for the use of tobacco (Gupta *et al*, 1989). The association of oral precancerous lesions with tobacco habits follows a pattern similar to that of oral cancer (Gupta *et al*, 1980). Because the prevalence of oral precancerous lesions is much higher than that of oral cancer, these lesions provide useful clinical markers for oral cancer. They have been used as such in large-scale intervention trials (Gupta *et al*, 1992a).

A focus on precancerous lesions avoids much of the potential for measurement bias and confounding that affect most studies of diet and oral cancer (Marshall and Boyle, 1996) because many of these conditions, such as oral leukoplakia, would have no plausible effect on dietary intake. It should be noted, however, that oral submucous fibrosis (OSF) may affect intake to some extent because of associated symptoms, a common one being a burning sensation on intake of spicy food. An additional rationale for conducting a study in an Indian population included a probable wide range of variability in nutrient exposures (Rao, 1987; NIN, 1991).

The primary goal of this research was to test the relationship between precancerous changes in the mouth and dietary intake of specific nutrients; in particular the antioxidant vitamins, several minerals, the B-vitamins, and fibre

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through a population-based case-control study. These nutrients were chosen based on the availability of nutrient contents of foods commonly eaten in India (NIN, 1993; Hebert *et al*, 1998) and on a variety of laboratory (Shklar and Schwartz, 1993; Kandarkar and Sawant, 1996) and human experimental studies (Garewal and Schantz, 1995; Krishnaswamy *et al*, 1995; Prasad *et al*, 1995; Tanaka, 1995; Maher *et al*, 1997) especially relevant to India. A food frequency questionnaire (FFQ) specific to this population was developed and validated for collecting dietary information necessary to estimate exposure to these and a variety of other nutrients. In general, the results of the validation study indicated a higher level of accuracy than what is observed in studies conducted in the West. Besides examining relationships between the lesions and these specific nutrients we also sought to investigate the potential role of specific foods.

Subjects and methods

Subject recruitment/data collection

This study was conducted in one of the 12 taluks, Palitana, of Bhavnagar district, Gujarat state. Among 92 villages in this taluk, 20 that were geographically contiguous and not included in earlier studies (Gupta *et al*, 1980, 1992a) were chosen. A preliminary census was conducted for listing all households along with the identification information for each member of the household and their tobacco use status in each selected village.

A team consisting of dentists, social scientists, field investigators and a nutritionist visited each household on the house lists. As the first step in the recruitment/data collection process, a field investigator interviewed the potential study subject (males aged 15 years or over) and filled out a questionnaire containing basic demographic information and details of tobacco habits. Only males were included, as in earlier studies in Bhavnagar district very few females reported using tobacco and were diagnosed with oral precancerous lesions (Mehta *et al*, 1969b; Gupta *et al*, 1980). The subject was then examined by one of the authors (PNS) and an additional examining dentist for the presence of oral precancerous lesions. After examination by the dentist, the subject was classified as a case if he had an eligible precancerous change (either OSF or leukoplakia) or a lesion (an ulcer or a growth) suspicious of oral cancer. The first male from the same village, examined subsequently and found to be free of any oral mucosal lesion, and matched on age (±5 years) and tobacco use (yes/no) was selected as a control. The potential control pool thus consisted of all examined persons who were found to be free of lesions. The recruitment was halted when we had safely exceeded the predesignated goal of 250 cases and 250 matched controls. This was earlier than anticipated because of an unexpectedly high prevalence of OSF found during examinations.

The most common precancerous lesions in this region are OSF and leukoplakia (Pindborg, 1980). Oral leukoplakia was defined as a raised white patch 5 mm or more in diameter which could not be scraped off and could not be ascribed to any other diagnosable disease. OSF was diagnosed on the basis of palpable fibrous bands (Pindborg, 1980). For lesions suspicious of being oral cancer, the diagnosis was confirmed histologically.

Smoking of *bidis* and clay pipe (hookli) are the common forms of smoking tobacco. *Bidi* is a smoking stick prepared by rolling 0.15–0.25 g of sun-dried flake-form of tobacco, in a rectangular dried piece of *temburni* leaf (*Diospyrous melanoxylon*). It is sold in bundles of 25. *Mawa* is a preparation containing thin shavings of areca nut (5–6 g) with the addition of some tobacco (about 0.3 g) and few drops of watery slaked lime. The contents, kept on a piece of cellophane paper, are tied with a thread into a ball and the packet is rubbed vigorously on the palm to homogenise the contents. It is then opened and a portion, or the whole of it, is placed in the mouth. Other tobacco habits practised in the region are described elsewhere (Bhonsle *et al*, 1990).

The FFQ interview was conducted only if a subject was selected as a case or a control and after obtaining informed consent. To minimise the likelihood of bias, all data were collected in a blinded fashion (i.e., the interviewer was not aware of the status of the subject and the subject was not told of the presence or absence of the lesion until completion of the interview). Therefore, unlike most case-control studies, the FFQ was administered without anyone involved in the collection of the dietary data having knowledge of the subject's disease status.

The FFQ took about 25 min to complete. It consisted of questions on the typical frequency and quantity of consumption of 92 food items representing >95% of exposure to total energy, fat, fibre, iron, copper, zinc, calcium, ascorbic acid, β-carotene, and the B-vitamins in this population.

Statistical methods

Descriptive statistics were computed for all variables. These consisted of standard parametric statistics for continuous variables (e.g., the nutrient scores), and non-parametric frequency statistics for variables measured as counts or on an ordinal or nominal scale. Each target nutrient score was also categorised into quartiles of its respective distribution.

For this case-control study, the definitive multivariable analysis was conducted using a logistic regression model. Even though cases and controls were users of tobacco in some form, because of the strength of association between tobacco use and oral cancer and these precancerous lesions, some designation of tobacco habit was fit in all models. For leukoplakia, we fit one indicator variable indicating smoking (whether or not the person also chewed tobacco) *versus* chewing only (as the referent). For OSF, there were two indicator variables: one for chewing *mawa* (with any other tobacco exposure) and one for any chewing other than *mawa*; with the referent being non-chewers (i.e., smoking only). Any chewing in general, and *mawa* chewing in particular (but not smoking), have been shown to carry high relative risks for OSF (Sinor *et al*, 1990).

In most investigations of diet or smoking it is important to account for social and economic variables that often function as proxies for potentially important risk factors for cancer and therefore can act as confounders of such analyses. For this population we defined three economic classes described as follows. High status individuals were those: possessing a concrete or tiled house; owning a farm

employing servants; having a successful business or shop; or being a government officer. Middle status individuals were those: having a low-level government job; being a primary school teacher; owning a small shop; owning a house plastered with mud and cowdung; or owning a small-scale farm. Low status individuals were those marginally employed or unemployed individuals who could neither afford to live in their own house nor own their own business.

Dietary data were fit both as nutrient scores and as frequency of exposure to specific categories of food items. Nutrient scores and estimates of food frequency were fit both as continuous data and as quartiles, in separate models. Due to the fact that these dietary factors are highly correlated, it is important to model them separately from one another.

Analyses were conducted for all lesions together and separately for leukoplakia and OSF. Because dietary exposure estimates may be biased by overall errors in reporting (Willett, 1990; Bingham and Nelson, 1991) and some nutrients have a stoichiometric relation with total energy utilisation (Goodhart and Shils, 1980), we controlled for total energy intake in the logistic regression models focusing on nutrient exposures. All analyses were conducted using the personal computer version of SAS (1997). All logistic regression models were tested for goodness of fit using the Hosmer and Lemeshow statistic (Hosmer and Lemeshow, 1989).

Results

Of 5018 male tobacco users examined, 323 were found to have qualifying lesions, and thus met the criterion of being a case. Out of these, 318 cases could be exactly matched to an equal number of controls. These 636 study subjects, out of a total of 666, were used for analysis. Shown in Table 1, are the descriptive statistics of the study population, including the daily nutrient intakes, as estimated by the FFQ. Because nutrient data were modelled as quartiles of exposure, the cutpoints for the 13 nutrients of primary interest in this study are shown in Table 2. The distribution of lesions is also presented (Table 3).

All logistic models had diagnostics consistent with a good model fit. Results from models in which a particular nutrient or food category was found to be at least marginally significantly associated ($P \leq 0.1$) with either leukoplakia or OSF are shown in Table 4 (for nutrients) or Table 5 (for foods). In all models, irrespective of specific nutrient or food effects, virtually identical results were observed for all control variables. For example, in OSF models in which we controlled for dietary energy and no specific food or nutrient: relative to smoking alone, *mawa* chewing was associated with a marked elevation of risk (OR = 28.9; 95% CI = 3.8, 222.0). For other forms of chewing the risk was also elevated (OR = 10.4; 95% CI = 1.2, 89.8). Relative to low economic status, for middle economic status the OR was 0.90 (95% CI = 0.45, 1.83) and for high economic status the OR was 1.11 (95% CI = 0.47, 2.60). Relative to sedentary work, for occupations requiring physical activity the OR was 0.85 (95% CI = 0.51, 1.43). For dietary energy (kcal d^{-1}) the OR was 0.80 ($P = 0.08$). However, in the

Table 1 Descriptive statistics in diet and oral precancer study, Bhavnagar District, Gujarat*

	Cases		*Controls*	
	n	*(%)*	*n*	*(%)*
*Categorical variables**				
Males	318	(100.0)	318	(100.0)
Occupation‖				
Active	119	(37.4)	112	(35.2)
Sedentary	199	(62.6)	206	(64.8)
Education				
Illiterate	137	(43.1)	126	(39.6)
Primary	101	(31.8)	111	(34.9)
Middle	50	(15.7)	51	(16.0)
High School	24	(7.6)	27	(8.5)
College	6	(1.9)	3	(0.9)
Social category				
Forward	199	(62.6)	207	(65.1)
Backward	106	(33.3)	86	(27.0)
Schedule	13	(4.1)	25	(7.9)
Socio-economic status				
High	53	(16.7)	64	(20.1)
Middle	188	(59.1)	194	(61.0)
Low	77	(56.2)	60	(43.8)
Tobacco use				
No areca nut¶	164	(51.6)	175	(55.0)
Mawa	131	(41.2)	102	(32.1)
Areca nut with tobacco	2	(0.6)	14	(4.4)
Mixed with smoking	21	(6.6)	27	(8.5)
Continuous variables†	*Mean*	*(s.d.)*	*Mean*	*(s.d.)*
Age (years)	38.1	(14.7)	38.3	(14.3)
Height (in cms)	164.1	(5.5)	164.0	(5.6)
Weight (in kgs)	51.2	(9.4)	51.5	(9.7)
Nutrients†‡				
Total energy (Kcal d^{-1})§	2945	(942)	3051	(1056)
Total fat (g d^{-1})	124.6	(50.6)	131.7	(56.5)
Fat (% Energy)	37.1	(5.8)	37.9	(5.8)
Fibre (g d^{-1})	10.8	(4.3)	11.9	(5.4)
Iron (mg d^{-1})	33.4	(9.7)	34.6	(11.2)
Sodium (mg d^{-1})	368.7	(227.2)	356.8	(190.6)
Copper (mg d^{-1})	4.04	(1.24)	4.18	(1.41)
Zinc (mg d^{-1})	12.3	(3.6)	12.6	(4.0)
Calcium (mg d^{-1})	907	(425)	917	(396)
Ascorbic acid (mg d^{-1})§	4.1	(0.6)	4.2	(0.6)
β-Carotene (μg d^{-1})§	8.0	(0.5)	8.0	(0.5)
Thiamin (mg d^{-1})	2.02	(0.63)	2.11	(0.72)
Riboflavin (mg d^{-1})	1.82	(0.70)	1.81	(0.68)

*Values presented are the number and percentages of all cases and controls with the attribute

†Value is the mean and standard deviation (s.d.) by case and control status

‡Nutrients are daily amounts as calculated from the food frequency questionnaire, as described in the text

§Values for these nutrients are log transformed to normalise the distribution

‖Categories are defined as follows: Active included people engaged in farming, merchandising, and any type of labour work, whereas sedentary was defined as business men, professionals, skilled labourer (most of them diamond cutters), secretary, clerk and householders

¶Almost all of them (93%) were smokers. Rest were chewers of tobacco with lime

Table 2 Quartile designations of candidate nutrients, diet and oral precancer study, Bhavnagar District, Gujarat*

	Percentile values		
	25%	*50%*	*75%*
Total energy (Kcal d^{-1})	2335.3	2883.9	3535.0
Total fat (g d^{-1})	91.9	121.9	154.2
Fat (% Energy)	34.6	38.4	41.1
Fibre (g d^{-1})	8.0	10.4	13.7
Iron (mg d^{-1})	27.2	32.4	39.8
Sodium (mg d^{-1})	230.8	317.4	448.8
Copper (mg d^{-1})	3.3	3.9	4.8
Zinc (mg d^{-1})	10.0	12.0	14.4
Calcium (mg d^{-1})	634.9	834.8	1097.9
Vitamin C (g d^{-1})	40.2	65.9	96.1
β-Carotene (μg d^{-1})	2195.6	3082.7	4237.3
Thiamin (mg d^{-1})	1.6	2.0	2.4
Riboflavin (mg d^{-1})	1.4	1.7	2.1

*Based on the food frequency questionnaire

Table 3 Distribution of lesion types in diet and oral precancer study, Gujarat*

	Male	
	n	(%)
Submucous fibrosis	149	(46.9)
Leukoplakia	168	(52.8)
Carcinoma†	1	(0.3)
Total number of subjects with qualifying lesions	318	

*Tabulated values are the number of subjects (cases) with each lesion. The value in parentheses is the percent of total represented by this lesion
†Previously undiagnosed. Suspected to be oral cancer on clinical examination and later confirmed histologically

Table 4 Adjusted odds ratios for dietary nutrients in relation to submucous fibrosis and leukoplakia in diet and oral precancer study Bhavnagar District, Gujarat*

	Odds Ratio (95% CI)	*P-value*
Submucous fibrosis‡		
Fibre (g/d)	0.89 (0.81, 0.99)	0.02
Leukoplakia§		
Fibre (g d^{-1})	0.87 (0.79, 0.97)	0.01
Ascorbic acid (10 mg d^{-1})	0.95 (0.89, 1.01)	0.01
Ascorbic acid		<0.01†
quartile 2	0.82 (0.45, 1.49)	
quartile 3	0.48 (0.25, 0.95)	
quartile 4	0.45 (0.21, 1.00)	

*Results are based on a logistic regression model fitting social class/economic status, tobacco exposure, total dietary energy as control variables
†This is the *P*-value for the test of trend
‡Results based on 149 cases and 149 controls
§Results based on 168 cases and 168 controls

Table 5 Adjusted odds ratios for foods in relation to submucous fibrosis and leukoplakia in diet and oral precancer study Bhavnagar District, Gujarat*

Food groups	*Odds Ratio (95%CI)*	*P-value*
Submucous fibrosis‡		
Roots & tubers	0.69 (0.43, 1.12)	0.1
Onion	0.49 (0.20, 1.17)	0.1
Wheat preparation	0.93 (0.86, 1.01)	0.07
Fruit	0.85 (0.70, 1.04)	0.1
Leukoplakia§		
Pulse	0.40 (0.15, 1.09)	0.07
Roots & tubers	0.63 (0.39, 1.03)	0.06
Other vegetables	0.78 (0.61, 1.00)	0.05
Tomato	0.32 (0.12, 0.87)	0.03
Tomato		<0.01†
quartile 2	0.95 (0.53, 1.69)	
quartile 3	0.66 (0.35, 1.23)	
quartile 4	0.42 (0.22, 0.81)	

*Results are based on a logistic regression model fitting social class/economic status, tobacco exposure and total dietary energy as control variables
‡This is the *P*-value for the test of trend
‡Results based on 149 cases and 149 controls
§Results based on 168 cases and 168 controls

model shown in Table 4, fibre removed the effect of total energy.

In leukoplakia models in which we controlled for dietary energy and no specific food or nutrient: smoking relative to chewing alone showed an increased risk (OR = 8.69; 95% CI = 2.53, 29.79). Relative to low economic status, for middle economic status the OR was 0.79 (95% CI = 0.46, 1.36) and for high economic status the OR was 0.45 (95% CI = 0.22, 0.91). Dietary energy (kcal d^{-1}) did not affect the risk (OR = 1.00).

In the nutrient-based analyses for OSF, only dietary fibre was significantly protective after accounting for relevant covariates. It showed a strongly linear protective effect (OR = 0.89 on a continuous scale (g d^{-1}), $P < 0.02$, Table 4). For leukoplakia, fibre was similarly protective (OR = 0.87, $P < 0.01$). In addition, ascorbic acid appeared to be protective in a linear fashion (OR = 0.95, $P < 0.1$), but it also evinced a very strong trend in the quartile-based analyses ($P < 0.01$).

For OSF, a variety of foods were found to be marginally associated ($P < 0.1$) including roots and tubers, onion, wheat preparations, and fruits (Table 5). For leukoplakia, a number of foods were found to be significantly protective, especially pulse and tomato ($P < 0.02$).

Discussion

Studies attempting to relate diet with oral cancer must confront two major obstacles, one inherent in the relationships among relevant risk factors and the other a consequence of the distribution of oral cancer in human populations. In most populations, oral cancer is strongly related to either tobacco use or alcohol consumption or both (Marshall and Boyle, 1996) and, typically, these two risk factors are related to diet (Hebert and Kabat, 1990, 1991). As such, they can confound the effect of dietary factors. For

example, even in studies using serum levels of β-carotene (Zheng *et al*, 1993), unless smoking is carefully measured and controlled in analyses, inferences regarding dietary β-carotene will almost certainly be confounded because smoking is itself an important determinant of serum β-carotene levels (Stryker *et al*, 1988; Hebert *et al*, 1994).

Due to the fact that oral cancer is a very rare disease in most populations, it has been amenable to study using mainly case-control designs. Such designs are subject to biases in self-report, arising either directly or indirectly from changes in exposure to risk factors concomitant with the onset of disease symptoms (Hebert and Miller, 1988; Marshall and Boyle, 1996), or to beliefs held by research subjects regarding the causes of disease (Hebert *et al*, 1995). Because oral cancer is likely to affect the diets of oral cancer patients and diet-cancer hypotheses have been popularised in many populations, such studies are limited by the potential for biased dietary recall among the cases as compared to the controls (Marshall and Boyle, 1996). There are no reports in the scientific literature of any belief among Indian populations about diet causing cancer, though there are widely held beliefs about the relationship between food habits and health, more generally (Messer, 1997).

In this study, we were careful to enrol only users of tobacco and then to measure their exposure to tobacco products using methods that had been developed and refined through years of study in the Bhavnagar district (Mehta *et al*, 1969b; Gupta *et al*, 1980, 1992b). Gujarat traditionally has been (and continues to be) a dry state, therefore alcohol consumption is illegal, socially unacceptable, and the rate of consumption is generally quite low. Besides, it is known that alcohol intake is less influential for the risk of oral leukoplakia in Indian populations (Gupta, 1984). Therefore, we did not attempt to measure alcohol exposure in this population.

In designing this study, a decision was made to focus on precancerous lesions. In part, this was to increase outcome yield and in part to reduce the probability of biased dietary exposure estimates due to the presence of a condition that could affect the physical sensation and palatability of food among the cases. OSF, however, does affect palatability of food items to some extent, particularly due to associated oral symptoms (the most common being a burning sensation on the intake of spicy food). The prevalence of this condition in Bhavnagar district in an earlier study (Pindborg *et al*, 1968) was only 0.16% but turned out to be extraordinarily high in this study. This finding lends credence to a suspicion of an evolving epidemic of OSF in India (Babu *et al*, 1997).

Despite a possibility of a restriction in the intake of spicy food among OSF cases and consequent bias, we decided to include this condition in this study. This decision was based on our prior research indicating high relative risks of developing frank oral cancer in individuals with either leukoplakia or OSF compared to individuals without any precancerous lesion or condition, even after accounting for tobacco use in the form of chewing or smoking (Gupta *et al*, 1989). By studying these conditions earlier on in the natural history of the disease, there would be a better chance of determining diet during the more etiologically relevant period. The one oral cancer included in this study was early-stage disease without symptoms, but was confirmed histologically. Finally, in order to further reduce the probability of bias, we chose to withhold the diagnosis of any lesion from both the subject and the interviewer until the FFQ interview was completed.

This study used a custom-made FFQ with portion size and recipe database to estimate nutrient exposure in the target population. Because there is a sizeable fraction of the adult population that is illiterate, it was decided to have the FFQ administered by an expert interviewer. Previous testing of this instrument in a group of subjects from villages in the target population census area indicated a reasonable level of agreement when comparing nutrient consumption data derived from this FFQ to nutrient data derived from 6 days of 24-h diet recall interviews administered over a 1-year period.

The strongest and most consistent relationships observed in this study were the protective effects of fibre for both OSF and leukoplakia. In a hospital-based case-control study in China, it was found that dietary fibre derived from fruits and vegetables showed a strong negative association with oral cancer risk (Zheng *et al*, 1993), a result consistent with the effect of overall vegetable intake here. In another case-control study in the USA, fibre was also found to be protective (Marshall *et al*, 1992). Ascorbic acid was found to be protective for leukoplakia, consistent with a wide range of evidence (Marshall *et al*, 1982; Hinds *et al*, 1984; Verreault *et al*, 1989). This protective effect, found at very low levels of consumption in this population, is not inconsistent with a lack of effect of ascorbic acid for reversing leukoplakia that was reported at much higher doses (Kaugars *et al*, 1994, 1996). Thus, while reconfirming a previously reported strong relationship in this population between smoking and leukoplakia (Mehta *et al*, 1969a), and *mawa* chewing and OSF (Sinor *et al*, 1990), the present study revealed a protective effect of ascorbic acid on leukoplakia and of fibre on both leukoplakia and OSF.

The marginally protective effects of onion (and allium vegetables generally), fruits, and pulses, is consistent with a broad range of evidence concerning epithelial cancers (Committee on Diet NaC, 1982; Byers, 1988; US Dept of Health and Human Serv, 1988; Nat Academy of Sciences, 1989; AICR, 1997). Of all foods, the tomato was the most strongly protective for leukoplakia. This is consistent with other evidence in humans (Steinmets and Potter, 1996; Gerster, 1997), its inhibition of proliferation in cell culture (Levy *et al*, 1995), and its strong antioxidant properties (Stahl and Sies, 1996). There is one recent report about the possible effect of copper on OSF (Trivedy *et al*, 1997), although this interpretation was questioned (Meghji *et al*, 1997). In our study, we did not observe any effect of copper on OSF.

In summary, this study found protective effects of several nutrients and categories of foods in both OSF and leukoplakia. That we were able to observe these relationships using a design that obviated many of the possible reporting biases in conventional case-control studies of frank oral cancer, underlines two very important things. The first is the fact that these dietary factors play a role in the presence of tobacco use, the dominant risk factor for these con-

ditions. The second is that the public health message must be focused primarily on eliminating exposure to tobacco, in any of the forms in which it is currently used.

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Authors are responsible for the accuracy of the references.

Prevalence and Determinants of Coronary Heart Disease in a Rural Population of India

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ABSTRACT. Background. The prevalence and determinants of coronary heart disease (CHD) have been inadequately studied in rural areas of developing countries. Methods. Entire communities were surveyed in randomly selected villages in Rajasthan, India. A physician-administered questionnaire, physical examination and electrocardiogram (ECG) were performed on 3145 adults ≥ 20 years of age (1982 males, 1166 females). Fasting blood samples for determination of lipids were obtained from 202 males and 98 females. Prevalence of coronary risk factors—smoking, hypertension, sedentary life-style, obesity, and hypercholesterolemia—was determined. CHD was diagnosed on basis of past documentation, response to WHO-Rose questionnaire, or changes in ECG. Three methods were used: (a) documentation, history, and ECG criteria, (b) ECG-Q, ST, or T change, and (c) presence of Q waves. Results. Coronary risk factors: smoking was present in 31% males and 3% females, hypertension (≥140/90 mmHg) in 24% males and 17% females, hypercholesterolemia (≥200 mg/dl) in 22%, diabetes history in 0.2%, and irregular physical activity or sedentary habits in 55%. Other risk factors were lack of formal education in 44%, obesity (body-mass index ≥27 kg/m² in 6% and truncal obesity (waist-hip ratio ≥ 0.95) in 5%. The prevalence of CHD (clinical + ECG criteria) was 3.4% in males and 3.7% in females. According to ECG criteria only, it was 2.8% in males and 3.3% in females and according to Q waves only it was 1.6% in males and 2.2% in females. Multivariate logistic regression analysis showed that age and smoking in males and age and systolic blood pressure in females were associated with higher prevalence of Q wave CHD. In males, higher education level and prayer habit were associated with lower prevalence. Conclusions. Prevalence of CHD in this rural community is higher than in previously reported Indian studies. Smoking, hypertension, and sedentary life-style have high prevalence. Significant determinants of CHD are increasing age and smoking while education and prayer habit are protective. Copyright © 1997 Elsevier Science Inc. [CHIN 1997;50:203–209, 1997.

INTRODUCTION

Coronary heart diseases (CHD) is the leading cause of death in industrially developed communities [1] and is rapidly assuming a similar role in developing countries. It is estimated that CHD will be the single most important cause of death in India by the year 2015 AD [2]. In Indian urban communities a high prevalence of CHD approaching those of developed countries has been reported [3–6]. There is a rising trend in CHD prevalence, more at younger age [7]. Epidemiological studies in rural areas in India have shown a lower CHD prevalence [7–9] and the increase is slower as in the urban areas [7]. As rural communities have been relatively less influenced by recent social change, the CHD risk factors may be different [7].

The aims of the present study were to determine prevalence of CHD using clinical and electrocardiographic (ECG) criteria, to determine prevalence of various standard and unconventional risk factors, and to determine significant associations of CHD with various coronary risk factors.

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METHODS

Sample Population

To examine rural communities located at substantial distance from major towns, areas in this North-West Indian state of Rajasthan were evaluated where enthusiastic physicians and technicians were also available. Three villages, Bagoth, Badoo, and Janjila, in Tarbatsar tehsil (County) of Nagaur district in Rajasthan, were studied. These villages are situated 155 km from Jaipur and 65 km from Ajmer, the major towns in this region. The total population in these villages is about 9500. All adults ≥20 years were grouped to be examined and their names were obtained from Voters' Lists (Government of Rajasthan). 2188 males and 1968 females were eligible. The study was preceded by meetings with local leaders who co-operated in ensuring participation

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METHODS

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of subjects. A team of two doctors, social worker, three technicians, and three wardboys was employed. Female nurses were used for performing ECG in female subjects, but even then the response rate was low because of the traditional *purdah* custom prevalent in this state.

Proforma

A detailed questionnaire was prepared according to guidelines from the World Health Organization (WHO) [10], the United States Public Health Service [11], and a review of previous Indian studies [12]. The proforma elicited family history of hypertension and CHD; social factors such as education, housing, type of job, stressful life events, depression, and participation in religious prayer and yoga. Details of conventional risk factors—smoking, alcohol intake, amount of physical activity, diabetes, and hypertension—were enquired. Blood pressure was measured using standardized mercury manometer. At least two recordings were made at 5-minute intervals according to WHO recommendations [10]. When high blood pressure ≥140/90 mmHg was noted, a third reading was made after 30 minutes. Lowest of the three was recorded. Weight in light summer clothing was measured in kilograms on a calibrated spring balance. Height without shoes was measured in meters on a wall-mounted scale. Standing hip measurement at intertrochanteric level and supine waist measurement at the most prominent portion of abdomen with the person breathing quietly were taken. A 12-lead ECG using proper standardization was performed on all persons. To obtain fasting blood sample of 10% of the total study sample, a random 12% of the study participants were approached [13].

Diagnostic Criteria

In India and in many developing countries tobacco is consumed in various forms (rolled tobacco leaves [bidi], Indian pipes [hookahs], cigarettes, chewing tobacco, etc.) and some people use it in more than one form. Hence, it is difficult to accurately measure the amount of tobacco consumed. We therefore categorised users of any form of tobacco along with former smokers as "smokers." Physical activity was assessed by asking about both work-related and leisure-time activities as suggested by Paffenberger *et al.* [14]. Their criteria classify a person as leading a sedentary lifestyle who walks <9 miles/week, climbs <20 flights of stairs/week, or performs no moderately vigorous physical activity five days a week. In the study area, which is a desert, farming activity occurs only during two or three months of rainy season in a year so that most of the time, the population is either sedentary or intermittently physically active.

Hypertension was diagnosed when either the person was on antihypertensive medication or systolic blood pressure was ≥ 140 mmHg and/or diastolic blood pressure ≥90 mmHg [15]. Figures for WHO criteria [10] of hypertension (≥160 and/or 95 mmH_g) used by most previous Indian studies are also given. Obesity was defined as a body mass index ≥27 kg/m² and truncal obesity when waist/hip ratio was ≥0.95 [6,15].

The three diagnostic criteria for CHD [10] were: (a) history of documented angina or infarction and previously diagnosed CHD; (b) affirmative response to the Rose questionnaire; or (c) ECG changes, namely, Minnesota codes 1-1, 4-1, 5-1, 5-2, or 9-2. Isolated T inversion in lead V1 was ignored. In an uneducated rural population of India, reliance based on history may result in overdiagnosis or underdiagnosis because of poor interpretation of symptoms. Therefore, we diagnosed CHD when there were either ST-T changes or Q wave changes or Q wave changes in the ECG.

Statistical Analysis

The sample size was calculated by the formula $n = pq/e^2$. Here n is sample size, t is normal variate, p is proportion or prevalence of disease, and e is margin of error. From previous Indian studies in rural areas the prevalence of CHD varies between 1.48% [9] and 2.26% [8]—say 2%. Taking the margin of error e to be small (0.2%), the sample would be 2023. We proposed a larger sample size of 3000 as suggested by a recent Indian study [16].

The prevalence rates are in percent. Mean values are given with 1 SD. Analysis to determine significant risk factors of coronary risk factors with CHD prevalence was performed with logistic regression (SPSS V4.0.1, SPSS Inc., Chicago, USA). The dependent variable was presence or absence of CHD (diagnosed by Q-waves) and independent variables were age, years of education, smoking, physical activity, prayer habit, body-mass index, presence of hypertension, and systolic and diastolic blood pressure. Variables like smoking, sedentary habits, prayer habit, and hypertension were dichotomized (yes = 1, no = 0) and other variables were continuous numbers. Odds ratios and 95% confidence intervals were determined for (a) all variables individually, (b) after incorporating age as a continuous variable in the equation (age-adjusted), and (c) after addition of all other risk factors in the equation to determine the independent determinants of CHD prevalence (multivariate analysis). Two-tailed p values less than 0.05 were taken as significant.

RESULTS

A total of 3148 persons were studied. The response rate was 92.6% (1982 of 2180) in males and 59.2% (1166 of 1970) in females. The overall CHD prevalence determined by the presence of clinical or ECG findings was 3.5% (males 3.7%, females 3.7%). ECG changes (ST, T, or Q) were present in 3.0% (males 2.8%, females 3.3%). Q-waves changes were in 1.4% (males 1.6%, females 0.9%). The age distribution of CHD patients is shown in Table 1. The prevalence of CHD diagnosed by various criteria increased with increasing age in both males and females (Mantel-Haenszel test for trend, $p < 0.001$).

Prevalence (%) of coronary heart disease

Age group	Male (n = 1982) Nos.	Clinical +ECG	ECG changes	Q-wave	Female (n = 1166) Nos.	Clinical +ECG	ECG changes	Q-wave
	571	10 (1.8)	9 (1.6)	3 (0.5)	382	5 (1.3)	4 (1.0)	0 (0)
	495	13 (2.6)	10 (2.0)	6 (1.2)	342	9 (2.6)	8 (2.3)	2 (0.6)
	366	12 (3.3)	11 (3.0)	6 (1.6)	212	11 (5.2)	8 (3.8)	2 (0.9)
	268	11 (4.5)	8 (3.0)	4 (1.5)	127	11 (8.7)	11 (8.7)	2 (1.6)
	282	22 (7.8)	17 (6.0)	13 (4.6)	103	7 (6.8)	7 (6.8)	5 (4.8)
	1982	68 (3.4)	55 (2.8)	32 (1.6)	1166	43 (3.7)	38 (3.3)	11 (0.9)

Overall χ^2 for trend in all groups shows $p < 0.01$.

The standard risk factor prevalence is shown in Table 2. Illiteracy was common among males (51%). Hypertension (≥160/95) was in 24% males and 17% females. Hypertension (≥180/95) was in 8% males and 6% females. Obesity was present in 6%. Results of waist-hip ratio measurements were available in 399 males and 104 females. Truncal obesity was present in 5% males and 5% females. History of diabetes was present in 3 people (0.2%). Prevalence of other risk factors (Table 2) showed that lack of education was widely prevalent, reflecting the general level of literacy in rural Indian community. Agricultural workers, who are poorer than business or service class people, constituted a large number. Although only moderate to high grade physical activity was noted frequently, participation in mentally-relaxing activity, such as regular prayer, was noted in a large number (30%) of subjects. The majority of the population was vegetarian. The consumption of milk fat (ghee) was low; 60% consumed less than 1 kg ghee per month and only 6% greater than 2 kg per month.

Blood samples of 202 males and 98 females were studied. Of the persons who were offered the blood test 85% males and 70% females responded. These constituted 10.2% of males and 8.4% of females of the study sample. Mean serum cholesterol and lipoprotein levels are shown in Table 4.

TABLE 2. Prevalence (%) of coronary risk factors

	Male (n = 1982)	Female (n = 1166)	Total (n = 3148)
Alcohol and tobacco (current and past)	1006 (51)	54 (5)	1060 (34)
Nil/moderate physical activity			
Leisure time	363 (18)	88 (7)	451 (14)
Work related	333 (17)	79 (7)	412 (13)
	386 (19)	91 (8)	477 (15)
Diabetes	4 (0.2)	2 (0.1)	6 (0.2)
Hypertension ≥160/90	470 (24)	197 (17)	667 (21)
≥180/95	150 (8)	72 (6)	222 (7)
Waist-hip index ≥ 27	104 (5)	74 (6)	178 (6)
Waist-hip ratio ≥ 0.95	17/399 (4)	5/104 (5)	22/503 (5)

Classification of individuals with abnormal lipoprotein lipids was done according to recommendations of the US National Cholesterol Education Program (NCEP) [16]. There was a high prevalence of "borderline" or "high risk" total cholesterol (22.3%) and LDL cholesterol levels (21.7%). Low HDL cholesterol was observed in 29.7%.

Comparison of subjects with and without CHD revealed that mean age was higher in those with CHD (males 47 ± 16 versus 40 ± 15; females 45 ± 13 versus 37 ± 13; $p < 0.001$). Age as a coronary risk factor was also confirmed by logistic regression analysis ($p < 0.001$ in both males and females; Table 5). Analysis of lifestyle factors showed that religion, marital status, occupation, family structure, alcohol intake, and dietary habits were not significantly associated with CHD prevalence. As cholesterol lipoprotein and triglycerides estimations were done in small proportions, they were not analyzed as determinants.

Unadjusted, age-adjusted, and multivariate odds ratios were calculated to determine the significant associations of major coronary risk factors and those found important on univariate analysis (educational level, prayer habit) with CHD prevalence (Table 5). Unadjusted odds ratios (OR) show that, in males, age, educational status, prayer habit, smoking, and body mass index and, in females, age, educational status and systolic blood pressure were significant determinants. Age-adjusted OR (95% confidence intervals [CI]) show that in males smoking (OR 2.56, CI 2.04 to 3.21), educational level (OR 0.84, CI 0.57 to 1.01), and prayer habit (OR 0.26, CI 0.08 to 0.86) were significant; in females systolic blood pressure (OR 1.02, CI 1.00 to 1.03) was significant. Multivariate analysis showed that independent risk factors in males were age and smoking (OR 2.50, CI 1.09 to 5.73) while prayer habit (OR 0.25, CI 0.05 to 0.95) was protective. In females age was an independent risk factor.

DISCUSSION

This study shows that the prevalence of CHD in a rural community in western India using the criteria of history plus ECG changes or ECG Q, ST, and T changes or presence of Q waves alone is 3.53%, 2.95%, and 1.37%, respectively.

TABLE 3. Prevalence (%) of lifestyle variables and other risk factors

	Male	Female
Age (years)	39.87 ± 15	36.81 ± 3
Religion		
Hindu	1794 (90)	1065 (93)
Non-Hindu	188 (10)	81 (7)
Marital		
Married	1866 (94)	1146 (98)
Unmarried	105 (5)	10 (1)
Widowed	11 (1)	10 (1)
Occupation		
Agriculture	1303 (66)	180 (15)
Business	377 (19)	19 (2)
Professional	4 (.2)	3 (3)
Govt. service	298 (15)	31 (3)
Household	—	933 (80)
Educational status		
Uneducated	765 (39)	608 (52)
1–5 years	350 (18)	304 (26)
6–10 years	591 (29)	194 (17)
>10 years	276 (14)	30 (3)
Family structure		
Joint family	1544 (78)	970 (83)
Nuclear family	307 (15)	111 (9)
Not specified	134 (8)	85 (7)
Anger/grief	37 (2)	22 (2)
Prayer habit	533 (27)	423 (36)
Diet		
Vegetarians	1639 (83)	1021 (12)
Non-vegetarians	343 (17)	145 (12)
Ghee consumption/month		
≤1 kg	1200 (61)	689 (59)
1.1–2 kg	660 (33)	410 (35)
>2 kg	122 (6)	67 (6)
Alcohol intake	377 (19)	26 (2)

The standard coronary risk factors smoking, hypertension, and sedentary lifestyle are widely prevalent. Significant positive associations of CHD are with age, smoking (males), and systolic blood pressure (females).

Hospital based data [17] and epidemiological meta-analysis [7] show that CHD occurs at a younger age in the Indian population. Therefore we included individuals 20–29 years and results show that CHD exists in this age group also. In the present study confirmation of CHD was based on presence of Q-wave and using this criteria the CHD prevalence is 1.6% in males and 0.9% in females. Earlier studies from India used different criteria [3–5,8,9] and showed higher CHD prevalence. When the diagnostic criteria in the present study are extended to include past documentation, response to WHO-Rose Questionnaire and ST-T wave changes in ECG as done in previous studies, the prevalence increases to 3.4% in males and 3.7% in females, which is higher than in previous Indian rural studies [8,9]. However, the validity of both the past documentation of CHD as well as the affirmative response to WHO-Rose questionnaire have been questioned [18]. This would be more so in the case of an illiterate rural population where reliance on self-reported diagnosis of CHD may result in either [illegible] nosis or overdiagnosis. As diagnostic markers of CH[illegible] of the previous studies from India included such [illegible] ria as the presence of left bundle branch block, [illegible] heart block and presence of ST segment and [illegible] changes [3–5,7,8]. Many studies suggest that the[illegible] are not reliable enough to diagnose CHD and sp[illegible] in females where ST-T changes may be non-spec[illegible]

Dewan *et al.* [8] studied 1504 individuals in [illegible] (North India) while Jajoo *et al.* [9] studied 2433 [illegible] Vidharbha (Central India). In both these studies [illegible] diagnosed on the basis of presence of Q-waves [illegible] T wave changes or left bundle branch block. D[illegible] [8] reported a CHD prevalence of 14.5/1000 p[illegible] Jajoo *et al.* [9] 20.6/1000. When we re-analyzed [illegible] Dewan *et al.* [8] basing diagnosis on the presence [illegible] only the prevalence decreased to 3.3/1000. Jajo[illegible] not specify the prevalence of Q waves and furthe[illegible] not possible.

Our results are not comparable with urban-b[illegible] from India not only because ours is a rural-base[illegible] also because of different and varying criteria u[illegible]

[illegible] Determinants of Coronary Heart Disease

[illegible] lipoprotein lipids levels and prevalence of hyper-

	Male (n = 202)	Female (n = 98)	Total (n = 300)
[illegible]olesterol	169.7 ± 41	169.2 ± 40	169.6 ± 40
[illegible] value	157 (78)	76 (78)	233 (78)
	29 (14)	14 (14)	43 (14)
[illegible]59	16 (8)	8 (8)	24 (8)
[illegible]ity lipoprotein			
[illegible]olesterol	97.2 ± 39	101.5 ± 36	98.6 ± 38
[illegible] value	165 (82)	70 (71)	235 (78)
[illegible]	29 (14)	16 (16)	45 (15)
[illegible]59	8 (4)	12 (12)	20 (7)
[illegible]ity lipopro-[illegible] cholesterol	44.4 ± 14	44.4 ± 15	44.4 ± 14
[illegible] value	49 (24)	40 (41)	89 (30)
[illegible]glycerides	144.6 ± 54	131.2 ± 66	140 ± 59
[illegible] value	189 (94)	91 (93)	280 (93)
[illegible]50	12 (6)	6 (6)	18 (6)
[illegible]	1 (0.5)	1 (1)	2 (0.7)

[illegible] are in mg/dl. Numbers in parentheses are percentages.

[illegible]rivotham and Berry [3] studied a sample of 2030 per-[illegible] more than 30 years in city of Chandigarh in North [illegible] and reported a prevalence of 66/1000. In this study, [illegible]HD was diagnosed on basis of either Q-waves or [illegible]e complete heart block in ECG the prevalence was [illegible]0 which is more than the present study. In a study [illegible]hi reported by Chadha *et al.* [5], the criteria for [illegible]g CHD were entirely different. These authors in-[illegible]ll symptomatic cases as definite CHD and later [illegible]symptomatic individuals with either Q-waves or ST-[illegible] and showed CHD prevalence as 96.7/1000. Sub-[illegible] of the Delhi data in asymptomatic individuals [illegible]-wave prevalence as 14.2/1000 in 5621 individuals [illegible]4 years of age [19]. Although this prevalence rate [illegible] to our data, it is not comparable because of exclu-[illegible]symptomatic persons. We recently reported CHD [illegible]ce of 75.9/1000 and Q-wave prevalence of 19.9/[illegible] an urban population of Rajasthan (n = 2212) [6]. [illegible]dence rate is significantly higher than 13.7/1000 [illegible]esent study.

[illegible]considering all the criteria, the prevalence of CHD [illegible] study is higher compared with previous Indian [illegible]ulation studies and less than in urban populations. [illegible]anization is a well known phenomenon in the [illegible]e of CHD and could be an explanation for this [illegible]evalence. On the other hand, the Haryana [8] and [illegible]9] studies were reported twenty-two and eight [illegible] respectively, and the higher prevalence in the [illegible]udy may be an indication of the rising trend of [illegible]ndian rural populations [7].

Analysis of the prevalence of CHD risk factors shows that there is a high prevalence of smoking and hypertension in this population. Although the prevalence of smoking is similar to previously reported studies [8,9], hypertension is more prevalent. When WHO criteria are used for hypertension, the prevalence of 7% in the present study is more than in previous studies [3–5]. The mean serum lipoprotein lipid levels are lower than those reported from the Western countries [16], but are higher than a previously reported study from North India [20]. This may reflect a rising trend in lipid levels in the Indian population. The prevalence of hypercholesterolaemia in our subjects is not comparable to any other Indian study because of the newer criteria used for classification. However, while the prevalence of hypercholesterolaemia is less than in USA, as well as in several European countries, it is similar to the prevalence in China [21]. A low prevalence of diabetes could represent an artifact due to reliance on self-reported diagnosis in our study. A study from USA has suggested that self-reported diagnosis of diabetes accurately reflects the true prevalence [22].

We used stricter criteria for grading physical activity as compared with previous Indian studies [8,9]. Low grade physical activity is universal in a rural agrarian population, and moderate or high grade physical activity is related to agricultural cycles. We used the Paffenberger [14] criteria for physical activity assessment, validated in studies from USA and other developed countries. These criteria may not accurately reflect physical activity in a semiliterate population.

Univariate analyses confirm the importance of classical coronary risk factors, age and smoking. These factors are also independently associated with CHD prevalence in men as confirmed by multivariate analysis. Systolic blood pressure positively correlated with CHD in females. The significance of truncal obesity and hyperinsulinaemic states has recently been highlighted as an important coronary risk factor among South Asians living in Britain [23]. A precise relationship between CHD with serum cholesterol, other lipoprotein lipids, obesity, and truncal obesity has not been demonstrated in our study as the proportions where such measurements were made was small. Sedentary lifestyle has not emerged as an important risk factor. The absence of any significant association may reflect the protective influence of intermittent physical activity.

CHD prevalence was significantly greater among uneducated versus educated persons. This observation is consistent with international data, which show that CHD and coronary risk factors—smoking and hypertension—are more frequent among the uneducated [24]. Men who engaged in regular prayer had a significantly lower prevalence of CHD. Mental stress is important in the genesis as well as perpetuation of coronary atherosclerosis [25,26]; therefore mentally relaxing activities may be relevant in CHD. Our results show that persons who pray regularly had a lower prevalence of CHD. This was confirmed on univariate, as well

TABLE 5. Odds ratios for association of CHD prevalence (Q-wave) with coronary risk factors (logistic regression)

Risk factor	Male		Female	
	Odds ratio (95% CI)	*p* Value	Odds ratio (95% CI)	*p* Value
Age				
a	1.05 (1.02–1.07)	<0.001*	1.08 (1.04–1.13)	<0.001*
c	1.05 (1.02–1.08)	<0.001*	1.07 (1.03–1.12)	0.002*
Education				
a	0.64 (0.45–0.92)	0.017*	0.29 (0.08–1.05)	0.059
b	0.84 (0.57–1.01)	0.052	0.64 (0.16–2.52)	0.524
c	1.00 (0.66–1.51)	0.999	0.51 (0.11–2.32)	0.385
Prayer habit				
a	0.28 (0.08–0.91)	0.035*	1.47 (0.45–4.84)	0.528
b	0.26 (0.08–0.86)	0.027*	1.61 (0.48–5.43)	0.439
c	0.28 (0.08–0.95)	0.041*	2.39 (0.64–8.88)	0.194
Smoking				
a	2.95 (1.32–6.61)	0.008*	0.01 (0.00–3.97)	0.802
b	2.56 (2.04–3.21)	0.023*	0.01 (0.00–3.83)	0.786
c	2.50 (1.09–5.73)	0.031*	0.01 (0.00–7.04)	0.795
Sedentary habits				
a	1.63 (0.75–3.56)	0.217	1.18 (0.15–9.37)	0.873
b	1.79 (0.81–3.95)	0.147	1.60 (0.19–13.2)	0.661
c	1.18 (0.51–2.75)	0.698	1.14 (0.13–10.0	0.906
Body-mass index				
a	0.87 (0.76–0.99)	0.028*	1.01 (0.94–1.07)	0.828
b	0.88 (0.80–1.04)	0.053	1.00 (0.95–1.06)	0.921
c	0.92 (0.80–1.04)	0.172	1.00 (0.96–1.05)	0.824
Systolic BP				
a	1.00 (0.98–1.02)	0.974	1.02 (1.00–1.03)	0.031*
b	0.99 (0.98–1.01)	0.394	1.02 (1.00–1.03)	0.034*
c	1.00 (0.98–1.03)	0.748	1.04 (1.00–1.09)	0.057
Diastolic BP				
a	0.99 (0.96–1.02)	0.490	0.98 (0.95–1.00)	0.209
b	0.98 (0.95–1.00)	0.108	0.98 (0.96–1.01)	0.134
c	0.98 (0.94–1.02)	0.249	1.05 (0.98–1.09)	0.205
Hypertension				
a	1.69 (0.65–4.41)	0.284	1.86 (0.49–7.06)	0.363
b	2.47 (0.94–6.55)	0.068	0.85 (0.21–1.75)	0.820
c	2.23 (0.83–5.98)	0.112	0.90 (0.22–3.71)	0.885
Cholesterol	Small numbers			

Abbreviations: CI = confidence intervals, BP = blood pressure, * = significant, a = unadjusted odds ratio, b = age-adjusted odds ratio, c = odds ratio after addition of all the variables in equation.

as multivariate analysis. The exact mechanism by which prayer habit imparts protection against CHD is not clear and unknown neuro-endocrine mechanisms may be involved.

In conclusion, analysis of the present epidemiological data shows that there is a rising trend of CHD in the Indian rural population. Coronary risk factors, smoking and hypertension, are widely prevalent and are important in the aetiopathogenesis of CHD in these persons as in any other population. In addition, social factors that are frequent in rural communities in India but are also present elsewhere are significant. Increasing level of education and regular participation in stress-reducing activities such as prayers appear to be significant protective factors.

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Role of diet and alcohol in tobacco-related cancer at sites in the upper aerodigestive tract in an Indian population

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Cancers of the upper alimentary and respiratory tracts, for which tobacco is the major cause, constitute about one-third of all cancers among Indians. Probable changes in demography suggest that the incidence of these cancers will increase. Since a large segment of tobacco users remain cancer free, however, other factors may have a modifying effect on the risk of developing the disease. The modifying effect of diet on the occurrence of oral cancer was observed in an exploratory study in India in early 1970s. Subsequently, the role of various dietary factors and of alcohol were studied for cancers of all sites in the upper aerodigestive tract. The results indicate that intake of vegetables, fish and buttermilk (liquefied yogurt) was associated with a lower risk for upper aerodigestive tract cancers and that use of red chillie powder, a common spice used in Indian food, was a risk factor in a dose-dependent manner. Alcohol intake had a limited but significant influence on the risk for these cancers.

INTRODUCTION

Epidemiological studies indicate that 80-90% of human cancers are attributable to environmental factors and life style. The major differences in the incidence rates of various cancers among different countries, between the genders, and between migrant and native populations, as well as time trends, implicate environmental factors in cancer causation.

In each country, there are characteristic site patterns of risk due to local exposure factors and life styles. For example, the rate of cancers at all sites combined among Indian males is quite low when compared with rates for men in Connecticut, USA, Oxford, United Kingdom, and Miyagi, Japan (1-6), where the incidence rates are two- to three-fold higher (Table 1). The incidence rates of cancers of the oral cavity, pharynx and larynx in India, however, are some of the highest in the world (Table 1). The incidence of lung cancer, although low by international standards, is similar to that of oesophageal and pharyngeal cancers in the national context. Thus, in Indian males, cancers of the upper aerodigestive tract constitute 30-40% of all cancers, whereas they constitute only 12, 6 and 8% of cancers in Connecticut, Oxford and Miyagi, respectively. With the inclusion of lung cancer, however, cancers of the upper alimentary and respiratory tracts constitute 40-50% of cancer at all sites combined among Indian males and about 20% of cancers among Indian females.

The use of tobacco as a major risk factor for cancers at these sites is well established (7-10). Quantification of the risks associated with different tobacco habits has also resulted in high values. Even so, not all heavy chewers and smokers develop cancer; thus, it is likely

Table 1

Average annual age-adjusted incidence rates of cancers of the upper alimentary and respiratory tracts in males per 100 000 population

Registry	Oral cavity (140-145)[a]	Pharynx (146, 148)	Oesophagus (150)	Larynx (161)	Lung (162)	All sites combined (140-208)
India[b]						
Ahmedabad	21.1	16.9	10.5	10.2	13.9	149.5
Bangalore	9.0	8.8	8.3	4.9	8.6	107.0
Bombay	13.4	11.8	11.4	8.0	13.8	120.5
Madras	12.0	6.8	7.4	4.9	7.5	91.1
Nagpur	15.3	9.7	14.1	13.1	8.6	122.2
Poona	14.8	5.7	12.8	11.2	11.3	127.6
Others[c]						
Connecticut, USA	10.6	3.7	5.3	8.2	60.9	303.0
Oxford, UK	5.2	1.2	3.8	3.9	69.3	268.5
Miyagi, Japan	1.9	0.4	13.8	2.2	25.5	208.9

[a]Figures in parentheses are ICD codes: 9th for Indian registries; 8th for other registries, with codes 140-207 for all sites instead of 140-208
[b]Source: refs. (1-5)
[c]Source: ref. (6)

that certain secondary factors, either external or internal, may have modifying influences on the risk, and diet and nutrition could be one such factor. This paper reviews the role of diet and also of alcohol in the pathogenesis of cancers of the upper aerodigestive tract.

ROLE OF DIETARY FACTORS

Nutrition and diet can act in several ways. Nutrients, food additives and contaminants (like aflatoxins) can act as complete carcinogens or pro-carcinogens. Dietary deficiencies or excesses can lead to biochemical malfunction, which in turn may initiate or promote a neoplastic process; they may also impede or enhance the delivery of carcinogens to the target tissue. They can result in metabolic activation or deactivation of carcinogens. Thus, diet and nutrition can interact with the host environment in several ways and alter the susceptibility of tissues to cancer induction and promotion (11). Generally, several dietary components are considered to act more as tumour promoters or antipromoters rather than as direct carcinogens.

An exploratory analysis of data collected in the 1950s in Bombay, India, indicated that certain dietary components may modify the risk of tobacco chewers and smokers for developing oral cancer (12). This formed the basis for a case-control study (13) conducted subsequently for all sites in the upper aerodigestive tract. Some of the results abstracted from this study are discussed below.

DIET AND CANCERS OF UPPER AERODIGESTIVE TRACT

Cancers of the oral cavity, pharynx, larynx and oesophagus formed the case group for this study. Two control groups were used. The results obtained with controls from the general population (using electoral rolls) are shown in Table 2. Information on usual diet before disease onset, in terms of the frequency and amount of intake, was obtained by a

Table 2

Relative risk estimates for cancers of the upper aerodigestive tract (with 95% confidence intervals) associated with consumption of different dietary items in Bombay, India[a]

Dietary item (level of comparison)	Cancer site			
	Oral cavity	Pharynx	Oesophagus	Larynx
Cereals and pulses				
Cereals (not daily *vs.* daily)	1.45 (0.8-2.5)	1.59 (0.9-2.9)	1.51 (0.9-2.7)	0.87 (0.4-1.9)
Pulses (not daily *vs.* daily)	1.57 (1.0-2.5)	1.90 (1.2-3.1)	1.11 (0.7-1.8)	1.48 (0.8-2.8)
Vegetables and fruits				
Vegetables (not daily *vs.* daily)	2.39 (1.4-4.0)	2.65 (1.6-4.5)	2.62 (1.5-4.4)	2.75 (1.4-5.3)
Fruits (<1/week *vs.* ≥1/week)	0.89 (0.5-1.4)	0.99 (0.6-1.6)	1.23 (0.8-2.0)	2.00 (1.0-4.1)
Animal products (<1/week *vs.* ≥1/week)				
Meat	1.21 (0.7-2.0)	1.13 (0.7-1.9)	1.46 (0.9-2.5)	1.12 (0.6-2.1)
Fish	3.28 (2.1-5.3)	2.23 (1.3-3.7)	3.77 (2.3-6.3)	3.94 (2.1-7.7)
Poultry	0.78 (0.1-5.2)	0.90 (0.1-7.0)	3.50 (0.3-48.9)	1.12 (0.02-48.3)
Eggs	0.83 (0.5-1.5)	0.43 (0.2-0.8)	0.79 (0.4-1.4)	0.64 (0.3-1.4)
Dairy products (not daily *vs.* daily)				
Milk	1.11 (0.6-2.2)	1.13 (0.6-2.3)	1.47 (0.7-3.0)	0.78 (0.3-2.0)
Buttermilk	3.71 (1.6-8.7)	3.68 (1.4-9.4)	2.44 (1.1-5.4)	11.09 (1.5-83.1)
Fat				
Groudnut oil (g/cu/month) (<600 g *vs.* ≥ 600 g)	2.91 (1.8-4.7)	2.93 (1.8-4.8)	1.99 (1.2-3.2)	2.61 (1.3-5.1)
Spices				
Red chillie powder (g/cu/month)				
< 75	1.00	1.00	1.00	1.00
75-99	2.61*	1.45	1.94	1.22
100-149	3.79**	2.33	1.99	2.05
≥ 150	3.94**	2.37**	2.85**	3.39**
χ^2 trend test	<0.001	<0.01	<0.01	<0.10
Beverages				
Tea (>2 cups/day *vs.* ≤ 2 cups/day)	1.21 (0.8-1.9)	1.46 (0.9-2.4)	2.39 (1.5-3.9)	1.10 (0.6-2.0)

[a]Source: ref (13): Comparison group; general population
Relative risk adjusted for age and tobacco use
*$p < 0.05$; **$p < 0.01$

questionnaire. Findings from the analysis based on the frequency of intake of several dietary items (13) are summarized in the table. The results are given in terms of relative risk estimates that were adjusted for the two important risk factors, use of tobacco and age. Adjustment was not required for sex or community, as all the patients were men and they belonged to one community with similar socio-economic status.

Cereals and pulses: These constitute the most common food items for all segments of the Indian population. Table 2 compares the risks of those who did not consume these items daily *versus* those who did. For those who did not include pulses in their diet daily *versus* those who did, the relative risk (1.9) was significant for pharyngeal cancer.

Vegetables and fruits: A two- to three-fold increase in risk was observed for men who did not consume vegetables daily *versus* those who did, and these were highly significant. The lower risks were consistent with the current hypothesis that vitamin A, ß-carotene and vitamin C have protective effects. Intake of fruits, however, showed no association; this was not surprising, since both the control and study groups were from the lower income stratum and, perhaps understandably, could not afford this relatively expensive food item.

Animal products: Risks were also assessed for men who ate meat, fish, poultry and eggs less than once a week *versus* those who consumed these items at least once a week. Only fish intake showed a significant relative risk, which was two- to four-fold higher for nonconsumers than consumers.

Dairy products: Milk intake was found to be relatively poor in both the study and control groups, and the relative risks were not significant. Butter was consumed by only 0.2% of the study group and was therefore not analysed. Nonconsumers of buttermilk (liquefied yogurt) were at significantly higher risk than consumers.

Fat: Information was obtained on the consumption of various types of fats and oils, and the quantity consumed was expressed in grams per consumption unit (cu) (one for a member of the family 12 years of age and above, half otherwise) per month (g/cu/mth). Groundnut oil was the most commonly used cooking medium (81-86% in different groups), and median consumption in the population control group was 600 g per cu per month while that of the whole study group was 400 g per cu per month. Men who consumed less oil were at a two-fold higher risk than those who used more. In contrast to the western diet, in which fat contributes 30-40% of the total caloric intake, in an average Indian diet fat consumption is low and contributes only 8-10% of the total caloric intake. High fat consumption in western countries was reported in several studies to be associated with higher risks for cancers of the colon and of endocrine-dependent sites (14,15); so the risk elevation even with low caloric intake from fat in this study is interesting.

Spices: Red chillie powder is an important spice in Indian food, and this emerged as a risk factor in a dose-dependent manner. With an increase in chillie use from <75 g to 150 g or more per cu per month, there was a one- to three-fold increase in risk, which was significant for all sites except the larynx. This observation is consistent with experimental findings that red chillies are mutagenic in bacterial test systems and are tumour promoters *in vivo* (16,17).

Beverages: Barely 2% of the study group drank coffee, but drinking of tea was common, the median intake being two cups per day. There was a significant, two-fold increase in risk for oesophageal cancer among men who drank more than two cups of tea a day as compared to those who drank two cups or less. For pharyngeal cancer, the risk was 1.5, which was only marginally significant.

When men who drank three, four, five or more cups of tea per day were compared with those who drank two cups or less per day, a significantly increasing trend of relative risk for oesophageal (2.0, 2.2 and 3.5) and pharyngeal cancers (1.1, 1.8 and 2.3) was observed. It is possible that it is the temperature of the tea and not the tea itself that is relevant, but it was not possible to study this aspect in our investigation.

Since this is the only case-control study on diet and cancer in India, the results need to be interpreted with caution. Furthermore, it was not possible at this stage to assess the attributable risks due to dietary factors, as has been done for tobacco (18).

DISCUSSION

A number of studies have reported similar results. In an extensive study by the International Agency for Research on Cancer, the role of several food items was investigated in the induction of oesophageal cancer in an area of high incidence (165 per 100 000) in Iran. Of the 45 food items listed (19), nine showed a significant association with the disease in both males and females. Tea drinking was one of them; a significant, almost two-fold increase in risk was observed among those who drank hot tea compared to those who did not. The other items included consumption of dairy products, raw vegetables and fruit; these were found to have a significant protective effect, the risks for higher *versus* lower levels of consumption ranging from 0.42 to 0.69. Consumption of meat, poultry and fish showed no association, nor was there a significant association with tobacco use or alcohol intake.

In a case-control study on oral and pharyngeal cancers in women in the southern USA, Winn *et al.* (20) reported a significant protective effect of vegetable and fruit consumption. A report from the Roswell Park Memorial Institute (USA), where large-scale questionnaire studies on diet are routinely conducted, also revealed a protective effect of vegetable and fruit intake, but not of meat or fish intake, on the development of oesophageal cancer in a dose-dependent manner (21). Using standard food composition tables, it was shown that higher dietary levels of vitamins A and C conferred protection. A similar protective effect of vitamins A and C was reported for laryngeal cancer (22), and the gradient in risk persisted even after adjustment for the effects of alcohol drinking and cigarette smoking.

It is not easy to quantify the contribution of diet to cancer risk because of the complexity and extreme difficulty of measuring in meaningful quantitative terms dietary intake prior to disease onset. Moreover, dietary items interact not only with each other but also with the host environment. Despite these complexities, certain consistent associations with specific food items have been observed.

It may be concluded that, although tobacco is known to be a major causal factor for some human cancers and efforts must be made to eliminate its use, the tumour promoting or protective role of certain dietary factors cannot be ignored. It is therefore suggested that a balanced diet adequate in protein and nutrient intake, especially fresh vegetables and fruits rich in minerals and vitamins, coupled with avoidance of high intake of fats and meat and strict surveillance of quality, preservation and storage practices, would be consistent with the lowest possible risk for cancer and other diseases for the Indian population.

ROLE OF ALCOHOL

Alcohol plays an important role in the pathogenesis of cancers of the upper alimentary tract, especially in conjunction with cigarette smoking. In the present study, alcohol was consumed in the form of a locally distilled brew.

The risks of alcohol drinking and tobacco smoking and chewing were assessed using log-linear models, which were translated into logistic regression models for the dichotomous response variable (23). Table 3 shows the

PH. 7.

Table 3

Estimates of odds ratios associated with regular habits obtained under fitted logistic models[a]

Adjusted odds ratios associated with	Cancer site		
	Oral cavity	Pharynx	Oesophagus
Smoking	7.4	5.6	4.7
Chewing	11.4	6.8	4.9
Alcohol drinking	1.3	2.2	[b]

[a]Source: ref. (23): Comparison group; general population controls

[b]Because of an age-alcohol interaction term in the model, estimates of odds ratios differ with age group and are 2.7, 2.6 and 0.6 for age groups 40-49, 50-59 and ≥ 60 years, respectively.

results abstracted from this study. The risks associated with alcohol intake *per se* were not as high as those associated with tobacco habits; for oral cancers, the adjusted odds ratio of regular chewers was 11.4, and that for regular smokers was 7.4, while for alcohol consumers it was only 1.3. Similarly, for pharyngeal cancers, the risk associated with alcohol drinking was lower than those associated with tobacco habits. Because of the presence of an age-alcohol interaction term in the model fitted for oesophageal cancer, a single risk figure could not be obtained; these varied from 0.6 to 2.7 in different age groups. The risks for a combination of habits can be obtained by multiplication, and they are high. In another study of oesophageal cancer from this region (24), similar risks were reported.

Pure ethyl alcohol is not likely to be carcinogenic to man, since studies in animal systems have invariably given negative results; but the possibility cannot be ruled out. Contaminants in alcohol might, however, play a role in the pathogenesis of cancer. It has been suggested that the mechanism of the alcohol-cancer association may be related to nutritional deficiencies, which would increase susceptibility to the carcinogenic potential of an external agent like tobacco. Alcohol may also act as a solvent and enhance penetration of carcinogens into target tissues (25). Although the effect of alcohol in inducing cancers of the upper alimentary tract has been demonstrated in several epidemiological studies, its mode of action in the carcinogenic process is still not clear.

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Risk Factors For Coronary Heart Disease — What Are They?

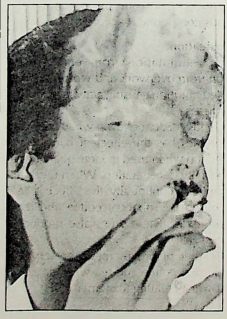
Dr Om Prakash, Head of the Department of Medicine, St Martha's Hospital, Bangalore.

Mr. Srinivasan, 48 years, is a businessman with a lot of drive and has an aggressive personality. He drinks only socially and smokes about 25 cigarettes a day — a habit he is unable to give up.

Five years ago he was noted to have high blood pressure (160/106) but he is irregular in taking his prescribed medications. His work keeps him busy; he often gets angry during the course of the day. He also carries his business papers home. He is reluctant to change his way of functioning.

Mr Srinivasan's father died suddenly, at the age of 44, presumably from a heart attack. His mother has diabetes and is on regular medication. While driving to work one day, Mr Sreenivasan got severe chest pain and he was sweating.

He was rushed to the nearby hospital with a cardiac care unit. He was noted to have acute myocardial infarction. He was given a drug (streptokinase) and other supportive measures. He made an uneventful recovery. He is now awaiting further tests to decide future treatment plans.



Could Mr Srinivasan's heart attack have been prevented? Could he have been more prudent and cautious? What are the coronary risk factors, which are commonly being talked about and written about?

A heart attack refers to a sudden and complete blockage of one or more branches of coronary arteries. It cuts off the supply of oxygen and nutrients, giving rise to death of part of the heart muscle. It is a potentially life- threatening condition, calling for immediate medical action.

Today, we have a better understanding of the condition and what causes it.

More important, we understand the various factors which singly, and in combination, conspire to lead to coronary atherosclerosis. (stiffening of the coronary arteries).

Such increasing knowledge of the risk-factors has been of immense help in preventing attacks, reducing the suffering and deaths due to acute heart attacks. Such reductions have been seen in the Unites States of America and other western countries.

Coronary risk factors include:

- Tobacco-smoking
- Hypertension
- Diabetes mellitus
- Obesity, and
- Cholesterol

Tobacco-smoking

We have such abundant evidence to conclude that tobacco-smoking is a major risk contributor in the causation of coronary disease. Different mechanisms play a part here. Even after two years of stopping smoking your chances of getting a fatal heart attack become as low as that of a life-time non-smoker.

In the United States of America, reduction in smoking has resulted in a gradual but substantial reduction in fatal and non-fatal heart attacks. The message, unfortunately, in our country has not yet been registered by a large majority of smokers.

Heart specialists in India feel that the prevalence of heart attacks in the younger populations may well be related to the increasing smoking habit.

Cessation of smoking is necessary in any primary preventive programme, especially so in patients who already have ischaemic hearts.

Apart from patient-education and emphatic counselling, mass education campaigns and similar other efforts have to be launched. Recourse may have to be taken to means such as nicotine substitution in the form of chewing gum or transdermal patches containing nicotine.

Hypertension

Elevated blood pressure is another major factor increasing the risk of coronary artery disease. Hypertension is most often symptomless. Hence, it is imperative that all adults have regular blood pressure check-ups done. This will ensure that hypertension that needs medical treatment can be detected early enough and appropriate action taken. Very often, what is needed is a change in the food habits and life-style.

Uncontrolled hypertension accelerates the process of atherosclerosis. Fur-

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Risk Factors for Coronary Heart Disease

ther hypertesnion causes strain on the left ventricle, thus increasing its energy demands and leading to insufficient blood supply.

Diabetes mellitus

It is well known that diseases of blood vessels are markedly aggravated and hastened by diabetes. The occurrence of diabetes and coronary artery diseases in the same individual is very common.

We have evidence that well controlled diabetes (by way of diet, exercise and if necessary drugs) retards the progression of coronary artery disease. We find this is true in both primary prevention of myocardial infarction as well as in the secondary prevention programmes.

Obesity

Coronary events are more common in fat persons; this is true even if the other variables like high blood pressure and diabetes are excluded.

Obesity, along with a physically slovenly and sedentary lifestyle, worsens the coronary disease. The realisation of this has led to a very active life-style along with weight reduction in the USA on a large scale. This, in turn, has led to the reduction of fatal and non-fatal heart attacks.

Cholesterol

We have known for many years the link between high levels of blood lipids and coronary events.

In recent years, it is being appreciated that one fraction of the blood cholesterol, the High Density Lipoprotein (HDL) is in fact a "protective" cholesterol. The Low Density Cholesterol is the one that is associated with myocardial events. Physical exercise tends to increase the HDL.

These five major risk-factors that contribute to coronary artery disease are modifiable. This means the risk can be reduced to a substantial extent by suitable action.

There are other factors that are not modifiable. These include the male sex (which is more subject to coronary artery disease).

The other factor that is unmodifiable is family history of vascular events in parents and close relatives. Though it is not yet clear as to how the genetic effect is transmitted, the fact remains that vascular events tend to run in families.

How does all this translate into practical terms?

An active life-style and diet that is poor in high calories and saturated fats, cessation of smoking or not starting to smoke, control of blood pressure by drugless measures and, if needed, by drug regimens, and weight reduction to an ideal weight, will go a long way in reducing the risk of coronary artery disease.

These measures are all the more important in those who have a family history of diabetes, hypertension or vascular diseases. There are major benefits to be had from these prudent life-style changes.

In our country, attempts are only now being made to educate the public at large as to the need for behaviour modification to reduce the coronary-proneness. These need to be done on a war- footing and on community basis, if any major measurable impact has to be made. ■

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Original Articles

Oral submucous fibrosis in India: A new epidemic?

P. C. GUPTA, P. N. SINOR, R. B. BHONSLE, V. S. PAWAR, H. C. MEHTA

ABSTRACT

Background. Oral submucous fibrosis (OSF) is a precancerous condition caused by use of the areca nut. The reported prevalence of OSF in Bhavnagar district during 1967 was 0.16%. We investigated whether the impression of an increase in the incidence of the disease was real.

Methods. A house-to-house survey was conducted in Bhavnagar district, Gujarat state. The use of areca nut-containing products and tobacco was assessed through an interviewer administered questionnaire. The oral examination was done by dentists. The diagnostic criteria for OSF was the presence of palpable fibrous bands.

Results. A total of 11 262 men and 10 590 women aged 15 years and older were interviewed for their tobacco habits. Among 5018 men who reported the use of tobacco or areca nut, 164 were diagnosed as suffering from OSF. All but four cases were diagnosed among 1786 current areca nut users (age-adjusted relative risk: 60.6). Areca nut was used mostly in *mawa*, a mixture of tobacco, lime and areca nut, and 10.9% of *mawa* users had OSF (age-adjusted relative risk: 75.6). The disease as well as areca nut use was concentrated (about 85%) in the lower (< 35 years) age group.

Conclusions. An increase in the prevalence of OSF, especially in the lower age groups, directly attributable to the use of areca nut products was observed. This could lead to an increase in the incidence of oral cancer in the future.

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INTRODUCTION

Oral submucous fibrosis (OSF) is a chronic, progressive, debilitating disease that was first reported from India in 1953.[1,2] Initially the disease was found only amongst people living in the Indian subcontinent or in Indian migrants to other countries. Later, it was reported from many South-east Asian populations.

In this disease the oral mucosa loses its elasticity and fibrous bands develop.[3] The epithelium is atrophic and there is a marked intolerance to spicy food. The opening of the mouth progressively reduces and in extreme cases it may be difficult for even a straw to pass into the mouth. The disease is precancerous[4,5] and carries a high relative risk (397.3 after controlling for tobacco use) for malignant transformation.[6] Spontaneous regression has not been reported and there is no effective or widely accepted treatment.

Several aetiological hypotheses for OSF have been proposed. The most prominent among them was its relation with intake of chillies. This was influenced by the fact that affected individuals showed a high degree of sensitivity to chillies as well as its occurrence mainly among Indians who used chillies liberally in their daily diet. However, this and other hypotheses have not been confirmed.

It has now been demonstrated that the chewing of areca nut is the most important aetiological factor for OSF. In case–control studies from Bhavnagar, Gujarat[7] and Karachi, Pakistan,[8] very high levels of relative risk for areca nut chewing were reported (109.6 and 94, respectively). A hospital-based prevalence study of 1790 patients[9] and a population-based prevalence study of 11 046 individuals,[10] diagnosed 136 and 335 OSF cases, respectively, all of whom were areca nut chewers. In an intervention trial, the incidence of OSF was lower (although not significantly) in the intervention cohort where there was a substantial decrease in smokeless tobacco and areca nut use due to health education, than in the control cohort.[11]

The practice of chewing areca nut in a betel quid is at least two millennia old.[12] It remained a rather personal habit in which a user purchased areca nut from the market or ordered a vendor to custom-prepare a fresh quid. Tobacco was introduced about four centuries back and currently almost all regular areca nut chewers use it with tobacco. This necessitates frequent spitting of a red colour juice, a scourge for almost all public places in India. This practice appeared to be slowly decreasing with increasing education, urbanization and unacceptability of spitting behaviour.

During the last two decades, the situation has changed once again and the practice of chewing areca nut has received a boost with the advent of 'pan masala'. These areca nut-containing products are industrially manufactured and commercially marketed. They are available in small convenient sachets and are backed by high profile advertisement campaigns. As a result the use of 'pan masala' and similar mixtures containing areca nut has again become quite common.

The prevalence of OSF was reported from population-based, house-to-house surveys in rural areas of six districts in India.[13,14] The highest prevalence (0.36%) was in Ernakulam district and the next highest, in Bhavnagar district (0.16%). The annual incidence per 100 000 was 13.5 in Ernakulam and 5.5 in Bhavnagar district.[15] Thus, OSF did not appear to be a very common disease. However, there is a widespread feeling among health professionals, especially dentists and otorhinolaryngologists in northern India, that there is a marked increase in the incidence of OSF.

The present study was undertaken in Bhavnagar district, Gujarat to investigate whether there was any increase in the

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prevalence of OSF and, if so, could it be attributed to an increase in the use of areca nut?

SUBJECTS AND METHODS

Bhavnagar district is located on the western coast of India in the state of Gujarat and has an area of 9259 sq km. In Palitana *taluka* of this district, 20 geographically contiguous villages were selected and all individuals aged 15 years and older were included in the study. A brief questionnaire on the use of areca nut and chewing and smoking of tobacco was administered by trained investigators to each individual during house-to-house visits. Those men who reported some kind of chewing or smoking habit were examined in natural daylight using two disposable wooden spatulas by the authors (PNS, VSP) who had been conducting similar studies in this area for many years. The visits and examinations were called off after 5018 male tobacco users were examined as more than the targeted oral precancerous lesions were accumulated.

The criteria for diagnosing OSF was the presence of palpable fibrous bands in the oral mucosa. This criteria has been used consistently in all our studies since 1966.[12]

The most popular method of areca nut use in Bhavnagar region is the chewing of *mawa*. This is a combination of areca nut, tobacco and slaked lime [$Ca(OH)_2$]. Areca nut is also chewed with betel quid. Some people chew tobacco with lime without areca nut. Application of commercially available dry snuff called *bajar* is also popular, especially among women.

The most common method of smoking in this region was *bidi*. This is made by putting a small amount (about 0.2 g) of coarse, ground tobacco on a rectangular piece of dried *temburni* leaf, hand-rolling it into a conical shape and securing the roll with a thread. Its length varies from 4 to 7 cm. Another common method of smoking tobacco was in a clay pipe. All these habits have been described elsewhere.[13]

RESULTS

A total of 11 262 men and 10 590 women were interviewed for their areca nut/tobacco habits. Figure 1 shows the age distribution of the sample for both sexes. The pyramid first increases but then tapers off rather steeply in older age groups.

Table I shows the distribution of tobacco habits among men and women. Among women, almost the only tobacco habit prevalent was oral application of *bajar*, practised by 11.6%. Tobacco use was much more common among men (67.6%). A variety of tobacco habits were prevalent, the most common being *bidi* smoking (31.3%), followed by *mawa* chewing (18.9%). Smoking was slightly more popular compared to smokeless tobacco use (35% *v.* 27.7%) with 4.8% reporting both kinds of use. Cigarette smoking was rather uncommon (0.2%).

Among women, the *bajar* habit was concentrated among older age groups whereas among men, smokeless tobacco use was concentrated in the lower age groups (Fig. 2), 76% of all smokeless tobacco users were less than 35 years old.

OSF was diagnosed among 164 men. The age and tobacco habit distribution shows that 70.7% were solely *mawa* chewers and an additional 22% used tobacco in other forms as well (Table II). Only 4 persons (2%) did not report any current areca nut use (they were past users). The disease seemed to be concentrated in lower age groups; 84.1% of the cases were less than 35 years old.

The highest prevalence of OSF was among *mawa* users (10.9%) and the lowest among those who did not use areca nut (0.12%). Compared to no areca nut use the age-adjusted relative risk for any kind of areca nut use was 60.6 (Table III).

Figure 3 shows the age distribution of the prevalence of OSF among men with some kind of tobacco habit and those with smokeless tobacco habit only. Among men with some kind of tobacco habit, the prevalence was high in the lowest age groups (15–19 and 20–24) and then fell sharply. In contrast, among smokeless tobacco users the prevalence fell rather slowly.

TABLE I. Distribution of tobacco habits among men and women

Tobacco habit	Male *n* (%)	Female *n* (%)
Any smoking	3942 (35.0)	16 (0.2)
Bidi	3526 (31.3)	15 (0.1)
Cigarette	19 (0.2)	– –
Pipe	397 (3.5)	1 –
Any smokeless	3124 (27.7)	1242 (11.7)
Mawa	2127 (18.9)	7 (0.07)
Betel quid	171 (1.5)	2 –
Tobacco	799 (7.1)	2 –
Bajar	27 (0.2)	1231 (11.6)
Mixed	544 (4.8)	1 –
Any habit	7614 (67.6)	1265 (11.9)
No habit	3648 (32.4)	9325 (88.1)
Total	11 262	10 590

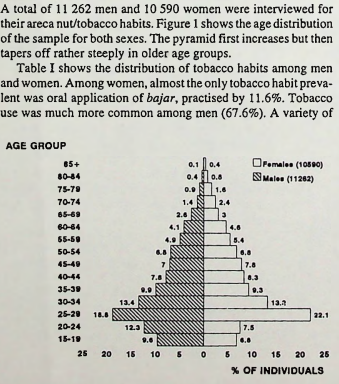

FIG 1. Age and gender distribution of the study population

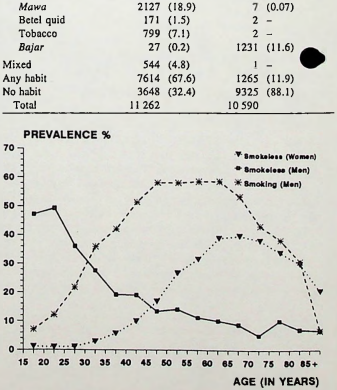

FIG 2. Age distribution of the prevalence of smoking among men and smokeless tobacco use among men and women

TABLE II. Age and tobacco habits of subjects with oral submucous fibrosis

Age (years)	*Mawa*	*Mawa* and others	Areca nut and others	No areca nut	Total
15–24	59	12	2	–	73 (44.5)
25–34	42	16	3	4	65 (39.6)
35–44	9	5	3	–	17 (10.4)
45–54	5	3	–	–	8 (4.9)
55–64	1	–	–	–	1 (0.6)
Total	116	36	8	4	164
	(70.7)	(22.0)	(4.9)	(2.4)	(100)

Figures in parentheses are percentages

TABLE III. Prevalence of tobacco use among subjects with oral submucous fibrosis (OSF)

Areca nut	Users	OSF	Prevalence % (age adjusted)	RR (age adjusted)
No areca nut use	3232	4	0.12 (0.16)	1.0
Areca nut use	1786	160	9.0 (9.7)	60.6
Mawa	1326	144	10.9 (12.1)	75.6
with tobacco	136	2	1.5 (1.5)	9.4
with smoking	324	14	4.3 (5.0)	31.3
Total	5018	164	3.2 (3.3)	

DISCUSSION

The prevalence of OSF in Bhavnagar district is available from a population-based house-to-house survey of 10 071 individuals aged 15 years and older, carried out in early 1967 by the same group of investigators.[13] In that survey, a total of 16 OSF cases were diagnosed; a prevalence of 0.16%. In the current survey carried out in 1993–94, using the same criteria and with one common examining dentist (PNS), 164 OSF cases were diagnosed among 5018 individuals examined with tobacco/areca nut habits; a prevalence of 3.2%. A total of 21 852 individuals were screened and even if we make the most extreme assumption that no OSF existed among the remaining 16 838 non-examined individuals, the prevalence still is 0.75%.

The old and the new prevalence are not equivalent for comparison because of the involved assumptions. Also in the older sample, the villages were selected by random sampling giving a representative sample of the entire district. In the current sample, geographically contiguous villages were selected from one specific *taluka* of the district. No other kind of selection, however, was allowed. Although the examinations were stopped before completing all villages, this is unlikely to have introduced any bias since the villages were not being examined in any specific order. Also, the age–sex distribution of examined individuals was compared with that of the entire screened sample; and these were identical.

It seems unlikely that this sample selection procedure can account for the large difference between the old and the new study since the people studied are from the same district. Such a large difference even on the most unfavourable assumption cannot be an artifact either.

The real difference in the prevalence is higher than apparent at first sight. In the older sample, not a single OSF case was found among men although 5227 were examined out of which 71% were tobacco users.[16] Thus among men, the prevalence increased from zero in 1967 to at least 1.46% in 1993–94 (164 among 11 262 men, again making the extreme assumption of zero prevalence among 6035 non-examined men).

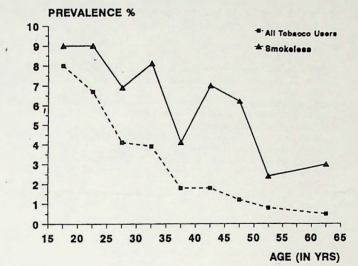

FIG 3. Age distribution of the prevalence of oral submucous fibrosis among all tobacco users and smokeless tobacco users only

Chewing of areca nut has been established as the main causative factor for OSF.[17] The present study shows that the trend in OSF prevalence closely followed the trend in areca nut chewing. The age distribution of OSF cases followed the pattern of smokeless tobacco users rather than that of smokers or the general population. OSF was diagnosed only among areca nut chewers since on detailed questioning, all four patients not using areca nut presently were past users. However, this information was not available for the rest of the sample so no indication regarding the relative risk for past areca nut use was possible. Thus while reconfirming the role of areca nut in OSF, this study also emphasized earlier findings that areca nut chewing in India almost always involves tobacco chewing as well.[18]

The findings in this study point towards an evolving epidemic of OSF in the rural population of Bhavnagar district. OSF is a progressive chronic disease with no known cure, yet 84.4% patients in this population-based study were less than 35 years old and 44.5% less than 25 years. The prevalence of areca nut chewing in the form of *mawa* chewing, followed a very similar pattern. The age-specific prevalence of OSF among smokeless tobacco users demonstrated a close and direct link between the two.

The reasons for this increased prevalence of areca nut chewing and consequent increase in OSF are not hard to locate. Areca nut is the main constituent of all 'pan masala' (betel quid mixture) that may or may not contain tobacco. Unlike for cigarettes, government taxes are low on these products and for 'pan masala' that does not contain tobacco, there is no restriction on advertising. This has led to an enormous increase in the use of all types of areca nut and smokeless tobacco in the Indian population, especially in north India as almost the entire 'pan masala' industry is concentrated in the north.

Thus, the perception of a substantial increase in the incidence of OSF in the north Indian population appears to be real. Given the degree of concomitant tobacco use among areca nut chewers and the high relative risk of malignant transformation of OSF, there is a possibility of an increase in the incidence of oral cancer. The epidemic needs to be stemmed urgently by taking measures to discourage the use of products containing tobacco and/or areca nut.

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Descriptive epidemiology of leukaemias in Greater Mumbai

B. B. YEOLE, D. J. JUSSAWALLA, S. H. ADVANI

ABSTRACT

Background. There is little data available on the occurrence of leukaemias in India. This is despite a large number of patients being diagnosed and treated at various cancer centres all over the country. We, therefore, analysed the available data of the Bombay Cancer Registry to ascertain the epidemiological characteristics of leukaemias in India.

Methods. The incidence and mortality rates of leukaemias by cell type and sex were obtained for the most recent 5 years (1989–93). The data of the past 30 years were used to study the time trends using a linear regression model based on the logarithms of the incidence rates.

Results. Leukaemias constituted 3.9% of all registered cancer cases and 5.4% of all registered deaths in Greater Mumbai. Males were affected more frequently than females. Myeloid leukaemias were the commonest. A bimodal age incidence was observed with the first peak in childhood, a trough bet weer to 19 years of age and a slow rise thereafter. Among the vari religious groups Hindus had the highest rate. An increasing trend in the incidence of all types of leukaemias was also observed.

Conclusion. The incidence of leukaemias in Greater Mumbai is comparable to world rates. There is a male preponderance in all cell types and an increase in incidence was observed over the last 30 years. The higher incidence of myeloid leukaemias observed by us might be related to under-reporting of chronic lymphatic leukaemia.

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INTRODUCTION

Leukaemias are conventionally distinguished by cell type (lymphocytes, myelocytes, monocytes) and clinico-pathological behaviour (acute, subacute, chronic). A comparison of the different subtypes is difficult because of the small number of cases and the varied accuracy of diagnosis, with different proportions remaining unspecified. As a group, leukaemias represent 3% of the world incidence of cancer. There is relatively little variation in the types of leukaemia occurring in different regions of the world. However, some variation in the incidence pattern related to various subtypes has been reported. There have been few reports on the epidemiology of leukaemias from developing countries including India.

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BUSINESS STANDARD (CALCUTTA) 18 APR 1998

Injurious to their health

Will the ban on the Rs 5,000 crore pan masala-gutka industry come through?

In two days from now, a flourishing, Rs 5000 crore industry, directly employing an estimated one lakh workers, could vanish without a trace. On Monday, a top-level meeting in the health ministry will be held to decide the fate of the pan masala and gutka products industry. The first item on their agenda: should this sector be banned on the grounds that its products are injurious to health?

The industry knows it is crunch time. Already the Delhi office of the All India Pan Masala & Tobacco Products Association (AIPMTPA) appears to be under siege. Bharat Thakkar, coordinator, spends most of his time lobbying with politicians, calling up journalists, and soothing the odd panicky industrialist. "We have presented our case to the prime minister," he says, "and politicians including Bansi Lal, Sushma Swaraj and Maneka Gandhi. We are trying to get an appointment with George Fernandes." He adds grimly, "But if this ban is enforced, people have to realise that this is not a question of 400-500 manufacturers. Crores of people depend on us. We will sit in protest outside every Vidhan Sabha in this country with our lakhs of supporters."

A paranoid and belligerent industry is now lashing out at cigarette manufacturers such as ITC and GTC for 'initiating' a sustained misinformation campaign. "According to the market information we possess," says Rasikbhai Dhariwal, president of AIPMTPA, "cigarette manufacturers are behind the move to ban this industry." Dhariwal is the owner of the Rs 350 crore Dhariwal Tobacco Products, India's largest pan masala/gutka manufacturer. "Cigarette manufacturers are running scared because we are eating into their market share."

Whatever the truth of that, there's no doubt that the industry has been caught napping. The case for a ban has been building up for some time now. In mid-1997 the Rajasthan High Court asked the central government to conduct an enquiry into the possible deleterious effects of gutka and pan masala. This order. Thakkar says, initiated the setting up of a committee; and the start of a research campaign in various government laboratories.

The results of the research is being contested heatedly even now. Both the anti and pro-gutka/pan masala lobbies often cite the same report. Those in favour of a ban say that the two products are directly responsible for cancer, especially of the oral tract. Thakkar disagrees vehemently. "No report so far has conclusively proved a causal link," he says. "There is no clear evidence."

But towards the end of 1997 the H Narasimhaiah committee recommended a complete ban on the manufacture, sale, storage and exhibition of gutka and pan masala. By then, also, the anti-gutka/pan masala movement had spread from Maharastra and Gujarat down to the South. In Kerala, for instance, the Cochin municipality banned all advertisement of the two products.

Soon after, in early 1998, and on the basis of the Narasimhaiah report, the Central Committee of Food and Supplies recommended that the health ministry ban all chewing tobacco and gutka products. This month the health ministry made out a notification to that effect. This order was to be signed on April 13.

For the industry it was a bolt from the blue. "We came to know of this notification 10 days ago", says Thakkar. Says an industry official, "It seemed as if the notification was intended to be passed in a clandestine manner. Our opponents did their homework."

The industry has had to learn several new lessons in the past few days. Its biggest weakness sources say, has been an inability to lobby effectively. "We do not have an organised lobby", says Thakkar. According to Dhariwal, "The industry is fragmented, with many local level players. There are at least five to six independent associations. We have been trying to organise more efficiently; the idea of a single association was mooted. But it may take time." Right now there are only two national players, Dhariwal, and the around Rs 300 crore Kothari Products, owned by MM Kothari.

The need to " work together" may be important. It was only last week, under threat of a ban, that the first ever national meet of gutka and masala manufacturers took place in The New Delhi Hotel in the capital. This when the organised sector market has around 400-500 players, with a combined turnover of Rs 2,500 crore (An estimated Rs 2,500 crore comes from the unorganised sector).

The health ministry meeting scheduled for 13 April was postponed by five days. Why this happened is as yet unclear, but sources say that the panicked industry had lobbied hard for the postponement. In the past week, the manufacturers have been trying to come up with a survival strategy. Industry lobbyists met with Atal Bihari Vajpayee to present their side of the case on the 15th. Says Dhariwal: "He did not have much time, but Pramod Mahajan gave us a hearing."

The industry now says that the ban on gutka and pan masala is unfair because it is yet to be proved that these are harmful. "We don't claim it is Chyawanprash," says Dhariwal, "but it is not as harmful as the tobacco lobby is making out. We carry a statutory warning on all our products. Our manufacturing procedures are open to examination by the government. And if gutka and masala are to be banned, so should cigarettes." Says Thakkar: "Cigarettes have a hundred per cent tobacco content; gutka and masala vary between eight and 12. So if you ban us, ban them as well."

The AIPMTPA is also trying to ram home the point that it has greater mass support, and leverage than one would suspect. " At least one crore vendors depend on this industry for their livelihood. We pick up almost 80 per cent, or 2,800 tonnes of the total arecanut produce in India annually. For lakhs of farmers in Karnataka and Assam we are their main source of income. Almost 50 per cent of the packaging industry is dependent on us, as is the attar/perfume sector. We contribute Rs 1,000 crore in excise to the centre and states every year. It isn't going to be that easy to implement a ban."

The solution, the industry says, is to implement uniform manufacturing practices. There is an implicit acceptance that poor quality gutka and masala churned out by the unorganised sector is a real problem. Their solution; allow the industry to organise better, and implement rigid manufacturing practices on even the small manufacturers. "We are ready to talk to the government; but are they?" says Harishbhai Lalwani, owner of Prince Gutka.

For the moment, manufacturers believe they have breathing space. Says Dhariwal: "We understand that the health ministry will not take a decision on the coming Monday. Some more time is required to carry out a comprehensive study of this industry. And, the politicians we have met have assured us that they will not shut down an industry that employs so many people". As a belligerent Lalwani states, "We never said this product is good for your health — it isn't. But I challenge anyone to try and ban it. Pen-pushers and politicians think they can take such decisions. But they will not be able to handle the consequences."

● MANISH KHANDURI

Picture by JAGAN NEGI

As the health ministry squares up to pan masala manufacturers, this could be a thing of the past

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THE TIMES OF INDIA (BOMBAY) 3 MAY 1998

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Leading you up the cancer path

Easy availability of gutka has resulted in oral submucous fibrosis reaching epidemic proportions, writes **Sameera Khan**

MGS

Courtesy: Tata Memorial Hospital booklet

WHEN nine-year-old Kanta, a slum-dweller doing menial household jobs, recently visited the OPD of St George's Government Hospital, Mumbai, she could barely open her mouth.

The culprit: the eight to 10 gutka pouches she had consumed every day over the past year.

The prognosis: Oral submucous fibrosis (OSF) — a disease which causes dense fibrous tissue bands to develop in the oral cavity, thereby damaging the inner lining of the mouth. A progressive disease, it is accompanied by soreness and a burning sensation. Due to atrophy (thinning) of the epithelium (inner lining of mouth), hot and spicy foods cannot be tolerated. The tongue is also affected and speech gets disturbed. Over a period of time, the mouth opening may get so reduced that meals have to be taken through a straw.

Doctors immediately advised Kanta to give up the gutka habit that was threatening not just to close her oral cavity but also increase her risk of getting oral cancer. Unfortunately, Kanta never returned for further treatment or medical advice.

"We are today seeing an increased incidence of OSF in the community, especially among younger people," says Dr Surendra Shastri, professor and head of department of preventive oncology, at Tata Memorial Hospital, Mumbai. "It's due to the easy availability and consumption of gutka and pan masala."

At the Tata Memorial OPD, it's now common to come across students of Class VII and VIII, who consume a minimum of five gutka packets a day, with signs of OSF. "Five years ago, we saw no cases of OSF in this young age group — now we see about four cases in the daily OPD," says Dr Shastri. "Clearly, it's just the tip of the iceberg."

According to Dr Prakash Gupta, senior research scientist, epidemiology unit of the Tata Institute of Fundamental Research, OSF has reached epidemic proportions in India. "In the 1950s, the only cases of OSF were among older people. In the 1990s, the prevalence has increased tenfold," says Dr Gupta. "And 80 per cent of these cases are in the under-35 age group."

The biologically active agents in gutka are tobacco — with the addictive nicotine — and arecanut. Regular chewing of these substances causes OSF. A recent TIFR population-based survey in villages around Bhavnagar, Gujarat, reveals that one in 30 of those who chew gutka (tobacco and arecanut) are prone to OSF. "The situation is alarming because there are no accepted lines of treatment for OSF, except for some surgical interventions to relieve the painful symptoms," says Dr Gupta.

Gutka also puts a person at risk for gingivitis (inflammation and recession of the gums) and pre-cancerous lesions such as leukoplakia (white patch) and erythroplakia (reddish patch) on the inner lining of cheek.

"Gutka also causes narrowing of the blood vessels which can lead to serious heart problems," says Dr J. Peter Rodrigues, honorary head of department of ENT at St. George's Hospital. "But what's really alarming is that when left unchecked, OSF can cause oral cancer."

Already oral cancer tops the list of cancers suffered by Indian men and ranks third among Indian women. About 1,00,000 Indians suffer annually from it. "Our greatest concern is that we will see a lot more cases of oral cancer in the future," says Dr Gupta. "The risk of developing oral cancer is 400 times higher among patients of OSF as compared to patients without OSF."

According to estimates at St. George's Hospital, 7.6 per cent cases of OSF finally get oral cancer.

Even those who chew non-tobacco pan masala are at risk. TIFR studies have revealed that OSF is more a result of the arecanut than the tobacco present in gutka. Besides, most non-tobacco pan masala chewers eventually move over to gutka.

"The only way to stop OSF and avoid the risk of oral cancer is to stop eating gutka," says Dr Rodrigues. But giving up the dangerous habit is a tough process and many former addicts complain of withdrawal symptoms, including craving, irritation, and lack of concentration.

"It's hard to give it up. Nicotine is habit-forming," says Dr Shastri. "We have a de-addiction programme at the Tata Memorial Hospital for tobacco and gutka-users but our success rate is as low as 12 per cent."

Still, there are those like Salma who for two years chewed five gutka packets a day. "I thought it was a mouth freshner but then I got addicted to it and couldn't do without it," she recalls. "When my mouth started burning and gradually closing, I was terrified. I made myself give up gutka completely. It was such a wise decision." One, that a lot more people in this country need to make.

'First ban cigarettes'

Banning chewing tobacco will drive the industry underground, activate the mafia, and increase smuggling, M. M. Kothari of Pan Parag tells **Sakina Yusuf Khan**

What do you have to say about the proposed ban on gutka and tobacco chewing products?

It is most unwarranted, and unfair to say the least. Chewing tobacco is part of our tradition. Our *raja-maharajas* and *sadhu-sants* patronised it from time immemorial. There was never any opposition to it. But today some vested interests are trying to impose this ban. In any case, there is no scientific basis for it.

How can you say that? It has been widely reported that the proposed ban was mooted to safeguard public health. It is also believed that these products are carcinogenic.

That's not true. Smoking tobacco is far more harmful than chewing tobacco. If the government is really serious about people's health, it should first ban cigarettes, which have been proved to cause lung cancer. Passive smokers are also affected. There is no such danger with chewing tobacco.

Besides, the government cannot impose a ban without conducting a proper epidemiological study that definitively links oral cancer with tobacco chewing. The clinical studies on oral submucous fibrosis patients carried out so far are not enough evidence.

If it's not health, what other reason could the government possibly have for proposing this ban? After all, it will lose Rs 1,000 crore in excise duty and Rs 300 crore as sales tax.

True, it will be losing a lot of revenue. But it is contemplating the ban because of pressure from powerful multinational tobacco companies. These companies want to destroy this domestic industry and and capture the market.

Do you think the industry might go underground if the ban is implemented?

It certainly will, thereby making it even more hazardous as there will be no quality control. Smuggling across the border will also increase. Since cultivation of tobacco cannot be stopped with one sweeping legislation, chewing tobacco will become a commodity in the hands of the mafia.

In any case, bans never work. Prohibition in Andhra and Haryana and their subsequent withdrawal prove the inefficacy of such shortsighted legislation.

If incentives are given to switch to other businesses within a reasonable time-frame, would you find that acceptable?

We are not worried for ourselves. Most of us (the 300-odd gutka manufacturers in the country) have other businesses alongside. We are fighting for the 10 crore tobacco and arecа-nut farmers, processors, silver beaters, perfumeries, packers transporters and pan-shop owners who will be adversely affected by this ban. Can the government guarantee alternative employment for all of them?

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PAAN MASALA

A New Way to Die?

Recent studies show India's favourite condiments are heightening the risks of an oral-cancer epidemic. Doctors want an urgent restriction on sales and advertising.

By SAMAR HALARNKAR

EVER EATEN DINNER WITH A straw? Anil Vaswani does. Slowly, the 36-year-old hardware store owner sucks in a bowl of bland, watery gruel. His mouth is no more than the size of a large button; the muscles have tightened into hard bands of tissue, no longer so flexible as to open wide enough to swallow the *samosas* and *dhoklas* he loves so much. Through his unnaturally pursed lips, Vaswani painfully tries to explain how he came to be this way. All that emerges is an incomprehensible mumble.

Vaswani has an extreme case of submucous fibrosis, a silent ailment that is spreading like wildfire through India. Far more frightening than struggling to keep your mouth open, submucous fibrosis is often a precursor to oral cancer—victims have a 400 times greater risk of getting this cancer than a normal person—a disease that literally eats away your face and ends, inevitably, in a slow, lingering death.

New evidence confirms what scientists long suspected: the disease springs from those pint-sized, silver-foil or plastic sachets of *paan masala*—a powdery mixture of arecanut (*supari*), lime, betel nut and a few other ingredients—and its relative, *gutka*. A study done jointly by the Regional Cancer Centre and the John Hopkins University in the US shows that 19 out of 22 popular *paan masala* brands (*see graphic*) have mutagens, substances that can transform ordinary human cells into uncontrolled cancers.

Paan masala is a 1990s icon of Indian society. It's convenient to carry and available anywhere—in the remotest villages and even in medical stores. Film stars like Vinod Khanna, Shammi Kapoor and Ashok Kumar promote it with glee, little realising they may be endorsing a message of death.

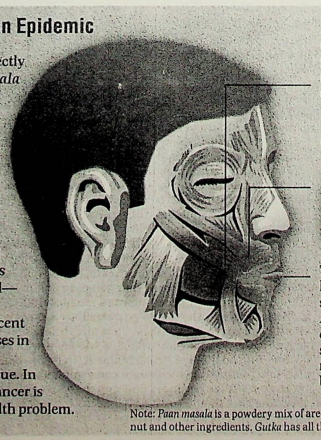
"We are observing a big epidemic of submucous fibrosis across India," says Dr Prakash Gupta, an epidemiologist at the Tata Institute of Fundamental Research (TIFR) in Mumbai, who has studied the deleterious effects of *paan masala* for more than two decades. "We are now afraid we will see an epidemic of oral cancer in the near future." *Gutka* (it contains tobacco; *paan masala* may or may not have tobacco) creates cancer in half the time that cigarettes take to do so, warn doctors. The cancer breaks out any time from five to 10 years after the advent of submucous fibrosis.

Oral cancer already accounts for 10 per cent of all cancer cases, drastically different from the West where such cancers rarely occur. If *paan masala*'s pro-

Graphic by JAI

Genesis of an Epidemic

New studies directly indict *paan masala* and *gutka* for causing submucous fibrosis (SMF), an incurable, irreversible disease. Victims are 400 times more at risk of contracting oral cancer—death is slow and painful—than a normal person. Ten per cent of all cancer cases in India affect the mouth and tongue. In the West, oral cancer is not a public health problem.



Arecanut triggers the synthesis of collagen, a tough, fibrous protein that stiffens the muscles of the mouth. The mouth size shrinks. In extreme cases, only a button-size opening is left.

The epithelium (skin cells) atrophies. As the skin wastes away, carcinogens like tobacco act easily. In traditional *paan*, the leaf prevents direct contact between the ingredients and the skin.

The tongue loses its rough outer layer and becomes smooth and white. An SMF patient cannot consume spices, and is reduced to eating bland food.

Note: *Paan masala* is a powdery mix of arecanut, lime, betel nut and other ingredients. *Gutka* has all these and tobacco.

liferation is not checked, doctors fear the deadly disease will begin peaking in numbers after its incubation period is over, around the turn of the century.

The submucous fibrosis epidemic—it runs into uncounted millions—is a phenomenon directly related to the exploding consumption of *paan masala*. "There is incontrovertible evidence of the link," says Gupta. "*Paan masala* must be considered a hazardous product."

An unpublished TIFR study in Gujarat shows just how the contagion has taken hold. In 1967 TIFR scientists found that one in 800 people had submucous fibrosis; today the incidence has skyrocketed to one in 30. Other kinds of tobacco use also cause the disease, but nine out of 10 of the victims in Gujarat are users of *paan masala*.

Little wonder. The *paan masala* industry has grown from an estimated Rs 200 crore in 1992 to well over Rs 1,000 crore today. There are no restrictions on advertising, no standards and no testing protocols. The warning is microscopic and often absent: "Chewing of *paan masala* is injurious to health." And that's in English, a language alien to most *paan masala* consumers.

Disturbingly, many of the brands may not contain their prime ingredient, *paan*, or betel nut. They contain only the *masala*, which is an amalgam of ingredients, many unknown, says Dr Babu Mathew, professor of community oncology, Regional Cancer Centre, Thiruvananthapuram. The flavouring agents are trade secrets (the packet only names major ingredients), but the two main known disease-causing agents are tobacco and arecanut.

A number of recent studies from India and Pakistan confirm that arecanut is the main cause of submucous fibrosis, inducing the production of a protein that cripples the mouth's muscles. That finding undermines a great social tradition: for the last 500 years, *supari* has not only been chewed but also forms an important part of religious rituals, from pujas to marriages.

"Anything taken in excess is harmful, even *gulab jamuns* and chocolate," says M.M. Kothari, manufacturer of India's largest selling brand, Pan Parag.

"If you thought smoking was bad, this is deadly. *Paan masala* is even killing children."

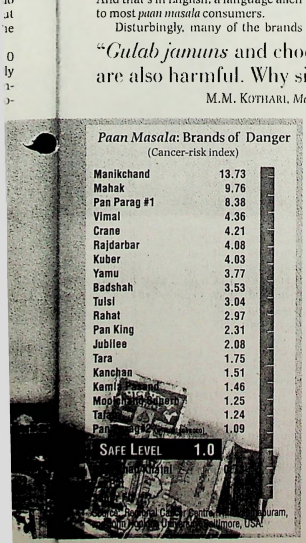
SUCHETAN PRADHAN, *Prosthodontist, Mumbai*

"*Gulab jamuns* and chocolates taken in excess are also harmful. Why single out *paan masala*?"

M.M. KOTHARI, *Manufacturer, Pan Parag*

***Paan Masala*: Brands of Danger**
(Cancer-risk index)

Manikchand	13.73
Mahak	9.76
Pan Parag #1	8.38
Vimal	4.36
Crane	4.21
Rajdarbar	4.08
Kuber	4.03
Yamu	3.77
Badshah	3.53
Tulsi	3.04
Rahat	2.97
Pan King	2.31
Jubilee	2.08
Tara	1.75
Kanchan	1.51
Kemi[illegible]	1.46
Mod[illegible]	1.25
Taj[illegible]	1.24
Pan[illegible]	1.09
SAFE LEVEL	1.0



Source: Regional Cancer Centre, Thiruvananthapuram, and Johns Hopkins University, Baltimore, USA.

and the father of the modern *paan masala* industry. He freely admits that *gutka* is harmful, but points to the statutory warning carried on the packs. Kothari, who's built a multi-crore *paan masala* empire from scratch in the last decade, says, "We have no objection to a ban, but then the Government must stop cigarettes too." He knows that is unlikely to happen in a hurry.

Despite the overwhelming evidence of the damage that *paan masala* is causing, the Government is clearly hesitant to act against a powerful commercial lobby. "*Paan masala* manufacturers are growing rich at the expense of our lives," Maharashtra Health Minister Daulatrao Aher declared before the state Assembly earlier this year. A vociferous advocate of a ban on *paan masala*, Aher can do little until the Centre acts—and there's no immediate sign of any restrictions being imposed.

Two years ago, the Rajasthan High Court asked the Health Ministry to examine the carcinogenicity of *paan masala*. A committee constituted by the Directorate-General of Health Services is currently reviewing papers on the subject. Officials say animal studies have been cleared to test the carcinogenicity of *paan masala* ingredients, but they haven't yet begun. None of this is required, say researchers, who accuse the Government of ignoring all available evidence against the concoction.

Meanwhile, the *paan masala* rage is spreading, especially among the Indian middle class and the rich. One reason is that *gutka* is a form of tobacco that's socially acceptable. As Kothari says, "A son can offer *gutka* to his father, but he cannot offer a cigarette." Most worrying, say doctors, is *gutka*'s gleeful adoption by the young: some chewers are no more than six years old. "*Paan masala* is killing them," says an agitated Dr Suchetan Pradhan, a prosthodontist who has been witnessing a "tremendous" increase in submucous fibrosis among his patients in his upmarket Mumbai clinic. "If you thought smoking was bad," says Pradhan, "this is deadly."

The *paan masala* craze has hugely displaced traditional *paan* chewing, which ended up as red, dribbly spittle splattered on walls and pavements. Most new victims are below 35 years of age. Even the south, traditionally a *paan masala*-free area, has succumbed. "At least a dozen boys below 17 (suffering from submucous fibrosis) have been registered as outpatients at our hospital," says Mathew. "The youngest is 11 years old and he used to consume at least six packets a day."

Forget about a ban. It hasn't happened with cigarettes, and it won't happen with *paan masala*. But what the Government can do is to first ensure that *paan masala* is not freely advertised and promoted as it is today on the media, especially television, which reaches into the Indian hinterland. Manufacturers use a loophole that frees non-tobacco products from advertising restriction like cigarettes. "But the *paan masala* sold has tobacco ... there must be no advertising or promotion," says Gupta.

The Government can also make consumption unattractive by simply slapping hefty taxes on *paan masala*. The money can then be used on spreading the message about its dangers—none of that is done today. There are no taxes on it, and the little sachets cost only a couple of rupees. Unless at least this much is done, millions of Indians could be reduced to sustaining their lives at the end of a straw—and adding on another way to die. ■

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Mawa chewing and oral submucous fibrosis in Bhavnagar, Gujarat, India

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Mawa is an areca-nut preparation containing tobacco and lime. Its use is very popular among the youth in Bhavnagar. Recently, there has been an increased occurrence of submucous fibrosis in this area. A case-control study on submucous fibrosis in Bhavnagar showed a relative risk of 109.6 for all forms of areca-nut use, 106.4 for *mawa* chewing and 780.0 for chewing *mawa* as well as betel quid (*pan*). The relative risks increased with the increase in the duration and frequency of areca-nut chewing; a bivariate analysis also showed a multiplicative effect. Clinically, submucous fibrosis in Bhavnagar differed in regard to age, sex and location distribution from cases in Ernakulam. These variations could be due to the differences in the type of areca-nut chewing in these areas — *mawa* chewing in Bhavnagar and betel-quid chewing in Ernakulam. The findings raise several research questions and indicate a need for public health measures against areca-nut containing products.

INTRODUCTION

Submucous fibrosis is a precancerous condition. The malignant potential of this condition is due to the atrophic epithelium that is often seen in submucous fibrosis and the action of carcinogens in tobacco upon it (1). Several factors, namely, the use of chillies (*Capsicum annum* and *Capsicum frutescens*) and nutritional deficiency states, were thought to be involved in its pathogenesis. Current epidemiological evidence highlights areca-nut (*Areca catechu*) chewing as an etiological factor in this condition (2-4).

A marked increase in the occurrence of submucous fibrosis has been seen recently, especially among the young, in Bhavnagar, Gujarat. This increase corresponds to the increasing popularity of *mawa* chewing in the population, especially among the youth. *Mawa* is a preparation containing thin shavings of areca nut with the addition of some tobacco and slaked lime (see paper by Bhonsle *et al.*, this volume). A case-control study was conducted to investigate the association between *mawa* and other forms of areca-nut chewing and oral submucous fibrosis (5). In this paper we describe some of the findings from that study and the differences in the clinical characteristics of the disease associated with *mawa* chewing in Bhavnagar and that with betel-quid (*pan*) chewing in Ernakulam district, Kerala.

MATERIAL AND METHODS

Submucous fibrosis was diagnosed on the basis of the presence of palpable fibrous bands, as per the standardized criteria (6) (see paper by Murti *et al.*, this volume). The case-control study was conducted in a dental clinic in Bhavnagar among 60 consecutive dental patients diagnosed with submucous fibrosis. Controls matched for age, sex, religion and

socioeconomic status were selected from among patients attending the same clinic who showed no evidence of oral submucous fibrosis or any other tobacco-associated oral mucosal lesion or condition. Prior to their examination, information on the type of areca-nut chewing, forms of tobacco use and other relevant information was recorded. All cases were photographed in colour.

The clinical features recorded in Bhavnagar were compared with those of 64 cases of submucous fibrosis reported earlier (3) from various population-based studies in Ernakulam district, which is about 2000 km south of Bhavnagar.

RESULTS

An overwhelming majority (97%) of the 60 individuals with submucous fibrosis in Bhavnagar were men; some 79% of these were under the age of 35 years.

There were no marked differences in the smoking habits between the cases and controls, implying that smoking is not an etiological agent in this condition.

Table 1 gives the relative risks for different types of areca-nut chewing habits. All cases occurred among people who were regular chewers of areca nut in one form or another, except one who was an occasional chewer. The overall relative risks were 109.6 for areca-nut chewing, 106.4 for *mawa* chewing and 780.0 for chewing *mawa* and betel quid.

Table 2 gives the relationship between the duration of chewing and its frequency per day. The relative risks increased with duration and frequency of the habits.

Table 3 shows the results of a bivariate analysis of the dose-response relationship according to duration and frequency. A multiplicative effect between duration and frequency of the chewing is clearly seen.

Table 4 shows the age and sex distribution of submucous fibrosis cases in both areas. Most of the (79%) individuals in Bhavnagar were in the age range 15-34 years, while in Ernakulam 94% were aged 35 years and over. This condition occurred overwhelmingly (97%) among men in Bhavnagar, whereas only 18% of cases were in men in Ernakulam.

Table 5 shows the location of submucous fibrosis in the mouth in the two areas. The buccal mucosa was affected more or less

Table 1

Association of submucous fibrosis with chewing habits[a]

Chewing habits	Cases		Controls		Relative risk
	No.	%	No.	%	
No habit	1[b]	2%	39	65%	1.0
Areca nut (no *mawa*)[c]	5	8%	7	12%	29.9**
Areca nut (no tobacco)[d]	4	7%	2	3%	78.0**
Mawa	30	50%	11	18%	106.4**
Mawa (with others)[e]	20	33%	1	2%	780.0**
Overall	60	100%	60	100%	109.6**

[a]Source: ref. (5)
[b]Occasional areca-nut chewer
[c]Betel quid with tobacco; betel quid without tobacco + tobacco-lime
**$p<0.01$
[d]Including betel quid without tobacco
[e]Mostly betel quid with tobacco

Table 2

Relationship between duration of chewing (in years), frequency of chewing (per day) and occurrence of submucous fibrosis[a]

Chewing habit	Cases		Controls		Relative risk
	No.	%	No.	%	
Duration (in years)					
1-5	17	29%	10	47%	1.0
6-10	16	27%	5	24%	1.9
≥11	26	44%	6	29%	2.5
Frequency (per day)					
1-5	16	27%	10	47%	1.0
6-15	37	63%	10	48%	2.3
≥16	6	10%	1	5%	3.8
Total	59	100%	21	100%	

[a]Source: ref. (5)

Table 3

Dose-response relationship between chewing habits and submucous fibrosis[a]

Frequency of chewing (per day)	Duration of chewing					
	≤5 years			>5 years		
	Cases	Controls	RR	Cases	Controls	RR
≤5	7	6	1.0	10	4	2.1
>5	11	4	2.3	33	7	4.0

[a]Source: ref. (5)

Table 4

Age and sex distribution of submucous fibrosis patients in Bhavnagar and Ernakulam districts

Age (years)	Bhavnagar	Ernakulam[a]
15-24	13 (22%)	—
25-34	34 (57%)	4 (6%)
35-44	10 (17%)	17 (27%)
≥45	3 (5%)	43 (67%)
Mean age	29.1	51
Sex		
Men	58 (97%)	18 (28%)
Women	2 (3%)	46 (76%)
Total	60 (100%)	64 (100%)

[a]Source: ref. (3)

equally in both areas, but its involvement in Bhavnagar was generally restricted to the posterior one-third (Fig. 1). In Ernakulam, there was a more generalized involvement of the buccal mucosa. The disease was clinically advanced in Bhavnagar and less severe in Ernakulam. Retromolar areas (100%), soft palate (95%) and the uvula (55%) were very frequently affected in Bhavnagar (Fig. 2), but less frequently in Ernakulam. The tongue and the floor of the mouth were involved in 59% and 22%, respectively, in Ernakulam, whereas in Bhavnagar they were either not involved or the involvement was negligible.

Seven individuals with this condition in Bhavnagar were siblings from three families. No similar observation was made in Ernakulam district.

Table 5

Location distribution of submucous fibrosis in Bhavnagar and Ernakulam districts

Location	Bhavnagar (n=60)		Ernakulam* (n=64)	
	No.	%	No.	%
Labial mucosa	30	50%	41	64%
Buccal mucosa	59	98%	62	97%
Retromolar area*	60	100%	14	22%
Hard palate*	—		12	19%
Soft palate*	57	95%	8	12%
Uvula*	33	55%	5	8%
Tongue*	1	2%	38	59%
Floor of the mouth*	—		14	22%

*Source: ref. (3)
*$p<0.01$

DISCUSSION

This paper demonstrates that *mawa* and areca-nut chewing in various forms are strongly associated with the occurrence of submucous fibrosis in Bhavnagar and that this disease exhibits specific regional variations in its clinical characteristics.

The upsurge of the *mawa* habit is a recent phenomenon in Bhavnagar. This habit, with some minor variations and under different names, is widely prevalent in other parts of Gujarat and also elsewhere in India. The high relative risks for different areca-nut chewing groups, observed for the first time, are consistent with other epidemiological observations which implicate areca-nut chewing in the pathogenesis of this condition. For example, Bhonsle *et al.* demonstrated in a review that 34-100% of individuals with submucous fibrosis chewed areca-nut in various forms (3). This habit was observed to be much more prevalent among the cases than in the general population (2), and the prevalence (7) and the incidence rates (8) were higher among areca-nut (betel-quid) chewers (see paper by Murti *et al.*, this volume). In the present study, chewing areca-nut alone, i.e., *supari* (see paper by Bhonsle *et al.*, this volume), was observed in 8% of cases in Bhavnagar; but this habit was practised by 67% of submucous fibrosis patients in Pune reported in an earlier study (3).

The above observations demonstrated a strong association of this condition with areca-nut chewing; similarly, a 10-year prospective intervention study showed a fall in the incidence of submucous fibrosis (4). In this study the annual incidence per 100 000 dropped from 21.3 among men and 45.7 among women in the control cohort to 8 and 29 in the intervention cohort, respectively. These findings also support the etiological role of areca-nut chewing in this condition.

It has been suggested that there might be a genetic susceptibility to areca-nut alkaloids and tannins in individuals with this disease (9,10). In this context, it must be noted that seven individuals with this condition were siblings from three families, sharing perhaps the same genetic predisposition and similar exposure to areca-nut chewing.

Submucous fibrosis exhibits notable regional differences in its age and sex distribution and its clinical characteristics; such variations are attributable to differences in areca-nut chewing practices in different areas (3). Similar observations were made in this investigation. The contiguous involvement of the posterior one-third of the buccal mucosa, retromolar areas (Fig. 1), soft palate and uvula (Fig. 2) in Bhavnagar could be due to the habit of keeping the *mawa* quid in the posterior part of the mandibular groove. In Ernakulam, exposure of the buccal mucosa to the betel quid is generalized; this may be responsible for the more diffuse involvement of the buccal mucosa.

Fig. 1. Involvement of posterior one-third of the buccal mucosa and retromolar area in a *mawa* chewer

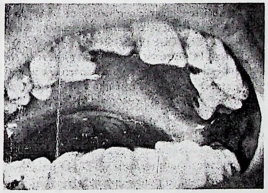

Fig. 2. Involvement of retromolar areas, soft palate and the uvula in a *mawa* chewer

Long-term studies on malignant transformation rates of submucous fibrosis among betel-quid chewers show that (see paper by Murti *et al.*, this volume) the mean age (51 years) of individuals with this condition in Ernakulam was higher than that in Bhavnagar (29 years). Correspondingly, the mean age of individuals with this condition who developed oral cancer (7.6%) in Ernakulam was 64.6 years (11). In view of the very low mean age (29 years) of the patients in Bhavnagar, it would be important to find out whether they develop oral cancer at an earlier age. It would also be important to know whether submucous fibrosis among areca-nut chewers with no concurrent tobacco use develops into oral cancer.

The health hazards of tobacco use are well recognized; consequently, tobacco control measures are receiving priority. While epidemiological studies have revealed no significant risk for oral cancer associated with areca-nut chewing (12), this habit certainly appears to be involved in the pathogenesis of oral submucous fibrosis, which is itself often a progressive disease with a burning sensation and dryness of the mucosa, with no effective cure. Furthermore, a recent study demonstrated a high relative risk (397.3) for oral cancer associated with this condition (13).

The popularity of areca-nut containing preparations such as *pan masala* (see paper by Bhonsle *et al.*, this volume) has increased tremendously within the last few years owing to a very sophisticated marketing campaign. In view of the serious consequences of submucous fibrosis and the etiological role of areca-nut chewing, a strict curb on the advertisement and use of these products is warranted.

Acknowledgments

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Tobacco-related cancers in Bombay, India: a study of incidence over two decades

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A study of the site-specific incidence rates of cancers of the upper alimentary and respiratory tracts over two decades among males in Bombay showed that the incidence of cancers of the tongue, oropharynx and larynx have decreased significantly, whereas that of oral cancer excluding the tongue has remained more or less stable. The incidences of cancers of the hypopharynx, oesophagus and lung increased only marginally, but successive birth cohorts showed no consistent pattern. Limited data on tobacco habits in Bombay indicate a marked decrease in the proportion of *bidi* smokers in younger cohorts, which conforms with the observed decline in the incidence of those cancers for which *bidi* smoking is the predominant risk factor. For cancers of the hypopharynx, oesophagus and lung, for which tobacco chewing or cigarette smoking is an equally or more important risk factor than *bidi* smoking, no consistent pattern was seen. Tobacco-related cancers constitute about 50% of cancers among men in India. As the recent national trends in *per-caput* consumption of tobacco are different from those in Bombay, the decline in predominantly *bidi* dependent cancers seen in Bombay cannot be extrapolated to the country as a whole. Consequently, control programmes are needed for all smokers in the country and especially for cigarette smokers in urban areas.

INTRODUCTION

Tobacco is a major risk factor for cancers of the upper alimentary and respiratory tracts, which constitute about 50% of all cancers among Indian men. This paper examines the trends in the incidence of these cancers over the years.

TRENDS IN TOBACCO-RELATED CANCERS

Data on site-specific incidence of cancer are available from the Bombay Cancer Registry for a period of over two decades (1,2), making it possible to assess trends in tobacco-related cancers. When the age-adjusted incidence rates for these cancers in five-year periods between 1964-82 (except 1964-66, which is a three-year period) were examined, the incidence of cancer of the tongue declined progressively, from 14 per 100 000 in the early 1960s to 9.7 per 100 000 in the period 1978-82, while those of cancers of other parts of the mouth remained more or less stable over the years, with an age-adjusted incidence rate of about 7 per 100 000 (Table 1). The rate for cancer of the oropharynx declined from 6.1 per 100 000 to 3.5 per 100 000 over the years, the decline being marked in the late 1970s and early 1980s. The incidence of cancer of the hypopharynx and oesophagus, however, increased from 7.3 to 10.0 per 100 000 and from 13 to 15 per 100 000, respectively. The age-adjusted incidence rate for cancer of the larynx declined from 13.8 to 10.1 per 100 000, whereas that for cancer of the lung increased marginally from 13.3 in the 1960s to 15.8 per 100 000 in the 1980s.

A clearer picture of changing incidence rates was obtained for each site by fitting a

Table 1

Site-specific age-adjusted incidence rates for cancers at major tobacco-related sites in males in Bombay, 1964-82

Site of malignant neoplasm	Age-adjusted incidence rate (world) per 100 000 per year			
	1964-66 (ref. 1)	1968-72 (ref. 2)	1973-77	1978-82
Oral cavity				
Tongue	14.0	12.6	10.2	9.7
Mouth (all other parts)	7.0	7.3	6.7	7.5
Pharynx				
Oropharynx	6.1[a]	5.6	4.5	3.5
Hypopharynx	7.3	7.7	8.7	10.0
Digestive organs				
Oesophagus	13.0	15.2	14.7	15.0
Respiratory organs				
Larynx	13.8	13.6	12.4	10.1
Lung	13.3	13.5	14.7	15.8
All sites	139.5	143.1	142.1	147.4

[a]ICD 7, 145: tonsils and oral mesopharynx

log-linear polynomial of the first order, which is the usual model for analysing trends in cancer incidence (3). The average percentage change in incidence was obtained and the significance tested by Student's *t* test.

For cancers of the tongue, oropharynx and larynx, the average percentage changes in incidence were -4.39, -3.73 and -3.16, respectively, and these were highly significant (Fig. 1). For cancers of the hypopharynx, oesophagus and lung, the average percentage changes were 1.23, 0.95 and 0.05, respectively, and these were not significant (Fig. 2).

The decline in incidence of cancers of the tongue, oropharynx and larynx has been reported to be due to a cohort effect, younger five-year birth cohorts in general having lower rates than older cohorts (4). However, for cancers of the hypopharynx and oesophagus, no clear pattern was discernible; for lung cancer, there seemed to be no cohort effect at all (Fig. 3).

We considered that a synoptic measure of the experience of each birth cohort would lead to better appreciation of the risk differentials between birth cohorts. On examining the age ranges for which the incidence data were available for each cohort, it was found that each cohort had two overlapping 15-year age intervals: one common to the five-year younger cohort and the other, common to the five-year older cohort. For example, the 1933 birth cohort had the age range 30-44 years common to the 1938 birth cohort and the age range 35-49 years common to the 1928 birth cohort (Fig. 4). Hence, a synoptic measure of risk in each birth cohort could be obtained by estimating the cumulative rate as defined by Day (5) over an appropriate age range. Accordingly, cumulative rates over an age range common to the five-year older or younger cohort were used to assess the risk differentials between adjacent cohorts.

A diagrammatic representation of cumulative rates in pairs of adjacent cohorts for the same age range is given in Figure 5 (4). It was observed that for cancers of the tongue, oropharynx and larynx, in each of the pairs of

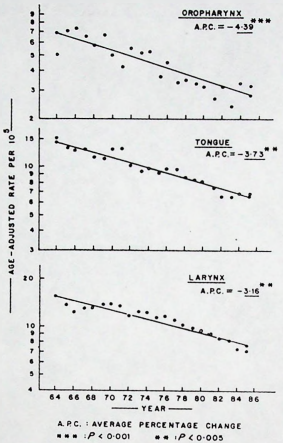

Fig. 1. Trends in age-adjusted incidence rates for cancers of the oropharynx, tongue and larynx in Greater Bombay, 1964-85

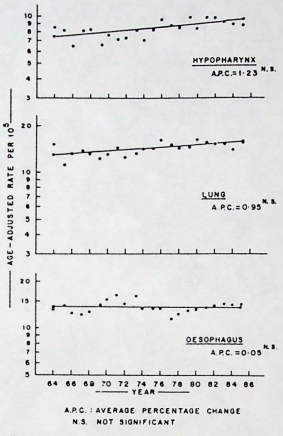

Fig. 2. Trends in age-adjusted incidence rates for cancers of the hypopharynx, lung and oesophagus in Greater Bombay, 1964-85

birth cohorts, the younger cohort had a lower cumulative rate. However, for cancers of the hypopharynx, oesophagus and lung, the pattern was not consistent; only cohorts born after 1928 seemed to have rates lower than those of five-year older cohorts, but for those born before 1928 the successive five-year younger cohorts had either similar rates or showed a reversal (i.e., younger cohorts having higher rates).

INTERPRETATION OF TRENDS

The observed changes in the incidence rates are not likely to be artefacts, as various indices have shown that the data of the Bombay Cancer Registry are reliable (6). This changing pattern, therefore, needs to be viewed on the basis of changing exposure to etiological factors. For that purpose, it is essential to know the risk factors for cancers at each of the sites, the associated risk ratios and the prevalence of risk factors in the population over the years. It must be pointed out that most Indian oncologists pool cancers of the base of the tongue with cancers of the oropharynx, as it has been found that the clinical behaviour, prognosis and etiology of cancers of the base of the tongue are similar to those of

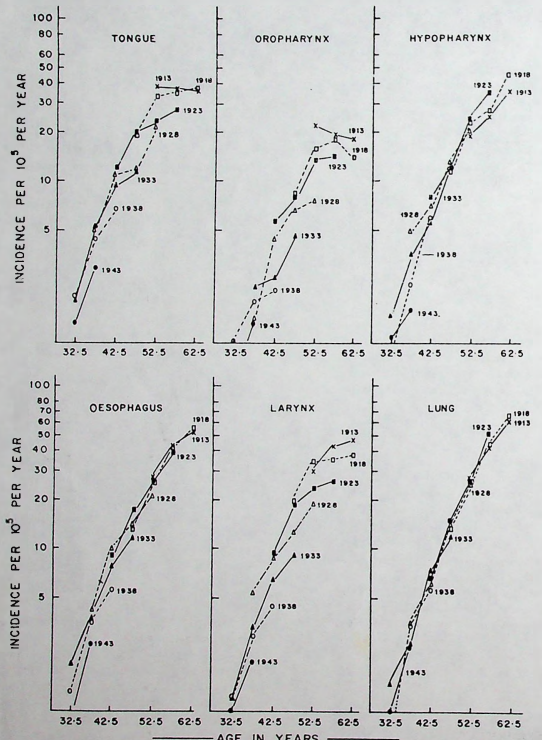

Fig. 3. Age-specific incidence of cancers of the tongue, oropharynx, hypopharynx, oesophagus, larynx and lung in cohorts born between 1913 and 1943

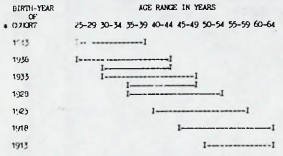

Fig. 4. Age ranges for which incidence data are available for various birth cohorts

oropharyngeal cancer (7). This practice is in contrast to the international classification, in which the entire tongue used to be grouped under one rubric. In Bombay, almost 75% of lingual cancers occur at the base of the tongue. It is therefore justifiable to consider that the risk ratio for cancer of oropharynx inclusive of the base of the tongue is appropriate for cancers of both the tongue and oropharynx.

The risk ratios obtained in a Bombay study for smokers and chewers as compared to nonusers of tobacco (8) are shown in Table 2. In this study, smokers who were predominantly *bidi* smokers had strikingly higher risks of cancers of the oropharynx, including the base of the tongue (11.8) and larynx (7.7), than chewers (3.3 and 4.6, respectively). In contrast, chewers had a higher risk for cancers of the oral cavity (excluding the base of tongue) and hypopharynx (6.0 and 6.2, respectively). Smokers and chewers had similar risks for oesophageal cancer. Risks for oral, pharyngeal and laryngeal cancers specifically among cigarette smokers are not available from India. Two studies in the west showed that the risk ratios for oral cancers in cigarette smokers were about 1.5 (9) and 3 (10); the risk for cancers of the pharynx taken as a group was not significantly higher in smokers (11); for cancers of the larynx, the ratio was between 3 and 6, depending on the frequency of cigarette smoking (12).

It is interesting that *bidi* smokers have a much higher risk of cancers of the oropharynx and larynx compared to cigarette smokers. For cancer of the lung, *bidi* and cigarette smokers in Bombay had two- to three- fold higher risks (13). Furthermore, *bidi* smoking and tobacco

Table 2

Risk ratios in smokers and chewers for tobacco-related cancers[a]

Site of cancer	Type of tobacco usage[b] S	C	SC	CgS
Oral cavity excluding base of tongue	2.8	6.0	10.1	1.5-3.0
Pharynx				NS
Oropharynx, including base of tongue	11.8	3.3	31.7	
Hypopharynx	3.6	6.2	16.9	
Oesophagus	2.2	2.5	6.2	
Larynx	7.7	4.6	20.1	3-6[c]
Lung (*Bidis*)	3.4			10-15
(Cigarettes)	2.4			

[a]Calculated from data in refs. (8-13)
[b]S, smoker; C, chewer; SC, smoker-chewer; CgS, cigarette smoker
NS, not significant
[c]Risk ratios here refer to western studies

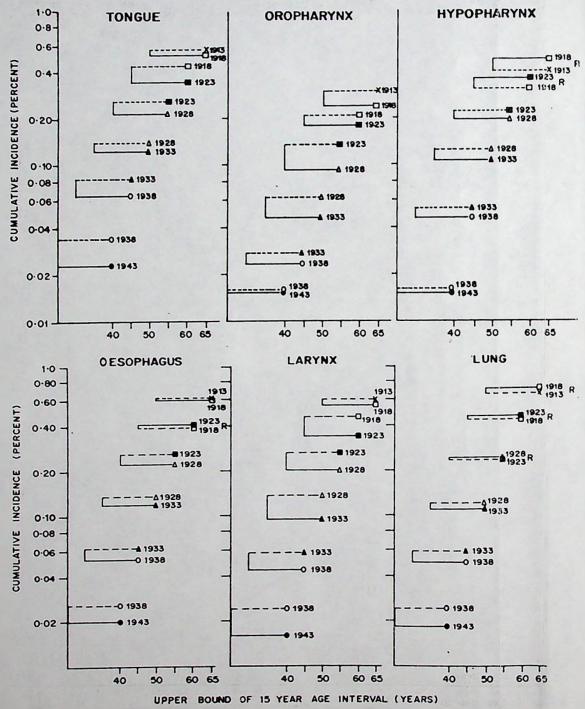

Fig. 5. Cumulative incidence rates over two overlapping 15-year age ranges for cancers of the tongue, oropharynx, hypopharynx, oesophagus, larynx and lung for various birth cohorts

chewing were found to be major risk factors for oral cancers and for cancers of the pharynx and larynx, and the risks attributable to tobacco usage were high, varying between 70 and 85%, depending on the site (14). Thus, the observed changes in incidence rates probably reflect the changes in tobacco usage that occurred in this population some 20 years ago. Data on the prevalence of tobacco usage in the population of Bombay over the years are not available to fully substantiate this hypothesis. An attempt to estimate the pattern of tobacco usage was made by considering limited data on prevalence by age available from a cohort study on blue-collar workers carried out in the 1970s (15). By approximating the habits in different age groups to the habit pattern in the corresponding birth cohorts, trends in the habits of cohorts born between 1921 and 1936 were assessed. These were used to interpret the cancer experience of cohorts born between 1913 and 1943.

Examination of the patterns in various birth cohorts showed a marked decrease in *bidi* smoking and a moderate increase in cigarette smoking in successively younger birth cohorts (Fig. 6). The pattern for those with dual habits, i.e., *bidi* smoking with tobacco chewing and cigarette smoking with tobacco chewing, is similar to that of people with the single habit of

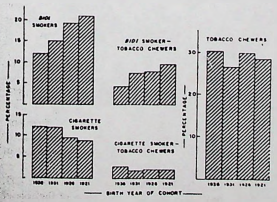

Fig. 6. Proportions of smokers and chewers in cohorts born between 1936 and 1921 (blue-collar workers in Bombay)

smoking. This situation would lead to successive younger birth cohorts having lower incidence rates of cancers in which *bidi* smoking is the dominant risk factor. This may explain the trends in the incidence rates of cancers of the tongue, oropharynx and larynx, which are the major *bidi*-related cancers in this analysis.

Tobacco chewing remained more or less stable in various birth cohorts; and the incidence of oral cancer, excluding the tongue, for which tobacco chewing is the dominant risk factor, was also stable over the years. For lung cancer, for which both *bidi* and cigarette smoking are risk factors, and hypopharyngeal cancer, for which chewing is a more important risk factor than smoking, it is difficult to explain the lack of consistency in the pattern in successive birth cohorts; it is probably due to the paucity of data. Perhaps, detailed data on a representative sample of the entire population would provide a plausible explanation. For oesophageal cancer, the risk attributable to tobacco was only 50% (14), and no explanation of the trend (or rather lack of it) can be given solely on the basis of the prevalence of tobacco usage.

In order to assess whether the trends observed continue in the same direction, the latest five-year data were considered. Interestingly, the incidence rates for cancers of the oropharynx and larynx have stabilized, at about 3.5 and 10 per 100 000, respectively.

FUTURE CANCER PATTERN IN THE COUNTRY

The pattern of tobacco-related cancers expected for the country as a whole on the basis of estimates of *per-caput* consumption of raw tobacco of different types, obtained from data published by the Ministry of Agriculture, is at variance with what was actually observed in Bombay (16,17). For instance, during the period 1951-81, the *per-caput* consumption of *bidi* tobacco increased from 145 to 191 g and that of cigarette tobacco from 55 to 115 g.

Table 3

Estimated per-caput *consumption of raw tobacco (in grams) in India*[a]

Tobacco type	1951-52	1960-61	1970-71	1980-81
Bidi	145	168	155	191
Cigarette	55	97	133	115
Chewing	140	143	94	54
Total	556	566	474	541

[a]Calculated from data in refs. (16, 17)

Consumption of chewing tobacco, however, decreased from 140 to 54 g (Table 3). The possible implications are that the incidences of *bidi*-related cancers, i.e., cancers of the tongue, oropharynx and larynx, are unlikely to show a decline in the near future. There is thus an urgent need to institute tobacco control programmes especially directed to all smokers in the country, with special emphasis on cigarette smokers.

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Oral health consequences of tobacco use in Ernakulam district, Kerala, India

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Bidi smoking and betel-quid (*pan*) chewing are the most common forms of tobacco use in Ernakulam district. They are strongly associated with oral cancer, various precancerous lesions and conditions, and others which do not seem precancerous. Nodular leukoplakia and submucous fibrosis are a very high-risk precancerous lesion and condition, respectively; other clinical types of leukoplakia also indicate a significant risk for oral cancer. Malignant transformation was not associated with leukoedema, leukokeratosis nicotina palati, palatal erythema, central papillary atrophy of the tongue, *pan*-chewer's lesion or oral lichen planus-like lesion. Most of these oral lesions remained stationary, some regressed and few recurred; submucous fibrosis, however, did not regress. Overall, tobacco use was found to influence the entire natural history of precancer, indicating the need to implement tobacco control measures.

INTRODUCTION

Ernakulam district in the State of Kerala, is on the south-western coast of India. In 1966, at the time of initiation of our epidemiological studies, the district had an area of 3340 km^2 and a population of 1 859 913 (1961 census). *Bidi* smoking and betel-quid (*pan*) chewing are the main forms of tobacco use in this area (see paper by Bhonsle *et al.*, this volume). In this paper we describe the oral health consequences of these forms of tobacco use on the basis of various epidemiological studies conducted over the past 24 years.

MATERIAL AND METHODS

Three main studies were conducted in Ernakulam district (Table 1). Phase 1 was a cross-sectional study among 10 287 villagers aged 15 years and over in 14 *karas* (*kara* is a smallest sampling unit) selected by random sampling (1). Some 59% of these individuals were tobacco users. Phase 2 was a 10-year prospective study of those examined in phase 1 (2). Phase 3 was an intervention trial in a new sample of 12 212 tobacco users in 23 *karas* (3). It consisted of a base-line survey and a 10-year follow-up of these individuals. An additional survey was carried out among 5099 people in five *karas* in the Parakadavu area (4), and people with lesions and matched controls were followed-up annually.

Prior to examination, the frequency of tobacco use, i.e., the number of times per day

Table 1

Main studies conducted in Ernakulam district

Studies	Population (no.)	Tobacco users (%)
Phase 1 and 2 (1966-77)	10 287	59%
Phase 3 (1977-88)	12 212	100%
Parakadavu survey (1971)	5 099	55%

an individual smoked or chewed tobacco, the duration of such habits and other relevant details were recorded by trained interviewers. Examinations were conducted in a house-to-house approach, and selected oral lesions were recorded as per standardized criteria (1,5). All lesions were photographed in colour at the initial diagnosis and subsequently whenever necessary. Several hundred oral lesions were biopsied, and smears were obtained for cytological examination as per the requirement of the particular survey.

LESIONS ENCOUNTERED

Almost all of the oral lesions were observed only among tobacco users. In this paper, the lesions can be grouped broadly as shown below on the basis of their frequency in groups with different habits.

Predominantly associated with smoking: (i) leukoedema; (ii) leukokeratosis nicotina palati; (iii) palatal erythema; and (iv) central papillary atrophy of the tongue

Predominantly associated with chewing: (i) *pan*-chewer's lesion; (ii) oral lichen planus-like lesion; and (iii) oral submucous fibrosis

Associated with smoking and chewing (mixed habit): (i) leukoplakia and preleukoplakia; (ii) oral lichen planus; and (iii) oral cancer

LESIONS PREDOMINANTLY ASSOCIATED WITH SMOKING

As mentioned earlier, *bidi* smoking is the most popular smoking habit, especially among men in this area. Overall, 17% of the 10 287 individuals examined in phase 1 smoked *bidis* (1).

Leukoedema: This is a chronic mucosal condition in which the oral mucosa has a grey, opaque appearance (Fig. 1) as though a greyish film were hanging over it like a veil. When the mucosa is stretched the lesion disappears, only to reappear when it is relaxed.

Epidemiology: The prevalence of leukoedema was 0.4%. About 16 (62%) of the 26

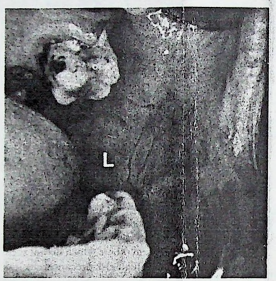


Fig. 1. Leukoedema (L) in the buccal mucosa of a *bidi* smoker

leukoedemas were seen among *bidi* smokers and the rest in people who smoked and chewed (1). The annual age-adjusted incidence rate of this lesion was 2.5 per 1000; it was 3.8 per 1000 among smokers (2).

Histological features: Leukoedema was characterized by accumulation of spongy vacuolated cells in the superficial epithelial layer, ballooning cells in the stratum spinosum and epithelial hyperplasia (6).

Natural history: Of the 87 leukoedemas (includes incidence lesions) followed-up over a 10-year period, 64% remained stationary and 36% regressed; no malignant transformation was observed (2).

Leukokeratosis nicotina palati: This lesion which is commonly seen among conventional smokers, consists of a greyish-white palate with small nodular excrescences having small central red dots, corresponding to the inflamed orifices of the minor salivary glands (Fig. 2).

Epidemiology: The prevalence of this lesion was 0.3%; 52% of the 31 lesions occurred among *bidi* smokers (1). The annual age

Fig. 2. Leukokeratosis nicotina palati in a *bidi* smoker

adjusted incidence rate among smokers was 1.7 per 1000; it was 0.7 per 1000 in those who smoked and chewed (2).

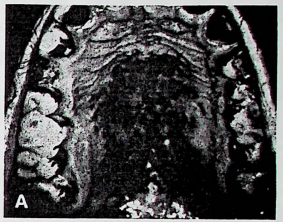
Natural history: Over a 10-year period, 66% of the 44 lesions remained stationary, 34% regressed spontaneously and none showed malignant transformation (2).

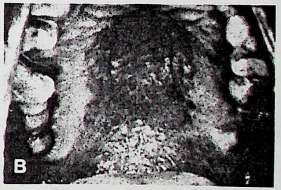
Leukokeratosis nicotina palati observed among conventional smokers must be distinguished from the palatal changes associated with reverse *chutta* smoking (see paper by Daftary *et al.*, this volume). Palatal changes in reverse smokers are multimorphic and precancerous, whereas leukokeratosis nicotina palati exhibits neither great variability nor malignant transformation.

Palatal erythema: Palatal erythema is marked by a diffused erythematous hard palate (Fig. 3A), occasionally extending to the soft palate.

Epidemiology: Of the 69 lesions observed among 7216 tobacco users (Table 2), 87% occurred among smokers, especially *bidi* smokers. This lesion was observed in only three women, which corresponds to the low prevalence of *bidi* smoking among women.

Clinical aspects: The lesion occurred either independently or sometimes with other lesions.





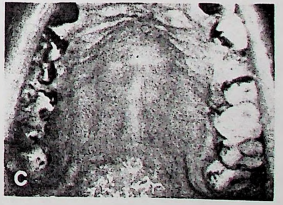


Fig. 3A. Palatal erythema in a *bidi* smoker

Fig. 3B. Palatal erythema with papillary hyperplasia in a *bidi* smoker

Fig. 3C. Regression of palatal erythema shown in *Fig. 3A*, following discontinuation of smoking; note loss of pigmentation

Table 2

Distribution of individuals with palatal erythema according to habit and sex

Habit	Men (n=6978)	Women (n=238)	Total (n=7216)
Smoking	58 (88%)	2 (67%)	60 (87%)
Smoking & chewing	8 (12%)	1 (33%)	9 (13%)
Total	66 (100%)	3 (100%)	69 (100%)

About 10% of the lesions were associated with palatal papillary hyperplasia (Fig. 3B) and 25% with central papillary atrophy of the tongue and bilateral commissural leukoplakias. This triad of lesions is comparable to the 'multifocal candidiasis' described in western literature (7).

Natural history: Over a 10-year period, 35% of the 69 lesions persisted, 56% regressed and 9% were transient, i.e., they regressed, recurred and regressed again (Table 3). Interestingly, the highest percentage (60%) of persistent lesions was seen among people who did not give up their smoking habits, while the highest percentage (75%) of regressed lesions occurred among those who discontinued or reduced smoking substantially (Fig. 3A and C). Most of the transient lesions were associated with inconsistent habit practices, i.e., among those who stopped their habits, restarted and stopped. These observations clearly indicate that palatal erythema is caused by smoking, particularly *bidi* smoking.

Central papillary atrophy of the tongue: This lesion has also been described in the literature as median rhomboid glossitis and localized atrophy of the tongue papillae (1). It consists of a well-defined, oval, pink area in the centre of the dorsum of the tongue devoid of lingual papillae (Fig. 4A).

Epidemiology: The prevalence of this lesion was 1%; it was present among 2.2% *bidi* smokers, 1.6% cigarette smokers and 0.3% nonusers of tobacco (1). In the 10-year follow-up study, the annual age-adjusted incidence rate among smokers was 1.5 per 1000 as compared to 0.8 per 1000 among nonsmokers (2).

Etiology: Central papillary atrophy of the tongue, is considered to be due to candidal infection, smoking or both (8). In this study, central papillary atrophy exhibited a strong association with smoking, particularly *bidi* smoking. This was exemplified by its higher prevalence (1) and incidence rates (2) among smokers, its long-term behaviour in relation to the cessation or reduction of smoking (see below) and the observation that 87% of the lesions occurred among *bidi* smokers (8). Interestingly, very few women had this lesion, due perhaps to the rarity of smoking among women.

Table 3

Behaviour of palatal erythema according to change in tobacco use over a 10-year period

Palatal erythema	Tobacco use: Unchanged/ increased		Reduced/ stopped		Not constant		Total	
	No.	%	No.	%	No.	%	No.	%
Persistent	15	60%	9	23%	—		24	35%
Regressed	9	36%	30	75%	—		39	56%
Transient	1	4%	1	2%	4	100%	6	9%
Total	25	100%	40	100%	4	100%	69	100%

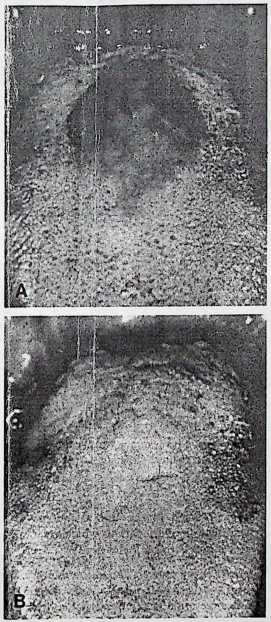


Fig. 4A. Central papillary atrophy of the tongue in a *bidi* smoker

Fig. 4B. Regression (repapillation) of the lesion shown in *Fig. 4A* following discontinuation of *bidi* smoking

Clinical aspects: Most of the 182 lesions studied were pink to dark-pink, oval or elongated; some were rhomboid or irregular (8). The mean length was 2.7 cm and the breadth, 1.3 cm. They were generally smooth, but some were fissured. In 69% of cases the lesion occurred independently; 14% had coexistent palatal erythema and 8% had leukoplakia. A triad of central papillary atrophy, bilateral commissural leukoplakia and palatal erythema, comparable to the 'multifocal candidiasis' described in western literature (7) was seen in 3% of cases. The remaining occurred with other lesions. Central papillary atrophy of the tongue must be distinguished from the atrophic candidiasis reported among people with human immunodeficiency viral infection (9).

Histological features: This lesion was marked by the absence of tongue papillae, the presence of slight parakeratinization of the epithelial surface, long slender reteridges and occasional pseudocarcinomatous hyperplasia. Chronic inflammatory cell infiltrate, chiefly of lymphocytes, was usually present within the epithelium and in the lamina propria. In a single periodic acid-Schiff section study of 12 biopsies, candidal hyphae were observed in 67% (8).

Natural history: Some 50% of the 182 lesions that were observed for 10 years were persistent (8), 43% regressed, i.e., repapillated, 5% regressed and recurred and 2% showed inconsistent behaviour (regressed, recurred and regressed). The highest percentage (65%) of persistent lesions was found among people who did not stop or reduce their habits, while the highest percentage (87%) of regressed lesions (Fig. 4A and B) was seen in those who stopped their habits. None of the lesions progressed to cancer.

LESIONS PREDOMINANTLY ASSOCIATED WITH BETEL-QUID CHEWING

Tobacco was most often chewed as an ingredient in betel quid (*pan*) by 33% of the women

and 35% men in Ernakulam district (see paper by Bhonsle *et al.*, this volume). Betel-quid chewing inevitably stains the mucosa bright red, due to the formation of *o*-quinone from water-soluble polyphenols, notably, leucocynidins, at the alkaline pH of 8-9 *via* secondary reactions (10). These stains can be washed clean or disappear with abstinence from chewing; however, it is not unusual to see persons with perpetually stained mucosa.

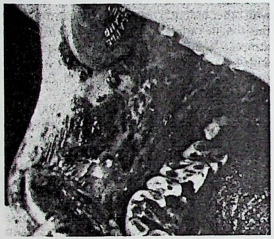


Fig. 5. Pan-chewer's lesion

Pan-chewer's lesion: This lesion consists of a thick brownish-black encrustation on the buccal mucosa (Fig. 5) at the site of placement of the betel quid. It was often seen among heavily addicted betel-quid chewers. It could be scraped off with a piece of gauze; it regresses spontaneously, more frequently when the habit is discontinued.

Epidemiology: The annual age-adjusted incidence rate of this lesion was 28 per 1000 among male chewers and 17.4 per 1000 among female chewers (2).

Histological features: These lesions showed pale-staining parakeratin-like surface layers of epithelium, containing round nuclear remnants, ballooning and vacuolated cells and epithelial hyperplasia.

Natural history: *Pan*-chewer's lesion is a specific entity and rarely progresses to leukoplakia. Over a three-year observation period, 26% of the 532 observed lesions were persistent, 45% regressed spontaneously and 29% recurred; malignant transformation was not observed in these lesions (2).

Oral lichen planus-like lesion: A characteristic lesion consisting of white, wavy, parallel, non-elevated striae that do not crisscross (Fig. 6A) (as in lichen planus) was observed. Sometimes, these striae radiate from a central erythematous area (Fig. 6B) at the site of placement of the betel quid.

Epidemiology: The prevalence of this lesion among 5099 individuals in Parakadavu was 0.7% (4). About 89% of the lesions occurred among betel-quid chewers and 11% among people with mixed habits. In a 10-year follow-up study of 10 000 villagers in Ernakulam district, the annual age-adjusted incidence rates among men and women were 0.7 and 2.2 per 1000, respectively (2). The peak incidence for women was in the 45-54-year age group. The incidence was zero among smokers and non-users of tobacco; 4.3 per 1000 among women who chewed. This lesion is thus entirely associated with betel-quid chewing.

Clinical aspects: The striae seen in these lesions were very fine, like fingerprints, and always occurred in the buccal mucosa and mandibular groove, locations which are in intimate contact with the betel quid.

Histological features: The lesion shows parakeratinized atrophic epithelium, liquefaction degeneration of the basal-cell layer and a band-like inflammatory cell infiltrate containing lymphocytes and plasma cells (4). Unlike lichen planus, this lesion shows hyperparakeratosis, and plasma cells in the juxtaepithelial region.

Natural history: A total of 42 lesions were followed-up for four years: 79% remained stationary, 21% regressed and two of the

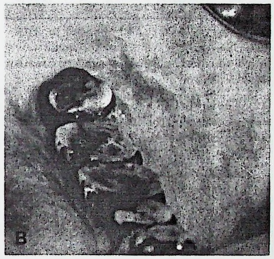


Fig. 6A. Oral lichen planus-like lesion in buccal mucosa

Fig. 6B. Radiating striae from a central erythematous area at the site of placement of betel quid

nine regressed lesions recurred (2). Although the histological features were similar to those of oral lichen planus, in view of its complete association with betel-quid chewing, it is regarded as a specific entity.

Oral submucous fibrosis: This is a chronic oral mucosal condition marked by rigidity of the mucosa of varying intensity (Fig. 7) due to fibro-elastic transformation of the juxta-epithelial layer, resulting in progressive inability to open the mouth (Fig. 8). When the tongue is involved, it is shrunken and hard (Fig. 9), with restricted mobility. Occasionally,

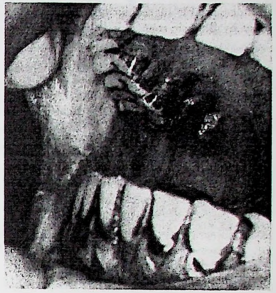


Fig. 7. Buccal mucosal involvement with blanching in oral submucous fibrosis

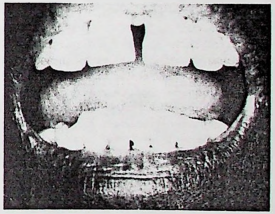


Fig. 8. Limited oral opening in submucous fibrosis; also shows shrunken tongue with impaired protrusion

pharyngeal and oesophageal involvement have also been observed. Submucous fibrosis occurs predominantly among Indians, Indians settled abroad and to a lesser extent in other Asiatics. Areca-nut *(Areca catechu)* chewing in any form is currently believed to be the primary etiological agent for this condition (11-13) (see also paper by Sinor *et al.*, this volume); areca nut is

an indispensable ingredient of betel quid (see paper by Bhonsle *et al.*, this volume).

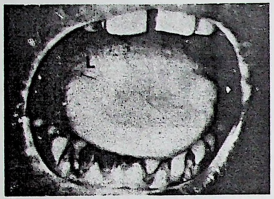


Fig. 9. Involvement of the tongue marked by absence of lingual papillae and restricted protrusion; note a homogeneous leukoplakia (L) on the dorsum and loss of pigmentation from the vermilion borders

Epidemiology: The prevalence (1,14) and the incidence (2) rates of submucous fibrosis are high in Ernakulam district as compared to other areas of India. The overall prevalence was 351 per 100 000; it was highest (1090 per 100 000) among betel-quid chewers (Table 4). The annual age-adjusted incidence rate was 7 per 100 000 among men and 17 per 100 000 among women (2); all new cases occurred among betel-quid chewers. The prevalence rates seem to be too high in comparison with the incidence rates because this condition does not regress like other precancerous lesions.

Clinical aspects: Submucous fibrosis affects people of each sex, but a definite female predominance was observed in Ernakulam (2,14), which was related to the extent of areca-nut (betel-quid) chewing (12). For example, in this area, most of the betel-quid chewers were women, so there were more women with this condition. Submucous fibrosis occurs in the age range 20-40 years, with some regional variation; for instance, the mean age of individuals with this condition in Pune was lower (37 years) than that in Ernakulam (51 years)

Table 4

Prevalence of oral submucous fibrosis according to tobacco habit[a]

Habit	No. examined	Prevalence	
		No.	Per 100 000
No habit	4 210	2[b]	48
Smoking	2 272	—	—
Chewing	2 661[c]	29	1090
Mixed	1 106	5	452
Total	10 249	36	351

[a]Source: ref. (1)
[b]Past chewers
[c]38 individuals who chewed *pan* without tobacco not included

(12). The age of individuals with this condition may also depend on the type of areca-nut chewing habit and the age at initiation of the habit.

Submucous fibrosis commonly affects the buccal mucosa (Fig. 7), retromolar areas and soft palate. The frequency of their involvement varies, however, with geographic area, depending on the type of areca-nut chewing (12). The earliest and commonest sign of this condition is blanching (15), which imparts a marble-like appearance to the mucosa. When the disease is fully developed, palpable fibrous bands develop in the buccal mucosa, soft palate and rima oris; they run vertically in the buccal mucosa and are circular around the rima oris. As the disease progresses, the mucosa becomes stiff and the oral opening may be restricted. Petechial spots resulting from the breakdown of connective-tissue support of the vasculature were observed in 11% of cases in one study (16). Submucous fibrosis is often associated with leukoplakia (Fig. 9), oral cancer and pigmentation changes (14). Most patients complain of a burning sensation, often aggravated by spicy food and excessive or decreased salivation.

Histological features: The most common histological features of this condition are

epithelial atrophy with juxtaepithelial hyalinization and collagen of varying density. A notable feature was the presence of epithelial dysplasia in 26% of cases (17).

Natural history: Unlike other precancerous lesions, submucous fibrosis does not regress, either spontaneously or with discontinuation of the habit. The most serious aspect of this condition is its precancerous nature (18). In a 17-year follow-up of 66 cases, oral cancer had developed in 0.4% of cases at the end of 10 years (2), 4.5% at the end of 15 years (17) and 7.6% at the end of 17 years (19). In an eight-year follow-up study of 25 cases, the relative risk of malignant transformation for submucous fibrosis, compared to that of tobacco users without any oral mucosal lesion or condition, was 397.3 (20).

Primary prevention: As mentioned above areca-nut chewing in any form is involved in the pathogenesis of this condition. There is no effective cure, so far, for this condition. Discontinuation of all forms of areca-nut and tobacco use would probably limit the extension of this disease and prevent malignant transformation. Stoppage of betel-quid chewing would probably lead to a decrease in the incidence of submucous fibrosis (21). This approach assumes great importance in view of the upsurge in *mawa* and *pan masala* usage in the country (see papers by Bhonsle *et al.*; Sinor *et al.*, this volume).

LESIONS ASSOCIATED WITH SMOKING AND CHEWING

The combined habit of smoking as well as chewing tobacco, mostly in betel quid (*pan*), was practised overall by 11% of the 10 287 individuals (1); almost all of them were men.

Leukoplakia: Leukoplakia, literally means a white patch. It was hypothesized initially as precancerous mainly because of its co-existence with oral cancer; it has a similar intraoral location as that of oral cancer. Leukoplakia is defined as a raised white patch of oral mucosa measuring 5 mm or more, which cannot be scraped off and which cannot be attributed to any other diagnosable disease. This definition does not carry any histological connotation (5).

Epidemiology: The prevalence of this lesion in Ernakulam district was 17 per 1000; it was highest (61 per 1000) among people with mixed habits (Table 5). The annual age-adjusted incidence rate was 2.1 per 1000 among men and 1.3 per 1000 among women; the highest incidence (6.0 per 1000) was among men who both chewed and smoked (2).

Table 5

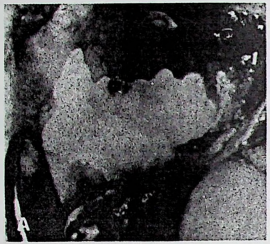
Prevalence of leukoplakia according to tobacco habit[a]

Habit	Total no.	Prevalence	
		No.	per 1000
No habit	4 210	8	2
Smoking	2 272	48	21
Chewing	2 661[b]	47	18
Mixed	1 106	67	61
Total	10 249	170	17

[a]Source: ref. (1)
[b]38 individuals who chewed *pan* without tobacco not included

Almost all leukoplakias in India occur in tobacco users. A definite dose-response relationship between leukoplakia and various forms of tobacco use in this area has been demonstrated (22). The dose-response relationship was stronger for smoking habit than for the chewing habit and remained significant after taking account of age, sex and type of tobacco habit.

Clinical aspects: Leukoplakias are classified into (i) homogeneous; (ii) ulcerated; and (iii) nodular types (5). Homogeneous leukoplakia is characterized by a raised formation of plaques or groups of plaques varying in size, with irregular edges (Fig. 10A). The lesions are predominantly white but may also be



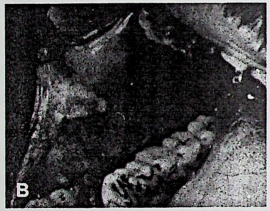


Fig. 10A. Homogeneous leukoplakia

Fig. 10B. Ulcerated leukoplakia

Fig. 10C. Nodular leukoplakia

greyish-yellow. Ulcerated leukoplakia consists of an area of ulceration sometimes surrounded by keratinized areas, pigmentation or both (Fig. 10B). Nodular leukoplakia shows many small white nodules on a erythematous base (Fig. 10C). Some 75% of the leukoplakias in this region were homogeneous, 20% ulcerated and 5% nodular leukoplakias (5). The risk for cancer varies with clinical type of leukoplakia (Table 6).

Leukoplakias occur from the age of 20 onwards. For men, the incidence increases steadily from the age of 20; for women, however, the peak incidence is in the age range 50-60 years, after which there is a drop (2). Most (88%) leukoplakias are located on the buccal mucosa, commissures and tongue (5). Ulcerated leukoplakias are associated with *bidi* smoking and are generally located in the commissures, whereas homogeneous leukoplakias associated with *bidi* smoking occur on the commissures and anterior part of the buccal mucosa; those associated with betel-quid chewing and mixed habits are often situated on the posterior part of the buccal mucosa. As mentioned above, in some instances commissural leukoplakias among *bidi* smokers occurred with palatal erythema and central papillary atrophy of the tongue, a triad comparable to the 'multifocal candidiasis' reported in western literature (7).

Histological features: Leukoplakias associated with betel-quid chewing showed hyperorthokeratosis in 82% and hyperparakeratosis in 12%; those associated with mixed habits of smoking and chewing showed hyperorthokeratosis in 63% and hyperparakeratosis in 23% (1). Overall, epithelial dysplasia was observed in 8%; nodular leukoplakias accounted for 71% of dysplastic leukoplakias. In a study of 723 leukoplakias in different areas of India, 14% showed superimposed candidal hyphae (23); nodular leukoplakias showed the highest frequency of candidal hyphae.

Natural history: Of the 225 leukoplakias studied over a 10-year period, cancer developed in 4% cases, 47% remained stationary, 42% regressed and 7% recurred (2).

Table 6

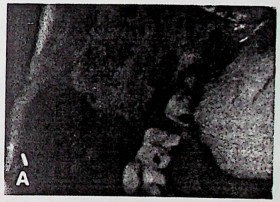
Relative risk for malignancy associated with various precancerous lesions and conditions[a]

Precursor lesion/ condition	Total no.	Average follow-up period (years)	No. of oral cancers	Transformation per 100 000 per year	Relative risk
Nodular leukoplakia	13	2.8	6	16 216.2	3243.2
Submucous fibrosis	25	6.0	3	1 986.7	397.3
Others[b]	26	2.6	1[c]	1 515.2	303.0
Ulcerated leukoplakia	105	4.4	1	218.8	43.8
Homogeneous leukoplakia	489	4.8	3	128.1	25.6
Lichen planus	344	3.7	1	78.9	15.8
None of the above	10 145	7.8	4	5.0	1.0

[a]Source: ref. (20)
[b]Includes nonspecific diagnoses, such as red area, ulcers and benign growth
[c]Preceding lesion, red area

Malignant transformation was most frequent (21%) in nodular leukoplakias (Fig. 11A and B), as compared to 2% in homogeneous leukoplakia (2). In another study (Table 6), nodular leukoplakia showed the highest relative risk (3243.2) among all precancerous lesions and conditions for developing into oral cancer, as compared to the risk for people with tobacco habits but no oral lesion.

Preleukoplakia: This lesion can be considered a precursor lesion to leukoplakia. It consists of a low-grade or very mild reaction of the mucosa, appearing as a grey or greyish-white but never completely white area with a slight lobular pattern and indistinct borders blending into the adjacent normal mucosa (5). The prevalence of this lesion was 2.4%; it was seen more often among people who chewed and smoked (5). The annual age-adjusted incidence rate was 3.1 per 1000 among men and 0.2 among women; the incidence was highest (5.6 per 1000) among men who smoked and chewed (2); of the 309 preleukoplakias followed-up over a 10-year period, 15% progressed to leukoplakia and two cases to cancer.



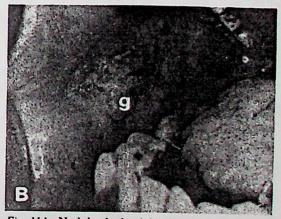


Fig. 11A. Nodular leukoplakia in the buccal mucosa

Fig. 11B. Exophytic growth (g) that developed in the lesion shown in *Fig. 11A*

Oral lichen planus: Oral lichen planus is primarily a dermatological disorder. Various mucosal surfaces may be involved in this condition, either independently, concurrently with cutaneous involvement or serially. Oral mucosa, however, is, more frequently affected mucosal location. Oral lesions are suspected to possess some cancer potential. Interestingly, in our study oral lichen planus was found to be strongly associated with tobacco habits.

Epidemiology: The overall prevalence of oral lichen planus was 1.5%; it was highest (3.7%) in those people with mixed habits and lowest (0.3%) in nonusers of tobacco (24). The annual age-adjusted incidence rate was 2.1 and 2.5 per 1000 among men and women, respectively. It was highest (8.2 per 1000) among men who smoked as well as chewed tobacco; among women it was highest (4.5 per 1000) in chewers (2). The relative risk for oral lichen planus was highest (13.7) among those who smoked and chewed tobacco (25).

Clinical aspects: Oral lesions are diagnosed on the basis of presence of Wickham's striae. Oral lichen planus occurred predominantly among women. The buccal mucosa was the most favoured location. Oral lichen planus occurred in diverse morphological forms such as reticular, annular, linear, erosive or ulcerated and pigmented forms; of these, 20% were erosive or ulcerated lesions (24) and about 11% were associated with pigmentation (26).

Histological features: Sixty lesions were studied microscopically and epithelial atrophy was observed in 82%, hyperortho or hyperparakeratosis in 90%, and Civatte bodies in 78%. Band-like juxtaepithelial inflammatory cell infiltrate was present in all biopsies (24).

Natural history: Most oral lesions persisted; some regressed and recurred. The regression rates were highest in nonusers of tobacco and lowest in people with mixed habits (2). The malignant potential of this condition was assessed in 722 affected individuals (27): over a 10-year period (mean, 5.1 years), oral cancer developed in three patients (0.4%) who had erosive (atrophic) lesions; all of them used tobacco. In an eight-year follow-up study of 344 individuals with oral lichen planus (20), the relative risk for malignant transformation was 15.8 (Table 6); this, did not, however, attain the 5% significance level. Overall, the high prevalence and incidence rates among tobacco users as well as its natural history strongly support the hypothesis that tobacco does play an important role in this condition.

Oral cancer: The term oral cancer is used in this paper to denote squamous-cell carcinoma, which comprises over 95% of all oral malignancies in Kerala. This disease is the most serious oral health consequence of tobacco use. Earlier hospital-based studies showed oral cancer to be the most frequent cancer in Kerala (28,29). More recent data from the National Cancer Registry show that among all cancers, oral cancer ranks first and third among men and women, respectively (30).

Epidemiology: In a cross-sectional study of 10 287 individuals in Ernakulam district, 12 oral cancers were diagnosed (117 per 100 000) (1); six were diagnosed among 2661 (225 per 100 000) betel-quid chewers and six among 1106 (542 per 100 000) with mixed habits. Although there was a substantial number of (4210) nonusers of tobacco and (2272) *bidi* smokers in this study, no oral cancer occurred among them.

In a 10-year follow-up study of 10 000 individuals, the annual-age adjusted incidence rate of oral cancer was 16 per 100 000; the incidence was highest (32 per 100 000) among people with mixed habits (2). Interestingly, although there were substantial person-years of observation, none of the cancers occurred among nonusers of tobacco or *bidi* smokers. The average age of *bidi* smokers in this study was low (31.2 years), as compared to 52.1 years for male chewers, and 43.8 years for males who smoked and chewed (1); this perhaps explains the absence of oral cancers among *bidi* smokers. Tobacco chewing and smoking are recognized as causal factors for oral cancer (31-33). Thus, the occurrence of oral cancer exclusively among tobacco users in Ernakulam substantiates the hazardous nature of tobacco.

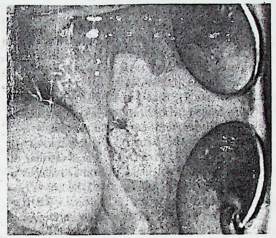


Fig. 12. Exophytic squamous-cell carcinoma in the buccal mucosa with an associated leukoplakia

Clinical aspects: Oral cancer is predominantly a disease of the elderly. For example, the average age of oral cancer patients, although based on small numbers, was 55 years (1). The age-specific incidence rates (2) showed that the peak occurrence of 57 per 100 000 per year was among people aged 55 years and above.

Oral cancer occurred more often among men. The buccal mucosa was the most frequently involved location in this region, and it often co-existed with leukoplakia (Fig. 12) or submucous fibrosis; it mostly arose from a precancerous lesion or condition (2,20). In a 10-year follow-up study, all 12 oral cancers developed from precancerous lesions or conditions (2), while in an eight-year follow-up study (20), 15 of the 19 oral cancers developed from precancer, giving a relative risk of 69.2. The relative risks for oral cancer associated with various precancerous lesions were significant for nodular leukoplakia, submucous fibrosis and others, including red area, ulcerations and ulcerated and homogeneous leukoplakia. The risk was not significant for lichen planus (Table 6).

POSSIBLE SOLUTIONS

This overview demonstrates that *bidi* smoking and betel-quid chewing are detrimental to oral health, as they are strongly associated with oral cancer, precancerous lesions and other mucosal pathologies. In view of these findings, specific studies for primary and secondary prevention were undertaken. Primary prevention was found to be feasible and effective (3,34,35) (see also paper by Gupta *et al.*, this volume). In the above-cited studies, oral examinations were conducted by dentists in a research set-up. The possibility of early detection of oral cancer by paramedical personnel in the governmental health care infrastructure was also explored in this area (36), and the results were encouraging (see paper by Mehta, this volume).

Acknowledgments

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A 10-year follow-up study for primary prevention of oral cancer among Indian villagers

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Oral cancer is caused by tobacco chewing and smoking. In this behavioural intervention study in Ernakulam district, 12 000 tobacco users were interviewed about their tobacco habits, examined for the presence of oral precancerous lesions and exposed to an intensive programme of health education on tobacco habits. The control cohort was a subset from an earlier study which used a similar methodology but with minimal behavioural intervention. Results after 10 years of follow-up showed that a higher percentage of individuals stopped using tobacco completely in the intervention cohort than in the control cohort. Several other indicators also showed that the intervention had been effective. As a result, the annual incidence of the most common oral precancerous lesion, leukoplakia, decreased substantially in the intervention cohort. Since most oral cancers are known to be preceded by oral precancerous lesions, the results demonstrate that primary prevention of oral cancer is feasible and practicable.

INTRODUCTION

It is a well-accepted fact that a high incidence of oral cancer in India and in several other South-East Asian countries is caused by the use of tobacco in the form of chewing and smoking. Most of this oral cancer, as much as 90% according to WHO estimates, is directly attributable to the chewing and smoking of tobacco (1). This indicates that oral cancer is amenable to primary prevention. The current study was undertaken to assess the feasibility and effectiveness of a primary prevention programme for oral cancer in a rural Indian population.

In large scale house-to-house cross-sectional surveys of over 150 000 individuals in rural India, the habits of tobacco chewing and smoking were strongly associated with oral cancer and precancer (2,3). A 10-year follow-up study of 30 000 individuals in three areas showed that all new cases of oral cancer and precancer developed exclusively among tobacco chewers and smokers, although a large proportion of the cohort consisted nonusers of tobacco. In addition all new cases of oral cancers developed among individuals with a prior diagnosis of oral precancerous lesions (4). When tobacco use was stopped or reduced substantially, the regression rates of oral precancerous lesions increased significantly (5). These results establish an almost complete association between tobacco use, oral cancer and precancer.

The present study was undertaken with two objectives: (i) to find out whether individuals in rural areas can be motivated to give up their tobacco habits through a concentrated programme of health education and (ii)

whether this programme would affect the incidence or risk of oral cancer. This study was conducted in three districts of India (see paper by Mehta, this volume) and the results from Ernakulam district in the State of Kerala in southern India where the incidence of oral cancer and precancerous lesions is known to be high, are discussed in this paper.

MATERIAL AND METHODS

Two distinct cohorts were selected and followed up at annual intervals for 10-years in Ernakulam district. In both cohorts, the base-line and annual follow-ups consisted of an interview and a clinical mouth examination for each individual in house-to-house surveys. In follow-up surveys, each individual was identified before the interview and examination from an alphabetical list of names cross-indexed with addresses and other identifying information.

The commonest method of tobacco smoking was *bidi* smoking and tobacco was chewed most commonly in *pan* (betel quid) (see paper by Bhonsle *et al.*, this volume). The commonest oral precancerous lesion was leukoplakia (see paper by Murti *et al.*, this volume).

The survey teams that went house-to-house consisted of dentists, interviewing clerks, drivers and local help. For the intervention study a social scientist was also a member of the team. The intervention cohort was subjected to a concentrated programme of health education about tobacco use in various different forms (see paper by Aghi *et al.*, this volume), whereas the control cohort was subjected to no such campaign.

Intervention cohort: The populations from selected *'karas'* (smallest population unit available through census publications) in Ernakulam district were screened, and all available tobacco users aged 15 years and over were chosen (12 212 individuals) as the study sample. Only temporary residents, very old, sick, infirm or psychologically disturbed people and those treated for oral cancer were excluded. The base-line survey for this intervention cohort was conducted in 1977-78, and 10 annual follow-ups were conducted thereafter.

Intervention: Special studies revealed that many people began to use tobacco and very often continued it because of its perceived medicinal value for disorders such as toothache and gastric disturbances (see paper by Bhonsle *et al.*, this volume). There was almost no awareness of any possible health consequence of tobacco use. The health education programme therefore consisted of two broad categories: (i) information for creating awareness regarding the relationship between tobacco use and oral cancer and convincing the target population of this relationship, and (ii) helping individuals to stop their tobacco use. In the health educational campaign, both personal and mass media communication were employed. For details see the previous paper by Aghi *et al.* in this volume.

The health educational programme was ongoing, dynamic and responsive to feed-back from the target population. All the intervention inputs were pretested before implementation and modified if necessary. The entire health education material was based solely upon scientific facts.

Control cohort: For this cohort, *'karas'* were selected by random sampling and the entire population aged 15-years and over was examined. The base-line survey was conducted in 1966-67 and the first follow-up survey three-years later. Eight annual follow-up surveys were conducted, providing 10-year follow-up results. For the purpose of this report, only a subset of the original cohort is included, namely tobacco users in the base-line survey.

Intervention: Although health education was not actively attempted in the control cohort, the conduct of the study itself provided some intervention input. The association between oral cancer and tobacco habits was explained to patients, especially while interviewing and conducting oral examinations. The examining dentists routinely advised patients to give up their tobacco habits, more forcefully if the patient had an oral precancerous lesion.

Statistical analysis: The incidence rates of leukoplakia were calculated using person-years method. The numerator for the incidence rate consisted of individuals with a diagnosis of oral leukoplakia in any of the follow-ups, but without a diagnosis of oral leukoplakia, submucous fibrosis or oral cancer in any previous examination. The denominator consisted of person-years of observation among individuals with no prior diagnosis of oral leukoplakia, submucous fibrosis or oral cancer. Variations with time in age and tobacco use were taken into account. Stoppage of tobacco habit was defined as complete discontinuation of any form of tobacco use at least six months prior to the interview.

RESULTS

Table 1 shows the cohort size and the follow-up details for the intervention and control cohorts. The control cohort was half the size of the intervention cohort. The loss to follow-up was higher in the control cohort (9.9% *vs* 0.9%), and correspondingly follow-up percentages were higher in the intervention cohort.

Figures 1 and 2 show the percentages of men and women who reported stopping of tobacco use at each follow-up in intervention and control cohorts. In the control cohort, there was some variation but no discernible trend. In the intervention cohort, there were very clear, significant, substantial positive trends for both men and women. Among men, the trend was almost constant throughout the 10-year period, whereas among women there was a decrease in the trend after six years.

Table 2 shows the number and percentage of men and women who reported stopping

Table 1

Follow-up details after 10 years for intervention and control cohorts

Follow-up details	Intervention cohort (n=12 212) (%)	Control cohort (n=6075) (%)
Re-examined[a]	93.2-81.2	74.8-71.4
Died[a]	0.7-11.7	2.9-10.3
Maximum followed up	98.4	87.2
Lost to follow-up	0.9	9.9

[a]The range is from the first to the last follow-up. The percentage decrease in the individuals re-examined and increase in deaths was fairly steady. The first follow-up of the control cohort was done three years after the base-line survey.

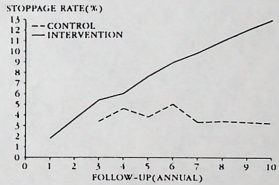

Fig. 1. Percentages of men reporting stoppage of their tobacco use at each follow-up in the intervention and control cohorts

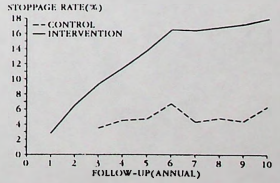

Fig. 2. Percentages of women reporting stoppage of their tobacco use at each follow-up in the intervention and control cohorts

Table 2

Comparison of stoppage of tobacco habit for 2, 3 and 4 successive years in the intervention and control cohorts

Stoppage	Intervention cohort		Control cohort	
	Followed up No.	Stopped %	Followed up No.	Stopped %
2 years				
Men	8279	11.2	3320	2.2
Women	3466	22.9	1778	7.1
3 years				
Men	8081	8.3	3208	1.7
Women	3391	18.0	1720	5.3
4 years				
Men	7901	6.3	3086	1.0
Women	3336	14.5	1676	4.0

their tobacco habit for two, three, and four consecutive years. These percentages were much higher in the intervention cohort than in the control cohort, showing that more people discontinued their tobacco habit for a longer time in the intervention cohort. The ratios were higher for men than for women.

Figures 3 and 4 compare distributions of the age at starting tobacco use of those individuals who stopped their tobacco use and those who did not, in the intervention and control cohorts, respectively. Those who started their tobacco habit later in life were better able to discontinue than those who started using it earlier. The pattern is similar in both cohorts, but the difference is less pronounced in the intervention cohort.

Figures 5 and 6 compare the distribution of frequency of tobacco smoking per day in the base-line survey and after 10-years in the intervention and control cohorts, respectively. Figures 7 and 8 provide the same information for tobacco chewing. Some individuals in the control cohort did stop tobacco use as indicated by zero frequency, but there was very little change in the frequency distribution after 10 years. In the intervention cohort, however, not only many more individuals stopped their tobacco habit, but there was a clear and significant shift towards the left for both smokers and chewers, demonstrating that their frequency of tobacco use had decreased.

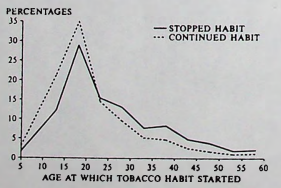

Fig. 3. Comparison of distribution of age at starting the tobacco use for those who stopped their tobacco use and those who did not, in the intervention cohort

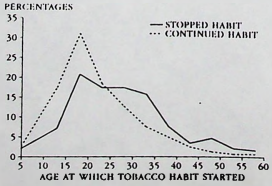

Fig. 4. Comparison of distribution of age at starting the tobacco use for those who stopped their tobacco use and those who did not, in the control cohort

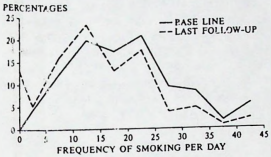

Fig. 5. Distribution of frequency of smoking per day in the base-line and 10th follow-up surveys in the intervention cohort

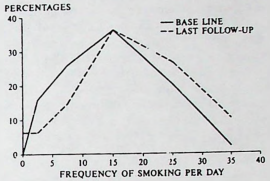

Fig. 6. Distribution of frequency of smoking per day in the base-line and 10th follow-up surveys in the control cohort

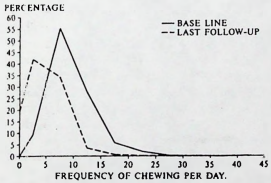

Fig. 7. Distribution of frequency of chewing per day in the base-line and 10th follow-up surveys in the intervention cohort

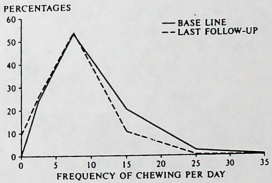

Fig. 8. Distribution of frequency of chewing per day in the base-line and 10th follow-up surveys in the control cohort

Table 3

Annual age-specific incidence rates (per 100 000) of leukoplakia in the intervention and control cohorts

Age group (years)	Intervention cohort	Control cohort
<34	77	255
35-44	256	677
45-54	262	846
55-64	373	756
≥65	234	507
Total	236	586
Age adjusted	186	470

DISCUSSION

The results described above corroborate the findings reported earlier after, one, five and

eight years of follow-up (6-8). Notably, the percentage of individuals who stopped their tobacco habit in the intervention cohort increased in successive follow-ups. This demonstrates that the effect of health education was cumulative over the years and helped not only in stoppage but even more in continued abstinence from tobacco.

Multiple logistic regression analysis of the five-year follow-up data showed that men who chewed were a difficult subgroup for stoppage of tobacco use, and the educational intervention helped them most (7). Interestingly, the trend in stoppage remained fairly constant for men over the 10-year period, but there was a decrease in the trend for women after six years. Further, this analysis showed that individuals in the higher age groups and those with a shorter duration of tobacco use were more likely to stop their habit. The present analysis demonstrates that it is easier to stop tobacco use if the individual started using it late in life. This confirms and explains the earlier finding.

The objective of the behavioural intervention programme was to stop tobacco use, and this was achieved to a fair degree. The educational programme helped in reducing the frequency of tobacco use in the intervention cohort, and this difference was as much or more pronounced in comparison with the control cohort as the stoppage of tobacco use.

In this study the comparison is not between the intervention and no intervention, but rather between programmed intervention and minimal intervention. It can be hypothesized that in the absence of such minimal intervention, the differences between the intervention and control cohorts would have been more pronounced.

As has already been demonstrared, leukoplakia is the most important oral precancerous lesion (see paper by Murti *et al.*, this volume), in that it is the most common and is the point of origin for most oral cancers (4,9). Therefore, a decrease in the risk of leukoplakia can be construed as decreasing the risk of oral cancer. This study shows that primary prevention of oral cancer is a feasible and practicable proposition, even among populations who have many misconceptions about the beneficial effects of tobacco.

The study has some limitations. The most important, perhaps, is the non-concurrence of the intervention and control cohorts. In terms of calendar time, the difference between the intervention and control cohort was ten years. Therefore the possibility that the observed differences were due to differences in time trends cannot be entirely ruled out. There is, however, no specific indication that time trend differences exist, or that they affect the validity of the conclusions in any way.

Although the possible benefits of health education in this study have been assessed only in terms of a decrease in the risk of oral cancer, it should be remembered that tobacco use is responsible for increase in the risk of many diseases, such as other cancers, especially those occurring in the aerodigestive tract, heart disease and respiratory disease. It has been estimated that in India tobacco use is responsible for at least 630 000 extra deaths every year (10). Thus, the positive effects of health education would undoubtedly be far greater than simply a decrease in the risk for oral cancer.

Acknowledgments

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Epidemiology of tobacco habits in Goa, India

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The Goa Cancer Society has conducted several epidemiological studies in Goa, India, to determine the prevalence of tobacco habits among schoolchildren and adults; to educate schoolchildren through a specially designed school curriculum on tobacco habits and intervention; and to assess the feasibility of using schoolchildren to bring about cessation of tobacco use by their parents or in the community. About 13.4% boys and 9.5% girls used tobacco, mostly smokeless tobacco. Usually, they had begun its use by the age of 5, and generally family members or friends had initiated them to tobacco. Among adults, nearly 33% of men and 20% of women used tobacco; smoking was the most common habit among men, while smokeless tobacco use was most common among women. Schoolchildren who received health education on tobacco and intervention methods were instrumental in achieving stoppage rate of 9.7% among adults. Furthermore, health education imparted a negative attitude to tobacco among the children.

INTRODUCTION

The State of Goa, which lies on the west coast of India tucked between the states of Maharashtra and Karnataka, became a part of the Indian Union in 1961 after being a Portuguese colony for several hundred years. As in many other parts of India, tobacco use is common in Goa. The prevalence of various types of tobacco habits and the practice of *dhumti* smoking in this area was reported by Bhonsle *et al.* (1).

In Goa, children seem to be a special target for tobacco advertising. Sweets and candies are sold which look exactly like cigarettes and are wrapped in packages similar to cigarette packets (Fig. 1). During the last few years, a tobacco product in paste form, described as 'creamy snuff', has been marketed in toothpaste-like tubes (Fig. 2) under various brand names. Initially, this product is used as a toothpaste; but soon it becomes addictive. Although it costs more than twice a regular toothpaste, its use has become popular.

Fig. 1. Candies that look like cigarettes

Ironically, unlike regular toothpaste, there is no sales tax on this product.

The Goa Cancer Society has undertaken several studies to elucidate the epidemiology of tobacco use in Goa and to explore strategies for

Fig. 2. Creamy snuff in a toothpaste-like tube

effective intervention. Children are considered effective agents for change, particularly in rural India where a school-going child may be the only literate member of the family. In this study, they were educated specifically with a view to conveying intervention messages to their parents.

MATERIAL AND METHODS

For this study, the State of Goa was divided into three zones: north, central and south, with rural populations of 227 000, 213 000 and 244 000, respectively. The requisite number of villages was selected by random sampling from each zone (21 from the north, 25 from the centre and 27 from the south), from which a population of 50 000 was selected. There were 73 schools in these 73 villages; 31 schools were selected by random sampling, and a questionnaire was distributed to 6271 schoolchildren in grades 5-10. Information was collected on age, gender, kinds of tobacco habits, age at starting those habits and the possible influence of parents and family members on the habit. This survey was done in 1986-87.

In 1987-88, another survey of a total of 29 713 individuals over the age of 15 years in three zones was done through house-to-house visits by selecting a 40% systematic sample from the 73 villages mentioned above. Information on age, gender and details of tobacco used was collected by trained investigators from 10 009, 9801 and 9903 individuals in each zone, respectively.

In 46 selected villages in the north and central zones, education about tobacco habits was given through children. Two booklets, one for 4th and 5th grade students and one for 6th to 9th grade students, were introduced during the academic year 1987-88. These booklets contained information on the history of tobacco, its ill-effects and advice on giving up tobacco habits. Class teachers were given a three-hour course on how to teach this information in four periods, each of 45 min. It was expected that children would not only benefit from this education but would convey the messages to their parents and spread the information in the community. In 25 villages of the central zone, the information was also spread by multi-purpose health workers and *Anganwadi* (child welfare) workers. The remaining 27 villages in the southern zone served as controls.

A sample of 448 boys and 332 girls from the intervention area were re-interviewed and a sample of 432 boys and 289 girls from the non-intervention area were interviewed after two-years to assess the changes in their attitude towards tobacco. These interviews were through self-administered questionnaires.

For the community-based intervention, results are available on 1159 tobacco users in the intervention area of the northern zone and 659 from the control area after about 1.5 years of the base-line survey.

RESULTS

Tables 1 and 2 give the results from the self-administered questionnaire among 6271 schoolchildren. Tables 3-6 and Fig. 1 give results from a community survey of 29 713 adults. Table 7 assesses the effect of the educational intervention in the community.

Table 1 shows the prevalence of tobacco use according to age and sex among the 6271 schoolchildren. The prevalence was higher (13.4%) among boys than girls (9.5%) and higher in the age group 15-18 years (15.4%) than in the age group 10-14 years (10.6%).

Table 1

Prevalence of tobacco use according to age and sex among schoolchildren aged 10-18 years

Age	Boys (%) (n=3443)	Girls (%) (n=2828)	Total (%) (n=6271)
10-14	10.6	9.4	10
15-18	15.4	9.7	12.7
Total	13.4	9.5	11.7

Table 2 shows the types of habits prevalent in the 731 tobacco users among the 6271 schoolchildren. Most (98%) of the boys and girls used tobacco in smokeless form, the commonest being *mishri*, followed by tobacco paste, i.e., creamy snuff, and chewing.

On the question of age at starting tobacco use, the response rate was low: 48% of boys and 52% of girls. Among those who responded, nearly one-third of the 223 boys and one-half of the 152 girls said that they had begun to use tobacco before the age of 5.

The response rate to the question about the people who influenced initiation of tobacco use was also not very high, namely, 62% among boys and 56% among girls. Family members were most influential for initiating tobacco use (boys, 60%; girls, 84%), although among boys other persons like friends (17%) and teachers (10%) were also influential.

Table 2

Prevalence of different types of tobacco habits among schoolchildren

Habit	Boys		Girls	
	No.	%	No.	%
Smoking	13	3	5	2
Mishri	256	56	177	66
Creamy snuff	212	46	128	47
Chewing	66	14	36	13
Single	388	84	219	81
Multiple	73	16	51	19
Total	461	100	270	100

Table 3 shows the distribution of the prevalence of tobacco use according to age among 29 713 individuals in the community. About one-third of the men and one-fifth of the women used tobacco. The prevalences increased rapidly up to the age of 44 among men and 64 among women; but prevalence rates among women were almost half of those observed in men up to the age of 44.

Table 3

Prevalence of tobacco habits according to age and sex

Age (years)	Men		Women	
	No.	Prevalence (%) (n=4778)	No.	Prevalence (%) (n=3152)
15-24	4 815	3.9	4 027	2.3
25-34	2 894	24.6	3 497	11.8
35-44	2 159	49.3	3 043	25.9
45-54	1 952	63.8	2 297	35.4
55-64	1 505	62.7	1 578	41.9
≥65	1 038	53.3	908	42.3
Total	14 363	33.2	15 350	20.5

Table 4 shows the distribution of different types of tobacco use among men and women. Smoking was most common (82.8%) among men, while smokeless tobacco use was most common (67.3%) among women.

Table 4

Distribution of various tobacco habits according to sex

Habit	Men		Women	
	No.	%	No.	%
Smoking only	3957	82.8	1 031	32.7
Chewing only	217	4.5	1 476	46.9
Mishri only	163	3.4	349	11.1
Creamy snuff	71	1.5	62	2.0
Multiple	370	7.8	234	7.3
Total with habits	4778	100	3 152	100
Total without tobacco habits	9585		12 198	

Bidi smoking was the commonest smoking habit among men (63%) as well as women (60.8%). The second commonest smoking habit among men was cigarette smoking (24%), while among women it was *dhumti* smoking (27.3%).

Figure 3 shows the prevalence of tobacco use according to educational level and gender. Tobacco use decreased sharply with increase in the educational level; for example, among men the prevalence was 64% among illiterates, 46% among those with primary education and 14% among those with middle-school education. Among women, it was 38% for illiterates, 11% in those with primary education and 3% among those with middle-school education.

Figure 4 shows the cumulative percentage of men and women starting tobacco use by a given age. Over one-third of individuals started tobacco use before they attained 20 years of age and most of them before they were 30 years old.

Figure 5 shows the reasons for starting tobacco use. About 28% of men started tobacco use due to a friend's influence and 22% just to pass time. More women started using tobacco either for perceived medicinal

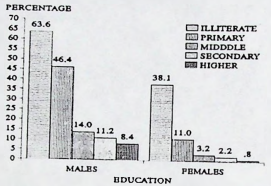

Fig. 3. Tobacco use according to educational level

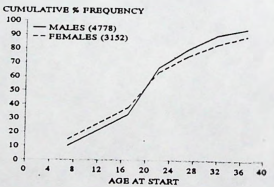

Fig. 4. Age at initiation of tobacco use among adults

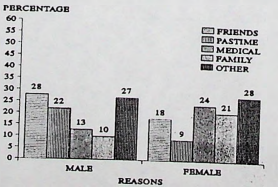

Fig. 5. Reasons for starting tobacco use in a community

Table 5

Attitude of schoolchildren to the question 'Are you likely to take up tobacco use in future?'

Attitude	Intervention		Non-intervention	
	Boys (%) (n=448)	Girls (%) (n=332)	Boys (%) (n=432)	Girls (%) (n=289)
Definitely not	80	87	62	65
May not	9	6	14	14
All others	11	7	24	23

χ^2Boys=8.2 with df=2
χ^2Girls=14.9 with df=2

Table 6

Attitude of schoolchildren to the question 'What would you do if a friend/relative offered you a tobacco product?'

Attitude	Intervention		Non-intervention	
	Boys (%) (n=448)	Girls (%) (n=332)	Boys (%) (n=432)	Girls (%) (n=289)
Definitely refuse and advise	82	89	59	60
Definitely refuse but not advise	10	8	16	15
All others	8	4	27	25

χ^2Boys=16.2 with df=2
χ^2Girls=23.0 with df=2

reasons (24%) or through family influence (21%).

Tables 5 and 6 show the differences in the attitudes of children in schools where educational intervention was performed after about two years, compared to those in schools where there was no intervention. The attitudes were determined by analysing responses to two questions: 'Are you likely to take up tobacco use in future?' (Table 5) and 'What would you do if your friend/relative offered you a tobacco product?' (Table 6). Although answers were given on five-point and six-point scales, respectively, they are presented in the tables, in terms of three categories by combining all extremes due to small numbers. For both questions, the difference between intervention and non-intervention schools was significant for boys as well as girls ($p<0.001$).

Table 7

Rates of stopping tobacco habits among men and women

Cohort	Men	Women	Total
Intervention			
Followed-up	705	454	1159
Quit	63	50	113
	(8.9%)	(11%)	(9.7%)
Control			
Followed-up	378	281	659
Quit	24	16	40
	(6.3%)	(5.7%)	(6.1%)

PH-7.

Table 7 shows rates of stopping tobacco use in the intervention and control areas in the community according to gender. Overall, a significantly higher percentage (9.7%) of men and women stopped their tobacco use in the intervention area compared with the control area. The difference was significant for women, but not for men.

DISCUSSION

This investigation showed that tobacco use in different forms is very common in Goa and its use generally starts at a very young age, mostly influenced by family members and friends. The finding that smoking is the most common habit among men and tobacco chewing is more often practised by women is similar to that of an earlier study in this region (1) and of studies in other parts of India (2). The present findings are also consistent with those of studies (3-5) in other parts of the country: that it is possible to motivate people in rural areas of India to quit their tobacco habits (see paper by Gupta *et al.*, this volume). Furthermore, the present investigation focused on the importance of desirability of including health educational material on tobacco in school curricula. It highlights the findings that such material is useful in shaping the children's attitude towards tobacco in a proper perspective and in propagating the intervention messages to their parents.

Acknowledgments

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POLICY AND LAW

Relevance to Human Cancer of N-Nitroso Compounds
Tobacco Smoke and Mycotoxins
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ANTIMUTAGENIC AND ANTICARCINOGENIC EFFECTS OF BETEL LEAF EXTRACT AGAINST THE TOBACCO-SPECIFIC NITROSAMINE 4-(*N*-NITROSOMETHYLAMINO)-1-(3-PYRIDYL)-1-BUTANONE (NNK)

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Earlier studies showed that betel leaf inhibits the mutagenic action of standard mutagens like benzo[*a*]pyrene and dimethylbenz[*a*]anthracene. Since tobacco-specific nitrosamines are the major carcinogens present in unburnt forms of tobacco, we studied the effect of an extract of betel leaf on the mutagenic and carcinogenic actions of one of the most potent, 4-(*N*-nitrosomethylamino)-1-(3-pyridyl)-1-butanone (NNK). Betel-leaf extract and hydroxychavicol suppressed the mutagenicity of NNK in both the Ames and the micronucleus test. In studies in mice, betel-leaf extract reduced the tumorigenic effects of NNK by 25%. Concurrent treatment with the extract also inhibited the decreases in levels of vitamin A in liver and plasma induced by NNK. Betel leaf thus has protective effects against the mutagenic, carcinogenic and adverse metabolic effects of NNK in mice.

The habit of chewing tobacco has been shown to be associated causally with oral cancer (Sanghvi, 1981; Bhide *et al.*, 1984; Winn, 1984). In addition, people who chew tobacco with lime have a higher risk for oral cancer than those who chew tobacco in a betel quid (Khanolkar, 1944, 1950), suggesting that betel quid contains some protective factor. We showed earlier that betel-leaf extract (BLE) inhibits the mutagenicity of benzo[*a*]pyrene and dimethylbenz[*a*]anthracene (Nagabhushan *et al.*, 1987). Since tobacco-specific *N*-nitrosamines are the only carcinogens present in unburnt tobacco products like chewing tobacco (IARC, 1985), we tested the effect of BLE on the mutagenic and carcinogenic effects of 4-(*N*-nitrosomethylamino)-1-(3-pyridyl)-1-butanone (NNK), which is a strong tobacco-specific carcinogen. We also tested the effects of hydroxychavicol, a phenolic antimutagen present in betel leaf (Amonkar *et al.*, 1986, 1989), against the effects of NNK.

NNK was synthesized according to the method of Hecht *et al.* (1983). BLE and hydroxychavicol were prepared according to procedures described earlier (Amonkar *et al.*, 1989; Padma *et al.*, 1989).

Antimutagenicity studies

The antimutagenic effects of BLE and hydroxychavicol against NNK were tested in the Ames test (Maron & Ames, 1983) and in the micronucleus test (Schmid, 1975). At a dose

of 200 μg/plate (Padma *et al.*, 1989), both BLE and hydroxychavicol suppressed the mutagenic action in *Salmonella typhimurium* strain TA100 of all three concentrations of NNK tested (Table 1) in the presence of an exogenous metabolic activation system.

Table 1. Effects of betel leaf extract (BLE) and hydroxychavicol (HC) on the concentration-dependent mutagenicity of 4-(*N*-nitrosomethylamino)-1-(3-pyridyl)-1-butanone (NNK) in *Salmonella typhimurium* strain TA100 with postmitochondrial rat liver fraction

NNK (μg/plate)	No. of *his*$^+$ revertants/plate		
	NNK alone	+ BLE (200 μg/ml)	+ HC (200 μg/ml)
0	123 ± 1	124 ± 7	89 ± 4
250	320 ± 9	284 ± 8	124 ± 14
500	499 ± 41	301 ± 10	222 ± 17
1000	824 ± 26	471 ± 4	374 ± 19

Values are means ± SE of eight plates from two independent experiments

In the micronucleus test, NNK at 500 mg/kg body weight induced 1.3 ± 0.05 micronuclei per 100 polychromatic erythrocytes as compared to 0.3 ± 0.02 in controls given distilled water. In the presence of BLE and hydroxychavicol, the numbers of micronuclei were 0.5 ± 0.04 and 0.9 ± 0.05, respectively, which were significantly different from that in NNK-treated animals. Animals treated with only BLE and hydroxychavicol showed 0.4 ± 0.025 and 0.42 ± 0.025 micronuclei, respectively.

Anticarcinogenic effects

The anticarcinogenic effect of BLE against NNK was tested in long-term studies on inbred male Swiss mice. NNK (1 mg/day three times a week; total dose, 22 mg) was administered on the tongues of mice following a 3–4 h administration of atropine (1% in drinking-water) to decrease salivation and facilitate retention of the nitrosamine in the oral cavity, as is the case with chewers. BLE was supplied in drinking-water (2.5 mg/animal per day) for the duration of NNK treatment. After treatment, animals were killed periodically to monitor tumour incidence or when moribund. All dead animals were autopsied and tissues fixed in 10% formalin for histological analysis.

In the group treated with NNK alone, 19/29 (65.5%) animals had tumours (17 lung adenomas, three forestomach papillomas and two hepatomas) while in the group treated with NNK and BLE, 11/27 (41%) animals had tumours (eight lung adenomas, three forestomach papillomas and one hepatoma). The per cent decrease in tumour incidence is not statistically significant.

Effect of BLE on vitamin A status in liver and plasma

The levels of vitamin A in both liver and plasma have been shown to be depleted by treatment with NNK (Padma, 1988). We studied the effect of BLE at 12-14 and 20-22 months on vitamin A levels, using the method described by Neeld and Pearson (1963). The results are shown in Table 2. Animals treated with BLE alone had significantly higher levels

of liver vitamin A than untreated animals at both time points, while the levels in plasma were elevated only during the earlier period.

Table 2. Levels of vitamin A in the liver and plasma of Swiss male mice treated with 4-(*N*-nitrosomethylamino)-1-(3-pyridyl)-1-butanone (NNK) alone or in combination with betel-leaf extract (BLE)

Treatment	Vitamin A levels at	
	12–14 months	20–22 months
Liver		
Untreated controls	208.2 ± 10.8	196.1 ± 6.4
NNK alone	32.7 ± 1.4	57.3 ± 4.0
BLE alone	261.1 ± 13.2	245.3 ± 8.8
NNK + BLE	148.8 ± 2.6	135.9 ± 3.9
Plasma		
Untreated controls	91.1 ± 1.3	100.4 ± 3.0
NNK alone	34.1 ± 1.3	59.2 ± 6.2
BLE alone	216.6 ± 12.2	105.2 ± 5.5
NNK + BLE	93.0 ± 1.9	110.1 ± 5.9

Results are means for six animals ± SE

The levels of vitamin A in the livers of the animals treated with NNK and BLE were significantly lower than those in untreated controls at both times, but the levels were significantly higher than those in animals treated with NNK alone. The levels of circulating vitamin A in animals treated with NNK and BLE were comparable to the control levels at both intervals but were significantly higher than those in animals treated with NNK alone.

Potential use of BLE as an anticarcinogen

Our study shows that BLE is nonmutagenic in both the Ames and micronucleus tests. These results are consistent with previous reports in which betel leaf was found to be nonmutagenic in the Ames test (Shirname *et al.*, 1983; Nagabhushan *et al.*, 1987) and in the V79 and human lymphoblastoid cell lines (Umezawa *et al.*, 1981). Our observation that betel leaves are not carcinogenic is also consistent with the results of previous studies in mice (Bhide *et al.*, 1979) and rats (Mori *et al.*, 1979).

BLE has been shown to suppress the mutagenicity of polycyclic aromatic hydrocarbons (Nagabhushan *et al.*, 1987), as well as that of NNK and *N'*-nitrosonornicotine (Padma, 1988), and to be anticarcinogenic against benzo[*a*]pyrene in the hamster cheek pouch model (Rao, 1984) and in the forestomach tumour model in mice (Padma, 1988), against dimethylbenz[*a*]anthracene in the rat mammary tumour model (Rao *et al.*, 1985) and against *N'*-nitrosonornicotine in Swiss mice (Padma, 1988). The antimutagenic and anticarcinogenic action of BLE against this wide variety of agents may be attributed to the presence of compounds like chlorophyll, phenolics like eugenol and hydroxychavicol (Amonkar *et al.*, 1986) and vitamins like A, ascorbic acid (Aykroyd, 1963) and vitamin E (unpublished data) in betel leaves.

We found that vitamin A levels were elevated in both liver and plasma of BLE-treated animals. It has also been observed that BLE induces a significant increase in liver ascorbic acid levels (Padma, 1988). Vitamin A has been shown to exert a protective action against carcinogens (McCormick & Moon, 1982; Goodwin *et al.*, 1986), and ascorbic acid has been shown to prevent the initiation of skin tumours following the application of a promoter (Slaga & Bracken, 1977). The protective effect may therefore be mediated partly by vitamin A and ascorbic acid.

Thus, the inclusion of betel leaf may reduce the carcinogenic risk of tobacco chewers, and these results support the hypothesis that betel-quid chewers may have some protection against cancer (Khanolkar, 1944, 1950).

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BETEL QUID AND ORAL CANCER: PROSPECTS FOR PREVENTION

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Betel-quid chewing is an ancient and socially accepted practice. The introduction of tobacco reinforced this practice, and now almost all habitual chewers of betel quids include tobacco. It is well established that chewing of betel quid with tobacco causes oral cancer and is largely responsible for the high incidence of oral cancer in several South Asian countries. The feasibility of primary prevention of oral cancer was studied in a population-based prospective intervention study. A cohort of 12 212 betel-quid chewers and smokers was exposed to a programme of health education for stopping chewing and smoking and subjected to annual examinations for detection of oral precancerous lesions. Evaluations after one, five and eight years showed that primary prevention of oral cancer is feasible and practicable. Early detection of oral cancer is an important control measure. In a secondary prevention study, 53 basic health workers were trained in the detection and referral of lesions suspected of being oral cancer. Over one year, they examined more than 39 000 high-risk individuals, resulting in the detection of 20 cases of oral cancer. The sensitivity and specificity of their diagnoses was assessed through a re-examination of a 5% sample: we concluded that it was possible to incorporate a secondary prevention programme into the existing health care system.

The chewing of betel quid is a very ancient practice in India and many other South Asian countries. References to this habit in stone and other inscriptions are about a millenium old, and literature references are about two millennia old. Betel-quid chewing has been part of religious and cultural rituals and enjoys complete social acceptance.

Basically, the betel quid consists of betel leaf, areca nut, lime and condiments, and sweetening and flavouring agents, which depend upon individual and local preferences. Tobacco was introduced into India, as everywhere else, from the New World in the sixteenth century by Europeans. It soon became an ingredient of the betel quid and because of this association enjoyed social acceptance.

The relationship between betel-quid chewing and oral cancer was postulated in the late nineteenth and early twentieth centuries by British surgeons, who noted that oral cancer was rare in Great Britain but common in India. Subsequently, several studies have been made of this association. The terms used to describe the habit have not been consistent, however, and the same terms have been used differently in different studies. This has resulted in a considerable amount of difficulty in interpretation. A major source of

confusion was the description of the habit as 'betel-nut' chewing, with the occasional addition of tobacco. This description led to the impression that the addition of tobacco to the chewing quid was of little or marginal prevalence. This impression was corrected comparatively recently by population-based house-to-house surveys of chewing habits in six different areas of India. Chewing habits were widespread in three of the six areas, and in these three areas 92-98% of chewers who did not smoke included tobacco in their quid (Mehta *et al.*, 1969, 1972). These findings demonstrate that the betel-quid chewing habit is usually the habit of chewing betel quid with tobacco.

'Chewing habit' is another loose term, which may include areca-nut chewing, tobacco-lime chewing and betel-quid chewing. Unless otherwise specified, the term betel-quid chewing implies the chewing of betel quid containing tobacco. Although the prevalence of tobacco chewing has been declining over the last few decades, it is estimated that there are still at least 40 million regular tobacco chewers in India.

Betel quid and oral cancer

The relationship between betel-quid chewing and oral cancer has been reviewed extensively (IARC, 1985). The association has been demonstrated in numerous case-control and cohort studies, and evidence from experimental studies points in the same direction. The overall evaluation of the IARC working group was that the evidence is sufficient for the carcinogenicity of betel quid with tobacco, meaning that chewing of betel quid with tobacco causes oral cancer. Neither the epidemiological nor the experimental evidence for the carcinogenicity of betel quid without tobacco was sufficient (Gupta *et al.*, 1982). This does not mean, however, that the chewing of betel quid without tobacco is an innocuous habit. Areca nut in betel quid causes oral submucous fibrosis, which is a debilitating disease with no known cure (Bhonsle *et al.*, 1987); it is also a precancerous lesion (Murti *et al.*, 1985). A person with submucous fibrosis who is exposed to carcinogens in tobacco in the form of chewing or smoking has a higher risk of developing oral cancer than persons without the disease.

It has been estimated that about 30% of oral cancer can be attributed to the habit of chewing betel quid with tobacco (World Health Organization, 1984). Betel-quid chewing and tobacco smoking have a synergistic effect on the risk for oral cancer, and the combined habits of chewing and smoking are quite common. Thus, an additional 50% of oral cancers can be attributed to the combination. It is therefore clear that betel-quid chewing is the single most important factor responsible for the high incidence of oral cancer in India and other South Asian countries.

Betel quid and oral precancer

Betel-quid chewing is strongly associated with white lesions of the oral cavity, the most important of which is leukoplakia. In several hospital-based studies in India, leukoplakia was found to be highly prevalent among people who chewed betel quid and rare among those who did not chew betel quid and did not smoke. These findings were confirmed in population-based cross-sectional studies (Mehta *et al.*, 1969, 1972). The most compelling evidence came from a ten-year prospective study of a random sample of 10 287 individuals in Ernakulam district with annual follow-ups (Gupta *et al.*, 1980). Not a single new leukoplakia was diagnosed among individuals who did not chew or smoke, although there

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Control of Tobacco-related Cancers and Other Diseases.
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Population impact of adverse reproductive outcome attributable to maternal tobacco use in India

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The prevalence of tobacco use among women in India ranges from 10 to 62%. Tobacco is used by women predominantly in its smokeless forms; overall, an estimated 10% of Indian women chew tobacco and 2.5% smoke *bidis*. Nevertheless, the potential health hazards of maternal tobacco use to reproductive outcome are not well documented. Preliminary estimates showed a three-fold risk of stillbirths among women in India who chewed tobacco during pregnancy and a two fold increase in perinatal mortality for babies born to *bidi* smokers in Bangladesh. The odds ratio for low birthweight (2.5 kg or less) associated with *mishri* use during pregnancy was 3.2 for all babies in Bombay, 6.96 for girls and 1.6 for boys. From these estimates, about 17% of stillbirths, 9% of perinatal mortality and 17% of birthweights of 2.5 kg or less are attributable to maternal tobacco use during pregnancy. Estimates for 1986 showed that nearly 457 000 deaths among infants and children under five years could be attributed to maternal tobacco use. Additional indirect effects may be increased infant mortality due to premature birth and diversion of income from nutritional needs to tobacco. These estimates emphasize the necessity for stopping tobacco use during pregnancy and the need for appropriate antenatal efforts.

INTRODUCTION

Maternal cigarette smoking is harmful to the unborn fetus, newborn, neonate and growing child in various ways. Cigarette smoking during pregnancy adversely affects the growth of the unborn fetus, resulting in low birthweight, increased numbers of stillbirths and increased perinatal, neonatal and infant mortality (1). It is also associated with a decrease in the male:female ratio of newborns (2,3) and with an increased prevalence of infections (4). Further, it slows or adversely affects the respiratory, mental, emotional and behavioural development of the child at newborn, infant, under-five and over-five stages (1,4).

Tobacco is used in various forms throughout India and South-East Asia (see papers by Bhonsle *et al.*; Pindborg *et al.*; this volume), but very little is known about its adverse effects on pregnancy, a topic which has been reviewed recently (5,6). Studies from Pune (7) and Jabalpur (8) in India and from Bangladesh (4) showed that maternal tobacco chewing (7,8) and *bidi* smoking (4) during pregnancy result in offspring of low birthweight. A three-fold increase in the number of stillbirths was seen among tobacco chewers (7), and increased placental weights were also reported (9,10). A two-fold increase in perinatal mortality was associated with *bidi* smoking (4). Perinatal mortality was twice as high among illiterate and less well educated women than among educated women and among those who had had little or no antenatal care compared to those who had sought antenatal care. Less well educated women were more likely to be *bidi* smokers and to have sought no or less

antenatal care. Thus, lack of education, *bidi* smoking and lack of antenatal care seem to be interrelated. Furthermore, the scarce income of poorer, less well educated women may be diverted from nutritional and other needs to the purchase of tobacco (11), which would add indirectly to the adverse effects of tobacco.

Relative risk estimates for the effects of maternal use of smokeless tobacco during pregnancy are available from a preliminary study in Bombay, India (12). In this study, 33% of the 500 women were *mishri* users, and they had a nearly three-fold greater risk of bearing an offspring with low birthweight (2.5 kg or less) than nonusers of tobacco. Female babies had a nearly seven-fold risk of weighing less than 2.5 kg ($p<0.0005$); for male babies, the birthweights showed no significant difference. The relative risk for having a baby weighing 2 kg or less was 5.4, and that for having a baby weighing 2-2.5 kg was 2.76.

This paper assesses the extent of premature births and other adverse effects associated with maternal tobacco use during pregnancy in India.

MATERIAL AND METHODS

In order to estimate the population impact of adverse reproductive outcomes due to maternal tobacco use in India, one must know the prevalence of tobacco use among women during pregnancy and the relative risk estimates. Relative risk estimates are available from the studies (4,7,8,12) described above. There has been no nationwide prevalence survey of tobacco use in India, but studies in some selected rural areas show that 10-62% of women use tobacco in one form or another (13,14). Overall, it has been estimated that at least 10% of women use smokeless tobacco, and an additional 2.5% smoke (15). Thus, it can be calculated that, in 1986, about 20.5 million women of reproductive age (15-44 years) were using tobacco in India.

RESULTS

Table 1 shows the population attributable risks associated with tobacco use for stillbirth and birthweight of 2.5 kg or less in all babies

Table 1

Estimated impact on reproductive outcome attributable to maternal tobacco use in India, 1986

Reproductive outcome	Odds ratio	Population attributable risk (%)	
		Smokeless tobacco users	*Bidi* smokers
Stillbirth[a]	3	15.7	4.8
<2.5 kg birthweight[b] (both genders)	3	15.7	4.8
<2.5 kg birthweight[b] (girls)	7	37.5	13.0
<2.0 kg birthweight[b]	5.4	30.5	9.9
2-2.5 kg birthweight	2.8	15.3	4.3
Perinatal mortality[c]	2	9.0	2.4

[a]Source: ref. (7)
[b]Source: ref. (12)
[c]Source: ref. (4)

Table 2

Estimated deaths from adverse reproductive outcomes due to tobacco use in pregnancy, India, 1986

Reproductive outcome	Deaths ($\times 10^3$) due to		
	Smokeless tobacco use	Smoking	Both
Stillbirth @ 25/1000 livebirths[a]	96	28	124
Prematurity-related deaths @ 41%[b]	151	43	194
Perinatal mortality @ 53/1000 livebirths[c]	110	29	139
Total	357	100	457

[a]Source: ref. (16)
[b]Source: ref. (17); figures for prevalence of premature births not available
[c]Source: ref. (17)

according to gender. Some 9% of perinatal mortality and nearly 17% of stillbirths could be attributed to tobacco use during pregnancy.

The estimated population load of such adverse reproductive outcomes is shown in Table 2. Overall, 457 000 deaths, of which 124 000 were stillbirths, 194 000 prematurity-related deaths, and 139 000 perinatal mortality, were estimated to have occurred in 1986 due to maternal tobacco use during pregnancy.

DISCUSSION

Our analysis shows that nearly half a million deaths among infants and children aged less than five years might be due to maternal tobacco use during pregnancy. This is likely to be an underestimate, since the risks for stillbirths were calculated on the basis of 25 stillbirths per 1000 in Bombay City (16) and stillbirths may be underreported, since all deliveries do not take place in hospital.

The higher death rates due to premature birth among female infants and children under the age of five may be due to the low birthweight of female babies, which in turn could be the outcome of maternal use of smokeless tobacco (12). As these relative risk estimates may change in the future with the availability of additional data, the present results must be viewed with caution. They nevertheless provide an estimate of the size of the problem and signal the need for action.

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Tobacco-Related Cancers : Portends for the Future

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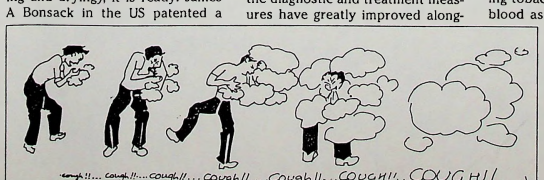
"Fire at one end and fool at the other", was how this cylindrical contraption was defined much before the health warning was made mandatory on cigarette packs. Christopher Columbus found the natives using tobacco in much the same way as it is used today, and being led to believe in its possible medicinal value, it was carried to France, Spain, Europe and the rest of the world, wherever colonies were established. Grown in more than 120 countries today, China leads, followed by the USA, India, Brazil and Turkey.

Tobacco belongs to the night shade family Solanaceae, and the genus, *Nicotiana* was named after Jean Nicot, French Ambassador to Portugal (1559-1561). Many varieties developed subsequently and a South American variety N. Tabacum is the major source of today's commercial varieties. Nicotine and other alkaloids which are nitrogen containing organic compounds are recognised as habit forming. The seeds are extremely tiny, one tablespoon can easily grow enough seedlings in 6 acres and harvesting takes place between 70-130 days after transplanting. After a process called 'curing' (wilting, yellowing, colouring and drying), it is ready. James A Bonsack in the US patented a machine in 1880 in which cigarette paper was filled with tobacco, formed, pasted, and cut into proper length by a rotary machine. Today it is a multimillion dollar industry, more than 7 million tons of tobacco are produced annually and more than 4 trillion cigarettes sold yearly. Nearer home it occupies prime spot through hoardings at traffic intersections. The industry owns luxury hotels, sponsors sports events and advertises it as the icon of the macho male whom the woman seeks! Today thanks to ceaseless efforts by the transnational tobacco conglomerates, production, distribution and marketing of cigarettes continues to grow. Cigarette advertisements continued in the pages of the 'Journal of the American Medical Association' until 1954, and even the American Cancer Society (ACS) has been cautious and conservative in challenging its $390 million annual tobacco industry!

The Health Hazard

Of the 676,000 annual newly diagnosed cases of lung cancer in men worldwide, 85% is attributable to cigarette smoking, and compared to men, women have a higher risk of developing cancer, and although the diagnostic and treatment measures have greatly improved alongside the understanding of smoking-related cancers, the risk is still dependent on the extent of exposure to tobacco smoke. Cigarette smoking is a major cause of cancer of the larynx, approximately 80% directly attributable to smoking, and a similar risk exists in those who smoke pipes or cigars, thus it is imperative to explode a myth! Regarding oral cancers a dose relation exists between the number of cigarettes smoked per day and cancers of the lip, tongue, salivary gland, floor of mouth, and hypopharynx, esophagus. Tobacco in its varied forms is responsible for 90% of cancers of the oral cavity. In 1992 the National Cancer Institute (NCI) of the US through a population based case-control study confirmed that cigarette smoking is a major cause of cancers of the renal pelvis, ureters, bladder and prostate. A case-control study of stomach cancer in Japan suggests that cigarette smoking plays a significant role in its causation. The strength and consistency of association of pancreative, colonic cancer, in smokers, and the epidemiological association between smoking and lymphoid and myeloid leukemia have resulted in identifying tobacco metabolites in bile and blood as the causative agents.



In the eighties smoking caused approximately 315000 deaths yearly in the US, which is greater than all the drug and alcohol and drug-abuse deaths, seven times more than automobile fatalities, and more than all American military fatalities of both the World Wars, and Viet-

nam combined! China, the largest producer of tobacco, is also the largest consumer. Smoking in the US is declining marginally, but the tobacco produced in the US finds its way elsewhere. In fact tobacco moghuls there have the clout to the extent that exports of various commodities from countries like Taiwan, Korea, Philippines etc. are linked to the import to these countries of the US brand of cigarettes.

Urge and Scourge - Why?

"Smoking relieves stress" - the stress that is relieved is that which resulted from being dependent on nicotine - the essence of addiction. Sales gimmicks are responsible for propagating the lure. Every documented report of health hazard has been countered by the promoters. Virginia Slims advertised that smoking keeps you slim and trim, aiming at the female clientele. Advertising strategies succeeded in boosting target sales in the US through catchy slogans. India never lagged behind in advertisement strategy.

Brands with purportedly low levels of tar and nicotine were promoted to calm widespread fears of lung cancer development from smoking when the first medical reports were published in 1964. Tar is a composite of more than 4000 solid products of combustion, containing nearly 40 known carcinogens. Similar adverse reports were offset by the introduction of the filtered brands with risk reducing claims. Of late considerable resources have been invested by tobacco companies in the development of cigarette prototypes in which tobacco is not burned, instead heated so as to provide with nicotine and flavour.

Passive Smoking

Documented reports suggest that two-thirds of smoke from a burning cigarette never reach the smoker's lungs but instead go directly into the air. Environment tobacco smoke (ETS) also called 'second-hand smoke' is defined as the combination of sidestream smoke emitted thus from a cigarette between puffs and the fraction of mainstream smoke exhaled by one who smokes. Considerable evidence is available to the effect that nonsmokers absorb and metabolise significant amounts of 'second-hand smoke' and even reports of possible increased relative risks of lung cancer and other diseases in the non-smoker are available.

Cessation Strategies

Around three hundred cessation strategies have been reported, from group therapy and hypnosis to over-the-counter pharmaceutical products either containing nicotine analogues or aversive chemicals. The Physicians' active involvement is vital of course. From pack-year history, today the metaphor is the 'inhalation count'. To put it this way, a pack-a-day smoking patient will breathe as many as one million doses of cyanide, ammonia, carcinogens and carbonmo-noxide in less than 15 years, not including the inhalation of other people's smoke.

Personalised approaches from all health care givers and individualisation of such messages is the cornerstone of success. Prevention nevertheless is better than cure, and like charity which has to begin at home, let all who have anything at all to do with health, stay away from tobacco.

Urgent versus Important

It is not enough that our country bans cigarette advertisement in televisions or the cigarette pack carry the 'health warning'. Common myths have to be debunked, that smoking relaxes you, relieves stress and so on. The fact that smoking causes cancer has to be impressed upon through positive strongly worded strategies through the media, be it radio or television. The life of an Indian is as important or more so, than the Indian tiger or our ecology, which seem to be a matter of priority, more to the powers that be. Appropriate measures to limit tobacco sales should be undertaken. Smoking should be banned in public places, much less in government offices and institutions. The right to smoke should not infringe upon the right of those who desire a smoke free environment. Breach of freedom is a crime and therefore through appropriate legislation smoking which violates an adopted code of conduct should be made punishable. "Knowledge puffeth off but wisdom lingereth". ■

DR. MANOJ SHARMA BAGS 1998 OSU ALUMNI AWARD

Manoj Sharma, Ph.D. Assistant Professor of Health Education at the University of Nebraska at Omaha, received the William Oxley Thompson Award for professional achievement by young alumni from the Ohio State University Alumni Association Inc., at its annual recognition banquet on 16 October, 1998.

Sharma earned his Ph.D in preventive medicine/ behaviour and health promotion from Ohio State in 1997. He has already made many contributions to the advancement of public health through his actions, research, and publications, and it is for these achievement that he was honoured.

The Ohio State University Alumni Association Inc., is a dues-supported organisation of graduates, former students, and friends of the university with more than 121000 members. Each year, the Association presents awards in several categories to honour those living alumni who personify Ohio State's tradition of excellence.

The VHAI family is proud of one of its former members getting such an esteemed recognition at an international level.

Correspondence

Oral submucous fibrosis, areca nut and *pan masala* use: A case–control study

Oral submucous fibrosis (OSF) is a chronic debilitating disease in which fibrous bands develop in the mouth. There is a marked intolerance for spicy food and opening the mouth becomes progressively more difficult. This disease does not regress and has no known cure. The most serious aspect of the disease is its precancerous nature. In a cohort study, the relative risk for development of oral cancer among OSF cases was 397.3 compared to individuals without any oral precancerous lesions after controlling for tobacco use.[1] Several aetiological factors have been proposed, and the current consensus seems to be the habit of chewing areca nut.[2] There is great concern about the increasing incidence of this disease in India, especially among adolescents and young adults.[3,4]

A case–control study was undertaken in the Government Dental College and Hospital, Nagpur, Maharashtra where 200 consecutively diagnosed outpatients with OSF over a period of one year (June 1996–May 1997) were selected as cases. Every fifth outpatient was designated as a potential control, roughly matched for age. Almost all patients and controls were in the age range of 15–54 years and 16% of cases and 38% of controls were women. Details of areca nut and tobacco use were obtained by an interviewer-administered, structured questionnaire in a face-to-face interview.

A wide variety of areca nut and tobacco chewing habits were reported; the most common (50%) being the use of *pan masala. Pan masala,* which literally means betel quid mixture, is a commercially manufactured product almost always containing tobacco and areca nut. This is widely advertised, aggressively marketed and the industry has grown from scratch to almost a billion rupees within a few decades. The next most popular habit among patients was the use of *kharra,* a betel preparation containing pieces of areca nut (7–8 g), a small amount of tobacco flakes, and drops of slaked lime, mixed, homogenized and wrapped in a cellophane paper ball. Other chewing habits were tobacco–lime and betel quid in different combinations. Table I shows the number of cases and controls according to the daily frequency of use of areca nut-containing products and the relative risk.

The relative risk and the trend for dose–response were highly significant ($p<0.01$). The relative risks were of the same order of magnitude as reported in earlier case–control studies.[5,6]

TABLE I. Relative risk of oral submucous fibrosis by the daily frequency of areca nut use

Frequency/day	Cases	Controls	Relative risk
No areca nut use	5	110	1.0
1	11	24	10.1*
2–3	65	42	34.0*
4–5	61	16	83.9*
≥6	58	5	255.2*
Any areca nut use	195	87	49.3*
Total	200	197	

*$p<0.01$, p for trend <0.01

The likelihood of an emerging epidemic of OSF seems to be justified by the present data. Over 70% of the cases were less than 35 years of age. Since almost all OSF cases use tobacco as well—and OSF is a high-risk pre-cancerous condition—an increase in the incidence of oral cancer can be predicted. In this study, 5.5% cases had associated oral cancer and 3.5% had associated leukoplakia. Urgent regulatory actions are, therefore, warranted to control the manufacture, marketing and consumption of products containing areca nut and/or tobacco, especially *pan masala.*

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Medical education and health needs of a community

There is disenchantment with the existing system of medical education in many developing countries because of its irrelevance to the prevailing health situation. Medical education must be based on the health needs of a community and requires to be modified based on a critical assessment of programme requirements and staff and system performance within the existing structure of health services. Health problems vary with the socio-economic and political situation in a country. Continuous situation analysis, planning, programming, implementation, management evaluation, reprogramming, and revaluation are necessary. Unfortunately, the health services sector and medical education lack interaction. As a result, the producer and the user are at cross-purposes. The outcome is a health scenario inconsistent with expectations. Today, India has the largest medical manpower in the world, but the health situation is far from satisfactory. Thus, the education of doctors and allied health professionals needs a thorough overhaul; a balance between technological and humanistic medicine, a more holistic approach covering promotive, preventive, curative and rehabilitative medicine, a suitably evolved health system with strong pillars of medical and ethical values, based on human suffering but without sacrificing scientific standards.

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The medical examination system

All countries spend a lot of money on technical education. Training medical personnel is more expensive than training other technical personnel. Undeniably, India needs more doctors who can deliver quality care to patients. Therefore, training of doctors is a hot and cold topic of discussion among medical personnel, hot because urgent reforms are needed and cold because of the frustration experienced by medical professionals over the listlessness that prevails.

The most important component in the training process is our system of examinations. Students in particular have lamented that the examination at the end of each course has assumed more than the necessary importance. This strikes an instant chord with teachers as well as students. The main reason for the negative reaction evoked by this important exercise is the flawed and sloppy manner in which it is conducted at all levels—undergraduate and postgraduate—throughout the country.

Students feel more strongly than their teachers about the urgency of reforms in the examination system. Understandably so, as they suffer the ills of the system while teachers are passively responsible. Yet, most teachers valiantly protect the flawed system, baulking any improvement in it.

What are the ills? Typically, the theory examination consists of either essay-type or short note questions, which are impossible to evaluate objectively and fairly. The objective type questions, more commonly referred to as multiple choice questions (MCQs) are superior and more objective in testing theoretical knowledge, but as very few teachers are trained in the art of formulating MCQs, these have been ignored. Surely, faulty MCQs are worse than the good old essay system. At the same time, training teachers in making

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Risk factors for acute myocardial infarction in Indians: a case-control study

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Summary

Background South Asians who have settled overseas and those in urban India have an increased risk of ischaemic heart disease (IHD). Reasons for this increased risk are unclear. Most studies have been based on migrants to western nations, so their findings may not apply to most south Asians, who live in their own countries. Therefore, we assessed the relative importance of risk factors for IHD among South Asians in Bangalore, India.

Methods We conducted a prospective hospital-based case-control study of 200 Indian patients with a first acute myocardial infarction (AMI) and 200 age and sex matched controls. We recorded prevalence of the following risk factors for IHD: diet, smoking, alcohol use, socioeconomic status, waist to hip ratio (WHR), blood glucose, serum insulin, oral glucose tolerance test, and lipid profile.

Findings The most important predictor of AMI was current smoking (odds ratio [OR] 3·6, p<0·001) of cigarettes or beedis (a local form of tobacco), with individuals who currently smoked 10 or more per day having an OR of 6·1 (p<0·001). History of hypertension and of overt diabetes mellitus were also independent risk factors (OR 2·68 [p=0·001] and 2·64 [p=0·004], respectively). Among all individuals, fasting blood glucose was a strong predictor of risk over the entire range, including at values usually regarded as normal (OR adjusted for smoking, hypertension, and WHR 1·62 for 1 SD increase, p<0·001). Abdominal obesity (as measured by WHR) was also a strong independent predictor across the entire range of measures (OR adjusted for smoking, hypertension, and blood glucose 2·24 for 1 SD increase; p<0·001). Compared with individuals with no risk factors, individuals with multiple risk factors had greatly increased risk of AMI (eg, OR of 10·6 for the group with smoking and elevated glucose). Lipid profile was not associated with AMI. In univariate analyses, higher socioeconomic (income) status (OR 0·32, p=0·005 highest *vs* lowest; OR 0·75 middle *vs* lowest) and vegetarianism (OR=0·55, p=0·006), seemed to be protective. The impact of vegetarianism was closely correlated with blood glucose and WHR.

Interpretation Smoking cessation, treatment of hypertension, and reduction in blood glucose and central obesity (perhaps through dietary modification) may be important in preventing IHD in Asian Indians.

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Introduction

Individuals of south Asian descent (India, Pakistan, and Bangladesh) have an increased risk of ischaemic heart disease (IHD) compared with most other ethnic groups.[1] The reason for this increased risk, which has been recorded both among south Asian migrants to other countries[1,2] and among Indians in urban India,[3,4] is unclear. Prevalence of conventional risk factors such as smoking, hypertension, and hypercholesterolaemia is no higher in south Asians than in other ethnic groups.[1,3-5] High triglyceride concentrations, low concentrations of high-density-lipoprotein (HDL) cholesterol, increased visceral fat, and insulin resistance are more prevalent among south Asians, and these factors have been proposed as reasons for the higher risk of IHD.[1,2,6,7] However, a variable that is more common among south Asians may not necessarily be associated with IHD risk. Conversely, a factor that is not more common among south Asians may still have an important relation with IHD. Further, since most studies have been based on migrants to western countries, the findings may not necessarily apply to the vast majority of South Asians who live in their own countries. Therefore, we conducted a hospital-based case-control study of patients with a first myocardial infarction in Bangalore, India, to assess the relative importance of the risk factors for IHD among south Asians.

Participants and methods

Cases

200 consecutive patients aged 30–60 years (inclusive) admitted to the coronary care unit of St John's Medical College Hospital with an acute myocardial infarction (AMI) were prospectively recruited as cases. AMI was defined as typical chest pain lasting at least 20 min and an electrocardiogram (ECG) showing ST elevation of at least 2 mm in two or more contiguous leads with subsequent evolution of the ECG and diagnostic enzyme changes (doubling of creatine kinase with at least 10% MB fraction). Patients were excluded if they had a history of heart disease, clinical evidence of liver disease, a change in diet in the previous month, or if a fasting blood sample could not be taken within 24 h of the onset of chest pain.

Controls

200 controls were prospectively selected either from individuals attending the hospital outpatients clinic (for refraction, otorhinolaryngology evaluation, or a general physical examination that they had requested) or from patients admitted for elective surgery for conditions that were unlikely to confound a comparative analysis (eg, cataract and herniorrhaphy). Individuals with any previous diagnosis of heart disease, history of exertional chest pain, clinical evidence of liver disease, dietary changes in the previous month, or a 12-lead ECG showing pathological Q waves, ST segment deviation, T wave inversion, bundle branch or atrioventricular block, tachyarrhythmia other than isolated atrial ectopics, or chamber hypertrophy were excluded. Controls were matched to cases for age and sex.

Variables

Data were prospectively recorded with standard forms. In all participants, age, sex, religion, monthly income, and educational level were recorded together with details of diet, smoking, alcohol use, and known history of diabetes mellitus and hypertension. Weight, height, and waist and hip circumferences were recorded for each person. Waist circumference was measured at the narrowest diameter between the costal margin and the iliac crest, and the hip circumference was measured at the greatest diameter over the buttocks. All interviews and anthropometric measurements were carried out by the same research assistant.

	Cases (n=200)	Controls (n=200)	
Age in years	47·3 (SD 8·0)	47·0 (SD 8·1)	
Male (%)	189 (95)	189 (95)	
Religion			
Hindu	146	151	3·5,* 0·174
Muslim	24	14	
Christian	30	35	
Marital status			
Single	4	9	2·86,* 0·239
Married	190	187	
Widowed	6	4	
Income per month			
<Rs 1999	91	74	10·66,* 0·005
Rs 2000–3999	81	78	
≥Rs 4000	28	48	
Level of education			
None	17	21	6·39,* 0·041
School	118	95	
College	65	84	
Serum lipids (mean, SD)†			
Total cholesterol (mmol/L)	4·83, 1·17	4·64, 0·96	0·08
Median (range)	4·71 (2·25–9·19)	4·69 (2·10–7·59)	
HDL cholesterol (mmol/L)	1·16, 0·26	1·15, 0·27	0·98
Median (range)	1·09 (0·65–2·43)	1·09 (0·73–2·59)	
LDL cholesterol (mmol/L)	2·76, 0·98	2·68, 0·82	0·14
Median (range)	2·73 (0·67–5·36)	2·75 (0·65–5·02)	
Total/HDL cholesterol	4·3, 1·14	4·2, 1·17	0·43
Median (range)	4·2 (1·3–7·3)	4·1 (1·6–8·3)	
Triglycerides (mmol/L)	2·00, 1·37	1·77, 0·97	0·11
Median (range)	1·68 (0·37–7·57)	1·51 (0·44–7·36)	

*p=2 df, †sign rank test in paired case-controls.

Table 1: Demographic, socioeconomic, and lipid data

Fasting blood glucose and lipids (total, low-density-lipoprotein [LDL] and HDL cholesterol, and triglycerides) were measured in all participants. Fasting serum insulin was measured in individuals without a history of diabetes; they also had a 75 g oral glucose tolerance test with measurement of a 2-h blood glucose (PPBG). In cases, fasting blood for lipids was taken within 24 h of onset of chest pain. Blood for fasting glucose, serum insulin, and PPBG was taken on the 9th or 10th day after admission. In controls, the blood tests were done on the same day as the lipid measurements; if patients were scheduled to have surgery, studies were completed before operation. Blood glucose, total cholesterol, and triglycerides were estimated on an automated system with standard kits (Boehringer Manheim GmbH). Enzymic methods were used: cholesterol oxidase/peroxidase-aminophenazone for cholesterol and glycerol phosphate oxidase/peroxidase-aminophenazone for triglycerides. HDL cholesterol was estimated with the precipitation method and glucose by the glucose oxidase method. Analyses were done on a Beckman Synchron CX4 Random Analyzer. LDL cholesterol was calculated as total cholesterol minus (HDL cholesterol +triglyceride/5). Serum insulin was estimated by RIA (Radio Immuno Assay Kit-1, the Board of Radiation and Isotope Technology, Bombay, India), which uses ^{125}I-labelled insulin. All biochemical analyses were done without knowledge of clinical information. The laboratory takes part regularly in an external quality assessment programme for lipids and glucose with satisfactory results.

Statistical methods

Comparisons of mean or median values or prevalence of a risk factor were conducted after matching each case with the next control subject recruited of the same sex and age within 5 years. A comparison of discrete variables in cases and controls was done with logistic regression accounting for the matching of cases with controls. Estimates of relative risk and 95% CIs were also done. For continuous variables, non-parametric analyses on paired values were used because of the skewed values obtained for many variables—eg, triglycerides. Multivariate analyses were conducted

Category	Cases (n=200)	Controls (n=200)	OR	95% CI	p
Smokers*					
Never	68 (34%)	119 (59%)	1·0†		
Former	32 (11%)	23 (12%)	1·9	0·93–3·90	
All current	110 (55%)	58 (29%)	3·6	2·20–6·03	<0·001
Current <10/day	30 (15%)	36 (18%)	1·6	0·82–3·07	
Current >10/day	80 (40%)	22 (11%)	6·7	3·51–12·8	<0·001
Type of tobacco‡					
Cigarettes alone	78 (39%)	54 (27%)	3·2	1·74–5·75	
Beedis alone	29 (15%)	16 (8%)	4·0	1·81–8·95	
Both	25 (12%)	11 (6%)	5·3	2·08–13·6	<0·001

*Combined data for beedis and cigarette smoking for never smoked at any time (never), smoked in the past (former), and any current smoker of cigarettes/beedis (current). †Referent. ‡Data are for category by type of smoking, including former and current smokers.

Table 2: **Smoking and risk of AMI**

with logistic regression methods on transformed values. The SAS (SAS Institute, Cary, NC) and BMDP (BMDP Statistical Software Inc, Los Angeles, CA) statistical packages were used for analyses. p values were two tailed. However, for data in which the overall sample of 400 subjects was divided by tertiles or by diabetic status, unmatched analyses were conducted. Analyses for the multiple logistic regression model excluded fasting insulin and PPBG concentrations because they were measured only in patients without diabetes

Results

The demographic characteristics and lipid data of the 200 cases and 200 controls are shown in table 1. Cases had significantly lower monthly incomes than controls, and significantly fewer of them had a college education. The odds ratio (OR) for AMI was 0·32 (95% CI 0·16–0·66) for the highest versus lowest income group and 0·75 (0·48–1·17) for the middle versus lowest income groups.

Life-style and diet

Smoking was an important risk factor. 132 (66%) cases and 82 (41%) controls had smoked or were current smokers of cigarettes or beedis (a local type of tobacco) (OR 3·1, 95% CI 1·94–4·90). This increased risk was also seen in those who only smoked beedis (table 2). When the data on cigarette and beedi smokers were combined, a dose-response effect was evident. Although alcohol was consumed by more cases (87, 44%) than controls (62, 31%) when the data were adjusted for the effect of smoking, alcohol was no longer a risk factor (p=0·221).

The high risk of IHD in Indians has been attributed to ghee (clarified butter) consumption,[14] but in our study regular use of ghee was broadly similar in the two groups (20/144, 13·9% in cases, 22/165, 13·3% in controls; p=0·739). Individuals were classified as being vegetarian or non-vegetarian by a simple questionnaire. 59 (30%) cases and 84 (42%) controls were vegetarians. Vegetarianism had a protective effect (OR 0·55, 95% CI 0·35–0·85; p=0·006), which persisted after adjusting for smoking, blood glucose, HDL and LDL cholesterol, and triglycerides but not after incorporating waist to hip ratio (WHR) into the analysis.

Glucose metabolism, WHR, and hypertension

36 cases (18%) were known to be diabetic compared with 18 controls (9%) (OR 2·64, 95% CI 1·31–5·30; p=0·007). Overall, cases had a higher fasting blood glucose than controls. This finding was expected since there were more known diabetics among the cases. After exclusion of patients with known diabetes, mean fasting blood glucose was higher in cases than in controls (p=0·003) (table 3). PPBG was 8·49 mmol/L (3·46) and 6·61 mmol/L (3·10), respectively (p<0·0001). Even after subjects with impaired glucose tolerance (PPBG ≥7·77 mmol/L) were excluded, fasting blood glucose remained significantly higher in cases (p<0·0001). Overall, after adjustment for smoking, hypertension, and WHR, a 1 SD increase in fasting blood glucose was associated with a 1·62 increase in risk of AMI. Cases had higher fasting plasma insulin (which was not measured in known diabetics) than controls (p=0·039); this difference was abolished after exclusion of patients with impaired glucose tolerance, p=0·239 (table 3). For fasting blood glucose and insulin, separate analyses were done for all participants together, for those not known to be diabetic, and for those with a PPBG of 7·77 mmol/L or less (table 4). All these analyses indicated a progressively increasing risk of AMI with increments of fasting blood glucose even within the range regarded as euglycaemic.

Although the body-mass index of cases and controls was similar (22·8 [SD 3·25] and 22·6 [4·06], respectively), the WHR was significantly greater in cases (0·92 [0·06] *vs* 0·89 [0·06], p<0·0001). When patients were divided into tertiles on the basis of WHR, fasting-blood glucose, and fasting plasma insulin, there was a progressive increase in risk for AMI with each increment in WHR and fasting blood glucose. Compared with those in the lowest tertile for WHR (cut-off values: ≤0·89, 0·90–0·93, ≥0·94), the ORs for those in the second and highest tertiles were 2·19 (95% CI 1·33–3·58) and 3·84 (2·33–6·32), respectively. After adjustment for smoking, hypertension, and blood glucose, a 1 SD increase in WHR increased the OR by 2·24.

A history of hypertension was significantly more common in cases than in controls (37, 19% *vs* 15, 8%; OR 2·69, 95% CI 1·42–5·11; p<0·001).

There were no significant differences between cases and controls in any of the lipid variables (table 1), and there was no pattern of risk when cases and controls were divided by tertiles according to the various lipids (data not shown).

	Patient group					
	All participants		Not known diabetic		PPBG <7·77 mmol/L	
	Cases (n=200)	Controls (n=200)	Cases (n=164)	Controls (n=182)	Cases (n=90)	Controls (n=143)
Age (years)						
Mean (SD)	47·3 (8·0)	47·0 (8·1)	46·2 (8·2)	46·3 (8·0)	45·0 (8·1)	45·9 (8·2)
Median (range)	48 (30–60)	48 (30–60)	46 (30–60)	47 (30–60)	45 (30–60)	45 (30–60)
FBG (mmol/L)						
Mean (SD)	6·77 (3·31)	5·55 (2·36)*	5·83 (2·16)	5·16 (1·84)*	6·05 (2·65)	4·83 (1·65)*
Median (range)	5·55 (3·00–26·09)	4·77 (3·05–18·65)	5·24 (3·00–20·31)	4·72 (3·05–18·65)	5·36 (3·22–20·31)	4·66 (3·05–18·65)
Insulin (mU/L)						
Mean (SD)	ND	ND	25·5 (18·5)	24·3 (26·7)†	23·3 (17·7)	22·0 (22·1)†
Median (range)	ND	ND	20·5 (1·9–101·7)	17·2 (3·9–217)	17·6 (1·9–90·8)	15·8 (3·9–126·0)

p values (cases *vs* controls) were *p<0·0001, †p<0·05, and ‡p>0·05. ND=not done.

Table 3: **Fasting blood glucose (FBG) and serum insulin**

	OR (95% CI) for each third			
	Lower	Middle	Upper	p*
All patients (n=400)				
FBG	1·0	2·15 (1·30–3·55)	3·70 (2·24–6·10)	<0·0001
Insulin	1·0	0·95 (0·53–1·70)	1·99 (1·11–3·56)	0·020
Not known diabetics (n=346)				
FBG	1·0	2·05 (1·24–3·37)	3·04 (1·73–5·33)	0·0002
Insulin	1·0	0·79 (0·47–1·33)	1·65 (1·98–2·77)	0·036
FPBG ≤7·77 mmol/L (n=233)				
FBG	1·0	1·58 (0·84–2·98)	5·48 (2·58–11·6)	<0·0001
Insulin	1·0	0·67 (0·35–1·30)	1·44 (0·74–2·81)	0·152
Cut off values for tertiles				
FBG (mmol/L)	≤4·72	4·73–5·77	>5·78	..
Insulin (mU/L)	≤13·8	13·9–24·2	>24·3	..

*Test for trend.

Table 4: **Relative risk in groups by tertile of fasting blood glucose (FBG) and insulin**

Stepwise-wise regression analysis

Stepwise logistic regression analysis was carried out for continuous variables (WHR; fasting blood glucose; total, HDL, and LDL cholesterol; and triglycerides) and for categorical variables (any smoking, history of diabetes mellitus and hypertension, income, and education level). The most predictive independent variables were smoking (p<0·001), WHR (p<0·001), fasting blood glucose (p=0·003), history of hypertension (p=0·017), and income (p=0·015). Smoking and WHR were associated with the highest risks. With receiver-operating-characteristics curves, cut-off values were chosen for high WHR and fasting blood glucose on the basis of the highest proportion of correctly classified cases and controls. To determine the effect of these risk factors, we considered

	Model		Adjusted OR (95% CI)
	Coefficients	SE	
Smoking	β_1=1·319	0·298	3·74 (2·08–6·73)
WHR >0·92	β_2=1·136	0·279	3·12 (1·80–5·40)
Hypertension	β_3=1·094	0·413	2·99 (1·32–6·75)
FBG ≥4·94 mmol/L	β_4=1·042	0·280	2·84 (1·63–4·93)
Income <4000 rupees /mo	β_5=0·9804	0·406	2·67 (1·20–5·94)
Non-vegetarian	β_6=0·2105	0·291	1·23 (0·70–2·19)

Adjusted OR of presence of single risk factor can be calculated from antilog of respective β-coefficient is. To calculate adjusted OR for combination of two risk factors, add β-coefficients and calculate antilog. For example, in individuals who smoke (β_1=1·319) and have an elevated fasting blood glucose (FBG) (β_4=1·042), the OR is calculated as e (1·319 + 1·042) = 10·6.

Table is based on matched case-control analysis. Data on fasting insulin and PPBG were not included since they were unavailable in diabetics. Recalculation of multiple logistic regression model without matching but also including fasting insulin and PPBG yielded the following results: intercept = −1·327, SE=0·237; smoking: β_1=1·252, SE=0·227, OR 3·5 (2·24–5·47); FBG ≥4·94 mmol/L, β_4=1·219, SE=0·299, OR=3·35 (1·88–5·09); hypertension β_3=1·064, SE 0·354, OR 2·90 (1·44–5·82); non-vegetarianism β_6=0·410, SE 0·228, OR=1·51 (0·99–2·36); WHR >0·92 β_2=0·244, SE=0·238, OR 1·28 (0·67–2·44).

Table 5: **Effect of multiple risk factors, modelled with logistic regression: prediction of cases versus controls**

smoking, hypertension, income, non-vegetarianism, WHR of 0·92 or more, and fasting blood glucose of 4·94 mmol/L or more. Table 5 shows the adjusted OR for each variable, with the independent predictive effect of each risk factor controlling for all others in the model. With the information in this table, the independent effect of risk factors and various combinations can be calculated. For example, individuals who smoke and have a raised glucose have an OR of 10·6. For an individual with the three risk factors of smoking, raised glucose, and hypertension, the OR is 31·7.

Discussion

Our study, which is probably the first prospective case-control study aimed at identifying the relation between risk factors and AMI in south Asians in India, shows that tobacco smoking, a history of hypertension, a high prevalence of diabetes, increased fasting blood glucose (even in those who are not diabetic), and an increased ratio of visceral to total body fat (WHR) are independent risk factors for AMI. Patients with multiple risk factors have a substantially increased risk for AMI.

Our study was conducted in a tertiary care hospital serving an urban and suburban population in Bangalore, a large south Indian city. Since the cases are confirmed cases of AMI not known to have had previous heart disease, the study avoids the problem of misdiagnosis associated with sole use of ECG diagnostic criteria (as has been done in prevalence studies) and of modification of risk factors by treatment of IHD. We also avoided problems associated with migration and acculturation since the study was done in India; it also allows comparison of risk factors among individuals within a relatively homogeneous ethnic origin and geographic region with and without AMI, rather than between populations.

Tobacco smoking is an important modifiable risk factor for IHD in western countries.[15] Studies on migrant Indian populations have not emphasised the importance of smoking.[2,12] The prevalence of smoking is increasing in India even as it decreases in developed countries. Our data show that it was the most important risk factor with a dose-related risk (cigarettes and beedis). McKeigue and colleagues[2] reported a similar relation between smoking and IHD among south Asians in the UK. Our study supports the conclusion that tobacco control programmes in India and other countries of the region could have an important public-health impact.

Despite low meat and fish consumption, even among non-vegetarians in India, our findings point to a significant protective effect of vegetarianism, which persisted after adjustment for smoking, lipids, and glucose concentrations. That the inclusion of WHR in the model substantially explained the potential impact of vegetarianism suggests possible ways for reducing the risk associated with central obesity. Vegetarianism among Indians is generally life long and is not necessarily associated with other healthy behaviours (eg, less smoking, more exercise) and therefore our data are less subject to confounding.

Lipid abnormalities are a widely accepted risk factor for IHD. Studies on Indian populations in other countries have reported that Indians generally do not have higher total or LDL cholesterol concentrations than white or Afro-Caribbean populations. They do, however, have

lower HDL cholesterol and higher triglyceride concentrations.[12,13,15,16] Although the mean HDL cholesterol was low and triglycerides were high in our cases, they were not significantly different from controls. In a survey of Asian men in Britain, McKeigue et al[17] reported that presence of major Q waves on ECG was associated with increased total cholesterol and triglycerides but not with reduced HDL cholesterol. Two small studies from India (Chaddha et al[14] with 11 cases and Dhawan et al[16] with 28) showed that total cholesterol and triglycerides were higher in individuals with IHD than in those without IHD. The data from our much larger study do not show significant differences in the concentrations of any of the usual lipid fractions in patients with and without AMI; this may indicate that in our population the serum lipids that we measured did not have an important causal role. Our study had 80% power to detect 11 mmol/L (6%) relative differences in total cholesterol. AMI alters serum lipids but this change occurs after the first 48 h whereas all our blood samples were taken within the first 24 h.[17,18] In addition, the fact that infarction tends to lower HDL cholesterol and raise triglycerides should exaggerate any difference in the concentrations of these lipid fractions. However, some of the cases in our study did receive intravenous heparin soon after admission which may lower serum triglycerides but not the other lipids.[18]

Known diabetes mellitus was a significant risk factor for AMI in our study, and both serum glucose and insulin were higher in cases than in controls. Although transient hyperglycaemia occurs in AMI, it is accompanied by a concomitant fall in serum insulin, in contrast to our findings. How long lasting are these transient AMI-related changes in insulin and glucose is unclear. According to Ryder et al,[19] blood sugar returns to normal in 3 days. Serum insulin is low in the early hours after AMI and returns to normal in a few hours to a few weeks.[20,21] If assessment of glucose tolerance is delayed after an AMI values may be altered by diet and changes in life style. Therefore, we measured blood sugar and serum insulin on the 9th and 10th day after admission. Fasting blood glucose was higher in cases than in controls even among patients not previously known to be diabetic and in those without impaired glucose tolerance. Our findings accord with several previous reports indicating a high prevalence of non-insulin dependent diabetes mellitus in Asians[22-24] and two previous studies showing the importance of diabetes and impaired glucose tolerance as risk factors for IHD.[4,5] Our observation of increasing risk with increasing blood glucose concentrations suggests that even high blood glucose within the euglycaemic range identifies individuals at higher risk of IHD. This is consistent with data from the Framingham Heart Study indicating a relation between glycosylated haemoglobin and IHD.[25] The lack of an association of fasting insulin levels (a crude measure of insulin resistance) with AMI in the euglycaemic group suggests that glucose may be more relevant to the development of IHD than hyperinsulinaemia in this population.

The WHR is a measure of abdominal obesity and a surrogate measure for visceral fat deposition.[26] McKeigue et al[8] found a significantly higher prevalence of major Q waves and positive ECG but not symptomatic IHD across tertiles of body-mass index and WHR. Central obesity is generally regarded as a more important predictor of IHD than is generalised obesity.[27]

The relation between IHD and economic factors depends on the state of the economic development of a country. In developing countries IHD is thought to be predominantly a disease of the upper income groups. As development progresses this relation may reverse.[28,29] Our findings that cases of AMI had a lower income and lower education than controls accords with a recent cross-sectional study conducted in a rural area of Rajasthan in which the prevalence of ECG abnormalities was inversely related to the level of education.[30] Our data are unlikely to be biased since hospital fees for patients admitted for elective surgery are similar to those for emergency care such as AMI. However, controls from outpatient clinics who request a general physical examination may have had a different social background. Of the 200 controls, 18 were in this category. If these 18 controls are excluded from the analysis, the findings remain largely unchanged. By contrast, Chadha et al[14] in a study from Delhi reported a lower prevalence of ECG abnormalities among people of a lower socioeconomic status than among those of a higher status. McKeigue and Marmot[31] found no difference in prevalence of IHD among South Asians in Britain from different socioeconomic backgrounds. These conflicting data suggest that India may be in a state of transition from a pattern of disease seen in developing countries to that seen in the more developed ones.

Our study may have some of the limitations inherent in a case-control design. Although the controls were hospital based, we carefully defined a group of individuals drawn from the same catchment area for whom enhancement or avoidance of putative risk factors were unlikely. Although controls from the community would have been ideal, hospital-based controls were easier to recruit and generally belonged to the same population as hospital-based cases. Further, all cases were defined prospectively with accepted criteria and all controls were carefully screened clinically to eliminate those who may have had subclinical disease. The values for several variables (eg, lipids, glucose, body-mass index) that we obtained in our controls are similar to those from an independent large cross-sectional study of 5455 (2488 of whom were male) urban and rural individuals in north India (K S Reddy, All India Institute of Medical Sciences, New Delhi, India). Without a prospective cohort study, it is difficult to assess the potential impact on risk factors, if any, of pre-existing silent IHD, changing risk factors among cases, and any treatment for diabetes mellitus and hypertension that patients may have received. However, such factors generally tend to reduce differences between cases and controls. Finally, the patients in this study are predominantly male and any extrapolation to women should be done cautiously.

Our findings suggest that, in addition to smoking and hypertension (which are important risk factors for IHD in most populations), central obesity and raised blood glucose are important across a wide range of values in south Asians. Although glucose intolerance, insulin resistance, hypertension, central obesity, high triglycerides, and low HDL cholesterol occur together and are associated with an increased prevalence of cardiovascular disease, the mechanism of the increased vascular disease associated with these syndromes is unclear.[32,33] In our study vegetarianism seemed to have a protective effect against AMI that was unrelated to risk factors other than WHR. This finding suggests that modifications in diet among non-vegetarians reduce visceral obesity, thereby lowering the risk of IHD.

Our data suggest that smoking cessation programmes aimed at controlling both cigarette and beedi use, control of blood glucose, treatment of hypertension, and reduction of visceral obesity, perhaps by diet, are likely to be key factors in the prevention of premature IHD in south Asians.

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PH-D

HOW TO STOP SMOKING.....

PREPARATION OF SURROUNDINGS

- Two weeks prior to *quit* date, limit your smoking to one room in your home.
- Clean and remove the smell of cigarette smoke from your home.

PREPARATION OF YOUR PHYSICAL SELF

- Get your teeth cleaned. With tar and nicotine removed from your teeth.
- Monitor your alcohol consumption.
- Reduce your caffeine consumption prior to quitting
- Get plenty of rest. Your body needs time to readjust without the drug, nicotine
- Drink plenty of fluids.
- Use healthy oral substitutes.

PREPARATION OF YOUR EMOTIONAL SELF

- Repeat to yourself your reasons for needing to *quit* smoking
- Plan activities for your first smoke-free week.
- Occupy your hands with other objects when you feel something is missing without a cigarette.
- Beware of cigarette advertisements.
- Never allow yourself to think that one cigarette won't hurt.

ENLISTING SOCIAL SUPPORT FOR YOUR *QUIT* DATE.

- Remind your friends and family that you are going through the quitting process and that it is important to you that they support you.
- Be assertive and direct when asking for support.
- *Working with a smoker.* It is important to make a request for support or at the very least for respect of your efforts to quit smoking by not smoking in your presence. You may also ask for a transfer to a work area that is somke free.

You'r *quit* date and the weeks that follow.

1. Visualize and reinterpret your physical systems as "*Symptoms of recovery*".
   Initial phase of quitting; you may experience a list of nicotine withdrawal symptoms (i.e. Restlessness, irritability, difficulty in concentration, sleep disturbances, dry mouth or sore throat, fatigue, coughing and Nicotine "Craving". These symptoms are short-term and necessary to the healing process. Try to think about them as symptoms of recovery". When you are feeling irritable and restless or having a "Craving" remind yourself that your body is healing.

Imaginary exercise of healing process.....!!
Close your eyes and imagine your lungs. See the black tar sitting on the tiny little air sacs that makes it hard for you to breathe at times. Each time you feel "uncomfortable" imagine this tar gradually being lifted off your lungs. Each breath that you take feels easier. You feel the clean air healing the wounded lung tissue. You see the 4,000-plus particles that are floating in your bloodstream being washed away. You feel your arteries relaxing and allowing blood to pass more readily through, cutting your risk for strokes and heart attacks. With each passing day you see more and more healing occurring inside your body.

2. *Pay attention to your "high risk" situations.* These are times, such as when you are stressed at work or finishing a meal, when you are most likely to desire a cigarette. Try either to avoid these situations or at the very least to have alternative strategies available.
3. *Use distraction techniques.* When you find yourself tempted to smoke a cigarette get some distance from the thought or situation. Distraction is a wonderful technique for preventing impulsive smoking.
4. *Reinforce your reasons for needing to quit smoking.* Remember, these reasons need to be specific and personal to you. These reasons will help get you through the periods of temptation.
5. *Repeat to yourself the benefits of quitting smoking.* Repeat the following list of benefits to yourself several times a day.

BENEFITS OF QUITTING SMOKING

1. Circulation improves.
2. Significantly decreases your risk for lung cancer and emphysema.
3. Increases lung and breathing capacity
4. Decreases allergies
5. Eliminates chronic bronchitis (which decreases energy level, resistance to infection, and predisposes one to emphysema) in a few months after cessation.
6. Reduces number of cavities and increases chance of keeping your own teeth (smokers have three times more cavities and gum disease than non-smokers)
7. Decreases risk of esophageal cancer by 500 percent.
8. Decreases risk of kidney cancer by 50 percent
9. Decreases frequency and intensity of headaches.
10. Decreases risk of osteoporosis

QUICK FIX COPING STRATEGIES.

Things You Can Do

1. Do relaxation exercises.
2. Go to a place where smoking is not allowed.
3. Take a walk.
4. Exercise.
5. Listen to your favorite music.
6. Drink fruit juice, water, or soda with lemon.
7. Take a hot bath.
8. Call a friend for support
9. Do some gardening.

THINGS TO THINK ABOUT OR SAY TO YOURSELF

1. Think about how many ways quitting will improve your health.
2. Think about how not smoking will help your loved ones.
3. Go over your reasons for quitting.
4. Imagine yourself as a non-smoker.
5. Think about how much better food tastes when you are not smoking.
6. "I can manage this without a cigarette."
7. "I have made it this far."
8. "My lungs are getting healthier."
9. "I can breathe better."
10. "NO!!!!"

MANAGING SYMPTOMS OF ANXIETY RELATED TO NICOTINE WITHDRAWAL

1. The symptoms of anxiety that you are experiencing are caused by the physical withdrawal process from nicotine.
2. This is your body's way of healing itself. The discomfort you are feeling will lead to overall healing and improved health. It is "good" pain.
3. These symptoms of anxiety will last for only a couple of weeks. The worst feeling will be around the third or fourth day after your last cigarette.
4. *Practise* visualizing how nicotine increases your heart rate and blood pressure. Next visualize how without nicotine your heart rate and blood pressure will return to normal.
5. You may want to picture your anxiety as a wave. You can feel it rise - but as you ride it out you can feel it subside. It passes without any action on your part.

Steps to Beating Depression – Related to Nicotine Withdrawal

- Recognize your triggers to depression
- Avoid isolating yourself.
- Push yourself to engage in small tasks. Depressed individuals often complain of no energy or interest in activities. Set small but reasonable goals for yourself. For example, force yourself to go to the grocery store or to a social function.
- Get support from those you trust.
- Seek professional help. You don't necessarily have to wait until the depression gets really bad to get professional help. The longer you wait to treat depression the worse it can get, and subsequently the harder it is to beat.

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Source : "HOW TO STOP SMOKING" – Lori Stevic-Rust & Anita Maximin.

PH 7.

TOBACCO, HEALTH AND DEVELOPMENT: AN INTRODUCTION

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The World Health Organisation (WHO) is in the process of negotiating its first international public health treaty, a proposed Framework Convention on Tobacco Control (FCTC). A major stimulus to this initiative has been recognition of the escalating burden arising from tobacco consumption and production in low- and middle-income countries, with serious and diverse social, economic and environmental impacts in addition to enormous implications for global health. With one or two exceptions, however, the development community has generally been slow to respond both to the challenges posed by the tobacco industry and to the opportunities presented by the FCTC process. This short paper highlights the importance and value of engaging with tobacco control for NGOs working with development issues, and provides links to easily accessible sources of further information. It serves as an introduction to key issues that will be developed during discussions at the forthcoming meeting of the Health and Development Forum to be held at the London School of Hygiene and Tropical Medicine on September 12th 2002 at 1.30pm.

Tobacco, Health and Equity

It is estimated that some 4 million deaths per year can currently be attributed to tobacco, or about 1 in 10 of all adult deaths. Such figures are set to rise dramatically such that by 2030 the annual death total will stand at around 10 million or 1 in 6 adult deaths. Consequently, around 500 million people alive today will eventually be killed by tobacco.

This burden is becoming increasingly inequitable in its distribution. Smoking related deaths were once largely confined to men in high-income countries, but the marked shift in smoking patterns to middle and low-income countries is being accompanied by rapidly rising trends in death and disease.

- Around half of all deaths from tobacco occur in the developing world, but this will rise to 70% by 2030.
- In China smoking accounts for around 1 in 3 of all adult male deaths, or around 100 million of the 300 million Chinese males now aged 0-29.
- Tobacco will kill around 80 million Indian males currently aged 0-34

Selling tobacco products to women has been described as the single largest product marketing opportunity in the world. While the epidemic may be in gradual decline among men, it will not reach its peak among women until well into the 21st century, and it is predicted that the current world total of around 187 million women smokers will reach 532 million by 2025. Such an increase, driven by economic and social change and by increased targeting of women by major tobacco companies, is liable to have enormous consequences for health, incomes and families across developing countries.

Sources:

WHO Tobacco Free Initiative (2001) Burden of Disease
http://www5.who.int/tobacco/page.cfm?sid=47
Gajalaksmi CK et al (2000) 'Global patterns of smoking and smoking-attributable mortality' in Jha P and Chaloupka F (eds) Tobacco Control in Developing Countries available at: http://www1.worldbank.org/tobacco/tcdc/009TO040.PDF

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Samet J and Yoon S eds. (2001) Women and the Tobacco Epidemic: Challenges for the 21st Century (Geneva: World Health Organization)
http://tobacco.who.int/documents/WoMonograph01.pdf

The Economics of Tobacco Control, Tobacco Production and Development

A fundamental obstacle to the development of comprehensive tobacco control programs has been the misplaced belief in the value of tobacco production and consumption to national economies. As a result of research led by the World Bank, it is increasingly clear that, for the vast majority of countries, increased taxation of tobacco products would not cause long-term job losses. Tobacco control actually presents policy makers with a virtuous circle, often combining substantial benefits for public health through reduced consumption with an expansion in revenues via increased taxation.

Notwithstanding the broadening evidence base that tobacco control makes good economic sense, it is clear that some countries are significantly reliant on tobacco production. Real dependence on the crop is, however, far less common than is often suggested. Of the 141 countries that export tobacco only 18 derive more than 1% of their total export earnings from it, and tobacco accounts for over 5% of export earnings in only 4, namely Kyrgyzstan, Macedonia, Zimbabwe and Malawi (at 8%, 16%, 32% and 58% respectively).

Importantly, however, improved tobacco control is not going to result in a sudden collapse. Rather, the number of people using tobacco products is expected to increase by over 500 million during the next quarter of a century. Tobacco control efforts do not focus on reducing supply, and any decline in overall consumption that could undermine employment in tobacco farming will occur over several generations.

Sources:
World Bank (1999) Curbing the Epidemic: Governments and the Economics of Tobacco Control http://www1.worldbank.org/tobacco/reports.htm
Campaign for Tobacco Free Kids (2001) 'Golden Leaf, Barren Harvest: The Costs of Tobacco Farming' http://tobaccofreekids.org/campaign/global/FCTCreport1.pdf

Globalisation, Trade and the Tobacco Epidemic

Globally, the tobacco industry is increasingly dominated by a handful of major companies. 75 percent of the world cigarette market is now controlled by just four companies: Philip Morris, British American Tobacco (BAT), Japan Tobacco and the China National Tobacco Corporation. Recent years have also seen the number of major companies involved in the purchasing, processing and shipment of raw tobacco fall from eight to three. The period from 1994-97 witnessed a 12.5% increase in unmanufactured tobacco exports globally, following a decade of negligible growth. Cigarette exports were relatively stable between 1975 and 1985, began to steadily rise thereafter, and grew by 42% between 1993-96.

Both the consolidation and expansion of the tobacco industry have been driven by trade liberalization. The opening of cigarette markets in Asia has been particularly significant, as shown by the impact of the so-called Section 301 agreements in Japan, South Korea, Taiwan and Thailand. Access to these markets was gained following threatened trade sanctions by the US and, in the Thai case, adjudication by GATT. It has been estimated that the opening of these markets increased per capita cigarette consumption by an average of 10% by 1991.

It is particularly important to note the inequitable impacts of trade liberalisation on tobacco consumption. Trade liberalisation has led to increased consumption of tobacco overall but, while it has no substantive effect on higher-income countries, it has had a large and significant impact on smoking in low-income countries and a significant, if smaller, impact on middle-income countries.

Sources:

Taylor A et al (2000) 'The impact of trade liberalization on tobacco consumption' in Jha P and Chaloupka F eds. Tobacco Control in Developing Countries, available at: http://www1.worldbank.org/tobacco/tcdc/343T0364.PDF

Hammond R (1998) 'Consolidation in the tobacco industry', Tobacco Control, 7: 426-428 (Winter) http://tc.bmjjournals.com/cgi/content/full/7/4/426?

Transnational tobacco companies and development

The tobacco industry has undoubtedly contributed to the widespread failure to perceive tobacco as a significant development issue, particularly in seeking to undermine the credibility of WHO's work to promote tobacco control. An examination by a WHO Committee of Experts of industry documents made available via litigation revealed the scale of efforts to portray such activities as a 'First World' agenda carried out at the expense of developing countries. Documents have identified the explicit use of the International Tobacco Growers Association as a front group for industry lobbying, a clear concern to stop developing countries becoming committed to tobacco control, to restrict WHO's funding and divide it from other UN agencies, and the creation of an international consortium to mobilize officials from developing countries to advance pro-tobacco positions.

Underlying such tactics has been a broad strategy of attempting to present the concerns of small tobacco farmers in developing countries as fundamentally aligned with those of the enormous transnational tobacco companies based in the United States, the UK and Japan. The extent of divergence in interests is becoming apparent, with increasing evidence of the poor economic returns, environmental damage and health impacts associated with tobacco production:

- In Brazil, a report by Christian Aid highlighted the role of BAT's local subsidiary Sousa Cruz in controlling the livelihoods of small-scale contract farmers and raised serious concerns about the health impacts of pesticides sold by the company.
- In Uzbekistan, where BAT has made a substantial investment, the British Helsinki Human Rights Group identified exploitation of local farmers amounting to *de facto* slave labour.
- In Kenya, there is rising concern about the substantial death toll from pesticide use and the rapid rate of deforestation attributable to tobacco.
- Cigarette companies are using progressively less tobacco per cigarette, adopting techniques such as using expanded or reconstituted tobacco, increasing profitability while reducing demand for raw tobacco.

Sources:

WHO Committee of Experts (2000) 'Tobacco Company Strategies to Undermine Tobacco Control Activities at the World Health Organization' http://filestore.who.int/~who/home/tobacco/tobacco.pdf

Christian Aid/DESER (2002) Hooked on Tobacco report on BAT subsidiary Sousa Cruz http://www.christian-aid.org.uk/indepth/0201bat/index.htm

British Helsinki Human Rights Group (2002) Uzbekistan 2002: British American Tobacco http://www.bhhrg.org

Campaign for Tobacco Free Kids (2001) Factsheets 'Tobacco and the Environment', 'Tobacco Industry Manipulation of Agricultural Issues' and 'Lowering Leaf Content, Boosting Profits' http://tobaccofreekids.org/campaign/global/

Towards the Framework Convention on Tobacco Control

The process of negotiating the FCTC was established by a unanimous resolution of the World Health Assembly in 1999, initiating a two-step process of Working Groups to establish technical foundations followed by an Intergovernmental Negotiating Body (INB). Semi-annual negotiating sessions of the INB have been held in Geneva since November 2000, with the fifth round set for October 2002. The FCTC is expected to take the form of a broad convention outlining legal parameters, structures and general obligations for all signatories, in combination with a number of protocols detailing more specific commitments to which states can choose to accede on a case-by-case basis. The objective is for a negotiated convention to be ready for presentation to the WHA in May 2003.

The FCTC process has been characterised by an attempt to secure broad participation both by member states and by civil society. One notable development has been the negotiation of coordinated positions among regional groupings prior to the INB meetings. The Johannesburg Declaration on the FCTC, for example, was adopted by the 21 countries of WHO's African Region in March 2001. This common front was widely perceived as having added weight to their contributions to the first INB session, emphasising a commitment to progressive control measures in combination with calls for assistance in agricultural diversification.

The FCTC process has aimed to encourage the participation of actors traditionally excluded from the state centric politics of UN governance. Public Hearings held in October 2000 provided an opportunity for interested groups to register their views prior to the start of inter-governmental negotiations. Over 500 written submissions were received, while 144 organisations provided testimony during the 2 day hearings, encompassing TTCs, state tobacco companies and producer organisations as well as diverse public health agencies, womens' groups and academic institutions.

The role of NGOs in the process has centred on the development and activities of the Framework Convention Alliance. This grouping of over 160 increasingly diverse NGOs was created to improve communication between those groups already engaged in the FCTC process and to address the need for a systematic outreach to smaller NGOs in developing countries. It has developed a valuable series of briefing papers and identified key issues in support of developing a strong Framework Convention.

Sources:

WHO (2002) 'Framework Convention on Tobacco Control: An Introduction' with links to all documentation and draft Chair's text http://tobacco.who.int/en/fctc/index.html

Bates C (2001) Developing countries take the lead on WHO convention, Tobacco Control, 10 (3): 209 http://www.ash.org.uk/html/international/html/inb2review.html

Framework Convention Alliance (2002) Briefings on Trade, Advertising, Smuggling and Packaging and Labelling, together with a list of 10 key issues for global tobacco control and the FCTC, available at www.fctc.org

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Building the evidence base for global tobacco control

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The tobacco control movement needs a global information system permitting routine monitoring of the tobacco trade, tobacco farming, the tobacco industry, the prevalence of tobacco use, associated mortality, and national resources for combating tobacco. The Tobacco Control Country Profiles database, a data collection initiative led by the American Cancer Society in collaboration with WHO and the Centers for Disease Control and Prevention, represents the first step in the development of such a system. Baseline data on several indicators of tobacco use were obtained from 191 Member States of WHO, two Associate Members, Hong Kong Special Administrative Region of China (Hong Kong SAR), China (Province of Taiwan) and the West Bank and Gaza Strip. The methods used to compile the data are described in the present paper.

Selected indicators from the database were analysed in order to demonstrate the potential utility and value of data derived from an information system devoted to tobacco control. The analyses covered gender-specific smoking prevalence by WHO Region, per capita cigarette consumption by Human Development Index (HDI) category, and average real annual percentage changes in cigarette prices between 1990 and 1999 for selected countries in each category. In 1998, men were almost four times more likely than women to be smokers. The prevalence of smoking among men was highest in the Western Pacific Region. The differential in gender-specific smoking prevalence was narrowest in the Region of the Americas and the European Region. It was wider in the South-East Asia Region and the Western Pacific Region. The lowest and highest per capita consumption of manufactured cigarettes occurred in the lowest and highest HDI categories respectively. In the medium HDI category, China's growing cigarette consumption after 1975 had a major bearing on the rise in per capita consumption. Cigarette price trends suggest that there is considerable scope for increasing taxes on tobacco products, particularly in low or medium HDI countries. The implications of the findings for future tobacco control efforts are discussed, as are issues surrounding the quality of available data, priorities for future data collection and the need to maintain and improve the information system in order to support such efforts.

Keywords: smoking, statistics; smoking, epidemiology; tobacco, statistics; prevalence; commerce; databases, factual, utilization; information.

Voir page 889 le résumé en français. En la página 889 figura un resumen en español.

Introduction

It has been estimated that some three million deaths are attributable to smoking annually and that the number could rise to ten million within 30 to 40 years (*1*). Effective action against tobacco requires countries to understand the magnitude of the adverse effects of smoking on their populations. As country representatives negotiate WHO's Framework Convention on Tobacco Control, the need for reliable and timely data on tobacco and its use is greater than ever before. The effects of tobacco use could be monitored through a global system routinely assembling information on the tobacco trade, tobacco farming, the tobacco industry, the prevalence of tobacco use, associated mortality, and national resources for combating tobacco. Anticipating the demand for a global information system to support new tobacco control efforts, WHO and the Centers for Disease Control and Prevention initiated the development of the National Tobacco Information Online System (known provisionally as NATIONS) in 1998. The baseline data for this system were collected for the Tobacco Control Country Profiles (TCCP) project, led by the American Cancer Society. The project has produced a monograph to be presented at the 11th World Conference on Tobacco or Health (Chicago, 6–11 August 2000).

In order to demonstrate the potential utility of the data available from the TCCP project and later from NATIONS, we have analysed gender-specific smoking prevalence, per capita cigarette consumption, and changes in cigarette prices. The analyses illustrate the type of comparison that can easily be made between regions and countries by means of data from

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the TCCP project, which represents the first step in the development of a global tobacco information system. In addition, we highlight issues surrounding the quality of available data, priorities for future data collection, and the need to maintain and improve the system in order to support tobacco control efforts.

Methods

For analyses of smoking prevalence we categorized 191 Member States of WHO, two Associate Members, Hong Kong SAR, China (Province of Taiwan) and the West Bank and Gaza Strip, thus allowing comparison with previous studies conducted by WHO. For analyses of manufactured cigarette consumption we categorized countries according to the Human Development Index (HDI) (*2*), whereby 174 countries are placed in high, medium or low categories based on life expectancy, educational attainment and income, giving a better measure of basic human capabilities or deprivation than income alone. This made it possible to examine how manufactured cigarette consumption varied with basic standards of living.

Country-specific statistics on smoking prevalence in the TCCP database were obtained through Medline literature searches, personal contacts with investigators and nongovernmental organizations engaged in tobacco control, and reports from health ministries, national statistical offices and WHO country representatives. The minimum inclusion criteria for a survey were the following items of information: date of the survey or its publication; characteristics of respondents (age and sex distribution); a description of sampling and data collection methods; and the questions used in assessing smoking behaviour.

When several studies from the same country met these criteria they were compared with respect to geographical coverage, dates, sample sizes, response rates and methods. Wherever different sources yielded contradictory data on prevalence, historical data were reviewed and experts working in the country were consulted. The most recent and representative studies on adult smoking prevalence were included.

Regional estimates of smoking prevalence were derived on the assumption that all studies reported current daily and occasional smoking among persons aged 15 years and older and that they reflected the smoking statuses of the populations in 1998. The gender-specific prevalence estimates for each country were weighted by the size of the male and female populations aged 15 years and above. The values were averaged so as to obtain WHO weighted regional prevalence estimates. Each of these was assumed to apply to an entire WHO region. The number of smokers in each region was estimated by multiplying the prevalence by the total population aged 15 years and above.

Data on per capita cigarette consumption in the TCCP were derived from production, import and export data in several electronic databases and national statistical yearbooks available for public scrutiny. Statistics on cigarette imports, exports and production were obtained from the United Nations Statistical Division's Commodity Trade Statistics, the Industrial Commodity Production Statistics databases, the United States Department of Agriculture, and the Food and Agricultural database.[1] For countries where these data were unavailable, figures from national statistical agencies and private research firms were used.

Cigarette consumption in each country was calculated as *production plus imports minus exports*, using a three-year moving average for the years 1975 and 1985. For high development countries, consumption was also calculated for 1995, a year in which trade and production data were not available for most countries in the medium and low development categories. In the medium development category, consumption was calculated for 1994, and in the low development category it was calculated for 1991. Average per capita consumption was estimated within each HDI category by combining the country-level consumption figures and dividing by the population aged 15 years and above. Adult per capita cigarette consumption in the medium development category is presented both including and excluding China and is calculated separately for China.

Data on cigarette prices, reflecting prices in the autumns of 1990 and 1999 unless otherwise noted, are presented by HDI category in US$ on the basis of values in local currencies and exchange rates in force when surveys were conducted (price and exchange rate data were obtained from the Economist Intelligence Unit). For countries where prices were sampled in more than one city, averages of all the city prices were calculated. Average annual real percentage changes in price between 1990 and 1999 were calculated using the percentage difference in local currency prices while taking into account or discounting for inflation. These calculations were facilitated by creating an inflation index based on estimates provided by the Economist Intelligence Unit.

Results

Prevalence of smoking

Data on smoking prevalence were available from countries with populations representing 55.4 % of the African Region, 96.3% of the Region of the Americas, 88.7% of the Eastern Mediterranean Region, 88.8% of the European Region, 96.9% of the South-East Asia Region and 99.3% of the Western Pacific Region (Table 1).

Men were almost four times as likely to smoke as women, yet 23% of females were smokers in the Region of the Americas and 23.4% were smokers in the

[1] The following product codes were used to identify data for analysis in each of the sources: code 1222, COMTRADE Standard International Trade Classification (Revision 2); code 3140-07, UNSD Production International Standard Industrial Classification of all Economic Activities (Revision 2); code 828, FAOSTAT.

European Region. Smoking prevalence among men was highest in the Western Pacific Region and lowest in the Eastern Mediterranean Region. Among women, smoking prevalence was highest in the European Region and lowest in the Western Pacific Region. There were about 1.235 billion adult smokers in a total world population of 5.926 billion (US Central Intelligence Agency's estimate of the world's population in 1998). On the assumption that there will be no change in the global prevalence of smoking, it can be expected that the number of cigarette adult smokers will reach 1.278 billion this year (2000) and 1.671 billion in 2020 because of changes in the world population (*3*).

Per capita consumption

The percentages of populations in the calculations of per capita consumption varied by HDI category and by year (Table 2). Fig. 1 presents estimates of per capita cigarette consumption for over 15-year-olds in 1975, 1985 and 1995 by HDI category.

The estimates for countries in the medium category are presented with and without China and separately for China. The highest per capita consumption of manufactured cigarettes occurred in the high development category and decreased between 1975 and 1995. Countries in the medium development category experienced a progressive 46% increase in consumption between 1975 and 1994, reaching 1139 cigarettes per capita in 1994. China experienced an increase in per capita consumption at a greater rate than that of the medium development category as a whole from 1975 to 1994. In total, China experienced a 128% increase in per capita consumption between 1975 and 1994. Without China's contribution to the medium development category, its per capita consumption would have decreased slightly between 1985 and 1994. Per capita cigarette consumption in the low development category remained fairly constant from 1975 to 1991.

Price of cigarettes

Table 3 presents trends in cigarette prices in various countries. Substantial increases in real cigarette prices, adjusted for inflation, occurred in only France, South Africa, the United Kingdom, and the USA. No increase or a substantial decrease in cigarette prices occurred in more than half the countries listed. This was especially true of imported brands.

Discussion

Using the TCCP database to support tobacco control

The analyses presented above demonstrate the utility of the data available in the database for supporting programme and policy planning for tobacco control. For instance, analyses of smoking prevalence and cigarette consumption can assist in identifying the countries with the greatest need for resources devoted to tobacco control efforts. Globally, some 30% of adults were estimated to be smokers in 1998. By 2020 the number of smokers will have increased by 35% if global smoking prevalence remains the same. Per capita cigarette consumption trends over 20 years, however, demonstrate the changing nature of the pandemic. If consumption trends continue as they have been since 1975, an increase in cigarette consumption will occur in economically developing countries and a gradual decrease will occur in economically developed countries. The countries with the greatest expansion in the cigarette market will be those with the smallest resources available for tackling the health problems associated with tobacco use. While these analyses used very broad economic categories, the TCCP database allows comparisons between countries, geographical regions or other groupings which might lend support to tobacco control initiatives.

Analyses of average real percentage changes in cigarette prices help to identify policy areas in which national governments can improve their efforts in tobacco control. The cigarette price trends in our study suggest that there is scope for increasing taxes on tobacco products, most notably in countries belonging to the low and medium HDI categories,

Table 1. **Gender-specific smoking prevalence by WHO Region, 1998**

Region	Weighted prevalence estimate (%)			Estimated numbers of smokers (millions)			Number of studies	% of total population represented by studies
	Male	Female	Total	Male	Female	Total		
Africa	36.2	9.4	22.9	59.6391	15.1086	74.7477	15	55.4
The Americas	34.7	23.0	28.7	98.0754	67.8454	165.9209	30	96.3
Eastern Mediterranean	34.2	8.7	21.8	49.7699	11.9266	61.6965	17	88.7
Europe	43.5	23.4	33.0	144.3112	84.6990	229.0102	40	88.8
South-East Asia	48.2	8.2	28.6	242.6307	39.4710	282.1017	6	96.9
Western Pacific	62.3	5.8	34.4	387.2792	34.9310	422.2101	23	99.3
Total	**47.9**	**12.4**	**30.2**	**981.7055**	**253.9816**	**1235.687**	**131**	**92.3**

Sources: American Cancer Society and World Health Organization, TCCP database.

Note: Several small countries for which population figures were not available did not contribute their population weight to the analysis.

where cigarette prices have failed to keep up with increases in the general price level of goods and services. Cigarettes were more affordable in 1999 than at the beginning of the decade. Increasing the price of tobacco products is arguably one of the most effective means of curbing their consumption (*4*). On average, a price increase of 10% can be expected to reduce the demand for cigarettes by about 4% in high-income countries and by about 8% in low-income and middle-income countries (*5*). The young (*6*, *7*) and the poor (*8*, *9*) tend to be more responsive to price changes than other groups of people. Analyses using data from the TCCP database, and later from NATIONS, can provide evidence in support of the World Bank's tobacco tax and price increase strategy and related policies.

Using the TCCP database for needs assessment

In addition to providing an evidence base for tobacco control, the database identified disparities between countries in regard to the amount and quality of data available for analysis. This indicated priority areas for future data collection and tobacco control surveillance efforts. For instance, smoking prevalence statistics were not found for 33% of the countries, provinces and territories. The prevalence of smoking in the African Region has probably been influenced by the lack of data because only half the Regional population contributed to the estimate, whereas the data for the other regions cover more than 85% of their populations. Compared to previously reported statistics the representativeness of Africa's regional smoking prevalence data has improved. In 1997, for example, WHO's Tobacco or Health Programme analysed regional smoking prevalence in the early 1990s (*10*). The new estimate covers 22% more of the African Region's population. The validity of estimates in developing regions can be expected to improve with increased access to country-specific data and increased capacity and resources for monitoring risk factors. Standardized survey methods would also increase the utility of regional estimates. In all regions there were variations between countries in the survey methods employed, and regional estimates were affected by the comparability of country-specific data.

The TCCP database made it possible to see ways in which consumption estimates could improve through standard reporting of country-level data to an information system. The accuracy of most per capita consumption estimates is limited by the information *not* included in each country's official trade and production statistics. In countries where the preferred cigarettes are not of the manufactured kind the TCCP data underestimate consumption. Country-level data related to the consumption of roll-your-own, bidi and kretek cigarettes would usefully supplement information on manufactured cigarettes from databases of the United Nations and the United States Department of Agriculture. This is particularly relevant to the Eastern Mediterranean Region and Central and Southern Asia, where tobacco consumption is likely to be underestimated if traditional forms of use are excluded from the calculations.

Table 2. **Population coverage by Human Development Index category in 1975, 1985 and 1995**

Level of human development	1975	1985	1995
High	97.8%	97.3%	87.6%
Medium	83.1%	85.9%	85.5%[a]
Low	77.2%	81.6%	73.7%[b]

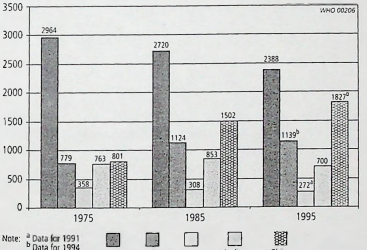
[a] Population coverage in 1994.

[b] Population coverage in 1991.

Source: American Cancer Society and World Health Organization, TCCP database.

Note: Coverage represents the percentage of the total population within each category that also reported consumption figures. Within each level of human development no population figures were available for certain countries, and these were not taken into account in the above calculations.

Fig. 1. **Annual per capita consumption by Human Development Index category (three-year moving average)**



Source: American Cancer Society and World Health Organization, TCCP database.

Routine data collection is less likely to provide the means of overcoming certain additional obstacles to estimating consumption, indicated below with a view to aiding the interpretation of TCCP data.

The calculations we used did not account for factors that increase or decrease the true volume of trade and production, such as smuggling and tax exemption. The consumption formula does not account for cigarette stocks held in reserve by cigarette wholesalers and retailers. This factor only becomes apparent if a very large net change in stock volume occurs from one year to the next. The per capita consumption calculation includes only persons aged 15 years and older in its denominator and thus does not account for younger smokers. The importance of this factor is greatest in certain developing countries where the largest proportion of the population consists of people under 15 years of age.

Table 3. **Cigarette prices in selected countries by human development level: 1990–99**

Country	Marlboro (US$ per pack of 20 cigarettes)			Local brand (US$ per pack of 20 cigarettes)		
	1990	1999	Average real annual % change	1990	1999	Average real annual % change
High human development						
Canada	3.85	3.50	−0.18	3.40	2.67	−1.67
Czech Republic	1.78	1.29	−5.66	1.05	1.15	−2.88
Denmark	4.64	4.37	−0.69	4.55	4.30	−0.67
France	1.98	3.26	7.40	1.20	2.76	14.86
Germany	2.86	2.87	−0.19	2.75	2.79	−0.09
Japan	1.75	2.58	1.01	1.61	2.30	0.70
New Zealand	2.63	3.81	4.78	2.67	3.62	3.78
Poland	1.34	1.21	−5.90	0.26	0.99	10.55
Sweden	3.90	4.32	3.20	3.72	4.20	3.45
United Kingdom	3.40	6.27	7.46	3.40	6.27	7.46
United States of America	1.74	3.16	4.72	1.71	3.04	4.39
Medium human development						
China	1.49	1.83	0.55	0.96	1.73	5.97
Costa Rica	0.89	0.69	−4.74	0.70	0.64	−3.63
Egypt	1.47	1.16	−6.52	1.10	1.16	−4.99
Hungary	1.46	1.01	−6.03	0.52	0.89	1.43
Kenya	2.15	1.59	−3.09	0.65	0.80	2.13
Mexico	0.52	1.07	0.16	0.45	0.86	−0.70
Malaysia	0.96	1.11	1.74	0.89	0.76	−1.50
Morocco	2.21	2.84	−0.76	0.98	1.45	0.78
South Africa	1.07	1.37	4.45	0.68	1.37	13.48
Thailand	1.16	1.09	−0.97	0.50	0.73	4.67
Turkey	1.66	1.32	−6.06	0.92	0.99	−4.44
Venezuela	0.46	1.44	3.06	0.46	1.28	1.49
Low human development						
Bangladesh	1.41	1.37	−1.25	1.13	0.85	−3.50
Côte d'Ivoire	1.87	0.94	−4.72	1.54	0.78	−4.67
Nigeria	1.26	0.83	−4.13	0.44	0.83	8.83
Senegal	1.15	0.80	−1.07	0.77	0.32	−5.09
Zambia	0.89[a]	2.03	−12.09	0.74[a]	0.64	−14.93

[a] 1993.

Source: Economist Intelligence Unit; calculations made by World Health Organization.

Both the wide range of analyses possible using TCCP data and the limitations of these data indicate a need for standardized data collection techniques at the country level and greater access to data by researchers working outside each country. In the future, NATIONS can be expected to increase access to data. The system will integrate information systems and data sources electronically to facilitate the tracking of country-specific information across a wide range of indicators, including smoking prevalence and tobacco consumption, laws and regulations, morbidity and mortality, industrial organizations, tobacco economics, and programmatic interventions against tobacco use. NATIONS will report time-trend data for each indicator and will update them periodically. In this way, the evidence base for tracking the progress of tobacco control policies will be increased and the common electronic framework necessary for storing and updating data, making information easily accessible to researchers, tobacco control advocates, and policy-makers over the Internet will be provided.

Conclusion

The results of these analyses using data from the TCCP database demonstrate the potential applications of an information system devoted to tobacco control. Because TCCP compiled data on a wide variety of indicators, from employment in tobacco manufacturing to pharmaceutical treatments for tobacco dependence, future analyses are not limited to the type of prevalence, tobacco consumption and price comparisons presented here. Nor are they restricted to groupings by WHO Region and HDI level. Unfortunately, neither TCCP nor NATIONS can directly meet the need for standardized survey and data collection methods at country level. This

requirement is best tackled through capacity-building at local level with leadership from WHO and others in accordance with defined principles (*11*). The establishment of a permanent electronic framework for data management and retrieval, however, may provide an incentive for improving and increasing tobacco control efforts by making the results of independent research available to the global tobacco control community. ◘

Résumé

L'information au service de la lutte antitabac

Le mouvement de lutte antitabac a besoin d'un système d'information mondial sur la culture et le commerce du tabac, l'industrie du tabac, la consommation de tabac et la mortalité qui lui est associée, ainsi que sur les moyens existant au plan national pour la lutte contre le tabac. La base de données par pays (Tobacco Control Country Profiles – TCCP) mise en place par l'American Cancer Society en collaboration avec l'OMS et les Centers for Disease Control and Prevention constitue une première étape vers l'établissement d'un tel système. Des données de base sur une série d'indicateurs relatifs à la consommation du tabac ont été recueillies auprès de 191 Etats Membres de l'OMS, de deux Etats Membres associés, de deux provinces de Chine et de trois territoires occupés. Le présent article décrit les méthodes utilisées pour synthétiser les informations.

Il analyse également les indicateurs employés pour les TCCP, de façon à mettre en évidence l'utilité et la valeur potentielles des données fournies par un système d'information spécifiquement voué à la lutte antitabac. Cette analyse porte sur la prévalence du tabagisme par sexe et par Région OMS, sur la consommation de cigarettes au regard de l'indicateur du développement humain (HDI) et sur l'évolution annuelle moyenne en valeur réelle du prix des cigarettes entre 1990 et 1999. L'article met également en avant certains problèmes concernant la qualité des données et la nécessité de maintenir et d'améliorer le système d'information afin de faciliter les efforts de lutte contre le tabagisme.

Globalement, les hommes étaient près de quatre fois plus nombreux que les femmes à fumer en 1998. C'est dans la Région du Pacifique occidental que le pourcentage d'hommes consommant du tabac était le plus élevé. S'agissant de la proportion respective de fumeurs et de fumeuses, c'est dans les Amériques et en Europe que l'écart entre les hommes et les femmes était le plus faible, et dans les Régions de l'Asie du Sud-Est et du Pacifique occidental qu'il était le plus marqué. En ce qui concerne les cigarettes industrielles, la consommation la plus faible et la plus élevée par habitant coïncidaient avec l'indicateur le plus faible et, respectivement, le plus élevé du développement humain. Dans la catégorie moyenne, l'augmentation globale de la consommation enregistrée depuis 1975 en Chine correspondait à une augmentation par habitant. Quant au prix des cigarettes, son augmentation était inférieure à la moyenne du renchérissement des biens et services, ce qui fait que les cigarettes étaient relativement plus abordables en 1999 qu'en 1990. Ces indications confirment qu'il existe une importante marge potentielle d'augmentation des taxes sur les produits du tabac, notamment dans les pays où l'indicateur du développement humain est faible à moyen.

L'analyse met également en lumière la contribution potentielle de la base de données TCCP au développement des programmes et politiques de lutte antitabac. Ainsi, les statistiques de la consommation des cigarettes permettent d'identifier les pays où le besoin de ressources dans ce domaine est le plus aigu. Les pays où le marché de la cigarette connaît la plus forte expansion sont à l'évidence ceux qui disposent des ressources les plus faibles pour faire face aux problèmes associés au tabac. De même, l'analyse de l'évolution du prix des cigarettes et autres données connexes permet de définir des domaines d'intervention dans lesquels les gouvernements pourraient renforcer leur contribution à la lutte antitabac, par exemple en augmentant le prix des cigarettes afin de faire baisser la consommation.

Le projet TCCP a révélé des disparités entre les pays en ce qui concerne le volume et la qualité des données disponibles pour l'analyse et permis d'identifier un certain nombre de priorités pour les futures activités de collecte de données et de surveillance. Ainsi, on n'a pas pu établir la prévalence de la consommation de tabac dans 33 % des pays, provinces et territoires occupés englobés dans l'étude. Dans la Région africaine, cette indication a été biaisée par le fait que seule la moitié de la population a été prise en compte dans les estimations. Les estimations relatives à la consommation de cigarettes pourraient être améliorées grâce à des systèmes de collecte de données standardisés au plan national. Dans les pays où les cigarettes les plus consommées ne sont pas les cigarettes industrielles, les données TCCP sous-estiment la consommation des populations concernées. Des statistiques sur la consommation des cigarettes roulées, des *bidis* et des cigarettes *kretek* permettraient de dresser un tableau plus complet que les données limitées aux cigarettes industrielles.

Le large éventail d'analyses autorisées par les données TCCP et les limites de ces mêmes informations confirment la nécessité de techniques de collecte des données normalisées au plan national et d'un meilleur accès aux données par des chercheurs travaillant en dehors des pays concernés.

Resumen

Acopio de datos estadísticos para la lucha antitabáquica mundial

El movimiento contra el tabaco necesita un sistema mundial de información para vigilar regularmente el comercio, el cultivo y la industria de ese producto, así como la prevalencia del hábito de fumar, la mortalidad

asociada y los recursos nacionales para la lucha antitabáquica. La base de datos sobre las características de los países en relación con la lucha antitabáquica, una iniciativa de recopilación de datos coordinada por la Asociación Estadounidense de Lucha contra el Cáncer en colaboración con la OMS y los Centros para el Control y la Prevención de Enfermedades, representa el primer paso en el desarrollo de dicho sistema. Se obtuvieron datos comparativos sobre varios indicadores del consumo de tabaco de 191 Estados Miembros de la OMS, dos Estados Miembros Asociados, dos provincias de China y tres territorios ocupados. Los métodos utilizados para compilar los datos se describen en el presente documento.

A fin de demostrar la utilidad y el valor potenciales de los datos derivados de un sistema de información dedicado a la lucha antitabáquica, se analizan los indicadores arriba mencionados. Los análisis versan sobre la prevalencia de tabaquismo por sexos por región de la OMS, el consumo de cigarrillos per cápita por categoría del índice de desarrollo humano (IDH) y los cambios porcentuales anuales reales promedio de los precios de los cigarrillos entre 1990 y 1999. Se destacan temas relacionados con la calidad de los datos y la necesidad de mantener y mejorar el sistema de información para respaldar la lucha antitabáquica.

A nivel mundial, los hombres tenían una probabilidad de fumar casi cuatro veces mayor que las mujeres en 1998, y la prevalencia más alta de tabaquismo masculino se registró en la Región del Pacífico Occidental. Las diferencias de prevalencia de tabaquismo por sexos eran menores en la Región de las Américas y la Región de Europa y mayores en la Región de Asia Sudoriental y la Región del Pacífico Occidental. Con respecto a los cigarrillos elaborados, el consumo per cápita más bajo y el más alto se registraron en las categorías más baja y más alta, respectivamente, del índice de desarrollo humano. En la categoría de IDH medio, el consumo creciente de cigarrillos en China después de 1975 tuvo una influencia predominante en el aumento del consumo per cápita. Los precios de los cigarrillos no aumentaron tan rápidamente como el nivel general de los precios de los bienes y servicios, y en consecuencia los cigarrillos fueron más asequibles en 1999 que en 1990. Estos resultados indican que hay un margen considerable para aumentar los impuestos que gravan los productos del tabaco, particularmente en los países de IDH bajo y medio.

Los análisis muestran el potencial que encierra la base de datos sobre las características de los países para apoyar la planificación de programas y políticas. Por ejemplo, los análisis del consumo de cigarrillos pueden contribuir a determinar en qué países se necesitan muchos recursos para la lucha antitabáquica. Los países con mayor expansión del mercado de los cigarrillos son evidentemente aquellos que tienen menos recursos disponibles para abordar los problemas asociados con el tabaco. El estudio de la variación porcentual de los precios de los cigarrillos y los análisis conexos pueden ayudar a identificar las esferas normativas en las que los gobiernos pueden mejorar sus esfuerzos de lucha antitabáquica, por ejemplo aumentando el precio de los cigarrillos como medio para reducir el consumo.

El proyecto reveló disparidades entre los países en cuanto a la cantidad y la calidad de los datos disponibles para efectuar análisis y mostró esferas prioritarias para los fines futuros de la recopilación de datos y los esfuerzos de vigilancia. No se encontraron estadísticas sobre la prevalencia del tabaquismo en un 33% de los países, provincias y territorios ocupados considerados. El análisis de la prevalencia del tabaquismo en la Región de África estuvo muy determinado por la falta de datos, ya que las estimaciones se realizaron sólo con la mitad de los habitantes de la Región. Los cálculos sobre el consumo de cigarrillos podrían mejorar mediante una notificación normalizada de los datos sobre los países. En los países donde los cigarrillos preferidos no son los elaborados, los datos que aporta esta base sobre consumo de cigarrillos por la población dan lugar a subestimaciones. Si se reunieran datos sobre el consumo de cigarrillos confeccionados manualmente y de cigarrillos de bidi y de kretek, se podría obtener un panorama más completo que el que ofrecen los datos sobre consumo de cigarrillos elaborados.

La amplia variedad de análisis posibles a partir de los datos de la base sobre las características de los países y las limitaciones de estos datos muestran la necesidad de técnicas estandarizadas de recopilación de datos a nivel de país y de un mejor acceso a los datos para los investigadores que trabajan fuera de determinados países.

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TOBACCO CONTROL IN INDIA

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Tobacco use has not been considered as a good habit by many societies, right from its introduction in 16th century. Availability of irrefutable scientific evidence on its health hazards from well-conducted cohort and case-control studies during 1950s supported the pleas for tobacco control. However, the anti-tobacco movement acquired a global nature after the publication of the official reports on the subject by the Royal College of Physicians[1] and the US Surgeon General[2]. Subsequently, thousands of scientific investigations have confirmed the association of smoking with various diseases, and have provided additional evidence implicating cigarette smoking as a cause of coronary artery disease, stroke, obstructive airway disease, peripheral vascular disease, pregnancy complications including intra-uterine growth retardation and a variety of neoplasms including cancers of oral cavity, larynx, oesophagus, urinary bladder, kidney, stomach, pancreas, cervix and more recently of haematopoietic system[3].

A long-term British study[4] that followed 34,439 male doctors for 40 years, concluded that about 50% of all smokers will eventually die from their habit. The median survival of smokers was 7.5 years shorter compared to non-smokers, and the decrease in survival was also dose-dependent. Review of the health hazards of exposure to environmental tobacco smoke (or passive smoking) shows that it damages the respiratory tract of adults, adversely effects the cardiovascular system and results in lung cancer[5]. Children of smokers have an increased frequency of respiratory and middle ear infections and are at risk of impaired lung function. Passive smoking increases the frequency & severity of asthmatic episodes, both in children and adults. Newer epidemiological studies are substantiating the risk of coronary heart disease due to passive smoking. Many hazardous substances have been identified in tobacco[3], but it has not been possible to identify all the components, which result into cancers or other diseases. Nicotine, tar, HCN, volatile aldehydes, nitrosamines are some of the identified hazardous substances in tobacco smoke.

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Despite progress made in identification of these hazardous substances, it has not been possible to identify chemical(s) whose removal may render tobacco safe. Thus, the most effective preventive measure for control of tobacco related diseases is to avoid tobacco use.

The total number of tobacco users in the World has been estimated at 1.2 billion, which is expected to rise to 1.6 billion during 2020s[6]. At present, tobacco use causes death of 3.5 to 4 million people globally, which is expected to increase to about 10 million during 2020s. Developing countries need to be concerned because 7 million of these deaths would be occurring in these areas, mainly due to increasing trends of tobacco use.

Indian studies have also recognized tobacco use as a major health hazard in India. Association of smokeless tobacco use with oral cancer was pointed out as early as 1908[7]. Subsequent Indian studies on tobacco have amply shown its association with major diseases entities, both in smoking as well as in smokeless form. Tobacco is used for smoking as well as in smokeless form in India[8]. Smoking of tobacco is mainly in the form of bidi, followed by cigarette, hukah, chilum, chutta, etc. The habit of smokeless tobacco (also referred as tobacco chewing) is also very common. Some common forms of smokeless tobacco include khaini, Mainpuri tobacco, mawa, mishri, etc. Careful review of Indian studies concluded that bidi smoking is also associated with the diseases caused by cigarette smoking and results in similar physiological changes[9]. Association of smokeless tobacco has been observed with cancers of oral cavity, pharynx, larynx and oesophagus, and precancerous lesions of oral cavity.

Prevalence of Tobacco Use in India

Information on prevalence of tobacco use in India is available from surveys carried out in general community. As per various surveys carried out during 1980s, the prevalence of tobacco use among men above 15 years of age varied between 46% and 63% in urban areas and between 32% and 74% in rural areas. Among women it varied between 2% and 16% in urban areas and between 20% and 50% in rural areas[10]. A survey in Mumbai city showed the prevalence

of tobacco use to be 69.3% among men over 35 years of age and 57.5% among women above 35 years[11]. A large survey in 2001 showed that the prevalence of current tobacco use above 10 years of age in Uttar Pradesh was 50.0% among men & 9.1% among women; whereas the prevalence in Karnatka was 41.0% among men & 14.9% among women[12].

Two nationwide surveys have been carried out in India for prevalence of tobacco use[13,14] covering rural as well as urban areas. The second and the most recent nationwide survey (carried out from July 1993 to June 1994) revealed that 23.2% males (any age) and 4.0% females (any age) consumed tobacco in any form in urban areas[13]. In rural areas the prevalence of tobacco use in any form was 33.6% among males and 8.8% among females. The reported prevalence of tobacco use in 1993-94 is less than the prevalence reported in the first national level survey (1987-88), which showed the prevalence of tobacco use among men to be 25.7% and 35.3% in urban and rural areas, and among women to be 5.95% and 11.1% in urban and rural areas, respectively. The reason for this decline is not clear. Based on age & sex specific rates for tobacco use in urban and rural areas, as reported in the second national level survey, it is estimated that in 1996, 184 million persons (150 million males and 34 million females) in India used tobacco[15]. It has also been estimated that about 112 million persons smoked tobacco, while 96 million used it in smokeless form.

Deaths due to Tobacco in India

Information on mortality rates associated with tobacco use in India is available from three cohort studies. The age adjusted relative risk of mortality due to tobacco use and the prevalence of tobacco use, applied to overall mortality of the country, suggested that at least 630,000 persons died in 1986 due to tobacco use[16]. Median risks as observed from these cohort studies, and the prevalence of tobacco use as found in the first nationwide survey of National Sample Survey Organization[14], when applied to the 1996 population, showed that about 800,000 persons in India died due to their tobacco habit in 1996[17]. Recent studies[18,19] indicate that the risk of death due to tobacco use may in fact be more than that identified earlier[16].

Magnitude of the Tobacco Related Diseases in India

Magnitude of three major tobacco related disease entities was estimated based on a careful review of Indian literature on risk estimates for development of these diseases; magnitude of these disease in India; and prevalence of tobacco use in the country[15]. Three disease entities under consideration were coronary artery disease, chronic obstructive lung diseases and cancers of oral cavity, pharynx, larynx, lungs & oesophagus. The prevalence of tobacco habit (smoking or smokeless form as applicable for the disease entity) was taken from the second nationwide survey on tobacco use (1993-94) by the National Sample Survey Organization[13]. The exercise revealed that the tobacco results into enormous morbidity in the country, being responsible for 42 lakh existing cases of coronary artery disease and 37 lakh existing cases of chronic obstructive lung diseases. It also caused about 154,000 incident cases of cancers in 1996.

Diseases due to Tobacco in India, 1996

Disease Entity	Total number in India	Cases due to tobacco use
Tobacco related cancers (Incident cases)	209,810	154,320
Coronary artery disease (Prevalent cases)	15,700,000	4,200,000
Chronic obstructive lung diseases (Prevalent cases)	14,000,000	3,700,000

Economic considerations of tobacco in India

The Ministry of Health & Family Welfare constituted an expert committee to undertake a comparative study on the economics of tobacco use inter-alia examining the tax revenue and foreign exchange earnings, employment and consumer expenditure on the one hand and the cost of tertiary level medical care facilities for treatment of tobacco-related diseases, losses due to fire hazard, ecological damage due to deforestation and disposal of tobacco-related waste on the other hand with a view to making an economic study of the impact of

tobacco consumption. The committee had members from the field of economics, health, health services, epidemiology, agriculture, tobacco trade, tobacco industry and trade unions. The committee suggested that tobacco economics should be studied in relation to it being a "de-merit good". The short-run, indirect macro economic, secondary benefits of tobacco use are easily outweighed by the conservatively estimated costs of three major diseases associated with the use of tobacco, as shown by an ICMR study. The report underlined the public health angle as critical to an approach towards tobacco use, while not ignoring the short run, secondary and indirect benefits to economy other than tobacco consumers who bear the brunt of the addiction[15].

The committee noted that information on costs due to tobacco related cancers, coronary artery disease and chronic obstructive lung diseases, are available through a study of the Indian Council of Medical Research. The average cost due to a case of tobacco related cancers (as experienced by the cohort[20]) for the year 1990-91 was Rs. 134,449. The average cost of a case of chronic artery disease[13] for 1992 was Rs. 14,909, whereas the average cost of a case of chronic obstructive lung disease was Rs. 11,952. Using the same discounting rate as used in ICMR study, the average cost of tobacco related cancers, coronary artery disease, and chronic obstructive lung disease, for the year 1999 was estimated to be Rs. 350,000, Rs. 29,000, and Rs. 23,300. The total cost to the country for the year 1999 due to these three disease entities was estimated at Rs. 27,761 crore[21].

Cost of Major Diseases due to Tobacco Use in India

	Tobacco Related Diseases		
	Cancers	Coronary Artery Disease	Chronic Obstructive Lung Diseases
Number due to tobacco use			
1996	154,300	4,200,000	3,700,000
1999	163,500	4,450,000	3,920,000
Average Cost (1999) (Rs)	350.000	29,000	23,300
Total Cost India (1999) Billion Rupees	57.225	129.05	91.336
Total Loss (1999) = Rupees 277.611 Billion or US $ 6.5 B			

Source : Rath GK & Chaudhry K[21].

The economics of tobacco use needs to be considered at the consumer level as well as its economy wide effects, including linkages and externalities to other sectors[15]. The commonly identified benefits of tobacco (like employment, contribution to GDP, export earnings, public earnings, inter-industry linkages. etc.) are at macro level and for the government (except for the perceived benefit for the users), while the costs are incurred by the tobacco users. For an existing product like tobacco, any change in pattern of use is likely to upset the regional/ local economies. Addictive properties of this de-merit good influences the rationality of choice for tobacco. India is the third largest producer of tobacco in the world. Tobacco provides on an average, 10% of India's total excise revenue, of which 88% is contributed by cigarettes. The economics of tobacco use has to take note of the multi-sectoral connections of tobacco. The returns to the farmers from tobacco cultivation are high, but the cost of production is also high and thus, the relative return from the crop may not be highest for tobacco. The expert committee on economics of tobacco use in India noted that in 1993-94, total tobacco employment was over 35.59 lakh.

Major efforts for tobacco control in India

Warning on cigarette packages/ advertisements: Recognizing the health hazards of tobacco, the Government of India promulgated The Cigarette (Regulation of Production, Supply and Distribution) Act 1975. Under the act, all packages and advertisements of cigarettes are to carry a statutory warning, "Cigarette smoking is injurious to health". The Act provides specific instructions related to minimum font size, colour contrast, etc. However, the Parliament's Committee on Subordinate Legislation in its 22nd report (December 1995) on this legislation, observed that these guidelines were often not followed[22]. Considering the issue of tobacco in totality, the Committee made wide-ranging recommendations, including, strong & rotatory warning in regional languages on tobacco products; ban on direct as well as indirect advertisement of tobacco products; prohibition of smoking in public places; initiation of measures for awareness on tobacco through health infrastructure, educational institutions and mass media; and initiation of efforts for persuasion of farmers to switch over to alternate crops. These recommendations of Parliament's committee resulted in

modification of the proposed comprehensive legislation on tobacco control.

Warning on smokeless tobacco products: In India, nearly half of the tobacco users consume tobacco in smokeless form. Realizing the need for a warning on smokeless tobacco products (which are classified as food material), the provisions under the Prevention of Food Adulteration Rules (1955) were applied in 1990, which necessitates that every package and advertisement of smokeless tobacco product should have a warning stating that "chewing of tobacco is injurious to health". Packages of arecanut should also state that "chewing of supari may be injurious to health". An expert committee of Directorate General Health Services also provided the minimum font size and other guidelines for this purpose.

Cabinet guidelines for smoking in public places: Cabinet secretariat by an administrative order in 1990, prohibited smoking in certain places such as hospitals, dispensaries, educational institutions, conference rooms, domestic air flights, A/C sleeper coaches in trains, sub-urban trains, A/C buses, etc. State Governments were also advised to discourage sale of tobacco products in and around educational and health related institutions. Direct advertisements of tobacco products had already been prohibited in government media, including Doordarshan and All India Radio. These cabinet guidelines were reiterated in 1998.

Comprehensive legislation on tobacco control: In view of various recommendations and experience on relative inefficacy of the existing legislation (the Cigarette Act), the Ministry of Health & Family Welfare initiated the process of formulation of a comprehensive legislation for replacement of the Cigarette Act (1975). The draft legislation had to undergo a second round of inter-ministerial consultations, in view of the recommendations of the Parliament's Committee on Sub-ordinate Legislation (22nd report - December 1995). The draft has undergone changes as per the suggestions of the Rajya Sabha's Standing Committee and currently proposes a ban on tobacco advertising; clear health warnings on all tobacco products; limit on levels of tar & nicotine; ban on smoking in public places; and ban on sale of tobacco products to minors. The legislation is expected to help in reduction of tobacco

use and in generating a social environment conducive to tobacco control. Legislation has also been promulgated by the states of Delhi, Kerala, Goa and Rajasthan, aimed mainly on prohibition of smoking in public places. Recently, many states such as Tamil Nadu, Maharashtra, Andhra Pradesh, etc., have imposed a ban on production and sale of gutka and pan masala-containing tobacco, as a short-term measure.

Multi-sectoral approach for tobacco control: The problem of tobacco in India is complex, in view of the varied nature of its use; association of a large number of sectors like health, agriculture, finance, mass media, labour, education, industry, welfare, etc.; unorganized nature of work for many tobacco products; dependence of a large number of people on tobacco production & processing; and need for action by many agencies. The situation necessitates multi-sectoral approach, wherein different sectors (government as well as non-government) identify themselves as contributor to a radical social change leading to tobacco control.

A major exercise involving different sectors was organized in July 1991, through organization of a national conference on tobacco or health. The conference recognized tobacco as a major public health hazard and noted that consumption of tobacco is not compatible with the goal of "Health For All". It also realized that an integrated educational, legislative and agro-economic strategy with an operational framework and political, administrative, financial & research support is needed. The conference recommended establishment of a National Tobacco Control Commission to plan, coordinate and monitor tobacco control activities; Prohibition of smoking in certain public places as per Cabinet Sceretariat O.M 27/1/3/90 (7.9.90); Ban on consumption of tobacco products in other public places; Ban on sale of tobacco to minors; Ban on advertising; Statutory warning on all tobacco products; Printing of tar & nicotine levels; Compulsory licensing of tobacco products; Afforestation by tobacco producers; Regulation of tobacco production; Preference for non-smokers in certain jobs; Study of tobacco economics; varied economic and agro-industrial restructuring measures aimed at reduction of involvement of government, Reduction of tobacco crop with rehabilitation of concerned, Removal of subsidies & guarding against involvement of foreign players, Increased taxation, etc.; Health education through various strategies; Involvement of

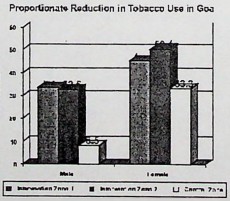
NGOs; Research; Development of a National action plan; and preparation of a White paper on government policy on tobacco.

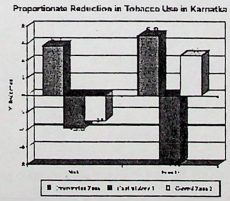
The multi-sectoral and inter-sectoral approach by the Government of India is amply demonstrated through inter-ministerial consultations, consultations with non-governmental organizations and public hearings related to the development of development of the comprehensive legislation on tobacco control; follow up actions on the recommendations of the Parliament's committee on sub-ordinate legislation (22nd report); study on economics of tobacco use in India; and development of a country stance for the framework convention on tobacco control by the World Health Organization. The Indian Council of Medical Research (ICMR) conducted operational research project for involving schools and community volunteers in anti-tobacco community education. The ICMR's collaborative project with All India Radio also showed the mechanism of inter-sectoral collaboration in cost-effective education through radio.

Community education on tobacco: In view of the deep-rooted nature, the eradication of tobacco habit would require concerted action resulting into a social change. Community education regarding tobacco and its health hazards would necessarily be an integral component of such an action plan. Anti-tobacco education needs to be targeted at decision-makers, professionals and the general public, especially the youth. Efficacy of educational activities in tobacco cessation had amply been demonstrated by various organizations. A study by Tata Institute of Fundamental Research, Mumbai, showed that after an intervention of ten years, a significantly higher proportion of persons in the intervention group stopped tobacco usage as compared to a control cohort[23]. No Tobacco Day (31st May) activities have been a regular feature since 1988, which generally comprise of educational advertisement(s) in newspapers along with a programme/ workshop in Delhi and at other centres by states. Tobacco has been included as a topic in books brought about by NCERT. National Cancer Control Programme also stresses on anti-tobacco education, in view of the fact that half of the cancers among men and about one fifth of the cancers among women in India pertain to tobacco related sites. The anti-tobacco community education activities have been initiated in about 60 districts through district level projects for control of cancers. India

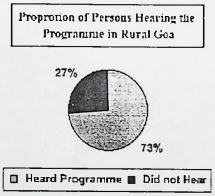
participated in WHO's SEAAT Flame project, under which an anti-tobacco flame traveled by road from Delni to Calcutta and from Delhi to Thiruvananthapuram. Educational programmes on tobacco through television have also been initiated.

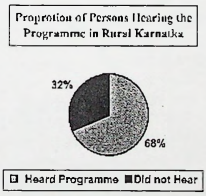
The Indian Council of medical research (ICMR) carried out operational research studies on anti-tobacco community education through involvement of existing infrastructures. The studies involved radio, health infrastructure, schools and community volunteers. The primary health workers in the areas utilizing health infrastructure also examine the oral cavities for presence of any pre-cancerous lesions[24]. The intervention through schools resulted in overall reduction of tobacco habit by 11.8% among men and 9.1% among women in one intervention zone and by 13.4% among men and 13.3% among women in a second intervention zone as compared to a decrease of 2.0% among men and 10.2% among women in control zone. Based on the experience of this project, Ministry of Education, state of Goa, included an 8 hour course on tobacco as a part of co-curricular activities for standard five and above. One-year intervention through community volunteers resulted in 26.3% males and 10.5% females quitting tobacco habit with another 10.1% males and 4.3% females being likely quitters (6 months had not passed since tobacco cessation). Intervention through health infrastructure achieved a reduction of tobacco habit in experimental area, amounting to 5.7% in the males and 6.9% in the females, as compared to an increase of 3.8% among male and 7.8% among female in one control area and an increase of 2.9% among males and 4.6% decrease among females.

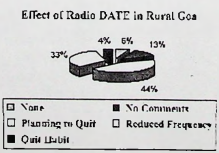


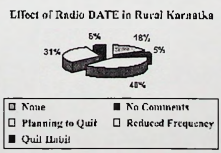


The collaborative project of ICMR and All India Radio (Radio DATE - acronym for Drugs, Alcohol, and Tobacco Education) was in the form of 30 weekly episodes of 20 minutes each25. Ten episodes focused on tobacco. The episodes were broadcast from 84 stations of All India Radio (out of 104 existing at that time) at prime time, simultaneously in sixteen languages. The Hindi prototype was sent to selected radio stations of All India Radio for translation in regional language, as per the specified guidelines. The broadcast was during a specified time (between 8.00 A.M. and 9.00 A.M. on Sundays, with a repeat broadcast during the week, generally in the evening). Two community based surveys in rural areas with no organized anti-tobacco programmes ahowed that about 4% tobacco users in rural Goa and about 6% users in rural Karnataka quit their habit after hearing the programme. About 32% of the potential listeners in Karnataka and about 27% of the potential listeners in Goa had heard at least one episode on tobacco.









Coverage of entire country for anti-tobacco education is a formidable job and can not be achieved without active support from Non-Governmental Organizations and mass media. They however, need support from the health departments for availability of reliable and impartial information on the subject. Support would be needed not only from health related non-governmental organization but also from other related sectors like education, economics, agriculture, welfare, etc.

Expert committee on health hazards of pan masala-containing tobacco

The Directorate General of Health Services constituted a committee to examine the scientific literature on health hazards of pan masala-containing tobacco. The committee realized that if this substance is a causative factor for oral cancer, then most of the users of this substance would be in incubation period and thus, epidemiological data not likely to represent correct picture. The committee examined scientific literature from point of view of in-vitro studies, animal studies, epidemiological data on combination of various substances in pan-masala-containing tobacco and data on tobacco mixtures similar to pan masala-containing tobacco. The committee recognized Pan Masala-containing tobacco to be an important cause of oral sub-mucous fibrosis and cancer. Based on this report, the Central Committee on Food Standards, recommended a ban on chewing tobacco, which was considered by the Government from logistic point of view. Various state Governments have banned the sale and production of such products as a short-term measure, till a long-term strategy for dealing with this substance is finalized.

Tobacco Control Cell

A Tobacco Control Cell has been established in the Department of Health, New Delhi, since August 2000, under Deputy Secretary (PH), with the aim of coordination of activities related to tobacco control, with the help of a 7 member Advisory Board. The current activities initiated through this cell include, educational programmes through mass media and schools, strategy papers for alternate crops and bidi workers, advocacy workshops for non-health sectors, and establishment of tobacco cessation clinics.

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PH-7

AMERICAN LUNG ASSOCIATION®

Stop Smoking ...

Control Your Weight!

Gain Your Freedom—Control Your Weight

If you've just quit smoking, or are about to, you deserve a lot of credit. It's not easy to do—you can face a lot of hurdles along the way. But 46 million ex-smokers have shown that it can be done, and without a doubt is one of the best things you can ever do for yourself and those you love.

Concern about gaining weight is a hurdle for most smokers. Some smokers refuse to quit smoking because they're afraid that they'll gain a lot of weight. Some others return to smoking after stopping for awhile, because they gain some weight and think they're better off smoking.

Cigarette companies have taken advantage of this for years. In the 1930's their ads told people to "Reach for a Lucky instead of a sweet." Today they tell you that "Slim" is the way to be. They want you to smoke as a way of controlling weight and coping with life's pressures—regardless of the consequences.

But the truth is you're never better off smoking. There are better ways to cope. Although it will take some work and take some time, you can quit smoking and control your weight for good.

How Stopping Smoking Affects Weight

Scientists have found that smokers are apt to weigh less than nonsmokers of the same sex, age and height, and that many smokers gain weight when they quit smoking. Smoking may affect the amount and types of food that smokers eat, and how their body processes the food, causing them to have a lower body weight.

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Quitting smoking can trigger changes in eating habits and the body's processing of food, resulting in weight gain.

• Metabolic changes.
Changes in the body's metabolic rate (the rate at which the body burns calories) may account for why many smokers gain a few pounds soon after quitting smoking. Smoking increases the smoker's metabolic rate and seems to make it easier for the body to expend calories and harder for it to store them—contributing to a lower body weight for smokers. When the smoker quits smoking, more calories are converted into tissue, resulting in some weight gain. Exercise is an effective way to combat these metabolic changes.

• Eating more.
It is likely, however, that smokers who gain a substantial amount of weight after quitting smoking also increase the amount of food they eat. Food in general may seem to taste and smell better, leading to bigger portions and extra helpings. Snacking may become a substitute for smoking and a new crutch in dealing with stress and other smoking triggers.

• Eating more sweet foods.
Current research indicates that many smokers develop cravings for sweet (high-sugar, high-calorie) foods after quitting smoking, and that eating more sweets is a significant factor in their weight gain. Some scientists think that nicotine affects the level of blood sugar (glucose) in the body, so that nicotine withdrawal triggers an increased craving for sweet foods. These scientists suggest that if a smoker avoids sweets after

quitting smoking, they probably will avoid much of the weight gain, too.

What You Can Do About It

There are many things you can do to help yourself succeed at quitting smoking and controlling your weight. But before you make changes in your diet and exercise, you have to make changes in your outlook—the way you look at smoking, weight and yourself.

Too many people get trapped in a vicious cycle of quitting smoking, gaining weight, and going back to smoking.

Breaking The Cycle

The key to breaking the cycle is to first make not smoking your #1 priority.

Do what you can now to avoid weight gain. But accept the fact that you still may gain a few pounds as a result of quitting smoking. If you do, chances are good that you can lose it after a few months, when you'll have control of not smoking and be better able to lose weight.

Keep in mind that you're only fooling yourself if you think that you can continue to smoke and stay healthy. Or that you'll be better able to quit smoking in a few years.

So quit smoking now and for good. The American Lung Association is ready to help.

10 Steps For Keeping The Weight Off

1) Make not smoking your #1 priority.

Maintain your freedom from smoking by using new ways to cope with life's pressures. Contact your local American Lung Association for

maintenance strategies for dealing with stress, using relaxation techniques and assertiveness, and coping with urges and feelings. Don't let concern about weight get in your way.

2) Exercise regularly.

Exercise is a big help in controlling weight and quitting smoking. Research suggests that exercise is a key factor in losing weight and, more important, in maintaining the loss.

Exercise can change your body composition, which in turn will help increase the rate at which your body burns calories, making it easier to keep the weight off. Physical activity helps you lose fat and develop muscle. It helps reduce tension and stress; you feel more relaxed and alert rather than exhausted and vulnerable to eating binges.

Your choices are infinite. You could take a walk after dinner or learn something new and different, like karate or dancing. Aerobic-type exercises, such as walking, jogging, swimming, bicycling and cross-country skiing, are best for improving your cardio-respiratory endurance.

Consult your doctor and plan a program tailored to your age and physical condition. Start out slow, make it fun, and stick to it.

3) Monitor your weight.

Weigh yourself regularly—at least once a week, under the same conditions—in order to note and respond to any changes in your weight. Gaining a few pounds after quitting smoking is common. Do what you can now to avoid weight gain and then lose any extra

weight once you're in control of not smoking.

4) Know what you're eating.

Just as it's important in quitting smoking to learn when and why you smoke, it's important in controlling weight to know what foods you're eating, how much, when, and why. Think about what triggers your eating.

5) Eat well-balanced meals regularly.

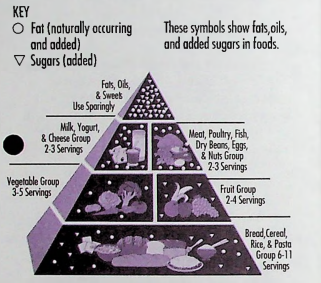
Weight control does not mean dangerous diets, skipping meals, and bad food. It means a healthy, balanced eating plan you can stick with.

Making smart food choices is the secret to controlling your weight. Simply "going on a diet" by cutting calories isn't the answer. If you cut calories too drastically, you won't get enough food to be satisfied, and you may not get enough of certain nutrients. Cutting calories also promotes temporary loss of fluids, instead of permanent loss of fat.

Instead, you'll need to change your basic eating habits.

Use the Food Guide Pyramid to guide you in your daily food choices from the six basic food groups. Make sure your meals are satisfying, to make up for the satisfaction you used to get from smoking. The government recommends that you eat 6-11 servings from the bread, cereal, rice and pasta group; 3-5 servings from the vegetable group; 2-4 servings from the fruit group; 2-3 servings from the milk, yogurt and cheese group; 2-3 servings from the meat, poultry, fish, dry beans, eggs and nuts group; use fats, oils and sweets sparingly.

The Food Guide Pyramid



6) Cut down on fat.

Focus on limiting fat to no more than 30 percent of daily calories. Fat is the biggest source of calories. Reducing calories from fat lets you eat more foods rich in nutrients. such as whole grains, fruits and vegetables.

Switch to leaner cuts of meat and low-fat dairy products. Broil instead of fry, and eliminate high-fat foods such as creams and oils. Serve and eat reasonable portions, no second helpings. Use smaller plates and bowls to give the impression of more food.

7) Snack well.

Limit your snacking by eating good regular meals. Learn new ways to cope with snacking triggers such as anxiety and boredom: try "deep breathing" and other relaxation exercises. Keep "safe" nutritious

snacks at hand: raw vegetables, unbuttered popcorn, fruits that must be peeled. Drink water and low-calorie beverages without caffeine.

8) Avoid sweets and alcohol.

Avoid sweet high-calorie foods and refined sugars. Try fresh fruits such as berries and grapes to satisfy cravings for sweets. Most alcoholic drinks contain 100-200 calories each, but no nutrients. Substitute calorie-free iced tea, mineral water, or seltzer with a squeeze of lemon or lime.

9) When you eat out, eat well.

Order wisely in restaurants. Ask for foods without extra oils and sauces; get salad dressing and butter on the side or not at all. Don't use high-calorie food or alcohol as a crutch in social situations.

It's okay to eat high-calorie foods on special occasions now and then, but plan ahead and fit them within your daily calorie quota.

10) Eat slowly.

Chew slowly. Rest your fork and knife between bites. Give your body 20 minutes to digest the meal and tell you it's satisfied.

If You're Pregnant Or A New Parent

Being pregnant or a new parent is a great reason to quit smoking, for you and your baby. Smoking during pregnancy can be very harmful to the fetus. After your baby is born, it's important to protect

him or her from breathing secondhand smoke. If you're pregnant or nursing, be sure to talk to your doctor about a proper diet before trying to control or lose weight.

Whatever Happens, u're Better Off Not Smoking

Controlling your weight along with quitting isn't always an easy thing to do. It may take some extra time and effort. But making the effort could mean the difference for you in getting off the "smoking and weight merry-go-round" for good. Don't be discouraged if you do gain a little weight. Chances are good that you can lose what you gain after three to six months, when you'll have control of not smoking and be better able to lose weight.

Remember that you are better off—in terms of your health, appearance, your sense of self-control—*not smoking.* So, be good to yourself and those you love. Stick with it! Stay free from smoking and do your best to control your weight. Call your local American Lung Association if you need help.

We need your support to fight lung disease, the third leading cause of death in the U.S. Call your local American Lung Association to find out how you can help.

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(1-800-586-4872)

National Web Site:
www.lungusa.org

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TOBACCO CONSUMPTION PATTERNS AND IT'S HEALTH IMPLICATIONS: THE INDIAN SCENARIO

By
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Oct. 2003

Abstract

Tobacco has become a major cause of death across the entire world. Around 9-lakh people die in India every year due to tobacco related diseases. In this context this paper tries to analyze the tobacco consumption pattern and its health implications in India using the latest National Sample Survey data on tobacco consumption. The paper finds that though there is reduction in tobacco consumption in India as a whole the rural India is showing a sort of substitution between different tobacco products. It has been also observed that the consumption of tobacco is more among the poor in India pointing to the fact that the consequent higher health care spending leaves them worse off. Thus the paper concludes that in spite of the huge Tobacco industry that is flourishing in India and the economic gains it gives to the country the burden it imposes on the country and it's masses in the form of various diseases and high morbidity is immense. Hence government policy needs to be targeted towards an effective control of Tobacco use.

Keywords: *Tobacco, Consumption, Health, India*

JEL Code: I12, I18, R22
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1. Introduction

It is well known that tobacco use in any form is potentially harmful from both economic and human development considerations. Tobacco has become a major cause of death across the entire world. It is estimated that by 2030, it would account for the death of about 10 million people per year; half aged 35-69. This is a matter of serious concern for the developing countries where more than 82 per cent of the world smokers reside. Incidence of daily tobacco consumption is about 50 per cent among males in low-income countries, which is in fact increasing over time (www.worldbank.org). The costs and consequences of this phenomenon are manifold. It leads to high morbidity due to ill health from tobacco use and hence, increased death rate. This would call for replacement of productive labor and thereby impose heavy economic costs on the society in the form of high spending on health care, training labor force for replacement etc. These factors could prove a serious threat to the development process of the poor countries. Hence much of the cost in the form of disease and death could be avoided with policy action aimed at regulating tobacco consumption.

Government of India has passed certain legislations in the past to curb tobacco use. But unlike in the past, legislation for curbing tobacco use has taken a qualitative change in the recent times mainly with the introduction of Cigarette and other tobacco Products (Prohibition of Advertisement, Regulation of Trade and Commerce, Production, Supply and Distribution) Bill, 2001. Nevertheless the Bill is yet to be implemented. Many state governments are also enacting various legislations to curb tobacco use in recent times. But in spite of all these tobacco use is widespread and continues unabated in India. This would raise a number of policy relevant questions: What is the pattern of tobacco consumption across various regions and social groups? Is it the poor or the rich, who consumes more of tobacco and thereby susceptible to various health calamities, bear the consequent economic costs? In this context we make a simple attempt to analyze the incidence of tobacco consumption at various levels and the associated health implications in India, which may help to underline the need for effective policy intervention by the government.

2.Tobacco economy in India

Some important features of the tobacco economy in India, which make a case for a serious academic study, are as follows:

- India is the second largest producer and fourth largest exporter of tobacco in the world. (Sundaram, 2003)
- In India an estimated 65% of all men and 33% of all women use some form of tobacco. (Shimkhada *et al.* 2003)
- tobacco is raised on an area of about 4 lakh hectares;
- Six million farmers are engaged in tobacco leaf production in India; and
- tobacco Industry supports nearly 100 million people in India either directly or indirectly. (Gupta Indrani & Shankar Deepa, 2001)

While these statistics depict a strong tobacco industry that is flourishing in India it has got a lot of health implications too. tobacco use has taken epidemic dimensions in India. This will reflect in a high burden of disease for the country not immediately but at a future date. The following statistics depict its severity in India.

- Around 9 lakh people die in India every year due to tobacco related diseases (The Hindu, June, 05, 2001)
- tobacco related cancers account for nearly half of all cancers among men and onefourth among women. (Shimkhada *et al.* 2003)
- India has one of the highest rate of oral cancers in the world
- Oral cancer accounts for one-third of the total cancer cases in India, with 90% of the patients being tobacco chewers. (www.cdc.gov/tobacco/who /india.htm)
- An estimated 8.3 million cases of coronary artery diseases and chronic obstructive airway diseases are attributable to tobacco every year. (Shimkhada *et al.* 2003)
- The treatment of tobacco related diseases in India costs 135.7 billion Rupees ($2.9 billion) every year and this is much more than the nationwide sale value of all tobacco products. (Pramod Mahajan, Hon'ble Minister, GoI, Jan 6,2001)

Given the above facts it is worthwhile to look at the prevalence of tobacco in India and also the associated health impacts. An analysis of this kind will really help in directing policy in such a way that maximum social benefits are achieved. Using NSS data for various years we try to analyze this.

3.The consumption patterns (National Scenario)

In India National Sample Survey Organization (NSSO) collects data on the prevalence of tobacco use along with its consumption expenditure surveys in India. Among the many million tobacco users in India 48% of them use Bidis, 38% use different chewing items and the rest 14% are Cigarette smokers (Sundaram, 2003). Following table gives the change in pattern of consumption of different tobacco products in India over the last decade as obtained from different NSSO quinquennial surveys.

Table 1: Trends in Per Capita Qty. & value of consumption of various tobacco Products per 30 days in Rural & Urban India*

All-India Rural	55th round, 1999-2000		50th round, 1993-94		43rd round, 1987-88	
Item	Qty. (no)	Value (Rs.)	Qty. (no)	Value (Rs.)	Qty. (no)	Value (Rs.)
Pan	0.83	0.78	0.64	0.39	0.65	0.21
Bidi	38.18	4.91	45.74	3.7	49.5	1.93
Cigarette	0.96	0.88	0.8	0.45	1.05	0.27
All-India Urban						
Pan	1.2	1.76	1.39	1.16	1.7	0.7
Bidi	22.13	3.12	32.39	2.79	38.67	1.6
Cigarette	3.24	3.68	3.65	2.45	4.89	1.47

*Source: NSS Report No.461 (55/1.0/4), 1999-2000.

The table clearly shows the differences in the consumption patterns of rural and the urban household in India. The table also shows the decreasing tendency in the consumption of

tobacco products between both the groups. The main observations that one can make from this data are:

- Bidi is predominantly consumed in the rural areas. It could be because of the low unit value of the Bidi and the low income of the rural mass.
- Bidi consumption has been steadily declining in both rural and urban areas.
- It is also interesting to note that the percentage decline in per capita Bidi consumption was more in urban (42.77%) than in rural (22.87%) India over this period of analysis. (Suryanarayana, 2002)
- Another interesting feature is that this decrease in Bidi consumption is more or less compensated by an increment in the consumption of pan in the rural areas. That is consumption of pan has increased in the rural areas. Where as this sort of a shift is not seen in the urban population. So it may be a sign that the urban populace, in general, is gradually decreasing the consumption of various tobacco products relative to their rural counterparts.
- Per capita number of Cigarette consumption, on the other hand, is more in urban India than in rural India. One obvious reason could be the higher price of Cigarette. It may be also due to some cultural factors, e.g. the taboo associated with smoking Cigarettes among some villagers (Sinha *et al.* 2002)
- There is a consistent decrease in Cigarette consumption in urban India where as, even though it has decreased in rural India over the period, it shows an increasing tendency in the last period of the study. From the year 1987-88 to 99-2000 the percentage decrease in Cigarette consumption was also very high (33.74%) in urban India compared to rural India (8.6%).
- The Pan consumption also has been steadily increasing in rural India while it showed a declining trend in urban area.

In sum one can safely conclude from the above statistics that the tobacco consumption habit of the urban household is showing a declining trend on the whole, while that of the rural household is showing a substitution between various tobacco products. The possible reasons for this kind of behaviors can be given only by further studies. One may think of the possible reasons like changes in the cultural aspects, tendency of rural population to imitate the urban mass, general changes in the consumption patterns, the effect of advertisements, lack of proper awareness etc.

4.Consumption Patterns at the state level

Now let us look at the behavior of consumption of various tobacco products at the state level. The following table shows change in the per capita annual consumption of Bidi and Cigarette at the state level calculated from the NSS reports for both the urban and rural population. A careful analysis of this table can shed a lot of light into understanding the problem at a disaggregated level.

Table 2: Per Capita Monthly tobacco consumption of different states both in Urban and Rural areas (in qty.)*

	Rural India		Urban India	
	Bidi (No)	Cigarette (No)	Bidi (No)	Cigarette (No)
State	1993-94	1999-'00	1993-94	1999-'00
Andhra Pradesh	48.06	38.95	2.80	3.52
Arunachal Pradesh	28.46	14.43	1.71	0.37
Assam	33.19	13.83	1.16	0.57
Bihar	10.63	6.92	0.13 ~	6.57 ~
Goa	34.84	16.55	4.54	3.78
Gujarat	74.17	63.84	0.16 ~	47.12
Haryana	80.50	80.01	0.12	0.42
Himachal P	72.67	62.60	0.93	1.66
J& K	70.72	32.30	3.04	7.45
Karnataka	51.55	42.63	0.65	0.67
Kerala	45.09	26.35	3.35	4.95
Madhya Pradesh	52.46	42.23	0.17 ~	38.38 ~
Maharashtra	22.17	16.43	0.39	0.01
Manipur	51.05	27.85	2.40	2.39
Meghalaya	37.07	49.24	4.67	2.73
Mizoram	10.12	9.08	0.98	5.17
Nagaland	63.07	37.53	5.78	0.85
Orissa	14.24	9.45	0.17 ~	14.64
Punjab	22.77	13.40	0.82 ~	32.02
Rajasthan	87.34	78.60	0.43 ~	56.95
Sikkim	20.48	8.12	2.85	1.95
Tamil Nadu	26.90	35.03	1.77	2.32
Tripura	94.66	79.29	3.32	2.11
Uttar pradesh	54.94	46.52	0.26 ~	36.21
West Bengal	65.96	61.61	0.89	0.66
A&N Island	24.09	13.73	4.29	0.84
Chandigargh	84.32	54.93	0.15	2.49
Dadra& N.Haveli	26.37	28.02	0.37 ~	35.78
Damen&Diu	63.93	11.16	0.72	0.98
Delhi	125.29	27.84	4.36	2.43
Lakshadweep	39.62	36.18	1.09	4.68
Pondichery	16.09	15.36	0.28	1.29
All India	45.74	38.18	0.80	0.96
	45.74	38.18	0.80	0.96
	32.39	22.13	3.65	3.24
	56.31	19.72	5.43	3.81
	43.12	30.60	4.77	9.57
	7.33	3.89	2.40	5.26
	32.39	22.13	3.65	3.24

*Source: NSS Report No. 461(55/1.0/4) for year 1999-200; Survekshana Oct- Dec 1996 for the year 1993-1994;

The behavior of the rural and urban households at the state level is very much in accordance with the National level statistics. It reflects an over all decline in the per capita consumption of tobacco in general with slight differences in rural areas. The main observations are as follows.

• Among the rural households Meghalaya, T.N & Dadra Nagar Haveli are the only

states/UT, which showed an increase in the Bidi consumption. Whereas 13 states (rural) show an increase in the Cigarette consumption, which is also the national level trend.

- Coming to the urban households Mizoram is the only state, which shows an increase in the Bidi consumption.
- The rural households of 11 states including 3 UT's have shown an increase in Cigarette consumption in the 55th round compared to the 50th round, which is in accordance with the national scenario.
- It is interesting to note that in both T.N & Dadra N Haveli consumption of both Bidi and Cigarette have gone up among the rural population.
- Similarly in Mizoram Consumption of both Bidi & Cigarette has gone up among the urban population.
- Haryana, Tripura & Rajasthan are the states with very high per capita consumption of Bidi.
- J&K, Tripura, Meghalaya, Kerala & Mizoram are the states with very high per capita consumption of Cigarette.
- It is interesting to note that in some of the states like Arunachal Pradesh, Maharashtra, Assam & Nagaland Cigarette consumption has fallen drastically.

This kind of information is good from the policy point of view in the sense that the states in which the consumption of both Cigarette and Bidi has increased, policy can be directed towards a desirable path. It may be also interesting to see why Cigarette consumption has fallen in certain states while it increased in most of the states between the last two rounds. Studying the associated health statistics for these states along with this can give us an insight into the relationships existing between the tobacco consumption and health hazards. Lack of proper data at a disaggregated level makes these

kinds of analysis nearly impossible. But even the limited data from various case studies can be of good help in this regard.

4.Consumption Patterns among different socio economic & age groups

The classification of tobacco consumption at such disaggregated levels is not available for the period of study conducted so far. But based on the data available for the period 1995-96 (52nd round) one can analyze the behavior of tobacco consumption of various socio economic and age groups. The following table will help us to understand the consumption patterns among males and females belonging to different age groups. The distribution of total tobacco consumption that we see in this table can help one to understand the nature of different socio economic groups in consuming various tobacco products.

Table 3: tobacco use prevalence (for 1000 population) among different Socio-economic groups. *

10-14 Yrs 15-24 Yrs 24-44 Yrs 45-59 Yrs 60+ All

RURAL MALE
Any tobacco 19 281 664 800 878 521
Smoking 10 220 488 680 626 397
Smokeless 11 81 324 300 450 232
RURAL FEMALE
Any tobacco 12 112 151 139 346 137
Smoking 3 9 59 44 54 38
Smokeless 10 105 134 102 300 118
URBAN MALE
Any tobacco 6 162 523 452 171 350
Smoking 3 41 345 393 125 227
Smokeless 4 129 306 92 66 193
URBAN FEMALE
Any tobacco 3 13 68 101 118 53
Smoking 1 2 4 25 25 7
Smokeless 2 11 65 79 95 47
* Source: NSS 52nd round (1995-96) calculated from Gupta *et al.* (2002)

Here again, as we saw in the tables above, the tobacco consumption in both smoking and nonsmoking form is more prevalent in rural India than in urban India. The following main observations can be made from the above table

- The prevalence of all forms of tobacco is more in the age group 24 years and above. But some WHO studies these days shows that the consumption by the lower age group is increasing.
- In all most all the age groups the male groups consume more of tobacco of any form compared to their female counterparts. This can be easily attributed to the social set up in the country.
- But interestingly the gap in consumption between male and female is much less in smokeless tobacco compared to smoking.
- In case of the 15-24 & 60+ age groups the prevalence of smokeless tobacco consumption is more among females than among the males.
- For the age groups 10-14 & 15-24 the prevalence of smokeless tobacco consumption is more than smoking, except for the rural male. The higher smoking prevalence compared to the smokeless tobacco in this age groups may be attributed to the fact that Bidi, which may be cheaper product, is the main constituent of smoking among this category. Adjusting for this factor one may like to conclude that smokeless tobacco is more prevalent than smoking among children and youngsters. This could be mainly due to the social sanctions on this group against smoking.

We can also have a look at the nature of consumption of different income classes and communities from the NSS 52nd round.

Table 4: The prevalence of tobacco consumption among different income groups and communities. *
Smoking Smokeless Any form

PH-7.

DEPARTMENT OF EPIDEMIOLOGY AND BIOSTATISTICS

(HOSPITAL BASED CANCER REGISTRY)

KIDWAI MEMORIAL INSTITUTE OF ONCOLOGY

Dr.C. Ramesh: PROF. & HEAD

WORLD: It is estimated that about 9 million new cancer cases are diagnosed every year and over 4.5 million people die from cancer each year in the world.

INDIA: The estimated number of new cancers in India per year is about 7 lakhs and over 3.5 lakhs people die of cancer each year. Out of these 7 lakhs new cancers about 2.3 lakhs (33%) cancers are tobacco related.

KARNATAKA: There would be about 1.5 lakhs cancer cases at any given time in Karnataka and about 35,000 new cancer cases are added to this pool each year.

The Department of Epidemiology and Biostatistics comprises of both the Hospital Based Cancer Registry and Population Based Cancer Registry. The Hospital Based Cancer Registry collects information on each and every patient registered at Kidwai Memorial Institute of Oncology in a predivised questionnaire devised by the National Cancer Registry Programme Project of the Indian Council of Medical Research. The Registry Provides Information on the Magnitude of cancer patients attending KIMIO, various types of cancers, the treatment particulars and its outcome, which enables the Insitution to plan for the management / control of the cancer disease. The information so collected by the registry enables initiation of epidemiological studies to find out various causative factors for different cancers and also play an important role in Cancer Control Activities. Over 16,000 new cases are registered every year with more than 20 % from neighbouring states of Andhra Pradesh and Tamil Nadu and Kerala.

The Faculty staff of the Department is also involved in teaching students of Undergraduate, Postgraduate students and also for Superspeciality courses in addition to involvement in many of the Research Projects / Clinical Trials conducted by various departments of the Institute.

Research Activities - Projects:

1. Cancer Atlas Project: The HBCR is involved in the Cancer Atlas Project of the WHO, ICMR under taken by the NCRP since 2001 and provide information on all non resident cases registered at KMIO.

2. Pattern of Care and Survival Studies: The HBCR has taken up the project titled "Pattern of Care and Survival Studies in Head and Neck Cancers, Cancers of Cervix and Breast".

All though thousands of cancer patients are receiving treatment from various cancer hospitals in India, no scientific evaluation of therapeutic efficacy in terms of pattern of care and survival has been done. The data from HBCRs of India has shown that Cancer of Cervix (28%) and Breast (16%) in women are most common and cancer of Head and Neck region constitute about 30 % of all cancer in

males and females. Realising the problem of follow-up of cancer patients wherein huge number of patients drop out from regular follow-up visits. ICMR decided to initiate pattern of care and survival studies on three of the most common cancers i.e Cancer of Cervix, cancer of Breast and Head and Neck Cancers. The project being carried out in all the HBCRs of India where Cancer Registry are established.

OBJECTS OF THE PROJECT:

1. To obtain core indentifying and diagnostic information in all patients in the particular center / Institution with cancer cervix / breast / head and Neck.

2. To record details of clinical stage and types of treatment of patients included.

3. To have periodic follow-up and record the patient and disease status in all patients suffering from these cancers so as to have clinical stage and treatment based on survival on these sites of cancer.

The project has already been in progress with grants funded by the ICMR. The duration of the project is of 3 years.

Two epidemiological studies - One on Oral Cancers and another one on Pharyngeal cancers are in progress which are aimed at investigating various risk factors in the causation of these two major sites of cancer.

Leading Sites of Cancer - Male:

Pharyngeal cancers (excluding cancer of nasopharynx) continue to be the most common form of cancers among males and accounts for 14.1% of the total cancers in males. Among Pharyngeal cancers, cancer of the Hypopharynx is the most predominant site of cancer accounting for over 68 % of the Pharyngeal cancers. The other common cancers among males in order are oral cavity (11.2%), Leukaemias (8.4%), Oesophagus (8.3%) and Lung (6.8%)

Leading Sites of Cancer - Female:

Cancer of the cervix uteri continues to be the most predominant site of cancer and accounted for 26.7% of all cancers in females. Cancer of the breast is the second most common site (16.6%) followed by cancers of oral cavity (11%), Oesophagus (5.7%) and ovary (5%). Over the years, a gradual decrease in the proportion of cervical cancers and marginal but steady increase in the numbers and relative proportion of breast cancers is observed.

Common Cancers:

The Commonest cancers among Males and Females seen at KMIO-2004-05 are as below:

MALE	FEMALE
Pharynx	Cervix
Oral Cavity	Breast

Leukaemia	Oral Cavity
Oesophagus	Oesophagus
Lung	Ovary
Lymphoma	Leukaemia
Stomach	Thyroid
Brain & Ner.Sys	Stomach
Larynx	Lymphoma
Liver	Pharynx

DEPARTMENT OF EPIDEMIOLOGY AND BIOSTATISTICS

(POPULATION BASED CANCER REGISTRY)

Kidwai Memorial Institute of Oncology

Dr.K.Ramachandra Reddy:Prof. & Head

The Population Based Cancer Registry at Kidwai Memorial Institute of Oncology was established during the year 1981 with the main objective of assessing the incidence/magnitude and type of various cancers in Bangalore and to provide a framework for controlling the impact of cancer on the community. The registry was included under the network project of the National Cancer Registry Programme (NCRP) of Indian Council of Medical Research (ICMR) and the actual registration of cancer cases was commenced in the year 1982. The registry covers the resident population of Bangalore Urban Agglomeration which has an area of 741 sq.kms and has an estimated population of 7.0 million as of 2007. The inclusion criteria for registration of cases is that patients who have lived in the defined areas of Bangalore Urban Agglomeration for a minimum period of one year at the time of fist diagnosis of cancer. The registration of cancer cases is done by active registration method. The staff of the registry visits all hospitals, nursing homes, diagnostic labs besides the base institution and death registration units in the defined areas to elicit the required information from cancer patients in a standard format. On an average about 5000 new cancer cases are registered in the registry area per year. During the period from 1982 through 2004 a total number of 73524 (34045 males & 39479 females) cases of cancers were reported to the National Cancer Registry Programme by the Population Based Cancer Registry of Bangalore. The average annual age adjusted rates of cancer among males & females were 96 and 120 per 100,000 persons respectively. Tobacco related cancers accounted for 34% of all cancers in males and 16% of all cancers in females and paediatric cancers accounted for 3% of all cancers in males and 2% of all cancers in females.

LEADING SITES OF CANCER

The first ten leading sites of cancer among males and females are shown in table. Ranking of these sites are based on the frequency of their occurrence. Among males, cancer of the stomach is the most predominant site of cancer constituting 9% of the total cancers among males followed by cancers of the lung (7.0%), oesophagus (6.6%), prostate (5.3%) and NHL (4.6%). Among females, cancer of the breast is the predominant site of cancer and has accounted for 24.6% of the total cancers in females followed by cancer of the cervix (15.9%), ovary (4.9%), oesophagus (4.7%) and mouth cancers (4.6%). The incidence of breast cancer among females in Bangaloreans is showing a steady and statistically significant increase as is the case in other Urban cities. Altogether, the first ten leading sites of cancers among males and females accounted for 53.1% of the total cancers in males and about 70.9% of the total cancers in females.

CUMULATIVE RISK : In the absence of other causes of death, the risk of developing cancer by an individual among Bangaloreans would be 15.1% in males and 16.8% in females (cumulative risk). In other words, one in six persons in either sex has the risk of developing cancer during their life time.

PH-7

Consortium for Tobacco Free Karnataka condemns BBMP move with tobacco manufacturer

Sunitha Rao R, TNN Jul 1, 2013, 06.06 PM IST

Tags:

- Consortium for Tobacco Free Karnataka
- BBMP

BANGALORE: As the BBMP decided to tie up with the ITC in its Zero waste management, and work on segregation of waste at source, the members of Consortium for Tobacco Free Karnataka (CFTFK) have taken objection.

"It's ironic but a fact that the theme for this year's World No Tobacco Day is prohibition on Tobacco Advertisement, Promotion and Sponsorships (TAPS) and a state-level consultation on ban on TAPS has been planned this week. In fact, BBMP itself is a district anti tobacco cell for the Bangalore Urban district," said an official release from the CFTFK.

Number of member organizations of CFTFK have written letters to the BBMP Commissioner expressing their concern over such collaboration.

According to S J Chander of CFTFK, such collaboration is sheer violation of section 5 of Cigarettes and Other Tobacco products (Prohibition of Advertisement and Regulation of Trade and Commerce, Production, Supply and Distribution) Act, as well as article 5.3 of the Framework Convention on Tobacco Control (FCTC) signed by Government of India, as it enhances public image of a tobacco company and amounts to an indirect promotion of tobacco.

Palike move to tie up with ITC flayed

Bangalore, July 1, 2013, DHNS

The move by BBMP to tie up with ITC for its Zero Garbage Model programme, which was launched on July 1, has been strongly opposed by the Consortium for Tobacco Free Karnataka (CFTFK).

A number of NGOs, academic institutions and healthcare delivery organisations that make up the consortium have demanded that the BBMP immediately disassociate itself from the tobacco company.

The consortium has said that any collaboration by the government with a tobacco firm, as is the case here, will mean an indirect promotion for the latter.

"While we appreciate the Palike's efforts to control tobacco use, it is ironical that it being the District Anti-Tobacco Control Cell (Bangalore Urban), the Palike should encourage the efforts of such tobacco companies in promoting their image," said Upendra Bhojani of CFTFK.

Enarada, Bangalore, July 1, 2013:

The recent decision by the Bruhat Bangalore Mahanagara Palike (BBMP) to tie up with a tobacco company (ITC) for its Zero Garbage Model programme has received objections from many corners.

Members of the Consortium for Tobacco Free Karnataka (CFTFK), that comprises NGOs, academic institutions and healthcare delivery organisations, today demanded that the BBMP disassociate itself immediately from the tobacco company.

It's ironic but a fact that the theme for this year's World No Tobacco Day is prohibition on tobacco advertisement, promotion and sponsorships (TAPS) and a state-level consultation on ban on TAPS has been planned this week. In fact, BBMP itself is a district anti tobacco cell for the Bangalore Urban district.

CFTFK members were concerned over the media reports on BBMP's collaboration with ITC (Indian Tobacco Company) for Zero Garbage Model programme launched on 1st July, 2013. Mr. S J Chander of CFTFK explained that "such collaboration violates section 5 of Cigarettes and Other Tobacco products (Prohibition of Advertisement and Regulation of Trade and Commerce, Production, Supply and Distribution) Act, as well as article 5.3 of the Framework Convention on Tobacco Control (FCTC) signed by Government of India, as it enhances public image of a tobacco company and amounts to an indirect promotion of tobacco."

ITC is the largest manufacturer of cigarettes in India. It is estimated that more than 10 lakh people die every year due to the use of tobacco in India. More than 1.5 crore people use tobacco in Karnataka.

"Such collaboration between government agency and a tobacco company not only enhances public image of tobacco company but also creates opportunities for tobacco companies to influence and interfere with public policies in general" Dr. Prem Mony of CFTFK added.

In past (2010), Karnataka high court had directed another government agency (Indian Tobacco Board, Ministry of Commerce and Industry, GOI) to withdraw its partnership with other tobacco companies for an event in Bangalore (Institute of Public health, Bangalore Vs Union of India and others), terming such partnership as indirect promotion of tobacco. The proposed collaboration would also amount to surrogate advertisement of tobacco.

Many member organisations of CFTFK have written letters to BBMP Commissioner expressing their concern over such collaboration. "While we appreciate BBMP's efforts to control tobacco use, being the District Anti-Tobacco Control Cell (Bangalore Urban) itself, the Palike should discourage tobacco companies' efforts in promoting their image through 'so called' corporate social responsibility (CSR).

As per WHO, activities that are described as "socially responsible" by the tobacco industry, aiming at the promotion of tobacco consumption, is a marketing as well as a public relations strategy", said Dr. Upendra Bhojani of CFTFK.

THE HINDU
2/7/13

The day when the Bruhat Bangalore Mahanagara Palike (BBMP) launched, with much fanfare, the Zero Garbage project in partnership with ITC Ltd., the Consortium for Tobacco-Free Karnataka (CFTFK) demanded the civic authority dissociate itself from the tobacco company.

In a press release in Bangalore Monday, CFTFK objected to the BBMP's partnership with ITC for the project.

Pointing out the irony of this partnership, it the theme for the year's World No Tobacco Day was prohibition on tobacco advertisement, promotion and sponsorship, and a state-level consultation on such a ban was planned for this week.

Besides, the BBMP was a district anti-tobacco control cell while ITC was the largest manufacturer of cigarettes in India.

According to S.J. Chander from CFTFK, BBMP's partnership with ITC "violates section five of Cigarettes and Other Tobacco Products (Prohibition of Advertisement and Regulation of Trade and Commerce, Production, Supply and Distribution) Act, as well as Article 5.3 of the Framework Convention on Tobacco Control signed by government, as it enhances public image of a tobacco company and amounts to an indirect promotion of tobacco".

In 2010, the Karnataka High Court had directed another government agency (Indian Tobacco Board, Ministry of Commerce and Industry) to end its partnership with tobacco companies for an event in Bangalore. It had termed such partnership as indirect promotion of tobacco, the release added.

"While we appreciate BBMP's efforts to control tobacco use...the civic body should discourage tobacco companies' efforts in promoting their image through so called corporate social responsibility," said Upendra Bhojani of CFTFK.

Keywords: BBMP, Zero Garbage project, anti-tobacco control cell, tobacco consumption, CFTFK, ITC, BBMP-ITC partnership

PH-7.

Kidwai Memorial Institute of Oncology

The Kidwai Memorial Institute of Oncology being a Regional Cancer Center, located in South of India. KMIO is catering to the poor and needy cancer patients from Karnataka and neighboring states. We register approx 17000 new cancer patietns each year. The Cancer Control Activitieswere establishment for our State. Mobile Cancer Education & Detection Unit (MCEDU), Cancer Detection Clinic:Community Programmes. In order to help thousands of poor and deserving cancer patients who need costly anti-cancer drugs for treatment "Kidwai Cancer Drug Foundation(KCDF)" was started from December 1991and provided these medicines at 50% low cost than the market price.
An ANTI-TOBACCO CELL:
The staff of Anti-tobacco Cell is involved in bringing about awareness among different categories of persons in the community on the harmful effect of tobacco usage through education wherever possible.Activities:Adoption of Schools/Colleges for anti-tobacco education.Organising & conducting training programmes for health personnel, teachers, VHG, etc. Conducting programmes to convey Anti-tobacco messages through guest lectures, exhibition, workshops, debates & painting competition. Adoption of taluk for Anti-tobacco education. Development of health education materials to the target group
Conducting tobacco related studies .
The Institute has initiated a program of Professional education, technology and expertise transfer through short-term education/training programme for undergraduate, postgraduate and staff of medical colleges/district hospitals and Primary Health Centres. The main objective of this training programme would be to train the medical personnel in prevention, diagnosis and treatment of cancer in early stages in their respective areas. This Institute is running postgraduate courses in MD (Radiotherapy) from the year 1987. Super Speciality Courses viz. M.Ch (Surgical Oncology) & D.M. Medical Oncology), PG diploma in DNM (Diploma in Nuclear Medicine) & DRP (Diploma in Radiation Physics), B.Sc. Medical Technology (Laboratory/Radiotherapy/Radio diagnosis) have also been started from 1. Sept. 1989. These courses are affiliated to Rajiv Gandhi University of Health Sciences, Bangalore and recognised by the Medical Council of India, New Delhi. Several multidisciplinary - multi centric global studies are on-going.

Finance:KMIO is recognised as a Charitable Institute by the Endowment Department of Karnataka, considering its commitment for services to poor cancer patients. The charges levied for cancer investigations and treatment, are well with in the reach of poor patients. In cases where the total treatment cost becomes too heavy such patients are financially assisted by various schemes like Free drugs from the Institute, Karnataka Chief Minister's Medical Relief fund, Poor Patients Welfare Fund, children Welfare Fund, Kidwai Cancer Drug Foundation, etc.,. The anti-cancer drugs sold at Kidwai Cancer Drug Foundation' are 40 to 60% cheaper than the market rates.

The annual budget of the Institute is about Rs.19 Crores out of which about Rs.9.50 Crores in spent on Salaries and Administrative over heads. The other items essential for patient care and hospital maintenance are drugs, diet, linen, surgical sutures, x-ray films, blood bank materials, laboratory reagents, hospital necessaries, water & electricity, maintenance of medical equipments and hospital buildings, replacement of obsolete equipments, etc.,. which cost annually at about Rs.9.50 Crores.

KMIO is recognised as one of the regional cancer centres by the Government of India. Patients not only from Karnataka but also from the adjacent areas of the neighboring States of Tamilnadu, Andra Pradesh, etc., In case of the latter the patients number is about 40% of the total no. of patients treated. The Government of Karnataka is extending substantial financial support to the Institute through Grant-in-Aid, annually, to the extent of about Rs. 10.00 Crores. Annually the Government of India is releasing Rs.75.00 lakhs for purchase of Medical equipments. Since the Institute is levying treatment charges at a very reasonable rate the revenue earned out of it is not substantial for the maintenance of the Hospital.

Health Systems Global

Improving performance through research and policy

PH - 7.

The Health Systems Global Thematic Working Groups

The thematic working groups are an important part of the society's operations. They provide a platform for member interaction and the exchange of experience on particular issues in health systems research. There are currently eight thematic working groups created and run by Health Systems Global members.

This flyer provides an overview of the eight groups, their aims and activities. You can also find more information about the thematic working groups and how to contact the coordinators on the Health Systems Global website (www.healthsystemsglobal.org).

If you have any questions or queries about the thematic working groups or if you wish to establish one, then please contact the Secretariat (healthsystemsresearch@cphiv.dk).

Supporting and Strengthening the Role of Community Health Workers in Health System Development

Community health worker programmes rely on staff who live and work at the community level. There is true potential for these services to strengthen delivery of health services through tailoring services to meet the needs and realities of individuals and households, and making more appropriate links between the community and the formal health system.

We are working to support the generation, synthesis and communication of evidence on the roll-out and functioning of community health worker programmes and to enable learning across geographical and political contexts.

This work includes: supporting dialogue online; arranging events; facilitating learning across the group; supporting research; and publishing and translating evidence into products which meet the needs of diverse audiences.

Ethics of Health Systems Research

The overall goal of the Ethics of Health Systems Research TWG is to initiate critical thinking and dialogue on the ethics of health systems research in low and middle-income countries. It aims to explore what ethical issues arise in relation to health systems research in low and middle-income countries, how they should be addressed, and by whom. Thematic working group activities include hosting webinars, workshops, meetings at bioethics and global health conferences, conference panels, and Google Group discussions.

Health Systems in Fragile and Conflict Affected States

Improvements in health systems in fragile and conflict affected states will not be possible with a 'business as usual' approach. These settings need special attention, policies and programming. The Health Systems in Fragile and Conflict Affected States Thematic Working Group brings together key actors interested in this area.

We promote the creation of new knowledge, improved policy and better communication among stakeholders to contribute to the development of responsive health systems. Our aim is to strengthen the research base and encourage the use of evidence in decision-making.

Medicines in Health Systems

Medicines play crucial clinical, public health, social, economic, political, and ethical roles in achieving the goals of health care delivery and financing systems. When used appropriately, medicines contribute to the health and well-being of individuals and populations; and they waste scarce resources when used unnecessarily or incorrectly. The thematic working group on Medicines in Health Systems will define medicines-focused activities that add value to ongoing global and national efforts to improve medicines availability, access, affordability, and use. Activities may include: facilitating constructive dialogue among stakeholders within and across systems; strengthening capacity of practitioners in generating evidence on medicines in health systems; disseminating applied research evidence early and efficiently to each relevant system stakeholder.

Health Systems Global

Improving performance through research and policy

SHaPeS: Social Science Approaches for Research and Engagement in Health Policy & Systems

SHaPeS aims to strengthen and raise the profile of social science approaches within the wider field of health policy and systems research. The group is particularly interested in qualitative and participatory approaches to research and analysis, and in conceptual and philosophical perspectives. Our primary interest is questions about health system performance that are difficult to study with the dominant health research methods. SHaPeS convenes a range of activities and discussions structured around four methodological clusters of engagement: participatory action research; policy analysis; theory-driven research; complexity science and systems thinking. There are several cross-cutting discussion areas: conceptualizing health policy and systems; research quality and rigour; linking research with policy and action; power in health policy and systems; capacity building; and working across disciplines.

Teaching and Learning Health Policy and Systems Research

The thematic working group is organized around ways to improve the teaching and learning of Health Policy and Systems Research (HPSR). The group will focus on issues in teaching and learning HPSR at educational institutions around the world, with an emphasis on research and its application in low and middle-income countries and disadvantaged populations, and address global, regional, and local policy and program priorities. Responding to interests of its members, the group is currently working on:

- Mapping out current approaches to teaching and learning HPSR around the world;
- Collecting and sharing curricula, courses, and other teaching and learning offerings in HPSR;
- Supporting ways to develop approaches to teaching multi-disciplinary research on health systems and policy for different target groups (undergraduate, graduate and post-graduate students, program managers, policy-makers);
- Supporting innovations in pedagogical approaches to teaching HPSR.

The Private Sector in Health

The non-state sector plays a significant role in delivering health care to people in developing countries. This poses both challenges and opportunities in terms of the quality, cost and availability of health services. The Private Sector Thematic Working Group seeks to enhance the quality, quantity, and accessibility of knowledge and evidence around the potential role this diverse set of actors has in delivering healthcare to the poor. The group will actively involve health researchers, practitioners, and policy-makers to encourage translation of research into policy and practice.

Translating Evidence into Action

The need for strong evidence to support health systems strengthening efforts globally has gained increasing attention in past years. However, there continues to be a gap between the creation of new and solid evidence from health systems research efforts and the translation of that same evidence into policy action. Policy-makers struggle to find, collect and understand context-specific evidence to support their own decision-making needs, despite existing knowledge. These challenges are not inevitable, and we propose that with the right level of support and interaction between researchers and decision-makers, the translation of research findings into actionable policy and programmatic guidance is an achievable goal.

This thematic working group focuses on the translation of health systems evidence into action, and support mechanisms to share best practices, lessons learned, and practical guidance and tools. The overall aim is to decrease the current gap between what we know and what we do.

We set out to:

- Enable researchers to support the use of health systems research by policy-makers and other stakeholders;
- Raise awareness among policy-makers, programme implementers, providers, citizens and the press/media about the need to value, demand and use evidence;
- Create opportunities for all Health Systems Global members to dialogue and share best practices in evidence translation;
- Collaborate with other Health Systems Global thematic working groups to promote evidence translation.