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A REVIEW OF CURRENT EPIDEMIOLOGICAL DATA AND ESTIMATION OF FUTURE TUBERCULOSIS INCIDENCE AND MORTALITY

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SUMMARY

The incidence of tuberculosis in 1990 is estimated at 7.5 million cases of which 3.1 million were in the South-East Asian region of WHO, 1.8 million in the Western Pacific region, 1.0 million in sub-Saharan Africa and 1.6 million in the remainder of the world. The estimates for South-East Asian and Eastern Mediterranean regions are higher than previously thought, while the estimates for the Western Pacific and African regions are lower. Forty-four percent of all cases occurred in China and India.

Annual incidence is predicted to increase to 8.8 million cases by 1995, 10.2 million by 2000 and 11.9 million by 2005, an increase of 58% compared with 1990 incidence. Demographic factors, such as population growth and changes in age structure of populations, will account for 77% of the predicted increases in incidence. Increasing incidence rates, particularly in Africa, will account for 23% of the increase in new cases. In the Eastern Mediterranean region and Central and South America, age-specific incidence rates are expected to fall during 1990-2005 but the total number of new cases will increase because of population growth.

It is estimated 315,000 (4.2%) of the 7.5 million incident cases of tuberculosis in 1990 were attributable to HIV infection. Over half of such cases occurred in sub-Saharan Africa where 23.8% of new cases of tuberculosis in adults aged 15-59 were attributable to HIV infection. By the year 2000, it is estimated that over 1.4 million (13.8%) of the forecast 10.2 million incident cases occurring annually will be attributable to HIV infection.

During the 10-year period 1990-1999 it is estimated that 88.2 million people will develop tuberculosis, of which 8.0 million cases will be attributable to HIV infection.

In 1990, 2.5 million persons are estimated to have died of tuberculosis. Assuming availability of treatment remains at its 1990 level, it is predicted 3.0 million tuberculosis deaths will occur annually by 1995 and 3.5 million deaths annually by 2000. Of the 3.5 million tuberculosis deaths predicted to occur annually by the year 2000, 0.5 million (14%) will be attributable to HIV infection.

During the decade 1990-1999 it is estimated that 30.0 million tuberculosis deaths will occur, of which 2.9 million will be attributable to HIV infection. Around 6.0 million tuberculosis deaths are expected in sub-Saharan Africa during the decade, 1.5 million (25%) of which will be attributed to HIV infection.

1. Introduction

WHO has declared tuberculosis a global emergency and warned that the disease claims millions of lives each year and that the situation will rapidly worsen unless immediate action is taken to curb its spread.

This document presents estimates of the present global situation and forecasts of increasing morbidity and mortality in the near future. Estimates are given for the world, WHO regions, and for selected countries.

Specific areas addressed in these forecasts include the impact of world population growth, the impact of demographic aging of the world's population, and the impact of the HIV epidemic.

The information presented here are forecasts of morbidity and mortality based on current levels of intervention. Tuberculosis is curable, and treatment is inexpensive. Much of the forecast burden of disease could be prevented if sufficient global resources were directed immediately towards the control of this disease.

2. Review of previous estimates of 1990 incidence

Tuberculosis incidence in 1990 was estimated for developing countries by Murray (*1*) and extended by Sudre (*2*) to include industrialised countries. Both authors based their estimates on a comprehensive review of survey data on annual risk of infection (ARI) in developing countries (*3*). Annual tuberculosis incidence was estimated by applying Dr Styblo's conversion factor, a 1% increase in ARI correlates to 50 additional smear positive cases per 100,000 population per year(*4*), to regional ARI estimates.

However, estimates based on such a methodology need to be interpreted with caution for a number of reasons. First, the conversion factor is based on measurements of certain populations and the validity of applying this to other populations is unknown. Second, the review of ARI only covered survey data up to 1985 (*3*) and few comprehensive surveys have been undertaken since 1985. Third, for most regions of the world there is sparse ARI data. For example, the estimates for the Caribbeans, Central and South America (46 countries) were based on survey data from two countries only. Fourth, previous immunisation with BCG excludes survey subjects from the calculation of ARI. In many areas where recent surveys were undertaken, most of the sample population had previous BCG immunisation and thus was excluded from the calculation. For example at least 80% of the survey population was previously immunised in Botswana and Malaysia, and at least 50% in a range of other countries, including Algeria, Argentina, Burundi, Libya, Republic of Korea, Samoa and Tanzania (*3*). Thus, subjects included in the ARI calculation in regions with high BCG immunisation coverage may not be representative of the population from which they were drawn.

On the basis of the above concerns about calculating global incidence of tuberculosis from survey data on ARI, a new set of estimates of tuberculosis incidence in 1990 have been produced using an independent methodology.

3. Tuberculosis incidence in 1990

WHO routinely collects data on the number of new tuberculosis cases in Member States each year (*5*). Within each WHO region, except the African region, an overall regional crude incidence rate was calculated by estimating the incidence in the most populated countries. Reliable notification data were preferentially used for these estimates. Notification data were considered reliable when provided by programmes with an established surveillance system. For countries with unreliable notification data, ARI was used to estimate incidence. Notification data are relatively poor for the African region, so a slightly different approach was used. The African region was divided into four geographic areas and within each area, a crude incidence rate was estimated based on the most reliable notification data (e.g., United Republic of Tanzania for East Africa, Côte d'Ivoire for West Africa).

Estimates of incidence based on notification data will partly reflect under reporting, and thus must be considered as conservative estimates. While notification data are of poor quality for many countries, and any estimates based on such data will seriously risk underestimating incidence, reliable data are available from other countries, particularly those where good tuberculosis control programmes are established.

Shown in Table 1 are the new 1990 estimates. Based on notification data, the number of incident cases of tuberculosis in 1990 is estimated at 7,537,000. While these estimates must be considered conservative, they are consistent with the ARI-based estimate of 8.0 million incident cases in 1990 by Sudre (*2*).

In the following sections, more detailed information is given on the calculation of tuberculosis incidence for each WHO region.

3.1 South-East Asian Region

The notification rate for India, the most populated country in the region, was 153 per 100,000 population in 1990. Not included in the Indian notification system were patients treated privately and patients hospitalised in the more than 40,000 tuberculosis hospital beds. Of the 438 administrative districts in India, only 378 had district tuberculosis programmes, and of these only 278 (63% of all districts) notified cases in 1991. It has been estimated that 57% of identified cases were included in notification reports (*6*). In many countries, relapse cases are usually included with incident cases in reports to WHO. For India it is not known what proportion of notifications were relapse cases, but other countries in the region have reported around 5% were relapse cases. This suggests tuberculosis incidence in India during 1990 was approximately 242 per 100,000 population.

In Indonesia, the second most populated country in the region, only 2,700 of the 6,000 health centres are currently included in the national tuberculosis programme. Notification data only includes smear positive cases and thus underestimates total incidence. Tuberculin surveys undertaken during 1983-87 in various regions including Java, Sumatra and Kalimantan found an ARI of 1.7-4.1%. In at least five districts the ARI was above 2.3% (*7*). ARI of this magnitude suggests an incidence rate at least as high as that for India where ARI is around 1.5-2%. For other countries of the region (e.g. North Korea, Mongolia, Myanmar, Thailand) notification data suggest an incidence rate half that of India.

The 1990 incidence rate for the South-East Asian region is estimated at 237 per 100,000 population. This is higher than the previous estimates of 165-200 per 100,000 given by Murray (*1*) and 194 per 100,000 population given by Sudre (*2*). Based on these calculations, it is estimated 3.1 million new cases occurred in the South-East Asia region during 1990, including 2.1 million new cases in India and 0.4 million in Indonesia.

3.2. Western Pacific Region

Thirty two countries were included in the Western Pacific region. The three industrialised countries of the region (Japan, Australia and New Zealand) have been excluded and grouped with Europe and North America.

In 1990, the population of the Western Pacific region was around 1,350 million, the most populated of all the WHO regions. Approximately 85% of the population live in China, with the remaining 15% spread across the other 31 countries. Thus, the incidence of tuberculosis in China strongly influences the overall regional incidence.

Murray (*1*) estimated an ARI of 1-2% for Asia while Sudre (*2*) estimated 1-2.25% for the Western Pacific region. However, data from the 1984-5 and 1990 national tuberculosis surveys of China suggest an ARI of around 1.0% (*8,9*). This suggests that previous estimates of tuberculosis in China, and thus the whole of the Western Pacific region, may have overestimated the situation.

The average notification rate for tuberculosis in China during 1987-90 was 49 per 100,000 population. Data from the 1984-85 national survey of China suggest that approximately 40% of cases had been registered (*8*). Recent notification data from China show that relapse cases account for approximately 7.5% of cases notified to WHO. Applying the 40% coverage rate to notification data and allowing for inclusion of

relapse cases, gives an estimated 1990 incidence rate of 113 per 100,000 population for China. This estimate is approximately 40% lower than the estimate of 192 per 100,000 population by Sudre (*2*).

Of the 15% of the region's population that live in countries other than China, half reside in the Philippines and Republic of Korea. During 1988-90, the Philippines reported 312 incident cases per 100,000 population and Republic of Korea reported 194 per 100,000 population. Assuming 7.5% of notified cases were relapses and a case-finding rate of 80% (a conservative estimate), the 1990 incidence estimate for the Philippines is 360 per 100,000 population and for the Republic of Korea is 225 per 100,000.

Only 8% of the population live in the other 29 countries of the region. For these countries, notification rates ranged from 30 to 300 cases per 100,000 population with a weighted average of 100 per 100,000 population. Allowing for 45% case-finding rate (reported by various countries within the region) and inclusion of relapse cases (7.5%), it is estimated an incidence rate of 205 per 100,000 could be applied to these countries.

For the entire Western Pacific region, it is estimated that there were 1.8 million new cases (136 per 100,000 population) in 1990, 28% lower than estimated previously. Around 1.3 million cases occurred in China.

3.3. African Region

Africa was divided into four geographical areas and within each area estimates of incidence were based on the most reliable notification data. For Eastern Africa, recent notifications ranged from 50 to 220 cases per 100,000 with a mean of 110 cases per 100,000. Tanzania, with one of the best tuberculosis programmes, reported approximately 105 cases per 100,000 population in 1990. Highest notification rates in East Africa were reported by countries with a high incidence of AIDS (e.g. Malawi, Zambia). Reports from national tuberculosis programmes suggest that relapse cases account for 5% of reported incident cases. Allowing for around 50% case-finding for all countries in the area, the 1990 incidence rate for Eastern Africa is estimated at 200 cases per 100,000 population.

In Central Africa, recent notifications range from 50 to 200 cases per 100,000 with a mean of 80 per 100,000 population. These rates are similar to those reported by Eastern Africa countries, suggesting an incidence rate similar to that estimated for Eastern Africa.

Notifications from countries in Southern Africa ranged from 170 to 225 cases per 100,000 population with a mean of 205 per 100,000. The Republic of South Africa reported 220 cases per 100,000 population. Allowing for inclusion of relapse cases (5%) and 70% case-finding, the underlying incidence rate for the Republic of South Africa was approximately 300 cases per 100,000 population. This rate was applied to other countries in Southern Africa.

West African notification rates are lower than other areas of sub-Saharan Africa. Notifications ranged from 20 to 140 cases per 100,000 population, with a mean of 50 per 100,000. Côte D'Ivoire, with one of the best surveillance systems in West Africa, reported 65 cases per 100,000 population in 1991. Relapse cases accounted for 5% of notifications and case-finding was estimated at 50%. This together with data from other countries in the area suggests an incidence rate of around 150 cases per 100,000 population in West Africa during 1990.

It is estimated that the 1990 incidence of tuberculosis for all Sub-Saharan Africa was 992,000 cases (191 per 100,000 population), 28% lower than previously estimated.

3.4. Eastern Mediterranean Region

Pakistan, the most populated country in the region, reported 169 cases per 100,000 population in 1988. No data is available on the proportion of relapse cases included in notifications from Pakistan. Data from other countries in the region suggest that around 5% of reported incident cases are relapses and a case-finding rate of around 65%. The 1990 incidence rate for Pakistan is estimated at 250 cases per 100,000 population.

Notification rates for other countries in the region, trend to fall into three categories. Allowing for 50% case-finding and inclusion of relapse cases, incidence rates for Djibouti, Somalia, Sudan and Yemen are estimated at 200 cases per 100,000 population. For Saudi Arabia, Syria, Oman, Qatar and Iran incidence is estimated at 100 cases per 100,000 population while for the remaining countries of the region, incidence is estimated at 50 cases per 100,000 population.

The 1990 incidence of tuberculosis for the entire Eastern Mediterranean region is estimated at 641,000 cases (165 per 100,000 population), similar to previous estimates. It is estimated 306,000 cases occurred in Pakistan and 335,000 cases in the other 22 countries of the region.

3.5. American Region, excluding USA and Canada

Included in this region were countries of the Caribbean, Central America and South America. Canada and the USA have been excluded and grouped with Europe and other industrialised countries. Of the 46 countries included in the region, 23 have populations of less than one million. Each of these countries reports only a small number of cases annually, and any estimates based on these numbers would be subject to Poisson variation. Of the other 23 countries in the region, notifications ranged from 20 to 180 cases per 100,000 population with a weighted average of 50 cases per 100,000. Brazil, the most populated country in the region reported around 50 cases per 100,000 population, although notifications only covered Rio de Janeiro.

Allowing for incomplete reporting, a case-finding rate of around 70%, and data from other countries in the region, the 1990 incidence for the region is estimated at 127 cases per 100,000 population (569,000 cases), similar to the estimate of Sudre (2). It is estimated 191,000 (34%) of these cases occurred in Brazil and 378,000 (66%) in the other 45 countries of the region.

3.6. European Region and USA, Canada, Japan, Australia and New Zealand

The region was considered in two section: (a) Eastern Europe and independent states of the former USSR and (b) Western Europe and the five other industrialised countries.

For Eastern Europe and independent states of the former USSR, the weighted average of 1990 notification rates was 42 cases per 100,000 population. Notification rates for Western European and other industrialised countries ranged from less than 10 per 100,000 in Canada, Denmark, the Netherlands, Norway and Sweden to more than 60 per 100,000 in Portugal. The weighted average of notifications for all Western European and other industrialised countries was 21 per 100,000 population.

If an 85% registration rate is assumed and allowing for 5% of reported cases to be relapses, the resulting estimates of 1990 incidence are 47 per 100,000 population for Eastern Europe and independent states of former USSR and 23 per 100,000 for Western Europe and the five other industrialised countries. For the entire region, it is estimated that 390,000 incident cases occurred in 1990 (31 cases per 100,000 population), similar to previous estimates.

3.7. Summary

It is estimated there were 7,537,000 incident cases of tuberculosis in 1990. Over 4.9 million cases (65%) occurred in the South-East Asian and Western Pacific regions and particularity in India (2.1 million), China (1.3 million) and Indonesia (0.4 million).

One million cases are estimated to have occurred in sub-Saharan Africa during 1990, 0.6 million cases in the Eastern Mediterranean region (including 0.3 million cases in Pakistan) and 0.6 million in the Central and South America (including 0.2 million cases in Brazil).

Around 0.2 million cases occurred in Eastern Europe and independent states of the former USSR and 0.2 million cases in Western European and other industrialised countries.

The global estimate based on notification data is similar to that estimated by Sudre (2) based on ARI data. This should allay some of the concerns expressed about the use of ARI for estimating incidence rates.

However, the two methods do yield different estimates for some regions. In particular, the notification-based estimates suggest a substantially greater incidence of tuberculosis in South-East Asia than previously thought. Conversely, a lower incidence in China and hence the entire Western Pacific Region was estimated when based on notifications.

4. Tuberculosis incidence in 1995, 2000 and 2005

In estimating future disease incidence, allowances were made for demographic factors (changes in the size and age structure of populations) and epidemiological factors (changes in age-specific incidence rates). To accurately allow for both demographic and epidemiological factors, age-specific incidence rates were estimated for the years 1995, 2000 and 2005 and then applied to age-specific population projections for these years.

This was undertaken at the regional level in two steps. First, data available at WHO on the age distribution of notified cases in each region during 1990 were applied to the 1990 regional crude incidence rates to derive 1990 regional age-specific incidence rates. Second, trends in regional notification rates during 1985-1990 were applied to the 1990 regional age-specific incidence rates to derive age-specific incidence rates for the years 1995, 2000 and 2005. This approach assumes that age-specific trends will remain unchanged. The derived rates were then applied to regional age-specific population projections to calculate the number of incident cases expected in 1995, 2000 and 2005.

In forecasting future burden of disease, it has been assumed that intervention (i.e. the activities of national programmes) remains at the 1990 level.

4.1. 1990 age-specific incidence rates

Age was categorised into four groups: 0-14 years, 15-34 years, 35-59 years and 60+ years. Table II shows the age structure of incident cases for each region in 1990, based on data supplied to WHO by national tuberculosis programmes. The majority of cases are aged between 15 and 59 years in each region. Variation between regions partly reflect differences in age structure of the underlying populations.

The number of incident cases aged 0-14, 15-34, 35-59 and 60 and older in each region was estimated by applying the age distribution of cases shown in Table II to the revised 1990 incidence estimates shown in Table I. Regional age-specific incidence rates for 1990 were then calculated by dividing these estimates by regional age-specific population estimates (*10*).

4.2. Trends in incidence rates

Trends in notification rates during 1985-90 were analysed to predict trends during 1990-2005. While notification-based data are subject to variation in completeness of reporting, they do provide a useful source of information and, when used with data on trends in ARI, trends in incidence rates can be estimated.

South-East Asian Region

In India, notifications increased by approximately eight additional cases per 100,000 population per year during 1985-90. This probably reflects improvements in completeness of reporting. It is also possibly the underlying incidence rate may be increasing. The extent of dual HIV-tuberculosis infection in the Indian population is unclear. However, it seems reasonably to assume there is a pool of persons with dual infection, and without intervention, the pool could be expected to increase. It is estimated the incidence of tuberculosis in India will increase during 1990-2005 by 0.4 additional case per 100,000 population per year, largely due to increasing prevalence of HIV infection.

For other countries in the region, notification data suggest annual incidence is decreasing by approximately 1.0 cases per 100,000 population per year. For the region as a whole, the weighted average trend is a reduction in incidence by 0.09 cases per 100,000 population per year. However, this trend could

be reversed if a marked increase in the prevalence of HIV infection among persons infected with tuberculosis occurs.

Western Pacific Region

Data from the 1979, 1984-85 and 1990 national surveys of China suggest the ARI among seven year old children was similar in each survey period (*8,9*). Data from these surveys also suggest the prevalence of infection among children aged 0-5 was higher in 1990 than in 1979. Analysis of registration data shows notifications have been increasing by approximately 0.5 additional cases per 100,000 population each year since 1986. Based on the available data, it is estimated that the annual incidence rate in China during 1990-2005 is likely to remain at the 1990 level, in the absence of intervention.

For most other countries in this region, notification rates have generally been falling in recent years by one case per 100,000 population each year. There are a few exceptions to this trend but mostly among the less populated countries.

The underlying annual incidence rate for the Western Pacific region as a whole is predicted to decrease by 0.13 cases per 100,000 population per year.

African Region

Around 1985 some African countries, particularly those in Eastern and Central Africa started reporting increases in tuberculosis rates. Although an increase in notifications for one country may reflect improved completeness of reporting, increasing notification rates across an entire region suggests that changes in reporting alone may not account for the increase.

For countries of Eastern and Central Africa with annual notification rates for AIDS of at least 10 cases per 100,000 population (e.g. Burundi, Congo, Malawi, Rwanda, Uganda and Zambia), tuberculosis notifications rates have been increasing, on average, by 10 additional cases per 100,000 population per year since 1985. The increase in notifications in Eastern and Central Africa correlates with the increasing prevalence of dual HIV-tuberculosis infections.

Increases of 5-10 additional tuberculosis notifications per 100,000 population have also occurred in other parts of Africa during 1985-90, including countries currently reporting less than 10 new cases of AIDS per 100,000 population per year (e.g. Cameroon, Equatorial Guinea, Mozambique, Senegal and South Africa). The interpretation of these trends is that the high prevalence of HIV infection seen initially in Eastern and Central Africa is now occurring in other parts of sub-Saharan Africa. In parallel with the spread of the AIDS epidemic, dual HIV-tuberculosis infection is increasing throughout the region. It is estimated, based on increases in notification during 1985-90, the underlying incidence rates across Sub-Saharan Africa will continue to increase by 10.0 additional new cases per 100,000 population per year during 1990-2005.

Eastern Mediterranean Region

Murray (*1*) estimated ARI to be decreasing during 1985-90 in the Eastern Mediterranean region. Notification data for this period confirm this trend. Notification rates fell in 13 of the 17 countries that have consistently reported cases to WHO.

However, the notification rate for Pakistan, the most populated country in the region, has been increasing in recent years by 4.0 additional cases per 100,000 population each year. It is thought the increase in the notification rate for Pakistan results from improved reporting. It is also possible that some increase in notifications could result from increases in underlying incidence rates. The prevalence of dual infection with HIV-tuberculosis in Pakistan is largely unknown, but thought to be relatively low. It is estimated, based on available data, that incidence rates in Pakistan will continue at their 1990 level during 1990-2005.

The weighted average of notification rates for other countries in the region is decreasing by around 1.0 cases per 100,000 population each year. Based on this, the underlying incidence rates for these other countries are predicted to decrease by 1.0 case per 100,000 population per year during 1990-2005.

For the Eastern Mediterranean region as a whole, underlying incidence rates are predicted to decrease by 0.68 cases per 100,000 population per year during 1990-2005.

American Region

It has been estimated that ARI was falling in Central and South America during 1985-90 (*1*). Analyses of notification data confirm this trend and suggest underlying incidence rates are falling by approximately 1.5 case per 100,000 population per year in the region.

Notification rates for some countries have risen in recent years, possibly due to the AIDS epidemic (e.g. Haiti, Honduras) but the impact of this on regional notification rates to date has been minimal because the population of the countries showing an upward trend are relatively small compared with other countries within the region.

Underlying regional incidence rates are predicted to continue falling by around 1.5 cases per 100,000 population per year during 1990-2005, unless the prevalence of dual HIV-tuberculosis infection increases appreciably.

European Region and USA, Canada, Japan, Australia and New Zealand

Tuberculosis notification rates increased during 1985-90 in several countries (including The Netherlands and USA) by approximately 0.5 additional cases per 100,000 population per year. However, for most other countries in Western Europe, notifications decreased during 1985-90 by 0.5-1.0 cases per 100,000 population per year. It seems reasonable to assume that rates in other countries in Western Europe will also increase in the near future, partly because of increasing migration of people to Western Europe from regions of the world with higher incidence of tuberculosis, and partly because of the increasing number of persons with dual HIV-tuberculosis infection. It is estimated that tuberculosis incidence in Western Europe and the other industrialised countries will either remain at their current levels or increase slightly during 1990-2005.

In Eastern Europe and states of the former USSR, notifications decreased during 1985-90 by approximately one case per 100,000 population per year. However, it is not clear that the decline in incidence rates can be maintained in these countries. It is assumed underlying incidence rates in Eastern Europe and states of the former USSR will remain at their 1990 level in the near future.

4.3. Incidence estimates in 1995, 2000 and 2005

The forecast trends in underlying regional incidence rates during 1990-2005 (section 4.2) were applied to 1990 age-specific incidence rates (section 4.1) to produce estimates of age-specific incidence rates for the years 1995, 2000 and 2005. These rates were then applied to age-specific population projections (*10*) to derive the number of incident cases expected in each year.

Table III shows the number of incident cases of tuberculosis predicted to occur in 1990, 1995, 2000 and 2005. The number of incident cases is expected to increase from 7.5 million new cases a year in 1990 to 8.8 million in 1995, 10.2 million in 2000, and 11.9 million new cases a year in 2005, an increase of 57.6% over 15 years. Around 4.5 million new cases annually can be expected in the South-East Asian region, 2.8 million in the African region and 2.5 million in the Western Pacific region by the year 2005.

The age-specific incidence rates for the Eastern Mediterranean region and Central and South America were predicted to fall during 1990-2005, but the actual numbers of incident cases are expected to increase. This indicates that demographic factors (changes in size and age structure of populations) are stronger than epidemiological factors (changes in age-specific incidence rates). The impact of demographic and epidemiological factors on the forecasts is examined below.

4.4. Impact of demographic and epidemiological factors

The effects of demographic factors (population growth and changes in the age structure of populations) were examined by fixing age-specific incidence rates at their 1990 levels (i.e., no change in age-specific incidence rates during 1990-2005) and applying these rates to age-specific population estimates for the years 1995, 2000 and 2005.

Table IV shows the expected increase in incidence due solely to demographic factors. With age-specific incidence rates fixed at their 1990 level, the number of incident cases of tuberculosis occurring each year increases from 7.5 million cases annually in 1990 to 10.9 million cases annually by 2005, an increase of 45%. This increase is due solely to demographic factors.

The influence of changing age structure is reflected in changes to the crude incidence rate. The global crude incidence rate (Table IV) is predicted to increase from 143 cases per 100,000 population in 1990 to 161 cases per 100,000 population by 2005, although age-specific incidence rates were fixed at their 1990 level. This occurs because the proportion of the world's population in the middle and older age groups is increasing and tuberculosis incidence rates are highest among these age groups.

While incidence is predicted to increase from 7.5 million cases annually in 1990 to 10.9 million in 2005 due to demographic factors only, it was forecast in Table III that incidence would rise to 11.9 million by 2005 when allowing for both demographic and epidemiological factors. This indicates that demographic factors will account for most of the predicted increase in annual incidence.

Shown in Table V are the predicted additional cases of tuberculosis, compared with 1990 incidence, due to demographic and epidemiological factors. Over three-quarters of the predicted increase will result from demographic factors, such as population growth and changing age structure of the population.

Less than 25% of the predicted increase will result from changes in age-specific incidence rates. These forecast changes due to epidemiological factors represents the balance between increasing rates due, largely, to the HIV epidemic versus falling rates due to effective intervention strategies. For example, by the year 1995, epidemiological factors are expected to account for 234,000 additional cases expected annually (Table V). This results from the 423,000 additional cases expected due to the HIV epidemic (see section 4.5), minus 189,000 additional prevented cases due to intervention strategies. Clearly the impact of prevention programmes, assuming they remain at their 1990 level, will be overshadowed by both population growth and the HIV epidemic.

While the number of new cases per year in each region is forecast to increase dramatically, the data in Table V indicate that prevention programmes are working. In South-East Asia, Western Pacific, Eastern Mediterranean and particularly the Americas, epidemiological factors (falling age-specific incidence rates) are preventing tens of thousands of additional cases from occurring each year. Unfortunately, at the global level, these achievements are overshadowed by the increasing age-specific rates in Africa.

The interpretation of above findings is that advances are being made in preventing new cases of tuberculosis, as seen by the falling age-specific rates. However, these efforts are insufficient to counter the strong effects of population growth, the demographic aging of populations, and the HIV epidemic.

Tables VI-XII show forecast annual incidence of tuberculosis in 1995, 2000 and 2005 at the regional level. The top half of each table shows predicted incidence due solely to demographic factors (age-specific rates fixed at 1990 levels), while the lower half of each table shows predicted incidence when allowances are made for both demographic and epidemiological factors.

In the South-East Asian region (Table VI), the benefits of a small decrease in age-specific rates will be overshadowed by the strong effects of demographic factors. By the year 2005, an additional 1.3 million cases will occur each year in South-East Asia. The effect of changing age structure of the population is clearly shown in the top half of Table VI. With age-specific rates fixed at their 1990 levels, the crude incident rate would increase from 237 per 100,000 population in 1990 to 257 per 100,000 in 2005. This results from the increasing proportion of people in the middle and older age groups.

The Western Pacific (Table VII), Eastern Mediterranean (Table IX) and American regions (Table X) all show a similar pattern: age-specific incidence rates are predicted to fall during 1990-2005 but the number of new cases each year will continue to increase due to population growth, and the crude incidence rates (all ages) will continue to increase because of the demographic aging of regional populations.

In sub-Saharan Africa (Table VIII), the number of incident cases each year is predicted to almost triple during 1990-2005. This is the only region where epidemiological factors are stronger than

By the year 2000, 1.4 million (13.8%) of the 10.2 million new cases expected to occur each year will be attributable to HIV infection. Substantial changes in the prevalence of HIV infection among persons infected with *M.tuberculosis* would alter the proportion of cases attributable to HIV infection.

4.6. Total incidence during 1990-1999

During the 10-year period 1990-1999 it is estimated that 88.2 million people will develop tuberculosis, of which 8.0 million cases will be attributable to HIV infection.

In South-Est Asia 35.1 million new cases of tuberculosis will occur during the decade, of which 2.8 million will be attributable to HIV infection. Around 20.5 million new cases will occur in the Western Pacific of which 0.4 million will be attributable to HIV infection, while 15.0 million cases will occur in sub-Saharan Africa of which 3.9 million will be attributable to HIV infection.

At the end of the decade, an extra 2.7 million tuberculosis cases will be occurring each year, compared with 1990. Around 1.1 of these additional cases (40%) will be attributable to the HIV epidemic.

5. Tuberculosis Mortality Estimates

Notification data from Western Europe and other industrialised countries suggest that around 7% of tuberculosis cases die of the disease (*17*). These deaths probably result from late presentation for treatment and failure to diagnose tuberculosis as the underlying disease. Notification data from Eastern Europe suggest a case-fatality rate of around 15%, while for Central and South America it was assumed that around 20% of tuberculosis cases die of the disease. For other regions, case-fatality rates were estimated using the approach of Murray and colleagues (1991). A case-fatality rate of 55% is assumed for cases not receiving treatment, and 15% for those receiving treatment (*18-20*). It is also assumed that all notified cases have been treated and that around 5% of treated patients are not notified (due to factors such as incomplete reporting or exclusion of patients treated privately). By applying these assumptions to notification data, it is estimated the case-fatality rate is around 35% in South-East Asia and the Western Pacific and slightly higher in the Eastern Mediterranean and sub-Saharan Africa (Table XIX).

Annual tuberculosis mortality was calculated by applying the regional case-fatality rates to the estimates of annual incidence. The number of tuberculosis deaths attributable to HIV infection was estimated by applying case-fatality rates to the estimates of HIV-attributable cases. These rates were conservatively assumed to be the same as those among HIV-uninfected cases.

Table XX shows the estimated number of tuberculosis deaths in each region of the world for the years 1990, 1995 and 2000. It is estimated that 2,530,000 tuberculosis deaths occurred in 1990 of which 116,000 were attributable to HIV infection. Around 1.1 million tuberculosis deaths occurred in South-East Asian in 1990.

By the year 2000 it is estimated, assuming the proportion of cases treated remains at the 1990 level, 3.5 million tuberculosis deaths will occur annually, almost 40% more than in 1990. Half a million of these deaths will be attributable to HIV infection, almost half of which will occur in Sub-Saharan Africa. In South-East Asia, 1.4 million deaths per year are anticipated by 2000.

The annual number of incident cases of tuberculosis is predicted to increase by 35.6% during 1990-2000 (Table III) while annual mortality is expected to increase by 38.7%. A higher proportional increase in deaths is expected because incidence is predicted to increase most in Africa where treatment rates are lowest and therefore risk of dying highest.

5.1. Total deaths during 1990-1999

During the 10-year period 1990-1999 it is estimated that 30.0 million people will die of tuberculosis, of which 2.9 million will be attributable to HIV infection.

demographic factors. Age-specific incidence rates are forecast to increase by around 10 additional cases per 100,000 population per year through to the year 2005. This increase is almost entirely due to the HIV epidemic.

In Eastern Europe (including independent states of the former USSR), Western Europe and other industrialised countries (Tables XI-XII), age-specific incidence rates are forecast to stay at their 1990 level during 1990-2005, but increases in the number of new cases are expected due to demographic factors.

Tables XIII-XVII show predicted incidence in 1995, 2000 and 2005 for selected countries: China, India, Indonesia, Pakistan and Brazil.

4.5. Impact of HIV epidemic

The interaction between HIV infection and tuberculosis infection has been reviewed elsewhere (*11*). HIV infection in persons with a prior tuberculosis infection dramatically increases their risk of developing tuberculosis.

Shown in Table XVIII is the prevalence of HIV infection by age among tuberculosis cases in 1990. Prevalence was estimated from WHO data on HIV seroprevalence in tuberculosis patients from 75 countries in 1989-1992. The data suggest that in 1990 around 25% of tuberculosis cases aged 15-59 were HIV seropositive in sub-Saharan Africa, 5% in Western Europe and industrialised countries and Central and South America, 2-3% in South-East Asia and 1-2% in the Western Pacific, Eastern Mediterranean and Eastern Europe. There was little HIV infection among cases aged more than 60. For children, there were limited data on the prevalence of HIV infection among those with tuberculosis. Data from Zambia suggest that 40% of children with tuberculosis were HIV seropositive (*11*). In Eastern Africa it is estimated that around 20% of children with tuberculosis were HIV seropositive in 1990. For other regions of the world, it is assumed few children with tuberculosis were HIV seropositive.

Estimates of the prevalence of HIV infection among tuberculosis cases in 1995 and 2000 (Table XVIII) were based on previous trends of HIV seroprevalence in tuberculosis patients and on consensus opinion of programme staff at WHO.

Among adults co-infected with HIV and *M.tuberculosis*, approximately 5-10% develop tuberculosis each year on average (*11-14*). By comparison, at most 0.2% of adults with *M.tuberculosis* infection only develop tuberculosis each year on average (*15*). Based on these data, the risk of developing tuberculosis for persons infected with both HIV and *M.tuberculosis* is at least 30 times higher than for persons infected with *M.tuberculosis* only. Using a relative risk of 30, the attributable fraction (*16*) (i.e., (relative risk - 1)/relative risk) for co-infection with HIV is 95%. Thus, 95% of tuberculosis cases co-infected for HIV are attributable to the HIV infection. The remaining 5% of co-infected cases would have developed tuberculosis irrespective of their HIV status and reflect the occurrence of disease in the absence of the HIV epidemic.

The number of incident tuberculosis cases in each region attributable to co-infection with HIV (Table XVIII) was calculated by applying the attributable fraction and the regional estimates of HIV seroprevalence among tuberculosis cases to the estimates of regional tuberculosis incidence in 1990, 1995 and 2000.

Of the 7.5 million incident cases of tuberculosis in 1990, 315,000 (4.2%) were attributable to co-infection with HIV. These cases would not have occurred if the persons were not co-infected with HIV. In sub-Saharan Africa, 25% of tuberculosis cases among persons aged 15-59 are estimated to have been HIV seropositive and 95% of such cases were attributable to HIV. Thus in sub-Saharan Africa, 23.5% of all tuberculosis cases among adults aged 15-59 during 1990 were attributable to HIV infection. Less than 2% of tuberculosis cases in the Western Pacific, Eastern Mediterranean, Europe and other industrialised countries were attributable to HIV infection.

By the year 1995 it is estimated 738,000 (8.4%) of the predicted 8.8 million new cases occurring each year will be attributable to HIV infection. These estimates assume the prevalence of HIV infection among tuberculosis cases will increase as shown in Table XVIII.

In South-East Asia 12.3 million tuberculosis deaths are forecast for the decade, of which 1.0 million will be attributable to HIV infection. Around 6.0 million tuberculosis deaths are expected in Sub-Saharan Africa, of which 1.5 million will be attributable to HIV infection.

6. Discussion

Nearly 90 million new tuberculosis cases and 30 million tuberculosis deaths are expected to occur through to the end of this decade without more effective intervention. For a disease where intervention is cost-effective (*21*), this is truly staggering.

These estimates are based on notification data and, because of under reporting of tuberculosis cases, must be considered conservative. This is reflected in our estimated 1990 incidence of 7.5 million new cases being slightly lower than previous estimates which were based on annual risk of infection data (*2*). Similarly, the estimation of tuberculosis mortality should be considered conservative. This study estimated 2.5 million tuberculosis deaths in 1990, compared with previous estimates of 2.9 million deaths (*2*). While the exact number of new cases and deaths is not known, the current and previous estimates are consistent in suggesting that between 7.5 and 8.0 million new cases and 2.5-3.0 million tuberculosis deaths occurred in 1990.

Current intervention strategies are expected to result in substantial reductions in age-specific incidence rates in the Eastern Mediterranean region and Central and South America, and to a lesser degree in the Western Pacific and South-East Asian regions. However, the total number of new cases in these regions is predicted to increase in the near future because of population growth.

The impact of the HIV epidemic is most evident in sub-Saharan Africa where the number of new cases per year is forecast to double by the end of the decade. In South-East Asia and other regions there has been little impact, to date, of the HIV epidemic on tuberculosis. However, by the year 2000 over 500,000 new cases and 200,000 deaths in South-East Asia will be attributable to HIV infection.

A number of assumptions were made in these analyses. It was estimated that 5% of all treated cases are not reported to WHO and that 100% of reported cases were treated. Limited global data are available on the completeness and quality of notifications. These levels were chosen as conservative estimates of the global situation. Earlier mortality estimates (*2*) used a case-fatality rate of 50% for HIV-positive tuberculosis cases, whereas the current estimates did not assume mortality was different between HIV-positive and HIV-negative cases.

Forecasting future incidence and mortality is difficult and can only be based on data available at the time of the modelling. Substantial changes in epidemiological factors, such as greater than expected increases in the seroprevalence of HIV among persons infected with *M. tuberculosis*, would increase the future burden of disease. Conversely, increased availability of treatment, would reduce the forecast number of future cases and deaths.

It has been demonstrated that effective application of short-course chemotherapy in well-managed national tuberculosis programmes produces excellent results, even under the most adverse conditions (*21*). Short-term chemotherapy of smear-positive tuberculosis cases is one of the most cost-effective health interventions available (*22*). A higher priority must be given to this disease, both by the countries most severely affected and by donor countries which invest in health care programmes in those countries.

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Table I. Estimated tuberculosis incidence in 1990.

Region	Sudre (2)		New estimates	
	Cases	Rate[1]	Cases	Rate[1]
South-East Asia	2,480,000	195	3,106,000	237
Western Pacific[2]	2,557,000	192	1,839,000	136
Africa	1,398,000	265	992,000	191
Eastern Mediterranean	594,000	155	641,000	165
Americas[3]	564,000	127	569,000	127
Europe and others[4]	409,000	34	390,000	31
All regions	8,002,000	152	7,537,000	143

[1]Crude incidence rate per 100,000 population
[2]Excludes Japan, Australia and New Zealand
[3]Excludes USA and Canada
[4]Independent states of former USSR, USA, Canada, Japan, Australia and New Zealand

Table II. Age distribution of incident tuberculosis cases in 1990/1991, based on data from national tuberculosis programmes.

Region	AGE 0-14 %	AGE 15-34 %	AGE 35-59 %	AGE 60+ %
South-East Asia	5	30	45	20
Western Pacific[1]	10	30	35	25
China	15	20	30	35
Africa	10	45	35	10
Eastern Mediterranean	10	35	40	15
Americas[2]	10	35	40	15
Europe and others[3]	10	30	35	25

[1]Excludes China, Japan, Australia and New Zealand
[2]Excludes USA and Canada
[3]Independent states of the former USSR, USA, Canada, Japan, Australia and New Zealand

Table III. Estimated tuberculosis incidence in 1990, 1995, 2000 and 2005.

Region	1990		1995		2000		2005	
	Cases	Rate[1]	Cases	Rate[1]	Cases	Rate[1]	Cases	Rate[1]
South-East Asia	3,106,000	237	3,499,000	241	3,952,000	247	4,454,000	256
Western Pacific[2]	1,839,000	136	2,045,000	140	2,255,000	144	2,469,000	151
Africa	992,000	191	1,467,000	242	2,079,000	293	2,849,000	345
Eastern Mediterranean	641,000	165	745,000	166	870,000	167	987,000	170
Americas[3]	569,000	127	606,000	123	645,000	120	681,000	117
Eastern Europe[4]	194,000	47	202,000	47	210,000	48	218,000	49
Western Europe & others[5]	196,000	23	204,000	23	211,000	24	217,000	24
All regions	7,537,000	143	8,768,000	152	10,222,000	163	11,875,000	176
Increase since 1990			16.3%		35.6%		57.6%	

[1]Crude incidence rate per 100,000 population
[2]Excludes Japan, Australia and New Zealand
[3]Excludes USA and Canada
[4]Includes independent states of former USSR
[5]USA, Canada, Japan, Australia and New Zealand

Table IV. Estimated change in tuberculosis incidence due to demographic factors only.

Region	1990		1995		2000		2005	
	Cases	Rate[1]	Cases	Rate[1]	Cases	Rate[1]	Cases	Rate[1]
South-East Asia	3,106,000	237	3,505,000	241	3,966,000	248	4,477,000	257
Western Pacific[2]	1,839,000	136	2,057,000	141	2,281,000	146	2,512,000	153
Africa	992,000	191	1,163,000	192	1,370,000	193	1,612,000	195
Eastern Mediterranean	641,000	165	760,000	170	907,000	173	1,047,000	180
Americas[3]	569,000	127	643,000	131	726,000	135	812,000	139
Eastern Europe[4]	194,000	47	202,000	47	210,000	48	218,000	49
Western Europe & others[5]	196,000	23	204,000	23	211,000	24	217,000	24
All regions	7,537,000	143	8,534,000	148	9,671,000	155	10,895,000	161
Increase since 1990			13.2%		28.3%		44.6%	

[1]Crude incidence rate per 100,000 population
[2]Excludes Japan, Australia and New Zealand
[3]Excludes USA and Canada
[4]Includes independent states of former USSR
[5]USA, Canada, Japan, Australia and New Zealand

Table V. Estimated additional cases of tuberculosis, compared with 1990, attributable to changes in demographic and epidemiological factors

Region	1995		2000		2005	
	demographic	epidemiologic	demographic	epidemiologic	demographic	epidemiologic
South-East Asia	399,000	- 6,000	860,000	-14,000	1,371,000	-23,000
Western Pacific[1]	218,000	-12,000	442,000	-26,000	673,000	-43,000
Africa	171,000	304,000	378,000	709,000	620,000	1,237,000
East. Mediterranean	119,000	-15,000	266,000	-37,000	406,000	-60,000
Americas[2]	74,000	-37,000	157,000	-81,000	243,000	-131,000
Eastern Europe[3]	8,000	0	16,000	0	24,000	0
Western Europe & others[4]	8,000	0	15,000	0	21,000	0
All regions	997,000	234,000	2,134,000	551,000	3,358,000	980,000
	81.0%	19.0%	79.5%	20.5%	77.4%	22.6%

[1]Excludes Japan, Australia and New Zealand
[2]Excludes USA and Canada
[3]Includes independent states of former USSR
[4]USA, Canada, Japan, Australia and New Zealand

Table VI. Estimated tuberculosis incidence in 1990, 1995, 2000 and 2005: South-East Asian region.

	AGE 0-14		AGE 15-34		AGE 35-59		AGE 60+		ALL AGES	
	Cases	Rate	Cases	Rate	Cases	Rate	Cases	Rate	Cases	Rate
------ Demographic factors only ------										
1990	155,000	31	932,000	207	1,398,000	515	621,000	740	3,106,000	237
1995	170,000	31	1,019,000	207	1,595,000	515	721,000	740	3,505,000	241
2000	180,000	31	1,131,000	207	1,838,000	515	817,000	740	3,966,000	248
2005	186,000	31	1,243,000	207	2,119,000	515	929,000	740	4,477,000	257
------ Demographic and epidemiological factors ------										
1990	155,000	31	932,000	207	1,398,000	515	621,000	740	3,106,000	237
1995	168,000	30	1,016,000	207	1,595,000	514	720,000	740	3,499,000	241
2000	175,000	30	1,126,000	206	1,835,000	514	816,000	739	3,952,000	247
2005	178,000	29	1,235,000	206	2,113,000	514	928,000	739	4,454,000	256

Table VII. Estimated tuberculosis incidence in 1990, 1995, 2000 and 2005: Western Pacific region, excluding Japan, Australia and New Zealand

	AGE 0-14		AGE 15-34		AGE 35-59		AGE 60+		ALL AGES	
	Cases	Rate	Cases	Rate	Cases	Rate	Cases	Rate	Cases	Rate
	------ Demographic factors only ------									
1990	248,000	70	423,000	80	579,000	166	589,000	487	1,839,000	136
1995	264,000	70	438,000	80	662,000	166	693,000	487	2,057,000	141
2000	281,000	70	429,000	80	784,000	166	787,000	487	2,281,000	146
2005	274,000	70	414,000	80	947,000	166	877,000	487	2,512,000	153
	------ Demographic and epidemiological factors ------									
1990	248,000	70	423,000	80	579,000	166	589,000	487	1,839,000	136
1995	261,000	69	433,000	79	659,000	165	692,000	487	2,045,000	140
2000	274,000	68	420,000	79	776,000	165	785,000	486	2,255,000	144
2005	264,000	68	401,000	79	932,000	164	872,000	486	2,469,000	151

Table VIII. Estimated tuberculosis incidence in 1990, 1995, 2000 and 2005: African region

	AGE 0-14		AGE 15-34		AGE 35-59		AGE 60+		ALL AGES	
	Cases	Rate	Cases	Rate	Cases	Rate	Cases	Rate	Cases	Rate
------ Demographic factors only ------										
1990	99,000	42	447,000	266	347,000	380	99,000	398	992,000	191
1995	115,000	42	526,000	266	406,000	380	116,000	398	1,163,000	192
2000	133,000	42	623,000	266	479,000	380	135,000	398	1,370,000	193
2005	150,000	42	736,000	266	569,000	380	157,000	398	1,612,000	195
------ Demographic and epidemiological factors ------										
1990	99,000	42	447,000	266	347,000	380	99,000	398	992,000	191
1995	251,000	92	626,000	316	460,000	430	130,000	448	1,467,000	242
2000	447,000	142	857,000	366	606,000	480	169,000	498	2,079,000	293
2005	686,000	192	1,152,000	416	794,000	530	217,000	548	2,849,000	345

Table IX. Estimated tuberculosis incidence in 1990, 1995, 2000 and 2005: Eastern Mediterranean region.

	AGE 0-14		AGE 15-34		AGE 35-59		AGE 60+		ALL AGES	
	Cases	Rate	Cases	Rate	Cases	Rate	Cases	Rate	Cases	Rate
					------ Demographic factors only ------					
1990	64,000	40	224,000	170	257,000	346	96,000	435	641,000	165
1995	73,000	40	261,000	170	311,000	346	115,000	435	760,000	170
2000	81,000	40	307,000	170	380,000	346	139,000	435	907,000	173
2005	86,000	40	350,000	170	452,000	346	159,000	435	1,047,000	180
					------ Demographic and epidemiological factors ------					
1990	64,000	41	224,000	170	257,000	346	96,000	435	641,000	165
1995	67,000	37	256,000	167	308,000	343	114,000	432	745,000	166
2000	67,000	33	294,000	164	372,000	340	137,000	429	870,000	167
2005	64,000	30	329,000	161	439,000	337	155,000	426	987,000	170

Table X. Estimated tuberculosis incidence in 1990, 1995, 2000 and 2005: American region, excluding USA and Canada.

	AGE 0-14		AGE 15-34		AGE 35-59		AGE 60+		ALL AGES	
	Cases	Rate	Cases	Rate	Cases	Rate	Cases	Rate	Cases	Rate
------ Demographic factors only ------										
1990	57,000	35	199,000	125	228,000	240	85,000	272	569,000	127
1995	60,000	35	217,000	125	267,000	240	99,000	272	643,000	131
2000	62,000	35	235,000	125	315,000	240	114,000	272	726,000	135
2005	64,000	35	251,000	125	365,000	240	132,000	272	812,000	139
------ Demographic and epidemiological factors ------										
1990	57,000	35	199,000	125	228,000	240	85,000	272	569,000	127
1995	47,000	28	204,000	117	259,000	232	96,000	265	606,000	123
2000	36,000	20	206,000	110	295,000	225	108,000	257	645,000	120
2005	23,000	13	206,000	102	331,000	217	121,000	250	681,000	117

Table XI. Estimated tuberculosis incidence in 1990, 1995, 2000 and 2005: Eastern Europe and independent states of the former USSR.

	AGE 0-14		AGE 15-34		AGE 35-59		AGE 60+		ALL AGES	
	Cases	Rate	Cases	Rate	Cases	Rate	Cases	Rate	Cases	Rate
------ Demographic factors only ------										
1990	19,000	20	58,000	45	68,000	56	49,000	75	194,000	47
1995	20,000	20	56,000	45	75,000	56	51,000	75	202,000	47
2000	19,000	20	55,000	45	81,000	56	55,000	75	210,000	48
2005	19,000	20	56,000	45	86,000	56	57,000	75	218,000	49
------ Demographic and epidemiological factors ------										
1990	19,000	20	58,000	45	68,000	56	49,000	75	194,000	47
1995	20,000	20	56,000	45	75,000	56	51,000	75	202,000	47
2000	19,000	20	55,000	45	81,000	56	55,000	75	210,000	48
2005	19,000	20	56,000	45	86,000	56	57,000	75	218,000	49

Table XII. Estimated tuberculosis incidence in 1990, 1995, 2000 and 2005: Western Europe, USA, Canada, Japan, Australia and New Zealand.

	AGE 0-14		AGE 15-34		AGE 35-59		AGE 60+		ALL AGES	
	Cases	Rate	Cases	Rate	Cases	Rate	Cases	Rate	Cases	Rate
------ Demographic factors only ------										
1990	20,000	10	59,000	22	68,000	27	49,000	37	196,000	23
1995	20,000	10	56,000	22	76,000	27	52,000	37	204,000	23
2000	19,000	10	55,000	22	82,000	27	55,000	37	211,000	24
2005	19,000	10	56,000	22	85,000	27	57,000	37	217,000	24
------ Demographic and epidemiological factors ------										
1990	20,000	10	59,000	22	68,000	27	49,000	37	196,000	23
1995	20,000	10	56,000	22	76,000	27	52,000	37	204,000	23
2000	19,000	10	55,000	22	82,000	27	55,000	37	211,000	24
2005	19,000	10	56,000	22	85,000	27	57,000	37	217,000	24

Table XIII. Estimated tuberculosis incidence in 1990, 1995, 2000 and 2005: China.

	AGE 0-14		AGE 15-34		AGE 35-59		AGE 60+		ALL AGES	
	Cases	Rate	Cases	Rate	Cases	Rate	Cases	Rate	Cases	Rate
------ Demographic factors only ------										
1990	193,000	64	257,000	58	386,000	132	451,000	444	1,287,000	113
1995	204,000	64	264,000	58	437,000	132	527,000	444	1,432,000	117
2000	216,000	64	255,000	58	512,000	132	595,000	444	1,578,000	122
2005	208,000	64	243,000	58	611,000	132	656,000	444	1,718,000	127
------ Demographic and epidemiological factors ------										
1990	193,000	64	257,000	58	386,000	132	451,000	444	1,287,000	113
1995	204,000	64	264,000	58	437,000	132	527,000	444	1,432,000	117
2000	216,000	64	255,000	58	512,000	132	595,000	444	1,578,000	122
2005	208,000	64	243,000	58	611,000	132	656,000	444	1,718,000	127

Table XIV. Estimated tuberculosis incidence in 1990, 1995, 2000 and 2005: India.

	AGE 0-14		AGE 15-34		AGE 35-59		AGE 60+		ALL AGES	
	Cases	Rate	Cases	Rate	Cases	Rate	Cases	Rate	Cases	Rate
------ Demographic factors only ------										
1990	103,000	31	619,000	212	929,000	526	413,000	756	2,064,000	242
1995	113,000	31	677,000	212	1,061,000	526	480,000	756	2,331,000	246
2000	120,000	31	752,000	212	1,222,000	526	543,000	756	2,637,000	253
2005	124,000	31	826,000	212	1,409,000	526	618,000	756	2,977,000	262
------ Demographic and epidemiological factors ------										
1990	103,000	31	619,000	212	929,000	526	413,000	756	2,064,000	242
1995	120,000	33	684,000	214	1,065,000	528	481,000	758	2,350,000	248
2000	135,000	35	766,000	216	1,231,000	530	546,000	760	2,678,000	257
2005	147,000	37	850,000	218	1,425,000	532	623,000	762	3,045,000	268

Table XV. Estimated tuberculosis incidence in 1990, 1995, 2000 and 2005: Indonesia.

	AGE 0-14		AGE 15-34		AGE 35-59		AGE 60+		ALL AGES	
	Cases	Rate	Cases	Rate	Cases	Rate	Cases	Rate	Cases	Rate
------ Demographic factors only ------										
1990	22,000	31	134,000	212	201,000	526	89,000	756	446,000	242
1995	24,000	31	145,000	212	226,000	526	102,000	756	497,000	246
2000	25,000	31	158,000	212	257,000	526	114,000	756	554,000	253
2005	25,000	31	170,000	212	290,000	526	127,000	756	612,000	262
------ Demographic and epidemiological factors ------										
1990	22,000	31	134,000	212	201,000	526	89,000	756	446,000	242
1995	20,000	26	141,000	206	225,000	521	101,000	753	487,000	241
2000	17,000	21	150,000	201	252,000	516	113,000	746	532,000	243
2005	13,000	16	158,000	197	282,000	511	124,000	741	577,000	247

Table XVI. Estimated tuberculosis incidence in 1990, 1995, 2000 and 2005: Pakistan.

	AGE 0-14		AGE 15-34		AGE 35-59		AGE 60+		ALL AGES	
	Cases	Rate	Cases	Rate	Cases	Rate	Cases	Rate	Cases	Rate
------ Demographic factors only ------										
1990	31,000	61	107,000	257	122,000	523	46,000	658	306,000	250
1995	35,000	61	124,000	257	147,000	523	55,000	658	361,000	254
2000	38,000	61	144,000	257	178,000	523	65,000	658	425,000	262
2005	41,000	61	165,000	257	213,000	523	75,000	658	494,000	269
------ Demographic and epidemiological factors ------										
1990	31,000	61	107,000	257	122,000	523	46,000	658	306,000	250
1995	35,000	61	124,000	257	147,000	523	55,000	658	361,000	254
2000	38,000	61	144,000	257	178,000	523	65,000	658	425,000	262
2005	41,000	61	165,000	257	213,000	523	75,000	658	494,000	269

Table XVII. Estimated tuberculosis incidence in 1990, 1995, 2000 and 2005: Brazil.

	AGE 0-14		AGE 15-34		AGE 35-59		AGE 60+		ALL AGES	
	Cases	Rate	Cases	Rate	Cases	Rate	Cases	Rate	Cases	Rate
------ Demographic factors only ------										
1990	19,000	35	67,000	125	76,000	240	29,000	272	191,000	127
1995	20,000	35	73,000	125	90,000	240	33,000	272	216,000	130
2000	21,000	35	78,000	125	105,000	240	38,000	272	242,000	135
2005	21,000	35	83,000	125	121,000	240	44,000	272	269,000	139
------ Demographic and epidemiological factors ------										
1990	19,000	35	67,000	125	76,000	240	29,000	272	191,000	127
1995	16,000	28	68,000	117	87,000	233	32,000	264	203,000	123
2000	12,000	20	69,000	110	98,000	224	36,000	257	215,000	120
2005	8,000	13	68,000	102	110,000	218	40,000	248	226,000	117

Table XVIII. Estimated number of HIV-attributable tuberculosis cases in 1990, 1995 and 2000.

region	1990			1995			2000		
	HIV +ve TB cases	TB cases	HIV attributed TB cases (%)	HIV +ve TB cases	TB cases	HIV attributed TB cases (%)	HIV +ve TB cases	TB cases	HIV attributed TB cases (%)
ADULTS AGED 60+									
All regions	0%	1,588,000	0	0%	1,855,000	0	0%	2,125,000	0
ADULTS AGED 15-59									
South-East Asia	3%	2,330,000	66,000 (2.8%)	10%	2,611,000	248,000 (9.5%)	20%	2,961,000	563,000 (19.0%)
Western Pacific[1]	2%	1,002,000	19,000 (1.9%)	3%	1,092,000	31,000 (2.6%)	6%	1,196,000	68,000 (5.7%)
Africa	25%	794,000	189,000 (23.8%)	35%	1,086,000	361,000 (33.3%)	40%	1,463,000	556,000 (38.0%)
Eastern Mediterranean	2%	481,000	9,000 (1.9%)	3%	564,000	16,000 (2.8%)	6%	666,000	38,000 (5.7%)
Americas[2]	5%	427,000	20,000 (4.8%)	10%	463,000	44,000 (9.5%)	20%	501,000	95,000 (19.0%)
Eastern Europe[3]	1%	126,000	1,000 (0.9%)	2%	131,000	2,000 (1.9%)	5%	136,000	6,000 (4.8%)
Western Europe[4]	5%	127,000	6,000 (4.8%)	10%	132,000	13,000 (9.5%)	20%	137,000	26,000 (19.0%)
All regions		5,287,000	310,000 (6.0%)		6,079,000	715,000 (11.8%)		7,060,000	1,352,000 (19.2%)
CHILDREN AGED 0-14									
East Africa[5]	20%	25,000	5,000 (19.0%)	25%	63,000	15,000 (23.7%)	30%	113,000	32,000 (28.0%)
Other African	0%	74,000	0	2%	188,000	4,000 (1.9%)	5%	334,000	16,000 (4.8%)
South-East Asia	0%	155,000	0	2%	168,000	3,000 (1.9%)	5%	175,000	8,000 (4.8%)
Americas[2]	0%	57,000	0	2%	47,000	1,000 (1.9%)	5%	36,000	2,000 (4.8%)
Other regions	0%	351,000	0	0%	368,000	0	0%	379,000	0
All regions		662,000	5,000 (0.8%)		834,000	23,000 (2.8%)		1,037,000	58,000 (5.6%)
TOTAL		7,537,000	315,000 (4.2%)		8,768,000	738,000 (8.4%)		10,222,000	1,410,000 (13.8%)

[1] Excludes Japan, Australia and New Zealand
[2] Excludes USA and Canada
[3] Includes independent states of the former USSR
[4] Includes USA, Canada, Japan, Australia and New Zealand
[5] Burundi, Kenya, Malawi, Mozambique, Rwanda, Tanzania, Uganda, Zambia, Zimbabwe

Table XIX. Estimated proportion of incident cases receiving treatment in 1990.

Region	Notified cases[1]	Expected cases	Percent notified	Case-Fatality treated[2]	Case-Fatality Rate[3]
South-East Asia	1,510,311	3,176,000	47.6%	50.1%	35.0%
Western Pacific[4]	875,098	1,839,000	47.6%	50.1%	35.0%
Africa	370,359	1,008,000	36.7%	38.6%	39.6%
Eastern Mediterranean	252,413	660,000	38.2%	40.2%	38.9%

[1]Notified cases based on most recent report (WHO/TUB/92.169)
[2]Calculated assuming 5% of treated patients are not included in notification data
[3]Calculated assuming 15% mortality among treated cases and 55% mortality among untreated cases
[4]Excludes Japan, Australia and New Zealand

Table XX. Estimated tuberculosis deaths in 1990, 1995 and 2000, assuming regional treatment coverage rates remain at their 1990 level.

Region	1990 Deaths		1995 Deaths		2000 Deaths	
	Total	HIV attributed	Total	HIV attributed	Total	HIV attributed
South-East Asia	1,087,000	23,000	1,225,000	88,000	1,383,000	200,000
Western Pacific[1]	644,000	7,000	716,000	11,000	789,000	24,000
Africa	393,000	77,000	581,000	150,000	823,000	239,000
Eastern Mediterranean	249,000	4,000	290,000	6,000	338,000	15,000
Americas[2]	114,000	4,000	121,000	9,000	129,000	19,000
Eastern Europe[3]	29,000	<200	30,000	<600	32,000	<900
Western Europe & others[4]	14,000	<500	14,000	1,000	15,000	2,000
All regions	2,530,000	116,000 (4.6%)	2,977,000	266,000 (8.9%)	3,509,000	500,000 (14.2%)
Increase since 1990			17.7%		38.7%	

[1]Excludes Japan, Australia and New Zealand
[2]Excludes USA and Canada
[3]Includes independent states of former USSR
[4]USA, Canada, Japan, Australia and New Zealand

5(b)

ORIGINAL ARTICLES

TUBERCULOSIS

Over the past two years, the World Bank has been undertaking, with a number of collaborators, a "Health Sector Priorities Review". The core of this Review is a series of studies on the public health significance of major clusters of diseases in the developing world and on the costs and effectiveness of currently available technologies for their prevention and case management. This analysis of tuberculosis supported as one of these studies has proven to be one of the most surprising; because of the tremendous burden of tuberculosis and the existence of interventions of proven efficacy that are some of the most cost-effective in the international public health armamentarium.

The present document (some clinical parts have been shortened for our readers who specialize in tuberculosis – the figures and content are final) comprises Chapter 11 of Evolving Health Sector Priorities in Developing Countries edited by Dean T. Jamison and W. Henry Mosley (see below in Introduction).

Tuberculosis in developing countries : burden, intervention and cost

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Introduction

Drafts of other components of the Review are now available from the Population, Health and Nutrition Division, Room S-6141, the The World Bank, Washington DC 20433. The conclusions of these studies, including the one on tuberculosis, do not necessarily reflect the policies of the World Bank.

Tuberculosis is an ancient disease that has long been a major public health challenge in the world, and remains a major health problem in developing countries. In the last century, tuberculosis was responsible for nearly one in ten deaths in Europe (Preston *et al.*, 1972). There is reliable evidence that irrespective of its magnitude, the tuberculosis problem in developed countries has been decreasing at least for the last 40 years, after the introduction of antituberculosis chemotherapy. In many developed countries, a steady decrease in mortality from tuberculosis in the pre-chemotherapy era was observed from the turn of this century if not before (Frost, 1937 ; Styblo, 1980). The elimination of tuberculosis in most developed countries will not be substantially influenced by AIDS because of the low prevalence of tuberculous infection in subjects aged 20 to 50 years in whom HIV infection is most frequent (Styblo, 1986, 1989).

On the other hand, in developing countries tuberculosis continues to be a major problem and there appears to have been virtually no tendency for tuberculosis to eliminate itself, in the absence of intensive control measures. Unlike in developed countries, HIV infection will result in a considerable increase of tuberculosis cases in those developing countries where both tuberculous and HIV infections are prevalent. Tuberculosis remains, therefore, one of the top priorities for action in developing countries, since tools exist to diagnose and cure infectious cases of tuberculosis and thus to decrease transmission of tuberculous infection.

The purpose of this article is to review the present status of tuberculosis in the world, with emphasis on the situation in developing countries, and to examine various policy options concerning the prevention and treatment of tuberculosis, with attention to their cost-effectiveness.

Tuberculosis incidence and mortality

Tuberculosis incidence

To put tuberculosis in the proper perspective we need to know the number and the age-distribution of new cases of tuberculosis which develop in a community each year, as well as the number and the age-distribution of patients who die from tuberculosis each year. Health information systems in developing countries are too incomplete to provide meaningful information on the incidence or mortality of tuberculosis (Styblo and Rouillon, 1981). We are forced to estimate the burden of tuberculosis indirectly using several epidemiological parameters. These include the average annual risk of

tuberculous infection and the incidence of smear-positive pulmonary tuberculosis, the proportion of all cases of tuberculosis that are smear-positive and case-fatality rates for smear-positive tuberculosis and other tuberculosis.

Annual average risk of tuberculous infection

Tuberculosis epidemiologists have used the ability to detect the presence of infection using skin tests to measure the prevalence of infection in communities. A technique has been developed for converting this information on prevalence of tuberculous infection into a series of annual risks of tuberculous infection (Styblo *et al.*, 1969a ; Sutherland, 1976). If several tuberculin surveys of the same population have been made at different times (using similar techniques and testing a representative sample of non-BCG-vaccinated subjects of the same age) the level of and percentage decrease in the risk of infection can be estimated. The annual risk of infection tells us the probability that any individual will be infected or reinfected with *M. tuberculosis* in one year. This measure has become the standard indicator of the tuberculosis burden in a community (Leowski, 1988).

Since the 1950's a variety of tuberculin sensitivity surveys in developing countries provide us with an approximate picture of the annual risk of infection in different regions of the developing world. Table 1 presents our best estimates based on a recent review of survey data on the annual risk of infection (Cauthen *et al.*, 1988). The annual risk of tuberculous infection is probably highest in sub-Saharan Africa, followed closely by South and East Asia. For comparison the annual risk of infection in the Netherlands in 1985 was 0.012 % (Styblo, 1989).

Incidence of smear-positive tuberculosis

The natural history of tuberculosis illustrates that the main source of infection are patients suffering from smear-positive pulmonary tuberculosis. For the rest of this paper, therefore, tuberculosis will be divided into two categories : i) sputum smear-positive tuberculosis, which will be referred by the shorthand smear-positive tuberculosis, and ii) other tuberculosis, which includes those cases of pulmonary tuberculosis that are sputum smear-negative and extra-pulmonary tuberculosis. As children rarely suffer from sputum smear-positive tuberculosis, most cases of tuberculosis in children will be included in the category other tuberculosis. (If children are smear-positive, they are, as adult patients, highly infectious sources of infection. If they are smear-negative/culture-positive or smear-negative/culture-negative they are much less infectious.) The above two categories are sometimes labelled infectious tuberculosis and non-infectious tuberculosis, respectively (*e.g.* Ministry of Health and Family Welfare, India 1986). The distinction between sputum smear-positive tuberculosis and other tuberculosis is particularly important when considering the policy options for tuberculosis control and prevention (Rouillon *et al.*, 1976).

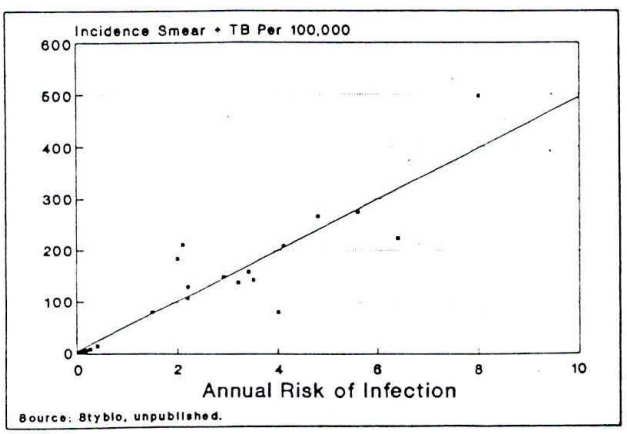

Figure I. The relationship between the annual risk of infection and the incidence of smear-positive tuberculosis.

Table 1. Estimated risks of tuberculous infection and their trends in developing countries, 1985-90

Area	Estimated risk of tuberculous infection (%)	Estimated annual decrease in risk of infection (%)
Sub-Saharan Africa	*1.50 - 2.50*	*1 - 2*
North Africa and Western Asia	*0.50 - 1.50*	*5 - 6*
Asia	*1.00 - 2.00*	*1 - 3*
South America	*0.50 - 1.50*	*2 - 5*
Central America and Caribbean	*0.50 - 1.50*	*1 - 3*

Source : Based on data presented in Cauthen *et al.* (1988).

Lack of data on smear-positive tuberculosis cases in developing countries makes it difficult to convey the enormity of the tuberculosis problem to the public health community. It is not possible to readily obtain reliable information on incidence of smear-positive tuberculosis in developing countries because case-detection rates can be only a fraction of the respective true incidence rates.

The relationship between the annual risk of infection and the incidence of smear-positive tuberculosis can provide one of the only means of estimating the incidence of smear-positive tuberculosis (Styblo, 1985, 1988). Styblo examined the relationship between the annual risk of infection and the incidence of smear-positive pulmonary tuberculosis using a variety of data sources from the developing and developed world. We have recomputed this relationship using only the results of a series of WHO sponsored surveys in developing countries and data from the Netherlands before chemotherapy was widely available. We must note that for some of these surveys data are available on the prevalence of smear-positive tuberculosis, not the incidence. In such cases, the incidence rates were derived using the historical observation that the prevalence of smear-positive tuberculosis was usually twice the incidence in the communities without widespread institution of chemotherapy (Holm, 1970). In these developing countries, the relationship beween the annual risk of infection and incidence of pulmonary smear-positive tuberculosis was linear. A least squared regression line (Figure I) gives an estimate of 49 cases of smear-positive tuberculosis per 100,000 for every 1 % annual risk of infection. The 95 % confidence interval for the coefficient is 39 to 59.

Table 2. Estimated incidence of smear-positive tuberculosis in developing countries, 1990

Area	Estimated number of cases			Incidence
	Low	Midpoint	High	rate
Sub-Saharan Africa	296,000	521,000	745,000	103
North Africa and Western Asia	53,000	146,000	239,000	54
Asia	1,142,000	2,298,000	3,455,000	79
South America	57,000	160,000	263,000	54
Central America and Caribbean	30,000	83,000	136,000	54
Total	1,578,000	3,208,000	4,838,000	77

Note : Based on the annual risk of infection for each region presented in Table 1, the 1990 population and an incidence of 39 to 59 cases per 100,000 for each one percent annual risk of infection.

Using the estimates of the risk of infection for different regions in Table 1 and the confidence interval for the relationship between incidence of pulmonary smear-positive tuberculosis and the risk of infection, the low and high estimates of the incidence of smear-positive tuberculosis for different regions in Table 2 have been calculated. The midpoint of the confidence interval of the estimates of smear-positive incidence is 3,208,000 cases or an incidence of 77 per 100,000 in the developing world. These must be viewed as only crude estimates, which nevertheless illustrate the continuing magnitude of the tuberculosis problem.

Age distribution of smear-positive tuberculosis

The age-distribution of incidence is important in determining the public health impact of smear-positive tuberculosis and the most appropriate means of preventing or controlling tuberculosis. From the historical record of developed countries and epidemiological models, the age and sex distribution of incidence appears to change as the annual risk of infection declines. As the majority of developing countries have an annual risk of tuberculous infection between 1.0 % and 2.0 %, we propose to use the age-distribution of the incidence of smear-positive tuberculosis from a developing country with an annual risk of infection in this range (Tanzania). There is no reason to believe that the epidemiology and thus the age distribution of incidence for a given annual risk of infection will vary substantially between communities. Because the tuberculosis control programme in Tanzania is well organized and captures the majority of tuberculosis cases, the age-distribution from Tanzania will be used as representative of the developing world where the risk of tuberculous infection is between 1 and 2 %. Figure II shows the age-distribution of smear-positive tuberculosis in Tanzania for 1985-87 (Chum *et al.*, 1987 ; Chum, 1989). The pattern is similar to other developing countries such as Mozambique, Malawi and Benin that have good reporting systems (IUATLD 1988). It is important to note that BCG coverage in Tanzania was roughly 50 % in 1983-87 (Bleiker *et al.*, 1987) – based on scar examination in the National Tuberculin Survey in Tanzania carried out from 1983 to 1987 on 80,000 schoolchildren from 20 regions selected at random which is below the officially reported average for the developing world (UNICEF, 1988). Thus, any effect such BCG coverage may have on preventing tuberculosis in children is partially represented in the age-distribution ; as world BCG coverage is probably higher than in Tanzania, the estimate for the incidence of smear-positive tuberculosis in children based on this age-distribution may be slightly high. Clearly, smear-positive cases are relatively rare in children ; smear-positive tuberculosis is concentrated in adults – more than 80 % of cases occur between the ages of 15 and 54, according to the data from Tanzania.

Incidence of other forms of tuberculosis

Estimates of the incidence of smear-negative pulmonary and extra-pulmonary tuberculosis are also needed. These forms of tuberculosis are particularly difficult to quantify as the major diagnostic tool used in developing countries, sputum microscopy, does not detect these cases. Because the diagnosis of extra-pulmonary tuberculosis is often based on clinical criteria, no survey data are available to estimate the relationship between the risk of infection and other tuberculosis. In the past, estimates of smear-positive tuberculosis have simply been doubled to provide a figure for other tuberculosis (Styblo and Rouillon, 1981 ; Leowski, 1988). The distribution of total cases between the categories sputum smear-positive and other tuberculosis cannot be accurately established. Whereas smear-positive tuberculosis and tuberculosis positive by culture only can be objectively determined, the number of culture-negative cases detected depends on various factors, such as active case-finding by Mass Miniature Radiography (MMR) extensively used in Europe in the 1950's, 1960's and 1970's, criteria for activity in asymptomatic cases detected by active case-finding, age-groups, etc. However, we will assume that **within each age-group** using the same diagnostic approach the percentage of cases that are sputum smear-positive and other should be the same relatively independent of the overall annual risk of

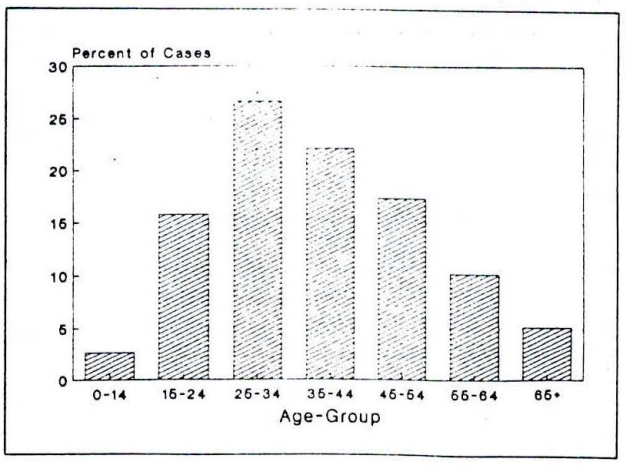

Figure II. The age distribution of smear-positive tuberculosis detected in Tanzania, 1985-1987.

infection. Using data for the United States and Norway, Figure III illustrates the proportion of all tuberculosis cases that are smear-positive by age (Galtung, 1955 ; CDC, 1989). Because the data set for the US is larger and no MMR was used on a large scale, we will use the ratio of cases of other tuberculosis to smear-positive tuberculosis within each age-group in the United States. Using the age-distribution of the incidence of smear-positive tuberculosis in Tanzania and the age-specific ratios of other to smear-positive in the United States, we have derived a rough estimate of the age-distribution of other tuberculosis shown in Figure IV. While the assumptions underlying these estimates of other tuberculosis may be challenged on many grounds, we feel it is preferable to make some objective attempt to estimate the age-distribution of smear-negative and extra-pulmonary tuberculosis in developing countries because it is an important input to policy decisions.

Our estimations imply that there are 1.22 cases of smear-negative and extra-pulmonary tuberculosis for every case of smear-positive tuberculosis in developing countries with an annual risk of infection between 1 and 2 % and an overall age-distribution similar to Tanzania. Table 3 provides low and high estimates of the number of new cases of smear-negative and extra-pulmonary tuberculosis for each region in the developing world. For all types of tuberculosis combined, Table 4 indicates that the incidence of tuberculosis exceeds 220 per 100,000 in sub-Saharan Africa.

Tuberculosis mortality

Case-fatality rates, untreated

In order to calculate tuberculosis mortality from the estimates of incidence derived above, we need to estimate the case-fatality rate. Without appropriate chemotherapy, tuberculosis is highly fatal. The results of several studies in developed countries before chemotherapy became available demonstrated mortality rates consistently in the 50 % to 60 % range (Drolet, 1938 ; Lindhart, 1939 ; Galtung Hansen, 1955). These observations were confirmed in the five-year study of the natural history of tuberculosis in Bangalore,

Table 3. Estimated incidence of other tuberculosis in developing countries, 1990

Area	Estimated number of cases Low	Midpoint	High	Incidence per 100,000
Sub-Saharan Africa	361,000	635,000	909,000	126
North Africa and Western Asia	64,000	178,000	291,000	66
Asia	1,393,000	2,804,000	4,215,000	96
South America	71,000	196,000	321,000	66
Central America and Caribbean	37,000	101,000	166,000	66
Total	1,926,000	3,914,000	5,902,000	94

Note : The incidence of other tuberculosis has been based on USA data showing the relationship between smear-positive tuberculosis and other tuberculosis by age combined with the age-distribution of smear-positive tuberculosis in Tanzania.

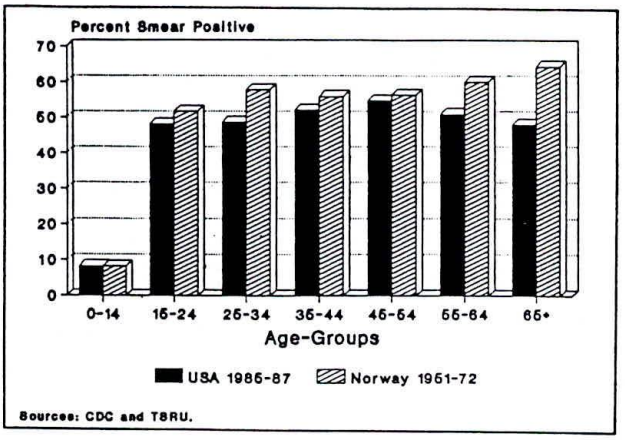

Figure III. The percent of all cases of tuberculosis that are smear-positive, USA 1985-1987 and Norway, 1951-1972.

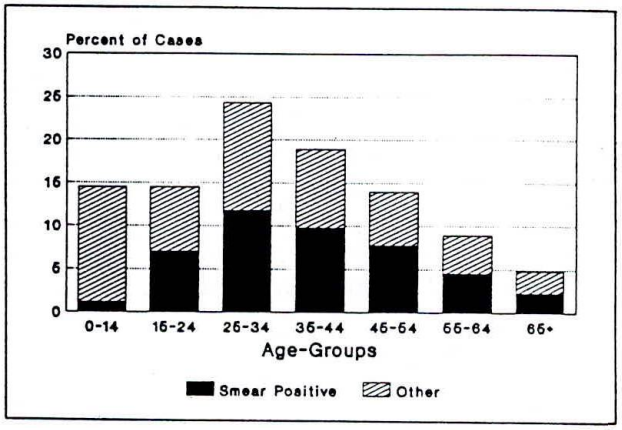

Figure IV. The estimated incidence of smear-positive and other tuberculosis by age for the developing world in 1990.

India : 49 % of bacteriologically confirmed cases (smear- and culture-positive cases or smear-negative and culture-positive) died within five years (National Tuberculosis Institute,

Table 4. Estimated incidence of all forms of tuberculosis in developing countries, 1990

Area	Estimated number of cases Low	Midpoint	High	Incidence per 100,000
Sub-Saharan Africa	656,000	1,156,000	1,655,000	229
North Africa and Western Asia	117,000	323,000	530,000	120
Asia	2,535,000	5,102,000	7,670,000	174
South America	129,000	356,000	584,000	120
Central America and Caribbean	66,000	185,000	302,000	120
Total	3,503,000	7,122,000	10,741,000	171

Bangalore, 1974). As expected, the case-fatality rate for smear-positive tuberculosis is even higher; Rutledge and Crouch (1919) and Lindhart (1939) reported 66 % mortality in these cases (no information is available from the Bangalore study). For the rest of this paper, we will assume that the case fatality rate for smear-positive tuberculosis is 60 % to 70 %, for other tuberculosis as a whole it is 40 % to 50 % and for all forms combined it is 50 % to 60 %.

Tuberculosis death rates in developing countries

The tuberculosis death rates in developing countries cannot be as high as implied by the incidence rates and a case-fatality rate of 50-60 % because a significant proportion of cases are detected and treated, which lowers the tuberculosis death rate. Accordingly, we adjusted our estimates for this effect by using estimates of the number of cases that receive treatment to derive the likely range of tuberculosis death rates in developing countries. For all those cases that are detected and receive treatment, we assume the case-fatality rate is reduced to 20 % after 5 years. For example, in the East African and British Medical Research Council surveys in Tanzania and Kenya the case-fatality rates for patients receiving standard chemotherapy were 12 % and 16 % respectively after 12 months (EAMRC 1977, 1979). In many countries, however, the case-fatality rate may be over 20 % for those receiving chemotherapy, after five years of follow-up, making the following estimates of mortality conservative.

Estimates of the percentage of new cases that are detected and treated are based on the number of cases of tuberculosis detected that are reported by countries to the World Health Organization (Table 5) (WHO, 1988). Because reporting is extremely variable, these estimates are based on the highest number of cases reported by each country for any year in the last decade. This is justified by the assumption that year to year variation in the number of cases reported, which can be greater than an order of magnitude, is due more to incomplete reporting of health service activities than to change in the epidemiology of tuberculosis. In addition, the highest number of cases reported in the last ten years has been adjusted upwards by 20 % to try and account for those cases that are detected in the private sector that do not report to the government ; in Asia where data for some large countries may include a large number of retreatment cases we have not adjusted the figures by 20 %.

Separate estimates for the percent of smear-positive and other cases are needed. As the primary means of detecting tuberculosis in developing countries is sputum microscopy, the detection rate of smear-positive tuberculosis is higher than for smear-negative or extra-pulmonary tuberculosis. Based on data from the National Tuberculosis and Leprosy Programme in Tanzania, we will assume that 60 % of detected cases are smear-positive and 40 % are other tuberculosis. The detection rate of the various forms of tuberculosis and the likely range of case fatality rates discussed above can be combined to estimate the tuberculosis death rates from smear-positive tuberculosis and other tuberculosis. Because the detection rate for smear-positive tuberculosis is higher despite a higher case fatality rate, the overall death rate from smear-positive tuberculosis is similar to the death rate from other tuberculosis.

Table 5. Estimated tuberculosis cases detected and case fatality rates in developing countries, 1990

Area	Estimated cases detected	Percent all cases detected	Estimated case fatality rates (%) Low	High
Sub-Saharan Africa	325,000	*28*	*41*	*48*
North Africa and Western Asia	223,000	*69*	*28*	*31*
Asia	3,087,000	*61*	*30*	*34*
South America	222,000	*62*	*32*	*36*
Central America and Caribbean	50,000	*27*	*41*	*49*
Total	3,907,000	*55*	*32*	*37*

Note : The calculations of effective case-fatality rates are based on the assumption that 15 % of those patients receiving standard chemotherapy die. As discussed in detail in the section on chemotherapy this is a conservative assumption.

Table 6. Estimated deaths from all forms of tuberculosis in developing countries, 1990

Area	Estimated number of cases Low	Midpoint	High	Deaths per 100,000
Sub-Saharan Africa	266,000	528,000	790,000	104
North Africa and Western Asia	33,000	99,000	166,000	37
Asia	771,000	1,709,000	2,646,000	58
South America	41,000	125,000	211,000	42
Central America and Caribbean	28,000	88,000	148,000	57
Total	1,139,000	2,549,000	3,961,000	61

Table 6 shows estimated deaths each year from all forms of tuberculosis for regions based on the calculations of the tuberculosis death rates discussed above. The wide confidence intervals reflect the cumulative uncertainty in the paremeters of the estimation procedure. Using the midpoints of the confidence intervals, the total number of deaths from tuberculosis in the developing world comes to 2,549,000. **Tuberculosis, therefore, accounts for approximately 6.7 % of all deaths in the developing world in 1990 (United Nations, 1989).**

Age-distribution of tuberculosis deaths

To estimate the age-distribution of tuberculosis deaths, we must take into consideration the age-distribution of new cases and the relationship between case-fatality rates and age. Clearly, the relationship is complex ; for example, the death rates may also vary by age because certain age-groups may be more likely to seek treatment and be cured. With hesitation, we will apply the age-specific case-fatality rates from London 1933-1934 to the age-distribution of total tuberculosis incidence derived above (Styblo, 1984). Tuberculosis case-fatality rates tend to increase steadily at older

Table 7. Distribution of tuberculosis deaths by age

Age-group	Czechoslovakia 1940	1931	Norway 1941	1951	1931	Netherlands 1941	1951
0-14	*11.7*	*11.8*	*10.3*	*8.0*	*24.0*	*19.4*	*13.6*
15-24	*22.0*	*30.6*	*25.4*	*10.8*	*22.4*	*20.3*	*12.8*
25-34	*18.7*	*25.9*	*25.4*	*24.4*	*20.8*	*20.7*	*16.9*
35-44	*14.0*	*14.5*	*16.1*	*19.5*	*11.7*	*13.1*	*12.8*
45-54	*12.5*	*7.7*	*9.6*	*13.2*	*7.7*	*9.6*	*11.6*
55-64	*11.4*	*5.0*	*6.6*	*10.7*	*6.3*	*8.2*	*13.4*
65+	*9.7*	*4.5*	*6.5*	*13.4*	*7.1*	*8.7*	*18.9*
Risk of infection	*5.5* (1938)				*3.7*	*1.8*	*0.5*

Age-distribution of deaths have been adjusted using the population age-structure of the developing world in 1990.

ages. Figure V provides the crude estimates of the age-pattern of tuberculosis deaths in a country with an annual risk of infection of 1 % to 2 % where the probability of detection is equal for smear-positive tuberculosis across all age-groups and equal for other tuberculosis across all age-groups.

This estimated pattern can be compared to the age-distribution of tuberculosis deaths in Western countries when the annual risk of infection was similar to that now seen in the developing world. Table 7 illustrates the age-distribution of tuberculosis deaths adjusted to the age-structure of the developing world in Czechoslovakia, Norway and the Netherlands (TSRU, 1966). The percentage of deaths in children under 15 ranged from approximately 10 % to 20 %. In the Netherlands, the tuberculosis death rates in children were considerably higher than in Czechoslovakia even at lower risks of infection. Clearly, there are other variables that are major determinants of the reported age-distribution of tuberculosis death rates. One explanation may be the high rates of *M. bovis* infection in the Netherlands at the time. According to our estimates for Tanzania, less than 8 % of tuberculosis deaths occur in children under age 15, which is less than in the three

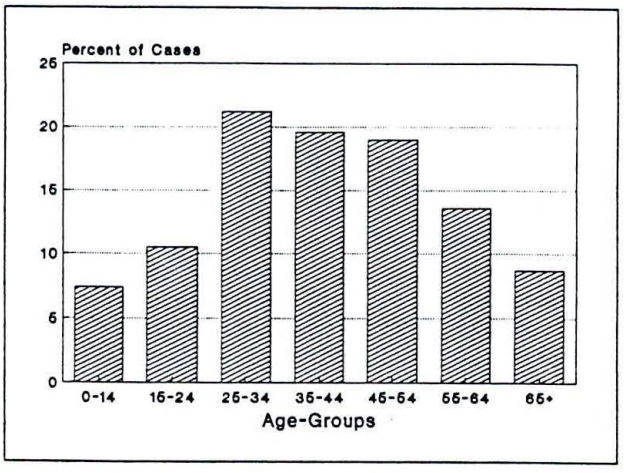

Figure V. Estimated age-distribution of tuberculosis deaths in the developing world in 1990.

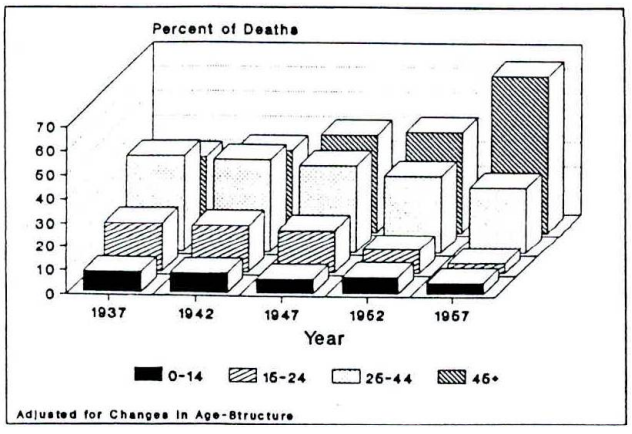

Figure VI. The shifting age-structure of tuberculosis deaths as the annual risk of infection declines, USA 1937-1957.

developed countries in Table 7. This may be due to the higher BCG coverage in Tanzania now than in these countries at the time. Variation in the age pattern of tuberculosis deaths highlights the tentative nature of the estimates presented here. The basic conclusion, however, that tuberculosis is concentrated in the adult age-groups, appears to be robust.

As the discussion above implies, the age pattern of tuberculosis deaths shifts towards higher ages as the annual risk of infection declines. Using data from the US which has been adjusted to the 1990 age-structure of the developing world, Figure VI demonstrates how the mean age of death increases as the risk of infection declines. The number of deaths in children declines faster than the annual risk of infection; this relationship will become important in considering the cost-effectiveness of BCG.

Trends in incidence and mortality

Using the midpoints of the ranges of the annual risk of infection in Table 1, population projections, and the rates of decline in the annual risk of infection also reported in Table

1, cases and rates of tuberculosis in 2015 have been estimated (Table 8). These estimates are based on the assumption that the rates of decline in the annual risk of infection observed between 1970 and 1985 will continue into the future. In other words, the projections are based on the assumption that the socio-economic changes and tuberculosis control activities that caused the decline in the risk of infection in the last two decades will continue at the same rate. Such projections suffer from all the same limitations that any projection of current trends does.

According to these assumptions, tuberculosis will remain a major problem in all developing world regions referred to in Table 8. In Africa, population growth will probably exceed the projected decline in the annual risk of infection, so that the absolute number of cases will increase. **These projections for Africa have not taken into consideration the interactions between HIV infection and tuberculosis.** As discussed below, the annual risk of infection in Central and East Africa may stop declining or even increase in the next decades. The figures in Table 8, therefore, may be significant underestimates for Africa. The relationship between HIV infection and tuberculosis will be explored more fully below.

Social and economic costs

There are few if any studies of the actual costs or consequences of tuberculosis on the family, community or economy in developing countries. The special burden of ill-health and death caused by tuberculosis, however, follows from the age-distribution of its incidence. While morbidity and mortality in any age-groups has significant social and economic costs, deaths in prime aged adults who are the parents, community leaders and producers in most societies have a particularly onerous burden. The incidence of tuberculosis is concentrated in adults 15-64. For example, while the overall incidence of tuberculosis in Africa is estimated to be 230, in adults it is approximately 360 per 100,000.

One of the greatest costs to society and the economy from tuberculosis is mortality. It has been estimated that there are just under 10.6 million deaths in adults 15-59 in the developing world (Murray and Feachem, 1990). Of these, our figures suggest approximately 18.5 % are due to tuberculosis. Not all these deaths are preventable. **Of avoidable adult deaths, 26 % are probably due to tuberculosis.**

The consequences of adult death from tuberculosis on children and other dependents can also be great. Studies have shown that when a mother dies her children suffer higher rates of mortality (Greenwood *et al.*, 1987). One can speculate that similar relationships may exist for paternal death. Several studies from developed countries have shown that tuberculosis is concentrated in lower socio-economic groups, those households least able to cope with the burden of tuberculosis. Pryer (1989) found that children in households where one parent suffers from a serious debilitating disease such as tuberculosis, are two and half times more likely to be severely malnourished. **As tuberculosis deaths are concentrated in the segment of the population that is economically most productive, the economic cost of tuberculosis, in terms of lost production, must be greater than a disease that affects exclusively children or the elderly.**

Prevention

There are three major strategies for preventing tuberculosis : BCG vaccination, chemoprophylaxis and decreasing sources of infection through case-finding-treatment. Each will be discussed in turn.

BCG

The bacillus of Calmette and Guérin (BCG) was developed in 1921. Since that time, it has become one of the most widely used yet controversial vaccines. While BCG coverage has been up to now on average quite high compared to other immunizations, the effectiveness of BCG in preventing tuberculosis in adults remains controversial. Clinical trials in the United Kingdom and in the USA found that BCG was up to 80 % effective (Aronson *et al.*, 1958 ; Medical Research Council of Great Britain, 1972). Major vaccine trials in South India, however, found no effectiveness of BCG (Tuberculosis Prevention Trial, 1979). A variety of prospective trials in the developed world and more recent case-control studies in developing countries have reported effectiveness ranging from 0 to 80 % (Smith, 1987 ; Clemens *et al.*, 1983).

Many explanations and theories have been advanced to explain this variance including differences in strains of BCG, infections with other mycobacteria and differences in sus-

Table 8. Cases and deaths from all forms of tuberculosis, 2015

Area	Estimated number of cases			Deaths
	Smear +	Other	Total	
Sub-Saharan Africa	766,000	934,000	1,701,000	777,000
North Africa and Western Asia	98,000	120,000	218,000	66,000
Asia	1,871,000	2,283,000	4,154,000	1,391,000
South America	98,000	120,000	218,000	77,000
Central America and Caribbean	80,000	97,000	177,000	84,000
Total	2,913,000	3,554,000	6,468,000	2,395,000

Note : These projections are based on the following assumptions : 1) the current rate of decline in the annual risk of infection will continue over the next 25 years ; 2) the percent of cases detected will remain the same in each region ; and 3) the cure rate and implicitly the percent of cases treated with standard chemotherapy will remain the same for those cases that are detected and treated.

ceptibility due to factors such as nutritional status (Fine, 1989). While there is no consensus on the effectiveness of BCG, we will assume that BCG is between 40 % and 70 % effective in preventing tuberculosis in children 0-14 when given at birth. Some would argue that BCG given at birth may protect beyond 15 years ; there is, however, no evidence of this especially in developing countries.

BCG is given as early as possible in life, preferably at birth, in the vast majority of developing countries. In addition, one could give serious consideration to "indiscriminate (re)vaccination" (*i.e.* without prior tuberculin testing) at older ages, irrespective of vaccination at birth. Depending on the feasibility of coverage, BCG (re)vaccination could be given to children entering school, leaving school, pregnant women attending for prenatal care of other routine contacts of the population with health workers. For example, tetanus toxoid is now considered by many to be an integral component of prenatal care ; BCG could be delivered at the same time for only a small increase in the total cost. The actual effect of BCG (re)vaccination at older ages has not been thoroughly studied but there seems little reason that it would be harmful and it may have some beneficial impact.

We must realize, however, that vaccination of newborns with BCG is a problem in those developing countries where there is a high prevalence of HIV infection among mothers. The WHO Expanded Programme on Immunization, which is responsible for the programme of vaccination against six selected childhood diseases in the world, has been continuing BCG-vaccination of newborns and small children including when the mother is known to be or suspected of being HIV-infected. As of the time of writing, evidence remains inconclusive regarding the rate of adverse reactions after BCG immunization among symptomatic HIV-infected individuals. BCG should be withheld from individuals with symptomatic HIV infection (WHO, 1987). The current recommendations on HIV and BCG-vaccination will be reviewed in the fall of 1990.

The impact of mass BCG-vaccination on the epidemiological situation of tuberculosis was overestimated until the mid-1970's (Styblo and Meijer, 1976). As mentioned earlier, tuberculosis is largely transmitted by sputum smear-positive cases of pulmonary tuberculosis. From the age-distribution of smear-positive cases, it is clear that even complete BCG coverage can have little effect on the annual risk of infection. Total coverage with BCG, however, will have a major impact on tuberculosis mortality in children, if BCG is 40 % to 70 % effective as we have assumed. Based on the assumptions discussed above, complete coverage could reduce total tuberculosis mortality by approximately 6 %. BCG will most likely have very limited effect on the remaining 90 plus percent of tuberculosis mortality. Evidently, the expansion of BCG coverage alone cannot or should not be the sole means employed to control tuberculosis in any community.

Cost-effectiveness of BCG

For two principal reasons, generalizable estimates of the cost-effectiveness of BCG cannot be made. First, there may be substantial differences in the computed average and marginal costs of BCG programmes depending on the programme considered. Second, the cost-effectiveness of BCG **is inversely proportional to the annual risk of infection.**

When more than one vaccine is given at the same time, average costs for delivering each particular immunization are often calculated by dividing the cost per client contact by the number of vaccinations received. Thus the difference between marginal costs and average costs for a BCG programme will depend on whether BCG is delivered in an independent campaign or contact with mother and child or along with other immunizations such as the first DPT. The Expanded Programme on Immunization was, unfortunately, unable to indicate how BCG is delivered in each country. We conclude that the marginal cost-effectiveness of expanding BCG will necessarily depend on the location and timing of vaccination in a particular country.

As the annual risk of infection declines, *ceterus paribus*, the cost of vaccinating all newborns does not change. The benefits of BCG vaccination in terms of cases or deaths averted, however, will decline inversely to the risk of infection. For example, as the risk of infection declines from 2 % to 1 %, the cost per death averted will more than double. The increase in the cost per death averted is greater than the decline in the risk of infection because the age-distribution of deaths also shifts away from children as the risk of infection declines – see Figure VI. The expected relationship between the risk of infection and the cost per death averted by BCG is illustrated in Figure VII.

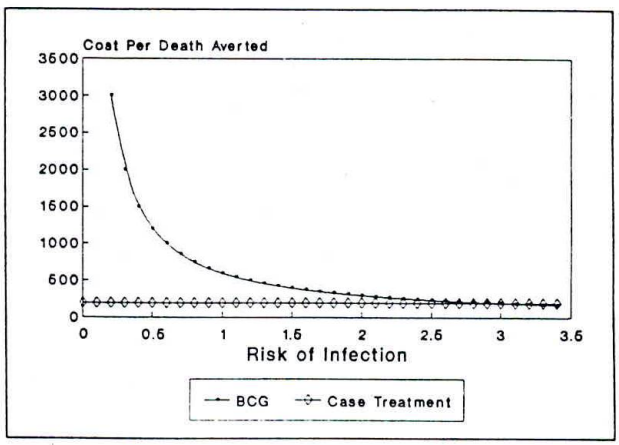

Figure VII. A hypothetical comparison of the cost-effectiveness of BCG immunization and case-treatment.

Only one study has attempted to cost a BCG programme and estimate its effect in a developing country. Barnum *et al.* (1980) estimated the cost of operating a BCG programme alone and also the marginal cost of adding a BCG programme to an existing DPT programme. His estimates of deaths averted were based on local incidence and case-fatality rates of tuberculosis and an assumed effectiveness for BCG of 50 %. We have recalculated using his original data the cost per discounted death averted in 1986 dollars. Deaths prevented by BCG vaccination now occur over the next 14 years, these are discounted to present value for comparison with interventions that avert deaths in the current time period. The cost per death discounted at 3 % was $ 644 for the BCG programme alone and $ 144 for the marginal BCG

programme – both prices are in 1986 US dollars. At the time in Indonesia survey data suggest the risk of infection was approximately 3 % ; regional surveys report annual risks of infection between 2 % and 4 % (Cauthen *et al.*, 1987). It must be stressed that these estimates of cost-effectiveness do not take into consideration the potential benefits of BCG in reducing leprosy (Fine *et al.*, 1986).

Chemoprophylaxis

Clinical tuberculosis can be secondarily prevented by treating patients with tuberculous infection. Chemoprophylaxis is applied either to freshly infected so-called tuberculin-converters or to those who have been infected with virulent tubercle bacilli in the more distant past. The latter either do or do not have abnormalities in the lungs on X-ray.

Tuberculin converters undoubtedly represent a very rewarding group in terms of chemoprophylaxis results and thus chemoprophylaxis policy has been adopted as a routine procedure in a number of low prevalence countries. However, mass chemoproplylaxis of converters is impossible, since their identification depends on repeated tuberculin tests of the population. On the other hand, a selective search for converters in high risk groups, such as close family contacts of smear-positive sources, is a feasible alternative. As discussed below 6-8 % of recent infections evolve into clinical tuberculosis. In developing countries, where large percentages of the population have been infected, the IUATLD recommends chemoprophylaxis (in HIV low prevalence countries) only for all non-BCG-vaccinated children aged 5 years or under, with no symptoms suspicious of tuberculosis. In children with symptoms chemotherapy should, of course, be given.

Chemoprophylaxis in tuberculin-positive subjects but who have not developed clinical tuberculosis would reduce the number of sources of infection, if given for 6 to 12 months. In most developing countries, this group is very large and resources would be far better directed to case-detection and treatment. However, chemoprophylaxis might play a very important role both in developed and developing countries in subjects with the dual HIV and tuberculous infections without clinical and bacteriological signs of tuberculosis. Research in this field is urgently needed.

Studies in developed countries have found cost-effectiveness rates per case averted on a 24 week regimen to be greater than $ 17,000 (Snider *et al.*, 1986).

Without accurate data to review the cost-effectiveness of chemoprophylaxis in developing countries, we can only make some comparisons to the costs per case treated. Since only 6-8 % of recent converters evolve into clinical tuberculosis, 12.5-16.7 recent tuberculin positive patients must be given chemoprophylaxis to prevent one case of tuberculosis assuming prophylaxis is 100 % effective. In tuberculin positive subjects as opposed to new converters, the ratio would be one or two orders of magnitude higher. The drug costs for chemoprophylaxis are lower than for treatment, but the costs of administration, screening, transport, delivery and monitoring would be similar. Thus, chemoprophylaxis is unlikely to be more cost-effective in developing countries than case-finding/treatment of patients presenting with symptoms suspicious of tuberculosis as discussed below. One exception may be in children under 5 exposed to an adult with active smear-positive pulmonary tuberculosis.

Decreasing sources of infection

It has already been suggested that the best way to reduce transmission of tuberculous infection and thus the number of tuberculosis cases is to cure patients with smear-positive tuberculosis. This was stated by Crofton (1962) already in the mid 1950's. A variety of epidemiological studies can be used to quantify this transmission effect. The number of new infections caused each year by a case of smear-positive tuberculosis can be estimated from survey data on the number of new infections and the prevalence of smear-positive tuberculosis. It has been estimated using data from developing and developed countries, that an undiagnosed and untreated smear-positive source of tuberculous infection would infect on average between 10 and 14 persons per year (Styblo, 1984 ; Sutherland and Fayers, 1975). Breakdown of primary infection with tubercle bacilli to clinical tuberculosis is the next link in the chain of transmission. Reference is made to three reports of newly infected subjects to determine the percentage that developed clinical tuberculosis : the MRC study (Sutherland, 1968) found 8.1 % of converters developed clinical tuberculosis within 15 years ; in Saskatchewan of recently infected individuals, 6.4 % developed clinical tuberculosis within a few years after primary infection (Barnet *et al.*, 1971) ; and a TSRU study of European data found 6.0 % of converters developed bacillary tuberculosis in five years (Sutherland, 1976). For the purposes of modelling transmission, we will assume that from 6 % to 8 % of new infections will eventually develop some form of clinical tuberculosis.

The studies cited above refer to the risk of developing clinical tuberculosis soon after primary infection. What about the risk of developing clinical tuberculosis in cases previously infected with tubercle bacilli, without or with a fresh reinfection ? As it is not possible to detect reinfection with tubercle bacilli by tuberculin testing, it cannot be discovered directly whether or not exogenous reinfection is important in the development of tuberculosis in an adult. It is evident that in countries with low annual risks of infection, tuberculosis in elderly and old persons is predominantly due to endogenous exacerbation among those remotely infected with tubercle bacilli. In developing countries, exogenous reinfection seems to play an important role in developing active tuberculosis in the adult population, since 0.5 % to 2.5 % or more of previously infected individuals are annually reinfected with tubercle bacilli as was the case in developed countries some 2 to 4 decades ago (Canetti, 1972 ; Jancik and Styblo, 1976). Strong evidence for the latter is the rapid decline in tuberculosis incidence in Eskimos over the space of 20 years, not only in children and young adults but also in elderly and old people, when aggressive case detection and adequate chemotherapy was introduced (Grzybowski *et al.*, 1976).

We will assume, therefore, that each undiagnosed and untreated smear-positive case will cause 10 to 14 infections per year of infectivity. These 10 to 14 infections will subsequently cause over the next few years 0.6 to 1.2 cases of tuberculosis. These cases will be approximately equally distributed between smear-positive and other tuberculosis. The mean period from infection to onset can be estimated more precisely from data reported by Sutherland (1968) as 1.4 years. These parameters highlight the importance of case treatment in preventing further cases and will be used in estimating the cost-effectiveness of treating smear-positive tuberculosis in the pages that follow.

Curative care

The subject of curative care can naturally be divided into tuberculosis detection and chemotherapy. Each of these will be addressed in turn, highlighting the policy options.

Case detection

There are two major issues in detecting cases of clinically significant tuberculosis : active versus passive detection strategies and the choice of diagnostic technology. Active detection means attempts to screen the population at large, or target populations such as military recruits, for evidence of tuberculosis. Passive case detection means screening and diagnosing only those patients who present to a health service provider because of symptoms suspicious of tuberculosis. In the 1950s and 1960's, the choice between active and passive detection in developed and developing countries was a controversial topic (Styblo *et al.*, 1967 ; Meijer *et al.*, 1971 ; WHO Expert Committee on Tuberculosis, 1974 ; Styblo and Meijer, 1980 ; Toman, 1979). In the last two decades, a consensus for passive case detection of tuberculosis in all countries has developed, and both the WHO and IUATLD advocate this policy.

There are three assumptions that underlie the wide acceptance of passive case detection as the primary strategy in tuberculosis control. First, 90 % of patients with smear-positive pulmonary tuberculosis have objective symptoms, such as cough (with or without sputum), fever, loss of weight or hemoptysis. These symptoms develop quite soon after the onset of the disease prompting the patient to seek medical advice. Second, the great majority of sputum smear-positive tuberculosis cases develop in a shorter period of time than the shortest feasible interval between two mass radiography survey rounds. That is why smear-positive tuberculosis cases were detected outside (usually earlier than) the periodic case-finding campaigns by the regular health services that the patient can consult whenever he feels ill. Third, appropriate diagnostic and curative care ought to be physically, socially and economically available. Most infections, before chemotherapy is instituted, would therefore occur within the family. Whereas in developed countries, it is estimated that 2-3 persons would be infected by a smear-positive case before its detection, this number may be 4-5 in developing countries, because of higher number of close contacts. No contacts will be infected after the start and completion of adequate chemotherapy.

The validity of these assumptions depends on local conditions, cultural perception of disease, access to care and the efficacy of health services.

Regardless of the technology used, active case detection is more expensive per case detected because the yield of tuberculosis per patient screened is lower. For example, if the incidence of smear-positive tuberculosis is 100/100,000 then more than 1,000 people's sputum would have to be screened to detect one case of smear-positive tuberculosis provided that the general population is screened. If specific high risk groups can be identified, the yield would clearly be higher. For comparison, screening patients who present with cough in Tanzania using sputum microscopy yields one patient in 10 cases with smear-positive tuberculosis. The second argument against active case detection is that cases actively identified may be less likely to comply with long drug regimens. Clearly, they did not yet consider their health to be impaired enough to seek treatment to start with. Moreover, a proportion of smear-negative cases with few or no clinical symptoms cure spontaneously and in a number of cases the disease is in regression (National Tuberculosis Institute in Bangalore 1974 ; Meijer *et al.*, 1971, Styblo *et al.*, 1967). In developing countries, active case-finding was studied by the Kenyan and British Research Councils in the late 1970's and early 1980's. There are seven reports on these studies and the conclusion in the last study is that a patient suffering from symptoms suggestive of pulmonary tuberculosis nearly always attends, usually several times, a health unit seeking medical advice (EAMRC, 1987). However, health workers at the peripheral level do not think in many instances of tuberculosis and do not send the sputum or do not refer the patient to the nearest microscopy centre for sputum examination for tubercle bacilli. In many developing countries, public transport is very rudimentary; even if available, it is not always affordable to poor people. Moreover, the Kenyan studies have shown that active case-finding, except in health units, is not feasible.

The second issue in case-detection is the choice of technology. At present, the major options are sputum microscopy, sputum culture and radiology. To illustrate the yield and likely cost of case-detection using microscopy (Ziehl-Neelsen), we shall examine data from the National Tuberculosis and Leprosy Programme in Tanzania. In that country, one in ten tuberculosis suspects screened by smear examination is identified as a smear-positive case. Normally, three smears are conducted on each patient. The costs of supplies and reagents alone for these thirty smears is $ 4.05. A microscopist can examine about 20 sputa per day and is paid US$ 45 per month. The effective cost per case detected in Tanzania is US$ 7.30. This is a high estimate since each case has three sputa examined to increase sensitivity ; the increased sensitivity achieved with the third smear is in fact small and could be sacrificed to reduce the cost.

Sputum culture is used to diagnose pulmonary tuberculosis in those patients that produced too few bacilli to be detected on a smear, to confirm sputum microscopy, and to characterize the type of mycobacterium. (Finally, culture is a prerequisite to sensitivity test examination.) As culture takes several weeks to yield results, it is not useful as a primary diagnostic tool in developing countries.

The third diagnostic tool is radiography. While it can be an effective tool particularly for diagnosing smear-negative pulmonary tuberculosis, the capital cost of an X-ray machine limits its use to those facilities with a high case load. In Tanzania, we can estimate that the cost per case detected for both smear-positive and smear-negative pulmonary tuberculosis combined to be around US$ 10. This calculation, however, attributes only one sixth of the depreciated capital cost of an X-ray machine to diagnosing tuberculosis, because we assume an X-ray machine in a district hospital would be used for many other purposes. An X-ray facility exclusively for diagnosing tuberculosis would be much more expensive. The calculation also assumes a case-load of at least 1,000 patients per year. The optimal use of radiography in passive case-detection clearly depends on the health system infrastructure, population distribution, and possibilities for referral. Usually, in 25-30 % of all pulmonary cases detected in a developing country, the diagnosis of smear-negative tuber-

culosis is based on X-ray of the chest with a pathology suspicious of active tuberculosis and on clinical examination.

New diagnostic technologies based on the enzyme linked immunoabsorbant assay or DNA probes for mycobacterial DNA or RNA are currently being investigated (Daniel, 1989 ; Bloom, 1989). If these approaches yield new tools that can be cheaply applied in developing countries, passive case detection may be improved especially for smear-negative and extra-pulmonary tuberculosis which are not diagnosed using sputum microscopy. Active case detection in some high risk groups would perhaps become feasible.

A limited number of interventions are available to improve the effectiveness of passive case detection. The most effective factor for improvement in case-finding is a high cure rate of diagnosed cases and a friendly relationship between the treating health staff and the patient. Public education can increase general awareness of the symptoms of tuberculosis and encourage suspects to seek medical advice resulting in diagnosis of tuberculosis and its treatment. Improved diagnostic skills of primary health care providers, transport of sputum or a patient to a microscopy center, and X-ray facilities, if available, can also improve the detection of both smear-positive tuberculosis and other tuberculosis. Finally, if diagnosis and adequate treatment are free, as recommended by WHO and IUATLD, more patients will seek care earlier.

Table 9. Examples of tuberculosis chemotherapy regimens used in developing countries

Regimen	Duration
New smear-positive cases	
Long-course (12 months)	
2SH/10TH	12
2SH/10EH	12
$2SH/10S_2H_2$	12
Short-course	
2SHRZ/6TH	8
2SHRZ/4HR or 2EHRZ/4HR	6
2HRZ/4HR	6
$2HRZ/4H_3R_3$	6
New smear-negative cases	
2STH/10TH	12
2SHRZ/6TH	8
Retreatment cases	
$2SHRZE/1HRZE/5H_3R_3E_3$	8
2SHRZE/1HRZE/5TH	8

S : streptomycin ; H : isoniazid ; R : rifampicin ; Z : pyrazinamide ; E : ethambutol ; T : thiacetazone. Subscripts refer to intermittent therapy where drugs are given a limited number of times each week.

Treatment

The six drugs recommended by WHO and the IUATLD and most commonly used in developing countries for tuberculosis are isoniazid, streptomycin, thiacetazone, ethambutol, rifampicin and pyrazinamide. These drugs are used in a host of combinations for different durations. See Table 9. However, despite the availability of powerful and potentially effective antituberculosis drugs, tuberculosis treatment programmes in most developing countries have not been very successful. Overall cure rates for most national programmes in poor developing countries are below 50 %. Evidently, the "standard" 12-month chemotherapy (isoniazid, streptomycin and thiacetazone) recommended by the WHO Expert Committee on Tuberculosis (1974) for use in developing countries is presently, and probably will be in the future, beyond the organizational resources of many of them.

While there are many interesting issues in tuberculosis treatment, this discussion will stress the choice between standard 12-month chemotherapy regimens that use fewer and cheaper drugs (isoniazid, streptomycin and thiacetazone), and short-course chemotherapy that lasts from 6 to 8 months and uses multiple and more expensive drugs (rifampicin and pyrazinamide). To compare these two approaches to chemotherapy, we must examine the relative effectiveness of each and the relative costs of each. Because of the great diversity in effectiveness and costs between countries, the emphasis will be on the key determinants of the effectiveness and costs of the two regimens. It should be stressed that the regimen with a higher cure rate leads to a more rapid reduction in the risk of tuberculosis infection and the incidence of active tuberculosis.

Effectiveness of chemotherapy

The effectiveness of standard and short-course chemotherapy depends on three major factors : (i) the cure rate ; (ii) acquired drug resistance ; and (iii) the impact on the trend of the risk of tuberculous infection. Without question, the most important of these factors today in nearly all contexts is the cure rate which decisively influences the remaining two factors.

The first determinant of the cure rate is the biological effectiveness of standard 12-month and short-course chemotherapy given under ideal conditions of 100 % compliance. With short-course chemotherapy after 2 months of treatment 85-95 % of smear-positive pulmonary cases will have converted to sputum negative status. Under standard 12-month therapy after 2 months 50 % will remain smear-positive. The "permanent" cure rate is a more important aspect of the treatment regimens. The schematic (Figure VIII) shows the

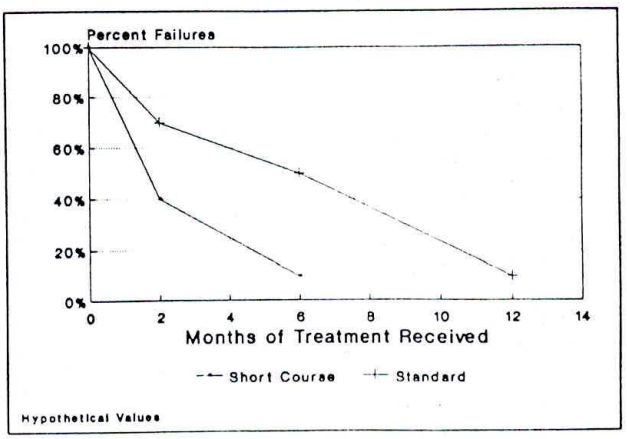

Figure VIII. The percent of patients failing therapy after 2 years of follow-up as a function of the number of months of chemotherapy completed hypothetical values.

percent of patients who will remain or become smear-positive, say, 2 years after the start of the (first) treatment (with no retreatment during the first 2 years) provided that chemotherapy is discontinued at each point in time. We shall refer to them as "failures". (If a patient remained or became smear-positive and died during the first 2 years, he/she will also be referred to as a "failure") (the upper part of Figure VIII above the interrupted lines). Under short-course chemotherapy (*e.g.* 2SHRZ/6TH), about 40 % may be "failures" at 2 months if they discontinue chemotherapy at that time compared with approximately 8-10 % if they complete 6 months of short-course chemotherapy. Under standard 12-month chemotherapy (*e.g.* 2STH/10TH), the "failure" rate in patients who discontinue after 2 months may reach 65-70 %, and in those who complete 6 months it might be approximately 50 %. The "failure" rate only begins to drop significantly on standard 12-month chemotherapy after 6 months. If treatment is stopped at 12 months, under ideal conditions of 100 % compliance approximately 10-15 % including deaths will become failures at two years.

Since standard 12-month and short-course chemotherapy both give high cure rates and do not lead to secondary resistance in controlled clinical trials compliance is the most important determinant of the cure rate in national tuberculosis programmes. There is a vast and detailed literature on compliance in general and on tuberculosis in particular (Haynes *et al.*, 1979 ; Fox, 1983, 1985 ; Chaulet, 1987 ; WHO Tuberculosis Chemotherapy Centre, 1963 ; Reichmann, 1987). Many of the factors that one might expect would influence patients compliance with antituberculosis drugs regimens, such as the severity of side effects, have not been empirically observed. There is a clear consensus, however, that the duration of treatment adversely affects compliance (Haynes, 1979). Moodie (1967) in unusual circumstances in Hong Kong found that most non-compliers dropped out in the first three weeks ; but all other studies have observed a steady drop out over time (EAMRC 1977, 1979). Improved net compliance due to a shorter regimen is a major advantage of short-course chemotherapy over standard chemotherapy. Given the relapse rate as a function of months of treatment discussed above, in a situation where patients continue to drop out over time, short-course chemotherapy will have a higher total cure rate.

The second major determinant of tuberculosis chemotherapy compliance is the degree of supervision of treatment. A spectrum exists from giving supplies of drugs for multiple months to patients all the way to hospitalization for the entire duration of treatment. Between these extremes, a wide variety of supervision strategies are possible, including daily visits to health centres, health visitors contacting patients in the home, periodic urine tests to monitor compliance and hospitalizations for the first 2 months of treatment. While increased supervision increases compliance in most settings (Haynes, 1979) ; increased supervision also means increased cost. The balance of this trade-off will depend on the specific institutional and cultural characteristics of each community. For example, in Madras, in areas where most of the population has ready access to health centres, entirely ambulatory care has been successful (Tuberculosis Chemotherapy Centre, Madras 1959, Dawson *et al.*, 1966). On the other hand, in many parts of rural sub-Saharan Africa, the only way to guarantee daily supervision of chemotherapy may be to hospitalize patients for the first 2 months of chemotherapy ; this has been the experience in 7 African countries (Tanzania, Kenya, Mozambique, Malawi, Benin, Senegal and Mali) (Styblo and Chum, 1987).

The rationale for hospitalizing patients to ensure close supervision of the initial intensive phase is much greater in short-course chemotherapy than in standard 12-month chemotherapy because 2 months of short-course chemotherapy will convert smear-positive sputum into smear-negative in about 90 % of patients and in the remaining 10 % in a further 2-4 weeks. Even if they stop taking drugs one or 2 months after they leave hospital many will not relapse. In Tanzania, approximately 50 % of smear-positive patients enrolled on standard 12-month chemotherapy remain smear and culture-positive at 2 months. For standard 12-month chemotherapy, it is crucial to continue to take regularly daily isoniazid and thiacetazone combined tablets for at least another 2-3 months to achieve 90 % sputum conversion.

In all probability, the patient's perception of the effectiveness of treatment and the balance between discounted future costs and benefits of treatment are also important determinants of compliance. In Tanzania and other IUATLD-assisted National Tuberculosis Programmes, it has been observed that both the perceived effectiveness of treatment and individual and group education of patients during the initial intensive phase of short-course chemotherapy positively affected compliance during the continuation phase.

Other possible determinants of compliance include the number of medications taken at each time, the number of doses per week and the costs to the patients of therapy. Combination tablets of isoniazid and thiacetazone and isoniazid and rifampicin have been in use in National Tuberculosis Programmes of many developing countries for several years. On the other hand, intermittent standard chemotherapy (streptomycin and isoniazid) has never been used on a large scale in developing countries. In India, it has been shown that intermittancy leads to increased irregularity (Pamra and Mathur, 1973). Also Blackwell (1979) could not validate the expected relationship between reduced number of doses and improved compliance. The advantages and disadvantages of intermittent standard chemotherapy will not be addressed further here. The common sense notion that increasing costs both in terms of time and money will decrease compliance has been confirmed in most studies (Haynes, 1979). To maximize compliance, tuberculosis chemotherapy should be free and the spatial and temporal ease of access to treatment should be improved. When alternative treatments are available in the private and public sector, patients may initially prefer to pay for therapy perceived as better, but when funds run out they may switch to the public sector (Uplekar, personal communication). This mixing of different drug regimens will tend to increase the failure rate and the probability of secondary resistance.

The second factor determining the effectiveness is the development of resistance. Under ideal conditions, such as in many clinical trials in patients with sensitive bacilli, the cure rates for both standard and short-course chemotherapy are over 95 %. In patients infected with tubercle bacilli that are isoniazid resistant, the cure rate with total compliance is greatly reduced (Shimao, 1987). Isoniazid resistance is already a major problem in many developing countries (Kleeberg *et al.*, 1980). A systematic application of short-course che-

motherapy referred to above (2SHRZ/6TH) in new smear-positive cases makes it virtually impossible to select for a bacillus resistant to all four drugs, provided that the 2-month initial intensive phase is closely supervised. Decreased development of resistance means that short-course chemotherapy is a substantially more effective long-term strategy for tuberculosis control than standard 12-month chemotherapy. It has to be stressed that acquired (and in contacts of the index cases, primary) resistance to both isoniazid and rifampicin results in incurability of the majority of such cases in developing countries with serious consequences for elimination of tuberculosis.

Costs of chemotherapy

The costs of any tuberculosis control programme comprise many components including drugs, staff costs, transport, training and the cost of hospitalization. While drugs form a considerable portion of the budget, probably from 20 % to 40 %, they are not the only cost. Cost differences between short-course and standard 12-month chemotherapy, however, center on drug costs and hospitalization costs. Table 10 shows prices for the five major drugs from three sources : the UNICEF (UNIPAC), and bulk purchase rates given to the IUATLD by major drug companies. Using different suppliers will substantially alter the relative costs of standard and short-course chemotherapy. Resolution of this question may pave the way for cheaper tuberculosis drug regimens -both standard and short-course. In general, the short-course regimen used in IUATLD National Tuberculosis Programme is approximately $ 25 more per patient than standard depending on the supplier.

Table 10. Costs of antituberculosis drugs

Drug	Unit	Unit cost IUATLD	Unit cost UNIPAC
Isoniazid			
Isoniazid	100 mg x 1000	$2.95	$2.70
Isoniazid	300 mg x 1000		$3.80
Isoniazid/ thiacetazone	300 mg/150 mg x 1000	$10.50	$9.11
Isoniazid/ thiacetazone	100 mg/50 mg x 1000	$4.80	$4.93
Streptomycin			
Streptomycin	1 gm vial	$0.07	
	1 gm vial	$0.09	
	1 gm x 50		$3.55
Pyrazinamide			
Pyrazinamide (CIF)	500 mg x 1000	$31.58	
Pyrazinamide	500 mg x 100		$8.34
Ethambutol			
Ethambutol	400 mg x 1000	$17.00	
Ethambutol	400 mg x 500		$17.13
Rifampicin			
Rifampicin	150 mg x 1000		$40.90
Rifampicin	300 mg x 1000		$58.00
Rifampicin/ isoniazid	150 mg/100 mg x 1000	$79.50	
Rifampicin/ isoniazid	300 mg/150 mg x 1000	$159.00	

The second potential source of cost differentials between short-course and standard 12-month chemotherapy is the level and intensity of supervision. Both standard 12-month and short-course chemotherapy should be given whenever possible on an entirely ambulatory basis. However, in rural areas, where 80-85 % of the African population live and where patients do not have easy access to a health centre, daily regimens may only be delivered in district hospitals. Not only will this improve compliance, but expensive and valuable drugs can be better accounted for in these conditions. For these reasons, short-course chemotherapy may justify higher hospitalization rates and more expense in some countries.

This discussion has thus far been implicitly restricted to the treatment of smear-positive tuberculosis. Once other forms of tuberculosis have been identified, treatment costs for other tuberculosis should be similar to standard 12-month chemotherapy except for serious forms of smear-negative tuberculosis, such as miliary tuberculosis, tuberculous meningitis, Pott's disease, etc., who should be enrolled on short-course chemotherapy (in cases with tuberculous meningitis, rimactazid should also be given in the continuation phase). For treatment of cases that failed to sputum or culture convert in the first round of treatment, the drug costs are particularly high because these patients harbour tubercle bacilli frequently resistant, in developing countries, to isoniazid and/or streptomycin. Many of them have to be treated with short-course chemotherapy for retreatment cases which should ideally contain 3 drugs to which the bacilli are sensitive. A retreatment regimen includes, as a rule, rifampicin and pyrazinamide. In the IUATLD-assisted National Tuberculosis Programmes the following regimen is used : 2SHRZE/1HRZE/5$H_3R_3E_3$ in patients resistant to isoniazid or 2SHRZE/1HRZE/5TH in patients sensitive to isoniazid. In programmes that are committed to treating all patients that present for care, retreatment must also be considered in examining short-course and standard 12-month chemotherapy. As failure rates are higher for standard 12-month chemotherapy, more resources would have to be devoted to retreatment of these patients.

Cost-effectiveness

The cost-effectiveness of tuberculosis treatment will vary depending on the type of tuberculosis case that is treated. In general, the cost per death averted directly and indirectly will be lowest for smear-positive tuberculosis, higher for other tuberculosis and highest for retreatment cases. While this statement may run counter to intuitive notions of the clinical costs of treating each type of tuberculosis, the rationale is based on the effect of interrupting transmission as explained more fully below. Treating smear-positive tuberculosis may be as much as twice as cost-effective as treating other tuberculosis because of the benefits of reduced transmission in the former. Whether a country with limited resources would choose to target treatment in adult patients to exclusively smear-positive tuberculosis is a difficult ethical, medical and economic choice. The calculations presented here pertain largely to treatment of smear-positive tuberculosis because little information is available on the results of treating other tuberculosis ; this emphasis should not be interpreted as a recommendation to treat only smear-positive tuberculosis.

Few studies have examined the cost-effectiveness of tuberculosis treatment in developing countries (Barnum, 1986 ; Joesoef *et al.*, 1989 ; Feldstein *et al.*, 1973). Two of these investigations reported that per case cured short-course chemotherapy was more cost-effective. They did not, however, report figures on the cost per death averted. To fill the gap in information on the cost-effectiveness of short-course and standard 12-month chemotherapy, we have analyzed the tuberculosis control activities over the last seven years of the National Tuberculosis and Leprosy Programme (NTLP) of Tanzania.

Our assumption and calculations are summarized in Tables 11 and 12. The NTLP has been assisted by the IUATLD since 1979. Excellent data are available on the results of both standard 12-month and short-course chemotherapy (Styblo and Chum, 1987, Chum *et al.*, 1988). Comparing the results of standard and short-course chemotherapy with the natural history of tuberculosis as documented in South India (National Tuberculosis Institute, 1974), we can estimate (Table 13) the net improvement in cure rates and death rates. For

Table 11. Assumptions used in estimating the effectiveness of standard 12-month and short-course chemotherapy in the National Tuberculosis and Leprosy Programme of Tanzania

Fate of 100 cases smear-positive tuberculosis with no treatment based on 5 year epidemiological study in South India (1974)

Year	Number of cases			Cured per year	Died per year
	Cured	Excreting bacilli	Dead		
0	0.0	100.0	0.0	0.0	0.0
1	18.5	61.3	20.1	18.5	20.1
1.5	27.8	42.0	30.2		
2	27.8	38.6	33.6	9.3	13.6
3	27.8	31.7	40.5	0.0	6.9
4	30.3	24.9	44.9	2.5	4.4
5	32.5	18.0	49.2	2.2	4.4

Fate of 100 cases smear-positive tuberculosis receiving standard 12-month chemotherapy based on treatment results in Tanzania*

Year	Number of cases			Cured per year	Died per year
	Cured	Excreting bacilli	Dead		
0	0.0	100.0	0.0	0.0	0.0
1	61.1	23.2	15.8	61.1	15.8
1.5	61.1	23.2	15.8		
2	61.1	21.3	17.7	0.0	1.9
3	61.1	17.5	21.4	0.0	3.8
4	62.4	13.7	23.8	1.4	2.4
5	63.7	9.9	26.2	1.2	2.4

Fate of 100 cases smear-positive tuberculosis receiving short-course chemotherapy based on treatment results in Tanzania*

Year	Number of cases			Cured per year	Died per year
	Cured	Excreting bacilli	Dead		
0	0.0	100.0	0.0	0.0	0.0
1	79.6	11.6	8.8	79.6	8.8
1.5	81.3	7.9	10.7	1.8	1.9
2	81.3	7.3	11.4	0.0	0.6
3	81.3	6.0	12.7	0.0	1.3
4	81.8	4.7	13.5	0.5	0.8
5	82.2	3.4	14.3	0.4	0.8

* Styblo and Chum (1987) ; Chum *et al.* (1989).

Table 12. Budgeted costs for tuberculosis chemotherapy, Tanzania, 1986

Cost category	STD	Short	Retreatment
Diagnosis			
Slides/reagents	$2.10	$2.10	
Sputum container	$1.95	$1.95	
Bacteriological			
Monitoring	$0.81	$0.81	
Culture	$1.50	$1.50	$1.50
Sensitivity			$3.90
Drugs	$17.00	$40.00	$65.00
Administration	$2.85	$2.85	$2.85
Labor costs and hospitalization	$67.65	$90.20	$169.12
Transport	$20.35	$20.35	$20.35
Training	$2.37	$2.37	$2.37
Supervision	$2.90	$2.90	$2.90
Capital 20 % depreciation	$3.22	$3.22	$3.22
Total cost per case	$122.70	$168.25	$271.21

Notes : 1) Labour costs and hospitalization include the salaries and wages of all staff working on tuberculosis control and the cost of hospitalizing all tuberculosis patients. As more disaggregated information was not available, the costs in this category have been distributed according to the hospitalization rate for each type of treatment (60 % standard, 80 % short-course, 100 % retreatment). This underestimates the cost per case treated for standard chemotherapy and overestimates the cost per case treated for short-course and retreatment because all staff costs are included in this category.

2) Drug costs are based on 1986 prices and 1986 exchange rates. Since that date the price has declined but the value of the US dollar has also declined.

3) Transport costs include 25 % of the entire purchase cost of all vehicles and operating expenses. The assumption that vehicles will last only 4 years on average may be overly conservative.

Table 13. Cost-effectiveness of standard 12-month and short-course chemotherapy for smear positive pulmonary tuberculosis in Tanzania, 1986

	Standard chemotherapy	Short-course chemotherapy
Cost per case treated	$123	$168
Cost per case cured at 18 months	$368	$314
Cost per death averted	$569	$514
Cost per death averted including one round of transmission	$275	$243

Note : Based on a 3 % discount rate.

standard 12-month chemotherapy and short-course, the cost per patient treated in 1986 US dollar was $ 122 and $ 168 respectively. In a programme where all patients that continue to excrete bacilli receive retreatment, this would raise the cost per case treated under standard 12-month chemotherapy to $ 186 and $ 190 for short-course chemotherapy.

Per case cured at the end of 18 months in excess of spontaneous cure, it was $ 368 for standard 12-month chemotherapy and $ 314 for short-course. Short-course chemotherapy is more cost-effective per patient cured. The difference would be greater except that in Tanzania approximately 80 % of short-course patients are hospitalized for the first 2 months and only 60 % of standard chemotherapy are hospitalized.

For standard 12-month chemotherapy, the cost per death averted was $ 569 and $ 514 for short-course, based on a three percent discount rate. These estimates are serious overestimates for two reasons. First, the benefits of treating patients relative to no treatment have only been examined for five years after treatment. In the South Indian epidemiological study tuberculosis patients were only followed for five years (National Tuberculosis Institute, Bangalore, 1974). Thus the improvement in the death rate due to standard 12-month or short-course chemotherapy has been underestimated by only examining the effect for five years. Second, treatment also reduced the number of new infections of tuberculosis. Using the lowest estimates of the number of cases that each case of smear-positive tuberculosis causes in one year derived in the section above, we can calculate the number of deaths averted by reduced transmission in one cycle. The resulting estimates show standard 12-month chemotherapy to cost $ 274 per death averted and for short-course chemotherapy only $ 242 per death averted.

These estimates of the cost per death averted through tuberculosis chemotherapy are specific to Tanzania but probably represent the higher end of the range for most other developing countries for four reasons. First, the hospitalization rate in Tanzania for short-course chemotherapy is especially high. Any country with a more developed peripheral health system could deliver short-course chemotherapy with a lower hospitalization rate. This observation must be tempered by the fact that the cost per bed-day in many developing countries is considerably higher than the $ 1.50 reported by the Tanzania Government. In a country where the cost per bed-day is $ 5, the cost of hospitalizating patients for 2 months would be increased by $ 210. Second, the benefits of chemotherapy over no treatment have only been considered for the first five years following treatment. Consideration of years 6, 7 and 8 if such data were available would reduce the cost per death averted. Third, the assumption on transmission were the lowest reasonable assumptions, not the midpoint of the expected range of cases transmitted per excretor. Fourth, the rate of capital depreciation was assumed to be extremely high 20-25 % per year. In other developing countries, the true cost per death averted may be considerably lower than $ 265 ; although in some countries where staff costs and hospitalization is more expensive, they may be higher.

Taken together the **studies on the cost-effectiveness of both standard 12-month and short-course chemotherapy show that tuberculosis chemotherapy is an excellent investment relative to virtually any health intervention.** Most interventions including immunizations and oral rehydration therapy yield estimates per death averted in the same range (Haaga, 1982). Second, the analysis clearly indicates that short-course chemotherapy is preferable to standard 12-month chemotherapy. The most significant advantages of short-course chemotherapy over standard 12-month chemotherapy are summarized in Table 14. Not only is it more cost-effective per death averted, as calculated above, but it provides other advantages not included in the estimates. The cure rate taking into consideration the natural history of tuberculosis for standard 12-month chemotherapy under excellent conditions is 63.7 % while under short-course it is 82.2 %. The percentage of cases requiring expensive retreatment is nearly three times greater with standard 12-month chemotherapy as compared to short-course chemotherapy. Finally the death rate with standard 12-month chemotherapy is nearly twice as high as with short-course chemotherapy. Short-course chemotherapy, because of a higher cure rate, will also accelerate the decline in the risk of infection by reducing transmission. Short-course chemotherapy will also limit the development of resistance to isoniazid and rifampicin in the long term. In summary, short-course chemotherapy for tuberculosis is an excellent cost-effective health intervention.

Table 14. Comparison of standard 12-month chemotherapy and short-course chemotherapy for smear-positive cases of tuberculosis based on data from the NTLP of Tanzania

	Standard chemotherapy	Short-course chemotherapy
Cost per death averted including one round of transmission	$275	$243
Percent of patients cured	*63.7*	*82.2*
Percent of cases requiring retreatment	*23.2*	*7.9*
Death rate after 5 years assuming no retreatment (%)	*26.2*	*14.3*

All these computations of cost-effectiveness have been based on the assumption that all patients treated for smear-positive tuberculosis do indeed have smear-positive tuberculosis. As the cost per case treated is high, false positives are a particularly onerous burden on the health system. In Tanzania, where a reference laboratory is available to monitor diagnoses made in the periphery, the false positive rate is low. The most important parameter from a cost point of view is the predictive value positive or the percent of cases diagnosed with tuberculosis who actually have the disease. In Tanzania, this is greater than 97 %. The cost per death averted must be divided by the predictive value positive to get the true cost-effectiveness in a particular situation. In countries with poorly trained microscopists or frequent atypical mycobacteria infections, the predictive value positive could be much lower than 95 %. The potential of wasting scarce resources on patients without tuberculosis puts a high premium on training health workers and microscopists to diagnose tuberculosis correctly.

BCG and case treatment

One would like to compare the two major interventions for

tuberculosis control : BCG and case treatment. They are, however, not truly comparable because even complete BCG coverage at birth will only affect 10 % of mortality. Case treatment is absolutely necessary to reduce the other 90 % of mortality. How does the cost-effectiveness of expanding BCG coverage compare to expanding case treatment activities ? The cost per death averted can be compared directly using the studies mentioned in the text above. Some may object that a death between the ages of 0 and 14 represents a greater loss of years of life than a death at age 35. However, if we choose to examine discounted years of life lost it will not significantly alter the comparison. A death at age 7, the midpoint for deaths averted by BCG, represents at a 3 % discount rate 29.7 years of life lost ; while a death at age 34 the average age of a tuberculosis death represents 23.4 years at a similar discount rate. Therefore, we can examine the cost-effectiveness of the two interventions using the cost per death averted bearing in mind that discounted years of life lost would change the relationship by less than 20 percent.

The cost per death averted through tuberculosis chemotherapy should change little as the risk of infection in a community declines. *Ceterus paribus*, the only change would be the slight increase in the cost of detection as more cases or cough would have to be screened per case of tuberculosis detected. This does not hold true for any immunization including BCG. The costs of vaccinating all infants will not change as the risk of infection declines, but the benefits in terms of deaths averted will decline proportionately to the risk of infection. In other words, the cost per death averted through BCG must be inversely proportional to the risk of infection. Figure VII shows two hypothetical curves for the cost per death averted as a function of the risk of infection. The curves are fitted to the single data point on BCG for Indonesia and the single point on case treatment for Tanzania. While the data are clearly weak, the principle is clear. At low annual risks of infection case treatment is substantially more cost-effective than expanding BCG coverage. At higher risks of infection, the costs of both interventions are of the same order of magnitude. This curve should not be interpreted to mean that countries with low risks of infection should curtail BCG vaccination activities. The discussion so far provides no insight into the savings from cutting back an existing activity versus the potential reduction in benefits. This discussion does not imply that the policy choice in tuberculosis control is between BCG and case-treatment. Some combination of the two is likely to be desirable in many countries. It does, however, indicate that BCG becomes relatively less attractive as the risk of infection declines.

Research priorities

This discussion of tuberculosis leads naturally to some general recommendations for tuberculosis research. These can be divided into six areas :

– **Epidemiology.** The wide confidence intervals in the estimates of incidence, prevalence and mortality highlight the need for epidemiological research. Many countries require basic information on incidence and mortality rates and their distribution by age and socio-economic status, in order to establish the importance of tuberculosis as a health sector priority. For those countries without vital registration, new survey techniques based on the verbal autopsy may provide the tools with which tuberculosis mortality can be quantified.

– **Prevention.** Because of the uncertain and variable effectiveness of BCG, a new effective vaccine would be a major tool, especially if it would also prevent tuberculosis in already infected individuals. Fine (1989), however, has pointed out that it will be difficult to test appropriately the effectiveness of any new vaccines for moral and technical reasons. Research is also needed to explore the most appropriate role for chemoprophylaxis in developing countries, especially in subjects infected with tubercle bacilli and HIV.

– **Diagnosis.** Development of new tools for the rapid and early diagnosis of tuberculosis would substantially improve case detection. Research into serological or sputum diagnosis that can be deployed at reasonable cost in peripheral health facilities in developing countries should be a priority.

– **Chemotherapy.** Development of new shorter acting, cheap drugs would help address two major issues in tuberculosis control : compliance and cost. While opportunities exist for developing new drugs (Sensi, 1989), relatively little research is underway. Another possibility that seems worth exploring is the use of depot preparations which would solve many of the compliance problems.

– **Programme design.** There is an urgent need for operational and health economics research on strategies for tuberculosis control.

Some key issues have been highlighted in this piece : what is the trade-off between the cost of supervision and the improvement in compliance, taking existing infrastructure into consideration ? What is the cost-effectiveness of alternative diagnosis strategies ? These and many other issues need to be addressed in an organised fashion.

– **HIV and tuberculosis interactions.** The interaction between HIV and tuberculosis has not been fully addressed in this piece. It is evident that immune suppressed patients with HIV and tuberculous infections have a high probability of developing clinical tuberculosis. In Central East Africa, tuberculosis programmes are already reporting a considerable increase in the number of cases of tuberculosis. The impact of any HIV-tuberculosis interaction in developing countries with a high prevalence of tuberculous infection on the annual risk of infection for the rest of the population is not yet known. Epidemiological study of these relationship has just begun and should be considered a priority for research.

Major operational conclusions

This review of tuberculosis can be summarized in five major points :

– The magnitude of the tuberculosis problem is simply staggering. Our estimates suggest that more than 2.5 million people die from tuberculosis each year. This is probably more than any other single pathogen ; the only disease that come close in terms of total deaths is measles, estimated to kill 2.5 million per year (Walsh, 1988). The burden of tuberculosis extents beyond mortality ; the annual incidence of new cases of all forms of tuberculosis is over 7.1 million cases in the developing world. Tuberculosis is unique amongst the major killers of the developing world in that it afflicts nearly all age-groups. Many children die from tuberculous meningitis and miliary tuberculosis. But the greatest burden of tuberculosis incidence and mortality is concentrated in adults 15 to 59. These are the parents, workers and leaders of society. This heavy toll of the care givers for the rest of

society makes tuberculosis a truly unique problem.

– In at least the last decade, tuberculosis has been ignored by much of the international health community. Shimao (1989) has outlined the decline of the human and institutional capacity to address the tuberculosis problem over the last decades which is but one symptom of a general lack of priority attached to tuberculosis action and research. Another example is the Institute of Medicine (1986) study of vaccine development priorities for the developing world. They classified diseases into three levels of priority for research on vaccines. While leprosy received significant attention tuberculosis was not even mentioned in the lowest priority group. Clearly, focussing international attention on tuberculosis is necessary first step if more resources are to be directed to combating tuberculosis.

– Existing diagnostic technology and chemotherapeutic agents can be used effectively in developing countries to cure tuberculosis. The IUATLD-assisted National Tuberculosis Programmes (e.g. Tanzania, Malawi) have shown that short-course chemotherapy can be applied on a national scale with excellent results. Cure rates approaching 90 % even taking into consideration compliance can be achieved in even the most difficult circumstances.

– Tuberculosis chemotherapy and BCG vaccination (in countries with high risks of infection) are some of the most cost-effective health interventions available in the health armamentarium. Our analysis of the National Tuberculosis and Leprosy Programme in Tanzania has shown that treating smear-positive tuberculosis costs less than $ 250 per death averted. The cost per discounted year of life saved is therefore substantially less than $ 10. There are few interventions that are as cost-effective as tuberculosis case-treatment. Given our estimates that slightly more than half of all new cases of tuberculosis receive some form of treatment that in most cases is not highly effective, we estimate that the total increased cost of treating all new cases of tuberculosis through a well managed chemotherapy programme to be less than 700 million US dollars per year.

– Evidence has accumulated that the HIV/tuberculosis interaction may significntly exacerbate the epidemiological situation of tuberculosis. The potential rise, due to this interaction, in the risk of infection in Africa and other regions depending on the spread of HIV makes all our operational conclusions about tuberculosis all the more pressing.

The combination of an enormous burden, years of neglect, the existence of effective interventions, the demonstrated interaction between tuberculous and HIV infections and one of the most cost-effective interventions available must make tuberculosis one of the highest priorities of action and research in international health.

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The relationship between the risk of tuberculous infection and the risk of developing infectious tuberculosis

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Introduction

The aim of this report is to study whether a uniform empirical relationship can be established between the annual risk of tuberculous infection in a community and the incidence of infectious (smear-positive) tuberculosis and, if so, to estimate this parameter*. Such information would be especially important for developing countries because it would enable them to estimate the incidence of smear-positive cases of pulmonary tuberculosis from the annual risk of tuberculous infection, without any further investigation.

Methodology

The relationship between the annual risk of tuberculous infection can be studied in communities where reliable information on both these variables is available.

We now have information on the annual risk of tuberculous infection in a number of developed and developing countries. Unfortunately, the incidence of smear-positive tuberculosis has only been reported in a few developed countries, mostly after World War II. Information on tuberculosis incidence in developing countries is very deficient and cannot be used for the purpose of this study, since it reflects the detection rather than the incidence rate.

However, there is reasonable evidence of the relationship between the incidence of tuberculosis and death from tuberculosis in the pre-chemotherapy era in developed countries. It has been shown that about half of the reported cases of tuberculosis resulted in death from the disease before the introduction of chemotherapy to tuberculosis treatment ; in other words, incidence was twice the mortality (1, 2, 3). It is also assumed that the prevalence of smear-positive tuberculosis is twice the incidence, or that the incidence is half the prevalence (4).

* A "parameter" is defined as a "constant" indicating the numerical value which links two variables together. In this case, we are aiming at establishing the relationship between the annual risk of tuberculous infection and the incidence of smear-positive tuberculosis in the general population.

Summary Table. Relationship between the risk of tuberculous infection and the incidence of smear-positive tuberculosis

	Ratio based on	Risk of infection (%)	Ratio between the risk of infection (%) and		
			mortality (rate)[1]	incidence (rate)[1]	prevalence (rate)[1]
Netherlands 1921-1938	mortality	*2.7 - 6.0*	19	38	
Netherlands 1951-1976	incidence	*0.038 - 0.4*		37	
Developing countries 1956-1951	prevalence	*2.0 - 8.0*		40-60	80-120[2]
Alaska Eskimos 1948-1951	mortality	*25*	26	52	
India long. study 1961-1968	prevalence	*1.5*		53	106
India prevention trial 1969-1971	prevalence	*4.1*		51	102

[1] Per 100,000.
[2] In Nigeria 53 ; in Somaliland 124 ; in Libya 283 ; in Zanzibar 283.

►Thus we shall adhere to the relationship :

Incidence** = mortality x 2

Incidence = prevalence** /2

** of smear-positive pulmonary tuberculosis.

While the relationship between incidence of and mortality from tuberculosis is well established, the evidence on the relationship between incidence and prevalence seems more doubtful, although fairly reasonable.

Material

As already mentioned, we are aiming at establishing the relationship between the annual risk of tuberculous infection and the incidence of smear-positive tuberculosis in the general population. For some countries we have data on mortality from tuberculosis, while for others information is available on prevalence or incidence of smear-positive pulmonary tuberculosis. The relationship between the two variables was studied on the basis of data from the following countries :

– ***Netherlands***

1) the annual risks of infection with tubercle bacilli for the periods 1910 to 1966 and 1967 to 1979 were published by TSRU, (5) and (6) respectively ;

2) the death rates from tuberculosis from 1921 to 1938 and the incidence of smear-positive pulmonary tuberculosis from 1951 to 1968 were used for the present study.

– ***WHO tuberculosis prevalence surveys in various developing countries carried out in the 1950s and 1960s***

1) the annual risk of infection was derived from data on tuberculin testing carried out by specialized WHO teams ;

2) there were estimates of the prevalence of smear-positive tuberculosis from the original WHO surveys.

– ***Alaska (Eskimos)***

1) the risk of tuberculous infection for Eskimo children was estimated as 25 % during the years 1948-1951 (7) ;

2) the mortality rate from tuberculosis among Eskimos in Alaska as reported in 1950 was used for this study (7).

– ***India***

Two studies are considered in this report : ***a)*** Tuberculosis in a rural population of South India : a five-year epidemiological study carried out in the 1960s (8) (hereafter referred to as "the longitudinal study") and ***b)*** Trial of BCG vaccines in South India for Tuberculosis Prevention carried out in the 1970s (9) (hereafter referred to as "tuberculosis prevention trial").

1) the risks of infection in the above two trials have been derived from the results of tuberculin testing among children and young adults ;

2) the prevalence of smear-positive pulmo-

nary tuberculosis cases in the longitudinal study and the prevalence of smear-positive cases in the prevention trial were used for this study.

Results

The relationship between the risk of infection and the incidence or prevalence of smear-positive pulmonary tuberculosis or mortality from tuberculosis concerning the data referred to in the previous section cannot be discussed in detail in this paper. A full report will be published in the Bulletin of the World Health Organization in 1986. A summary table shows the relationship between the risk of tuberculous infection and *the incidence* of smear-positive tuberculosis (the last but one column).

The summary table shows two areas (the Netherlands and Alaska with an Eskimo population) with tuberculosis mortality ; we have doubled the ratio to arrive at the relationship between the risk of infection and the incidence of smear-positive tuberculosis.

Table 1 shows the relationship between tuberculosis mortality and the risk of infection in the Netherlands from 1921 to 1938. The table shows that the average death rate from tuberculosis was 115 per 100,000 for 1921-1923, gradually decreasing to 48 per 100,000 for 1936-1938. The annual risk of tuberculous infection was about 6 % in 1922, decreasing to 2.7 % in 1937. The ratio of death to risk of infection was 19 for the whole period of 18 years, ranging from 18 to 20, although the mortality from tuberculosis and the risk of infection decreased more than twice during the period under study.

By multiplying the mortality ratio by 2, we obtain the ratio of incidence to infection. For the Netherlands, this incidence/infection ratio is 38 smear-positive cases per 100,000 population for each 1 % risk of infection (see the summary table).

The second set of information on the relationship between death from tuberculosis and risk of infection is on Eskimos in Alaska from 1948 to 1951. The risk of infection in Eskimos in the late 1940s and early 1950s was extremely high ; Comstock and Philip (7) estimated it to be in the order of 25 % (three quarters of Eskimo children were found to be "positive" at the age of 3-4 years).

The tuberculosis death rates were also extremely high with a figure of 650 per 100,000 general population. The ratio of incidence of smear-positive tuberculosis to risk is 2 x 26, *i.e.* 52 new smear-positive cases per 100,000 population for each 1 % risk of infection.

Table 2 shows that the ratio between the incidence of smear-positive tuberculosis and the risk of infection in the Netherlands in the 1950s and 1960s was 36 smear-positive cases per 100,000 for each 1 % risk of infection. It is seen that the rates of the risk of infection and the incidence rates were very low.

The relationship between the risk of infection and prevalence of smear-positive cases has also been studied, based on data taken from WHO tuberculosis surveys which sought to determine both the infection and disease prevalences in a number of African and Asian countries in the late 1950s and early 1960s. The material collected by the WHO teams is unique because the population studied was selected at random, the methods used (for tuberculin testing, bacteriological examination of sputa for tubercle bacilli by direct microscopy and X-ray examination of the chest) were standardized, and examination methods were entirely independent of one another.

The data presented in the summary table refer to 13 African countries. In 10 of them the risk of infection was between 2 % and 4 %. In Nigeria, the rate was higher than 4 %, in Bechuanaland higher than 5 % and in Somaliland it was about 8 %. The prevalence of smear-positive pulmonary tuberculosis (at all ages) was mostly between 200 and 300 per 100,000 of the general population ; however, in Swaziland, Bechuanaland and Somaliland, it was 500 or more per 100,000 general population.

The ratio of the prevalence of smear-positive cases to 1 % risk of infection in 10 of the 13 countries was between 80 and 120 per 100,000 population ; in one country, the ratio was smaller than 80 per 100,000 and in two countries it was

Table 1. Relationship between mortality from tuberculosis (all forms) and the annual risk of tuberculous infection, The Netherlands, 1921-1938

Year	Death rate from tuberculosis (per 100,000)[1]	Risk of tuberculous infection (%)	Ratio of death to risk[2]
1922	115.1	*6.02*	19
1925	100.3	*5.13*	20
1928	87.9	*4.37*	20
1931	70.5	*3.72*	19
1934	55.5	*3.16*	18
1937	47.7	*2.69*	18
1921-1938	–	–	19

[1] Average for 1921-1923, 1924-1926, etc.
[2] Expressed as mortality from tuberculosis per 100,000 general population for each 1 % risk of tuberculous infection.

Table 2. Relationship between the incidence of smear-positive tuberculosis and the annual risk of tuberculous infection, The Netherlands, 1951-1976

Year	Incidence rate of smear-positive tuberculosis (per 100,000)[1]	Risk of tuberculous infection (%)	Ratio of incidence to risk[2]
1952	13.9	*0.400*	35
1955	7.8	*0.265*	29
1958	5.7	*0.176*	32
1961	4.6	*0.116*	40
1964	3.2	*0.077*	42
1967	2.4	*0.051*	47
1973-1976	1.8	*0.038*	47
1951-1976	–	–	39

[1] Average for 1951-1953, 1954-1956, etc.
[2] Expressed as incidence of smear-positive cases per 100,000 general population for each 1 % risk of tuberculous infection.

higher than 120 per 100,000. By dividing the prevalence ratio by 2, we obtain the incidence ratio of 40 to 60 smear-positive cases of tuberculosis per 100,000 general population for 1 % risk of infection.

The data on the relationship between the prevalence of smear-positive cases and infection in two trials in India carried out in the 1960s show a ratio of 106 and 104 respectively, or an incidence of 53 and 52 smear-positive cases per 100,000 population respectively for each 1 % risk of infection. The risk of infection in the longitudinal study was about 1.5 % and in the prevention trial 4 %. The observed prevalence rates of smear-positive cases of pulmonary tuberculosis were about 160 per 100,000 in the former and 420 per 100,000 in the latter study.

* * *

The present material suggests a relatively constant ratio (lower for developed and higher for developing countries) between the risk of tuberculous infection and the incidence of smear-positive tuberculosis, irrespective of the level of the risk of tuberculous infection. We assume that in developing countries, 1 % risk of infection corresponds to an incidence of about 50 to 60 smear-positive cases of pulmonary tuberculosis. ■

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ANNUAL RISK OF TUBERCULOUS INFECTION

by

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I. INTRODUCTION

Risk of infection in a population is in many respects the most informative index of the magnitude of the tuberculosis problem (Sutherland, 1976; Pio, 1984). The risk of infection at a particular time indicates the current magnitude of the incidence and prevalence of infectious cases (Styblo, 1985) and also indicates the magnitude of the tuberculosis problem years into the future. An observed decline in the risk of infection would be the earliest indicator of a decline in the epidemic cycle of tuberculosis, resulting from tuberculosis control activities or improvements in living standards. A rising risk of infection would be an early indicator of changes in the other direction, signalling the introduction of new risk factors, such as the spread of human immunodeficiency virus (HIV) infection.

It is known that risk of infection has been declining for many years in developed countries, but remains at high levels in many developing countries (Styblo, 1984). In developing countries in the last decade, a number of surveys of infection prevalence have been carried out in national populations as well as in smaller populations.

Therefore a project was carried out to assess the current level and trend in the risk of infection in developing countries by reviewing and assembling tuberculin skin test survey data available since 1975.

II. METHODS

Tuberculin skin test data collected since 1975 for populations in developing countries were assembled from reports to the World Health Organization and from the published literature. Data from surveys of childhood age groups that were judged of sufficient quality were selected in order to provide as valid and up to date an assessment as practical of the magnitude of the risk of infection. Comparable prior data for the same countries were also selected in order to judge whether the risk of infection is likely to have declined.

Prevalence of infection observed in childhood age groups was used to derive the average annual risk of infection that would have resulted in the observed cumulative prevalence rate. Choosing younger age groups allows the calculated average annual risk to be bracketed within a relatively narrow period of time between the average birth date of the group and the date of the survey (Styblo et al, 1969).

Each survey was judged on the basis of available documentation for ability to represent the population and to detect the proportion infected at a particular time. A sample survey was judged to have measured the proportion infected in the target population if the probability sampling design and the estimation method appeared correct in concept and conduct, and skin testing technique appeared adequate to measure the proportion infected in the sampling units.

Basis for selection

Surveys were selected which met most of the following criteria:

Specified the sampling design including the sampling frame, staging, stratification, sampling units, allocation, sampling weights, and estimation formulas and documentation to support that the design was followed with adequate coverage.

Provided reaction-size distributions for surveyed age groups and for bacteriologically confirmed cases from the same population in order to assess the definition of infection and in order to judge technique.

Documented type and strength of antigen used, technique of administration and reading, and quality control procedures.

Specified the methods used to detect and eliminate persons with a history of BCG vaccination, and described BCG policy and actual coverage in the population age group surveyed.

Data assembled from selected surveys:

The area population represented and the survey period.

In the youngest age ranges for which sufficient numbers were tested and read, the number tested and read, the number counted as infected with M. tuberculosis, and the mean age.

Information documenting quality of the data.

Criterion of infection

Induration reaction size distributions observed in each survey were used together with general knowledge about the specific and nonspecific components of observable distributions to set a uniform criterion for counting infected persons in order to improve comparablility between surveys.

Because it can be assumed that nonspecific reactions to intermediate strength purified protein derivative tuberculins are only infrequently larger than the mode of the distribution of true reactions, an observed distribution of tuberculin reactions will be nearly free of contamination by nonspecific reactions above its mode.

Because of this, and because distributions among truly infected persons are symmetric, the number truly infected in a distribution contaminated by nonspecific reactions would be closely approximated by adding the number at the mode plus twice the number with reactions larger than the mode.

This method, described by Nyboe (1960) and by Comstock et al. (1971), was used to determine the number of infected persons in the selected groups when detailed reaction size distributions were available and when the mode of reactions among infected persons in the same general population could be estimated from distributions of either bacteriologically confirmed cases or older age groups in the population.

When such data were not available, a cutoff criterion was accepted as the second choice if it appeared reasonably adequate based on distribution data.

Prevalence

Prevalence at a particular calendar time for an age group was calculated as the number infected divided by the number tested and read. Reported prevalence figures were used when numerator or denominator counts were not specified.

Risk of infection

For comparability, a single uniform method was chosen to derive the approximate average annual risk of infection (Styblo et al, 1969, pg. 14). By this method, the annual risk of infection (R) for a group of average age (A) was derived from the prevalence (P) by

$$R = 1 - (1 - P)^{1/A}.$$

The slope per year (B) of the trend between two risk estimates R_i and R_j at years Y_i and Y_j was approximated by

$$B = 1 - (R_j/R_i)^{1/T} \quad \text{where } T = Y_j - Y_i.$$

Average age

Average age was calculated by taking the midpoint of a single year (e.g., 6.5 for age given as 6 at last birthday) or a range of years (e.g., 7.0 for ages given as 6 to 7, or 7.5 for ages given as 5 to 9). When available, the weighted average age was calculated from year-of-age specific frequencies for an age group.

Time at which average risk occurred

For purposes of calculating and plotting trends, the calendar time of occurrence of a particular average annual risk (Y_R) was considered to center approximately at the calendar time of the midpoint of the average lives of the individuals in the age-group. This was calculated by $Y_R = Y_S - A/2$, where A is the average age of the group and Y_S is the midpoint time of the survey. For example, a group of average age 6.1 years surveyed at 1978.9 was taken to contribute information about the annual risk of infection for a time interval centered at 1978.9 - 6.1/2 = 1975.85.

The midpoint time of the survey (Y_S) was calculated from the month, if stated, or the calendar year of the survey. For example, a survey stated to have taken place in 1975 was counted as occurring at 1975.5. A survey stated to have taken place from 1981 to 1982 was counted as occurring at 1982.0. A survey stated to have taken place from May 1952 to September 1953 was counted as occurring at 1953.04 (the midpoint between 4.5/12 + 1952 and 8.5/12 + 1953).

III. RESULTS

A variety of tuberculin skin-test surveys were found in the published and unpublished literature: National sample surveys, sample surveys of other large populations, school surveys, school BCG campaigns, and mass BCG campaigns.

Twenty-five countries were judged for the purposes of this project to have been adequately surveyed in whole or significant part since 1975.

Figures 1 and 2 display the results for each country by region. Table 1 contains the data used in the figures and describes the area population represented, the survey design, the level of BCG coverage in the age-group surveyed, and the antigen and criterion defining infection.

An arithmetic scale is used in Figure 1 in order to display the relative magnitudes of current estimates of annual risk of infection.

A logarithmic scale of annual risks is used in Figure 2 in order to represent constant percentage decreases or increases between current estimates and prior estimates as straight line trends.

Dark symbols in the figures indicate risk estimates based on 42 well-conducted national sample surveys in 16 countries. In Figure 2, dark solid lines are used to connect rates which are based on more than one large sample survey of the same country.

Light symbols in Figure 2 indicate risk estimates based on data representative of lesser populations.

Dark dashed lines in Figure 2 are used to connect risk estimates based on national sample survey data with risk estimates based on other substantial data such as tuberculin testing in the mass BCG campaigns. A light solid line was used to connect risk estimates from repeated surveys representative of lesser populations. A light dashed line was used to connect surveys of approximately the same population done in different years.

The symbol + was used in Figure 2 to indicate the average of a set of risk estimates which together would represent a larger population. Stratum estimates within sample surveys, plotted as separate points to reveal variation in risk, were displayed as a single estimate for the whole population in this way. Sets of small area estimates that were less representative of the whole population than would have been provided by formal probability sampling, such as the set of completed sampling units in a not yet completed national survey, or areas selected by judgement from geographic or economic strata in order to be representative of a large heterogenous population, were also combined in this way.

To indicate the extent of underlying variability, risk estimates from single surveys that were representative of only small areas are indicated in Figure 2 by unconnected light symbols.

Results by region

Africa. The most recent data for the eight countries included indicate current annual risks of infection around 1 to 2 percent. In the five countries for which comparable earlier surveys were available, trends over 20 to 25 years appear to be downward at 1 to 6 percent a year.

Data for the nearly completed national survey of Tanzania indicate an annual risk of infection of 1.1 percent, based on a population weighted average pooling of the samples. However, comparisons with earlier data available for three of the 18 regions in the sample do not together suggest a downward trend.

Surveys in Botswana and Lesotho suggest downward trends of about 6 and 1 percent a year, respectively. In the most recent survey in Botswana, however, BCG coverage in the age group surveyed had reached 83 percent, leaving only 17 percent who had by whatever circumstance missed vaccination, upon which to base the estimate.

No national surveys were available for Cameroon, but two surveys of the capital city, Yaounde, were available. These surveys indicate a level of annual risk of 0.6 percent in 1980 after a 20-year declining trend of 3.6 percent a year.

Survey data collected 30 years apart were available for Addis Ababa, the capital city of Ethiopia. These surveys indicate a 1.3 percent level of annual risk in 1979 succeeding a downward trend of 3.7 percent a year from the 4.1 percent risk level in 1949. A survey of selected villages in the Southwest, however, indicated a 3.8 percent annual infection risk in 1973. This suggests that within Ethiopia there is large variability in the level and perhaps also in the trend of infection risk.

Data from the 1976 sample survey of Gambia indicates an annual risk in 1971 of 1.9 percent. The trend of risk could not be assessed in Gambia, however. The only prior data available are from the 1958-59 survey of the capital city, Bathurst. The annual risk of infection in the urban stratum (4.4 percent) was higher than in the rural stratum (1.7 percent), which was nearly the same as the national level in 1971.

The annual risk of infection derived from skin test data for all military recruits in Burundi in 1981-82 was 1.2 percent. Data from an earlier survey among a scattered provincial population were selected in order to provide a rough comparison. The annual risk of infection in that group was 2.7 percent in 1955.

No comprehensive survey of the Nigerian population was available, but data from a survey of one emirate indicates an annual risk of 2.3 percent in 1973.

Americas. National sample survey data were available only from Argentina, but repeated surveys of large local populations within Argentina and also within Brazil were available. In the latest surveys, infection risks in these local populations varied ten-fold from 0.2 to 2 percent per year. Over time in these local populations, there was evidence of a steep decline in risk in Argentina, and a lesser decline in Brazil.

The annual risk of infection derived from the 1974-78 survey of the entire population of Argentina was 0.6 percent. Data from three surveys repeated in Santa Fe City and three surveys repeated in areas around Santa Fe City indicate low recent levels in that region of 0.2 to 0.3 percent annual risk, and indicate that the trend of the previous 12 to 15 years was steeply downward at a rate of 7 to 10 percent a year. The two trends described by the two sets of three survey points suggest that the decline was much steeper between the first two surveys but that the trend was nearly level during the 5 years between the second and third surveys. In the 1960-61 sample survey of another area of Argentina, Resistencia Province, the annual risk of infection was 0.5 percent.

Capitals of Brazilian States and Territories were surveyed in 1970-73 and again in 1980. The annual risk of infection was 0.8 to 1.9 percent in 1976 with evidence of a yearly downward trend of around 2 to 3 percent. A 1983 survey of the provincial population of Rio Grande Do Sol indicated a 0.4 percent annual risk of infection, with a 2.4 fold higher risk in southern than in northern rural areas.

South-East Asia. Only Thailand had national survey data available, but repeated surveys of local area populations were available for both India and Indonesia. In these populations, annual risks in the decade of the 1970's appear to have ranged from about 1 to 5 percent. Annual risks were highest in Indonesia.

Based on the 1977-79 national survey, the annual risk of infection in Thailand was 2.2 percent in 1974. Two earlier surveys, one of Bangkok and Chiengmai Province in 1960-64, and one of localities of Chiengmai and Kanchanaburi Provinces in 1954, indicate annual risks only slightly higher than in the national survey 16 to 24 years later.

In India, three large local populations were twice surveyed. Declining trends of 1.6 and 3.5 percent a year were apparent in two of these populations, but an increase of about 1 percent was apparent in the third population. Village surveys in 7 regions throughout India in 1972 indicate annual risks on the order of 1 to 2 percent. The village survey in Kashmir, compared to a 1978 sample survey of the Kashmir Valley, suggest a declining annual trend, but the populations may be only nominally comparable.

Indonesia has followed a policy since 1974 of withholding BCG and conducting 5-yearly surveys in nine special areas selected to be situated throughout the country. Three surveys have been completed in five of these areas, two in three areas, and one in another area. There are also three surveys available from an area with low BCG coverage. The latest surveys in these areas indicate a median annual risk of 2.3 percent (range: 0.7 to 3.9). Earlier data from the 1964-65 survey in rural East Java indicate an annual risk of 1.6 percent. Comparing the earliest to the latest survey in each of the nine areas with repeated surveys, the median downward trend in the annual risk of infection was 2.5 percent a year (ranging from a decline of 6.3 percent to an apparent increase of 3.4 percent a year).

Eastern Mediterranean (and Algeria). For the purposes of this project, Algeria is grouped in this region instead of with the African countries. National survey data were available for six countries, and repeated surveys of local populations were available for a seventh country in this region. Recent annual risk levels appear to be low to very low in Bahrain, Libya, Algeria and Kuwait (0.2 to 0.5 percent), but high in Afghanistan and Pakistan (1.8 and 3.5 percent, respectively). Recent levels of risk in the Syrian cities of Aleppo and Homs also appear to be very low (0.3 and 0.14, respectively). The trend of risk also appears to have decreased steeply in the current low risk countries, but not as steeply in Pakistan and appears to have increased in Afghanistan.

Four local areas sampled in 1980-84 for the nearly completed national survey of Algeria had also been canvassed in the 1949-52 mass BCG campaign. Repeated surveys were also available for the population of Blida. Based on these comparisons, annual risk of infection appears to have decreased about 6 to 7 percent a year in Algeria. A similar trend is apparent between risk estimates for the Syrian cities of Aleppo and Homs.

In Kuwait between 1972 and 1981, all school entrants (including non-citizens) were tuberculin tested prior to BCG vaccination. Compared to the 1962-63 national sample survey estimate, the annual risk of infection appears to have declined by 10 percent a year. In Bahrain, a decline of nearly 12 percent a year appears to have occurred between the 1969 national sample survey and mass tuberculin testing of students in 1981. A similarly steep rate of decline may have occurred in Eastern Libya, if the areas and populations covered in the surveys are comparable.

The annual risk estimate based on the 1974-78 national sample survey of Pakistan, which was completed except for Baluchistan, compared to the estimate based on the mass BCG campaign of 1949-54, suggests that the risk of infection declined by 4.2 percent a year, but that the risk was still high (1.8 percent) in 1972. The risk estimate based on the partially completed 1961-62 national survey is consistent with this trend.

The annual risk of infection in Afghanistan appears high (3.5 percent in 1978), without having much changed since 1958, compared with an estimate based on tuberculin testing program data collected in 1963 in selected schools around the country.

Western Pacific. Eleven national sample surveys were available for five countries in this region. In the Republic of Korea, the annual risk of infection appears to be declining, but remains high at about 2 percent. The risk appears to be about 1.8 percent in the Philippines, based on the recent national survey. Infection risk appears to be relatively low in Malaysia (0.4 percent) and Samoa (0.5 percent).

In China the annual risk of infection appears to have been 1 percent in 1975, based on areas without BCG coverage in the very large 1979 national survey sample.

Based on infection risk estimates from the five 5-yearly national surveys available from the Republic of Korea, the trend appears to be downward at 3.8 percent a year to a level in 1984 of 2 percent.

IV. DISCUSSION

Interpretation of this collection of risk and risk trend estimates must take into consideration the many potential sources of error, both in determining absolute levels of risk and in comparing risk estimates among countries or between periods within the same country. Some of these sources of error appear to have been adequately controlled, but the influence of other sources of error (identified and unidentified) must be acknowledged as unknown.

Tuberculin skin testing is a usefully accurate technique for separating groups at relatively high and low risk of future Mycobacterium tuberculosis disease, but is liable to varying degrees of error in identifying all the infected and specifying all the uninfected.

Sensitization to environmental mycobacteria is a source of nonspecific reactivity to tuberculin that is especially prevalent in tropical regions (Edwards and Edwards, 1960). There was evidence in reaction size distributions of a high prevalence of nonspecific sensitivity in several of the African and Asian populations surveyed, but distribution data for older groups or for bacteriologically confirmed cases were frequently available for locating the mode of the distribution of true infections and deriving their number by assuming the distribution to be symmetric.

There is underlying variability in tuberculin reactivity as evidenced by the variation between simultaneously applied identical tests in the same individual (Chaparas et al, 1985). Although this reduces precision of estimation, it is not expected to introduce systematic error.

A variety of antigen preparations and dosages were used, and these differed between countries and within countries over time. Estimating the number infected by using the symmetry of the distribution of true reactions about the mode would adjust for differences in specific biological potency between antigen preparations, but would not be effective in controlling for large differences in specificity of antigens.

The Mantoux method of administration was virtually always used, and all the selected studies measured induration of reaction. Techniques of measurement varied somewhat, but almost always consisted of transverse measurement at 48 or 72 hours after administration.

Waning of tuberculin reaction size over time, and complete reversion to zero reactivity are recognized to occur (Sutherland, 1971). To the extent reversions have occurred in a population, tuberculin test prevalence at a point in time will underestimate the proportion who were ever infected. But limiting to groups of about the same low average age may have minimized and kept comparable the effects of cumulative reversion.

Boosting is a potential problem in survey designs that retest the same individuals (Styblo, 1984). Boosting is the effect of an initial tuberculin test which, although it elicits slight or no reactivity itself, apparently acts as an antigenic stimulus able to recall waned or reverted preexisting mycobacterial sensitivity so that a subsequent test does elicit reactivity that is indistinguishable from conversion caused by M. tuberculosis transmission in the interval between the tests. Although some of the data compiled in this project came from surveys using a repeated testing design, the problem of boosting was avoided by selecting age groups too young to have been tested in earlier rounds.

BCG vaccination, a major component of tuberculosis control activities in developing countries, compromises the usefulness of tuberculin testing as a means to survey risk of infection. Tuberculin skin testing cannot distinguish between sensitivity caused by BCG vaccination and sensitivity caused by natural infection with M. tuberculosis, because BCG vaccination, unlike nonspecific sensitization, causes reactions that are distributed with nearly the same mode and shape as reactions caused by true infections with M. tuberculosis. For this reason the risk of infection in the whole population can only be inferred from risk measured in the unvaccinated.

In some of the countries for which survey data were selected, the policy was to vaccinate indiscriminantly without using tuberculin testing to select the as yet uninfected. In these countries, surveys limited to children without evidence of vaccination are subject to bias only to the extent that children selected for vaccination, either by choice or by local availability, are at a different risk of infection than the unvaccinated. This is a potentially severe source of bias if BCG coverage is very high.

In some of the surveys selected for this project, none of those surveyed had been vaccinated, either because BCG had not been introduced into that locale, or because BCG was withheld by policy until a later age. In other surveys, the unvaccinated were identified by physical examination to detect the characteristic scar. Levels of coverage by BCG were very low in some surveys, in which case representation of the whole population by the unvaccinated would be unaffected. In a few surveys, BCG coverage was so high that representation was demonstrably affected.

In other countries, the policy was to tuberculin test and vaccinate only those with weak or no reactions. In this situation, a later survey among children without BCG scars would be liable to severe overestimation bias. This was avoided by selecting age groups before the age of eligibility for selective vaccination programs in effect in a particular country.

Failure to test and measure every person in a survey sample can introduce a bias if those not reached by the survey are at a different risk of infection than those who were reached. A severe bias might also result from failure to measure a high proportion of those tested, because whether a survey participant returned for reading could well depend on whether there had been a reaction. Surveys with severe problems of this kind were not selected. Adequate coverage was a criterion for selection by this project, and was high in most of the surveys selected.

Although the average annual risk for a group lies in the calendar interval from birth to the time of the survey, it need not be at the interval midpoint. If the risk is changing substantially over time, as data from several of the surveys indicate, or varies with age, as has been suggested by the work of Sutherland (1976), and as might be expected in some of the diverse cultures surveyed, a complex model is necessary to estimate the risk at a particular time (Styblo, 1969). Limiting to young, narrow age groups was used as a way to bracket risk estimates within usefully narrow time intervals.

Average annual risk estimates for the same populations surveyed in different years are connected with straight lines in Figure 2 to indicate the average trend that would result in the observed risk estimates. An exponential trend is to be expected in the situation of a long-term constant ratio of the number of new cases produced by each existing case (Sutherland, 1976). However, without data for intermediate years, it is difficult to know the true shape of a trend line. In some instances where more than 2 surveys were available, the trend appeared to follow a fairly constant geometric decrease, but in other instances, the trend appeared to have changed over time.

Many ey reports presented more detailed analyses of infection risk and its trend, but for th rposes of this review, methods were adopted that could be simply and consistent pplied to all data. In the few instances of large disagreement, the present analysis be in error.

V. CONCLUSIONS

This attempt to review and compile data available from major surveys carried out in developing countries since 1975 falls far short of providing a comprehensive picture of tuberculous infection risk and trend in the entire developing world. The assembled data cannot safely be generalized beyond the specific target populations surveyed. However, the assembled data do provide several recent objective examples of apparent progress and lack of progress in tipping the balance against the tuberculosis epidemic.

The review found that since 1975 many large scale surveys have been successfully carried out in the developing countries, with impressive attention to correct procedure and technique.

In most of the countries repeatedly surveyed in whole or in part, risk of infection does appear to have diminished. In some of these countries, the decline appears to have been substantial, and current levels of risk have become very low in a few countries.

In other countries, however, rates of infection appear to remain high and there is no indication of decrease.

It may be speculated that general improvements in living standards and tuberculosis control programs are having an effect against the tuberculosis epidemic in some parts of the developing world as it already has in the more developed countries. In the rest of the developing world, however, very little is known of the current magnitude and trend of the risk of tuberculous infection.

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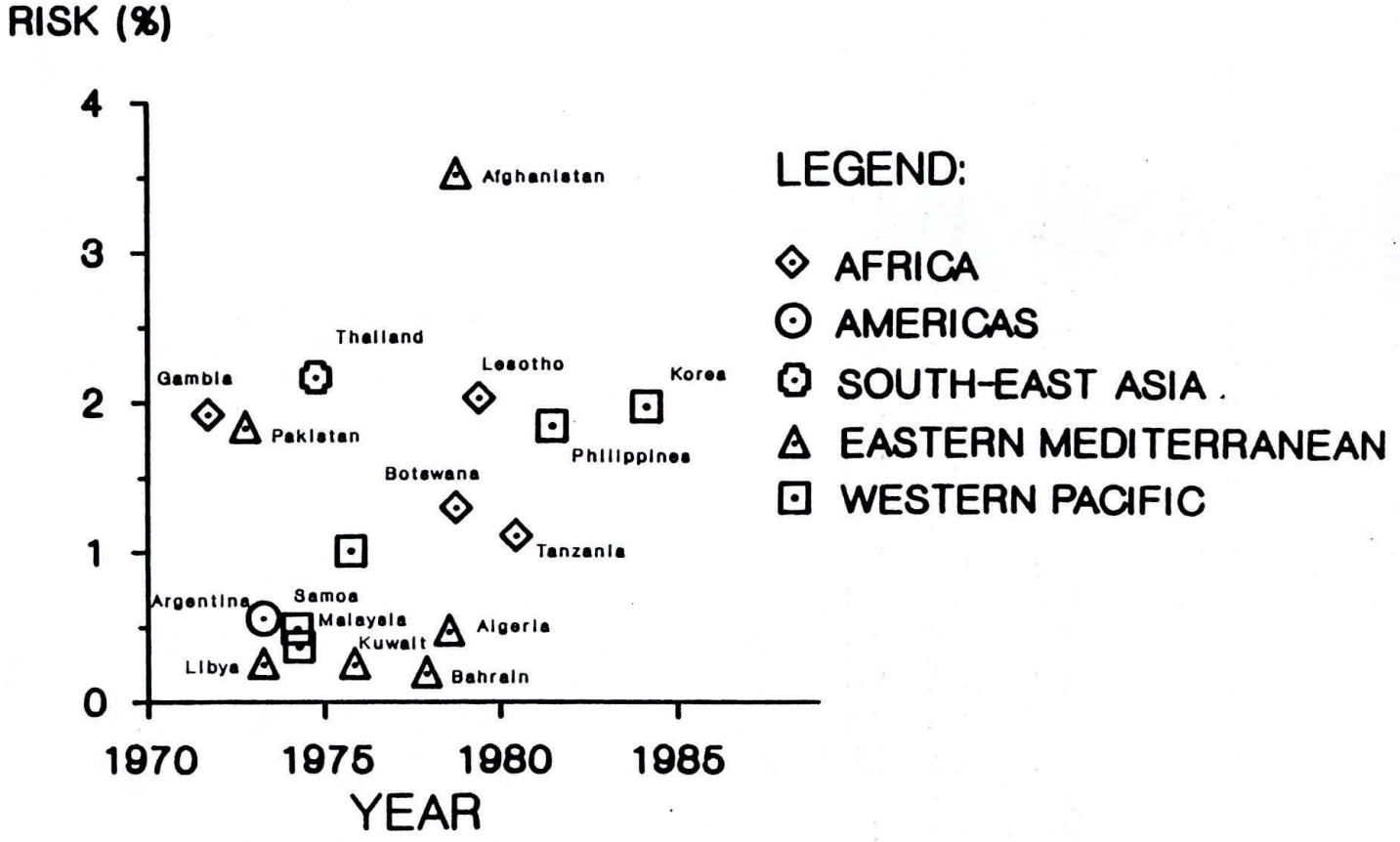
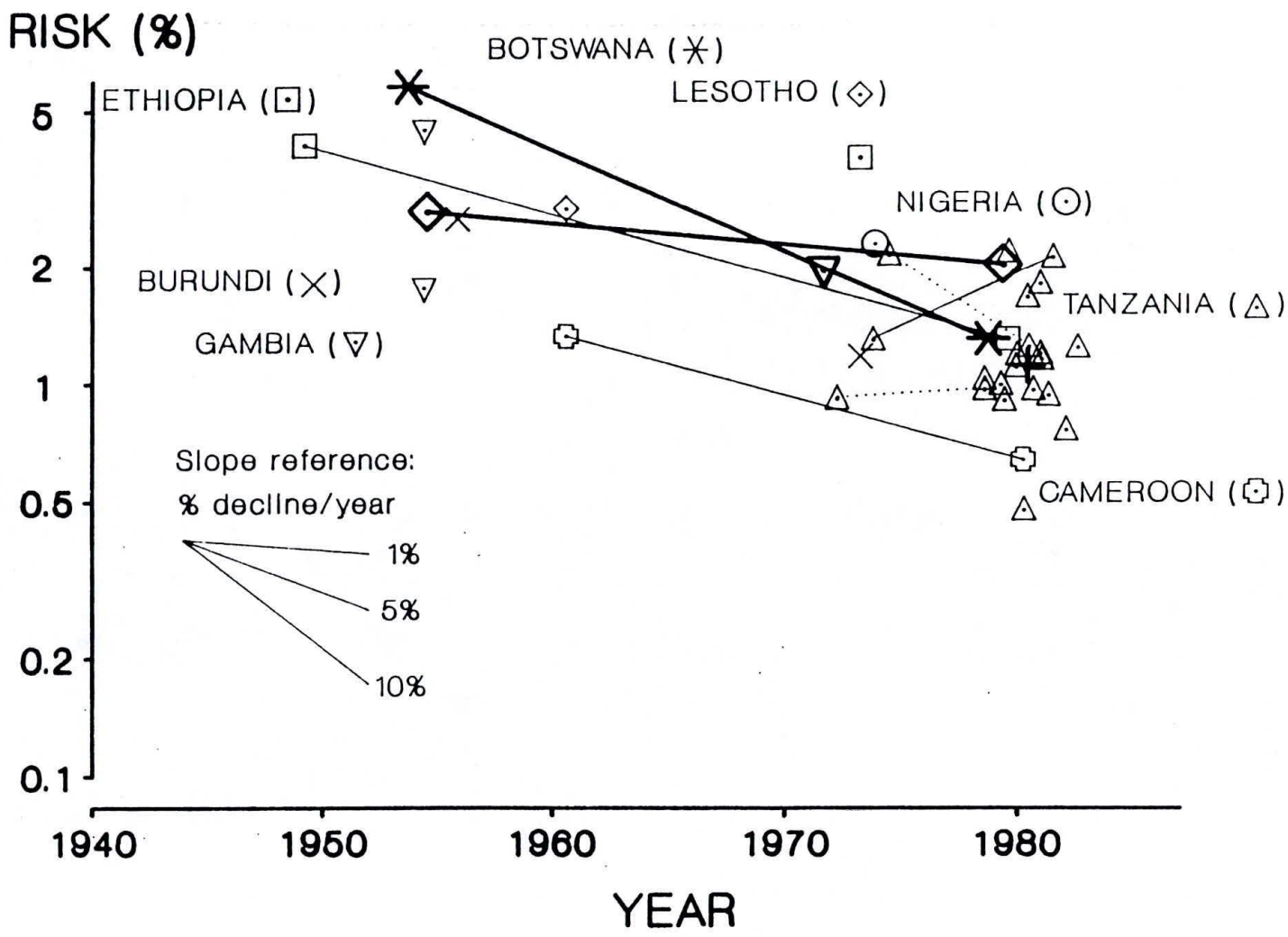
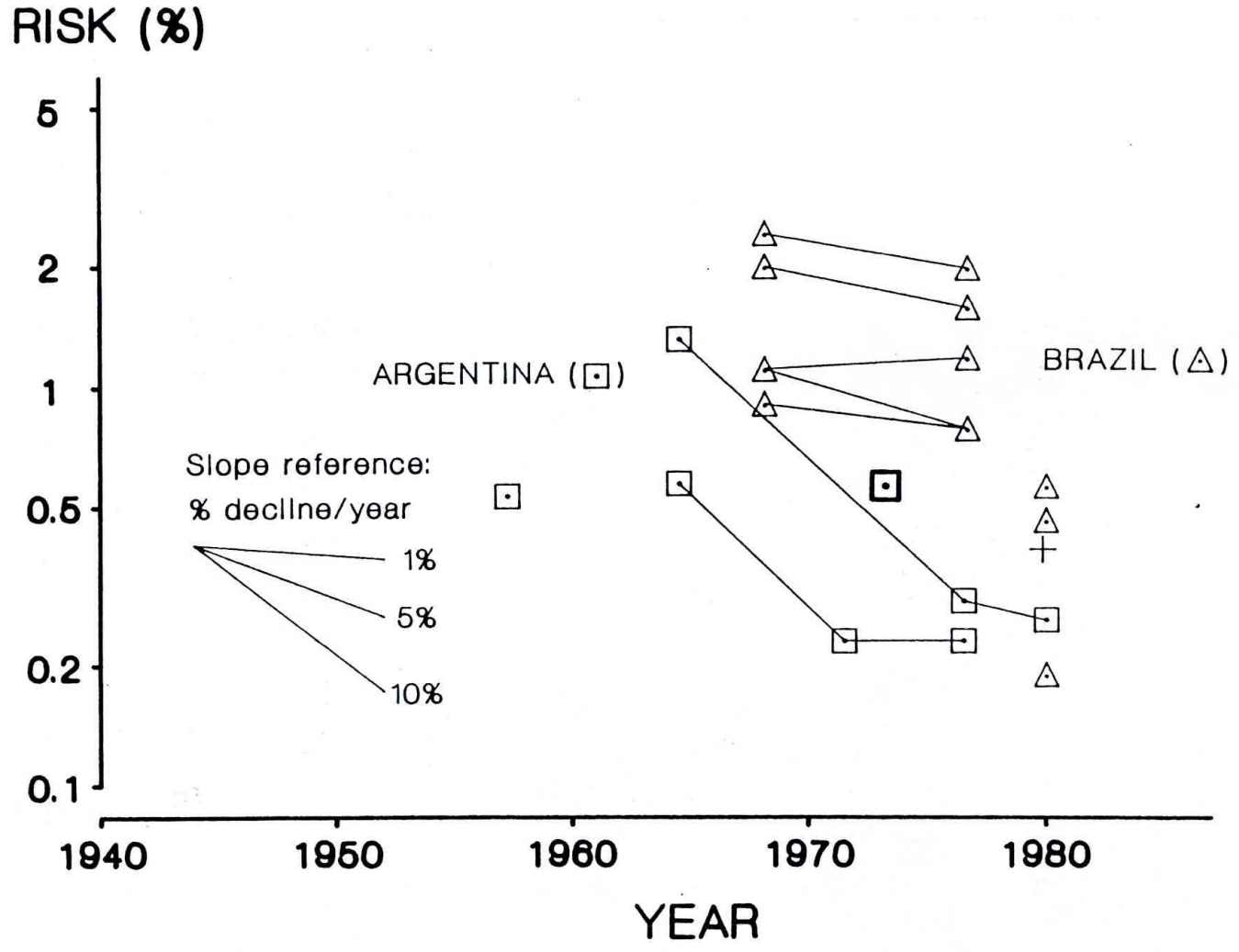
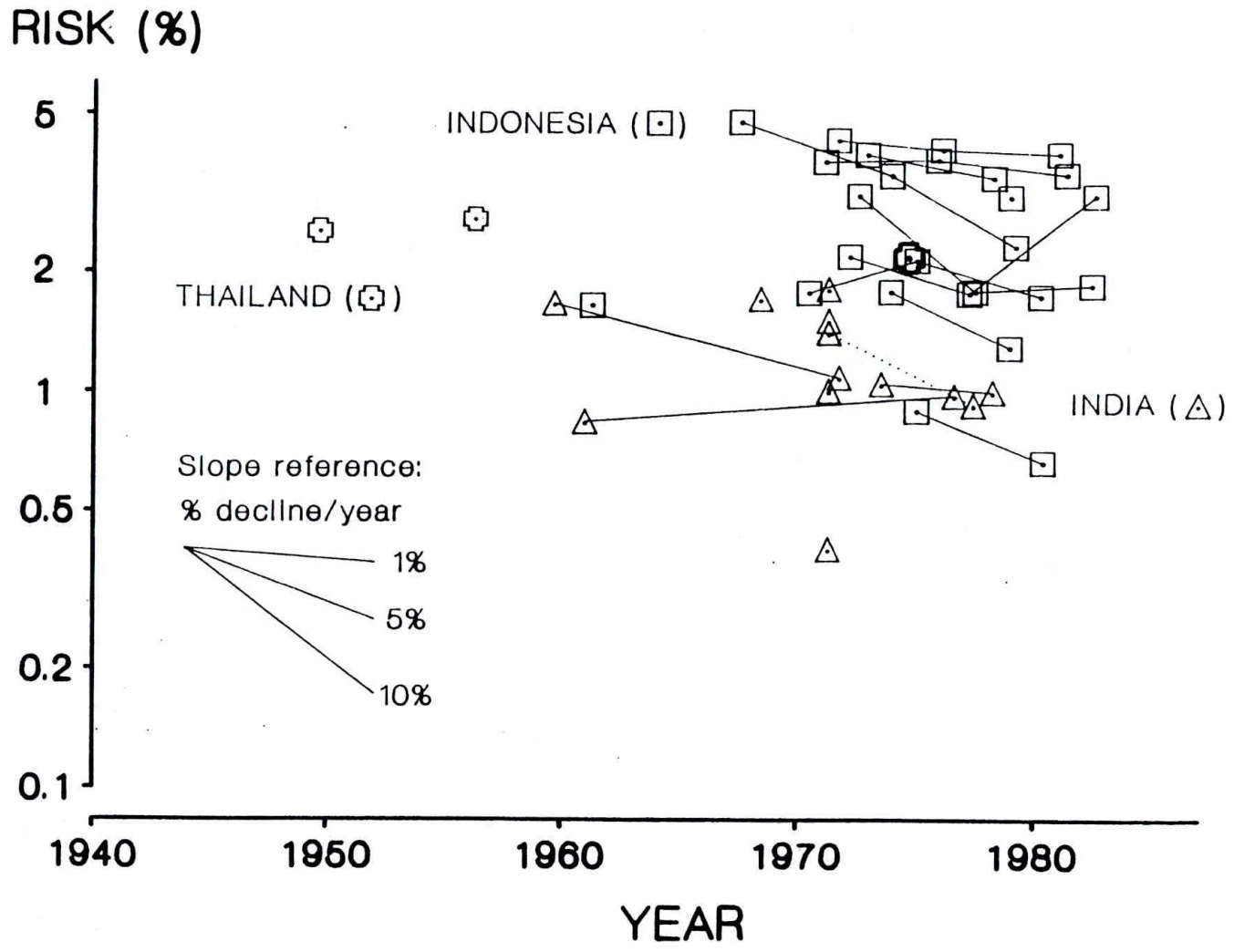
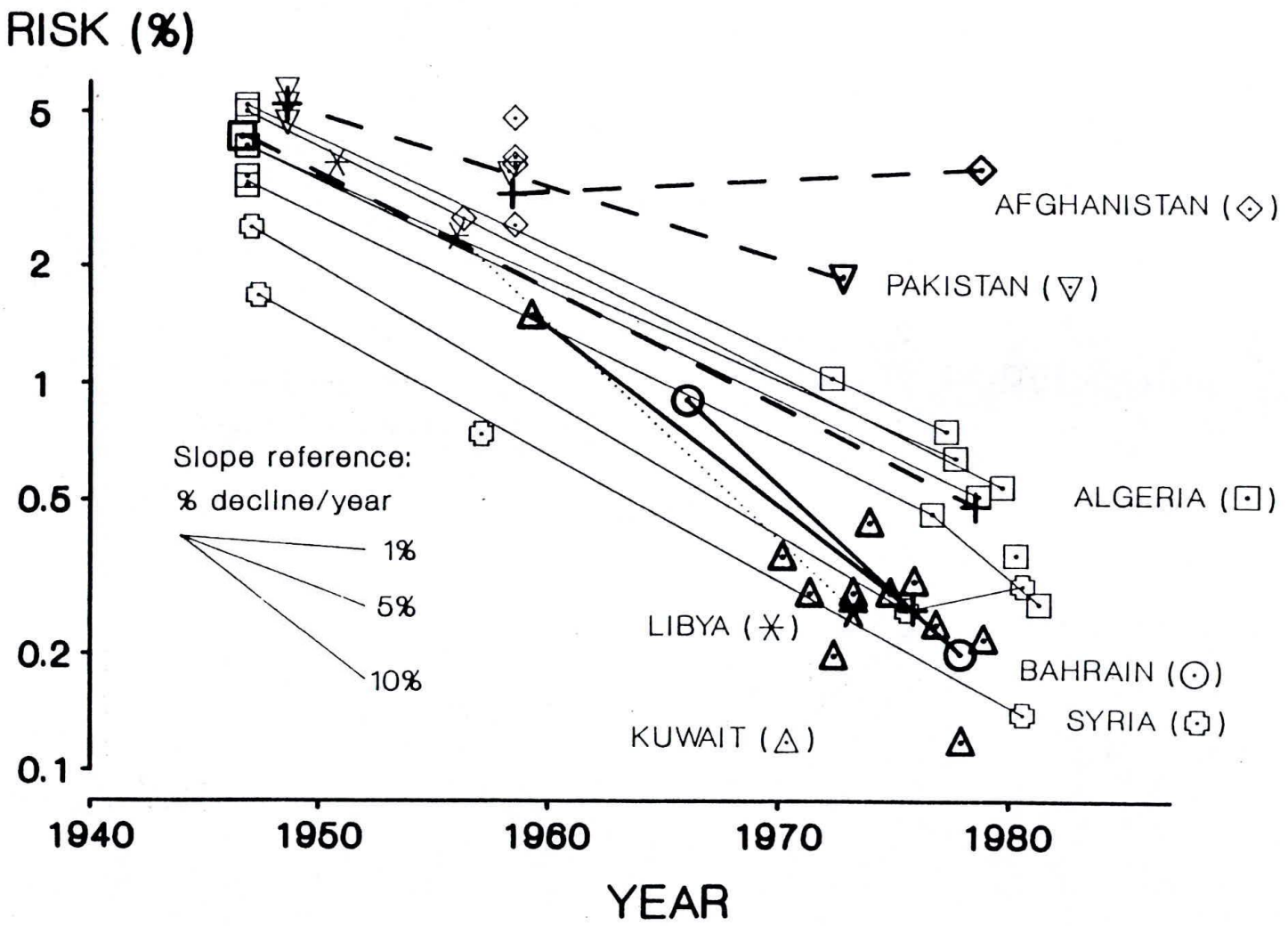
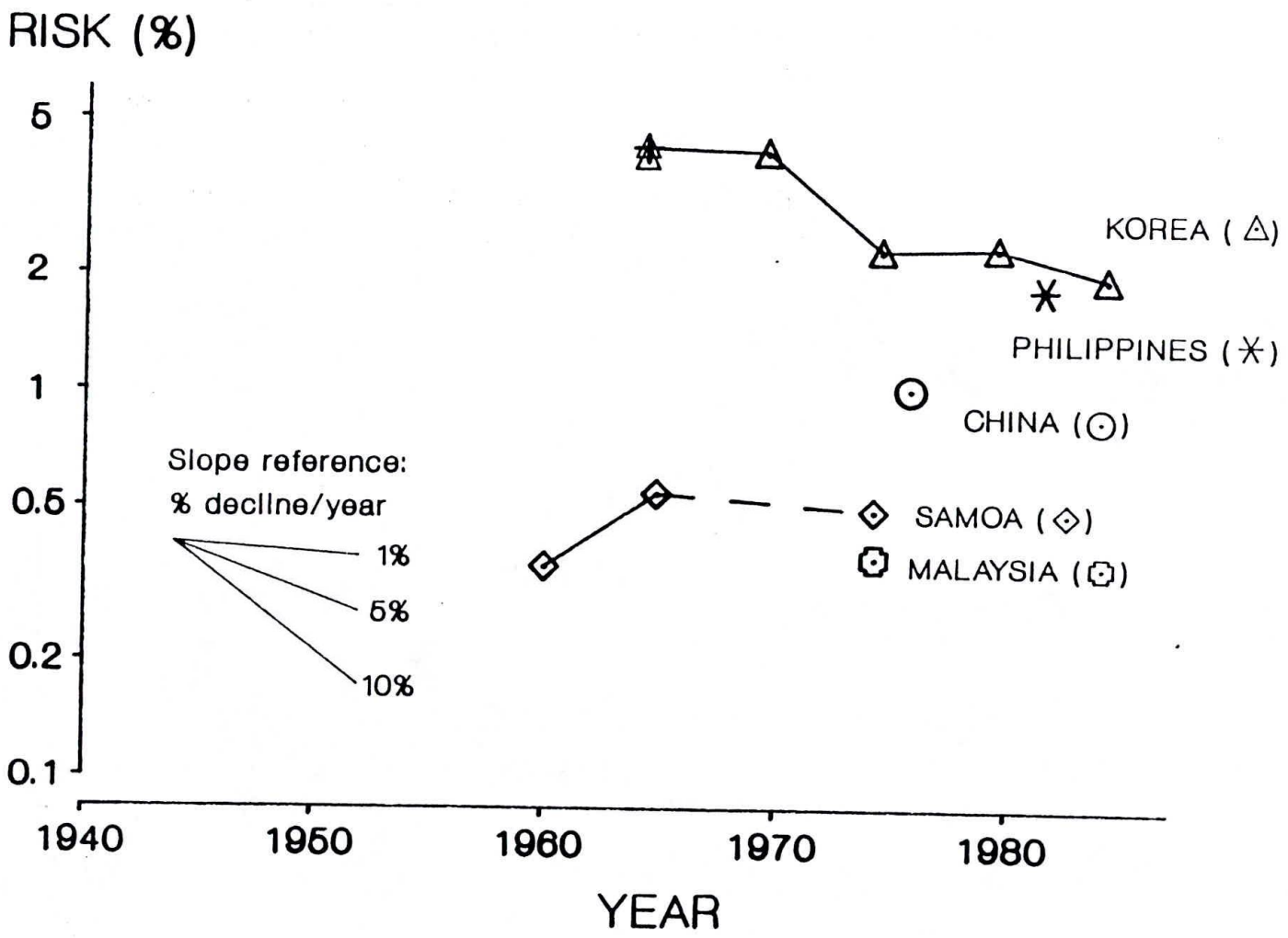

RISK (%)
4
3
2
1
0
1970
1975
1980
1985
YEAR
Afghanistan
Thailand
Gambia
Lesotho
Korea
Pakistan
Philippines
Botswana
Tanzania
Argentina
Samoa
Malaysia
Algeria
Kuwait
Libya
Bahrain
LEGEND:
AFRICA
AMERICAS
SOUTH-EAST ASIA
EASTERN MEDITERRANEAN
WESTERN PACIFIC


RISK (%)
BOTSWANA (✳)
LESOTHO (◇)
ETHIOPIA (⊡)
NIGERIA (⊙)
BURUNDI (×)
TANZANIA (△)
GAMBIA (▽)
Slope reference:
% decline/year
1%
5%
10%
CAMEROON (⊡)
5
2
1
0.5
0.2
0.1
1940
1950
1960
1970
1980
YEAR

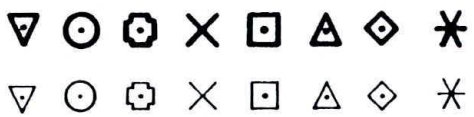

RISK (%)
5
2
1
0.5
0.2
0.1
ARGENTINA (⊡)
BRAZIL (△)
Slope reference:
% decline/year
1%
5%
10%
1940
1950
1960
1970
1980
YEAR


RISK (%)
5
2
1
0.5
0.2
0.1
INDONESIA (⊡)
THAILAND (⊙)
INDIA (△)
Slope reference:
% decline/year
1%
5%
10%
1940
1950
1960
1970
1980
YEAR

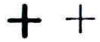

RISK (%)
5
2
1
0.5
0.2
0.1
1940
1950
1960
1970
1980
YEAR
Slope reference:
% decline/year
1%
5%
10%
AFGHANISTAN (◇)
PAKISTAN (▽)
ALGERIA (⊡)
LIBYA (✳)
BAHRAIN (⊙)
SYRIA (⊙)
KUWAIT (△)


RISK (%)
5
2
1
0.5
0.2
0.1
1940
1950
1960
1970
1980
YEAR
KOREA (△)
PHILIPPINES (✳)
CHINA (⊙)
SAMOA (◇)
MALAYSIA (⬡)
Slope reference:
% decline/year
1%
5%
10%

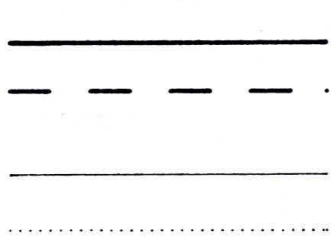
LEGEND



Survey estimates of risk



Average of risk estimates



Trend between risk estimated in different years

Dark symbols and lines are used to display risk estimates and trends for national populations and large parts of national populations.

Light symbols and lines are used to display risk estimates for subnational units.

Solid lines connect surveys that closely represent the same population.
Dashed lines connect surveys that represent approximately the same population.

TABLE 1. ANNUAL RISK OF TUBERCULOUS INFECTION IN DEVELOPING COUNTRIES BASED ON TUBERCULIN SURVEYS

1. WHO African Region (except Algeria) - Region Africaine de l'OMS (sans Algerie)

Year	Area Represented	Survey design	BCG (%)	Antigen and Infection Criterion	Survey Year Midpt.	Age (midpt.)	Tested N	Infected N	Prevalence (%)	Risk/year (%)
Botswana										
1981-82[ab]	Whole country	Sample survey	83.3	RT23 2TU, Mode=13	1982.0	0-14 (6.5)	257	...	8.17	1.30
1956-57[c]	Whole country	Sample survey	0	RT19-20-21 5 TU, Mode=16	1957.0	0-14 (6.6)	1450	472	32.55	5.79
Burundi										
1982-84[a]	Military recruits	All recruits	71.0	RT23 2TU, 9mm+	1983.5	18-22 (20.5)	912	195	21.38	1.17
1964[b]	Northern section of Muramvya Province	Sample survey	56.4	RT23 2TU, 9mm+	1964.6	15-19 (17.5)	202	76	37.62	2.66
Cameroon - Cameroun										
1984[a]	Yaounde	Sample survey of schools	58.4	PPD 71 10U, 9mm+	1984.5	7- 9 (8.5)	860	46	5.35	0.64
1964[b]	Urban Yaounde	Sample survey	...	RT23 2TU, 9mm+	1964.3	5- 9 (7.5)	326	31	9.51	1.32
Ethiopia - Ethiopie										
1983[a]	Addis Ababa	Sample of schools	49.4	RT23 2TU, 10mm+	1983.9	6-15 (8.6)	1251	133	10.63	1.30
1977[b]	Southwest area	Selected villages	...	... 2TU, 10mm+	1977.5	6-10 (8.5)	185	52	28.11	3.81
1953-55[c]	Addis Ababa	BCG school campaign	0	...	1954.7	7-14 (11)	...	...	37	4.1
Gambia										
1976[ab]	Whole country	Sample survey	0.7	RT23 2TU, Mode=15	1976.4	6-16 (9.4)	2397	399	16.65	1.92
1958-59[c]	Bathurst in 2 strata	Sample survey:	...	RT23 1TU, Mode=17	1959.1	5-14 (9.4)	..	..	16.38	1.89
	Urban stratum	at 50 per 1000					176	61	34.66	4.43
	Rural stratum	at 7 per 1000					400	61	15.25	1.74

1. WHO African Region (except Algeria) - Region Africaine de l'OMS (sans Algerie) (continued)

Year	Area Represented	Survey design	BCG (%)	Antigen and Infection Criterion	Survey Year Midpt.	Age (midpt.)	Tested N	Infected N	Prevalence (%)	Risk/ year (%)
Lesotho										
1981-82[a]	Whole country	Sample survey	70.4	RT23 2TU, Mode=14	1982.0	0- 9 (5.2)	158	...	10.13	2.03
1956-57[b]	Whole country	Sample survey	0	RT19-20-21 5TU, Mode=17,18	1957.0	0- 9 (4.9)	1101	142	12.90	2.78
1962-65[c]	Rural area around Maseru	Sample survey	0	RT23 1TU, Mode=19	1963.8	0- 9 (4.9)	10216	1342	13.14	2.83
Nigeria										
1977[a]	Kazaure Emirate of Kano State	School survey	32.1	RT23 2TU, Mode=15	1977.4	4-13*(7*)	...	...	15.0	2.29
United Republic of Tanzania - Republique-Unie de Tanzanie										
1983[acehij]	Arusha Region	Sample survey	52.4	RT23 2TU,	1983.6	7-14 (10.0)	3125	307	9.82	1.03
1984	Coast (Pwani) Region	of schools	37.6	Mode=17	1984.8	(9.6)	681	74	10.87	1.19
1984	Dar-es-Salam Region	in progress,	45.0		1984.8	(9.7)	1338	137	10.24	1.11
1986	Iringa Region	90% completed	57		1986.4	(10.1)	1723	156	9.05	0.94
1986	Dodoma Region		49		1986.9	(10.7)	1743	358	20.54	2.13
1987	Kigoma Region		49.1		1987.7	(10.2)	1188	143	12.04	1.25
1985	Kilimanjaro Region		52.4		1985.4	(10.2)	2324	111	4.78	0.48
1984	Lindi Region		31.3		1984.6	(10.3)	2665	240	9.01	0.91
1986	Mbeya Region		64		1986.5	(10.9)	1621	193	11.91	1.16
1986	Morogoro Region		67		1986.6	(11.0)	865	158	18.27	1.82
1984	Mtwara Region		41.8		1984.5	(9.7)	629	122	19.40	2.20
1985	Mwanza Region		...		1985.8	(10.2)	2420	...	9.5	0.97
1986	Rukwa Region		67		1986.4	(10.8)	385	47	12.21	1.20
1984	Ruvuma Region		46.1		1984.5	(10.4)	1412	140	9.92	1.00
1985	Shinyanga Region		...		1985.4	(9.8)	3666	...	11.6	1.25
1985	Singida Region		...		1985.7	(10.5)	985	...	16.3	1.68
1987	Tabora Region		...		1987.7	(11.2)	1794	...	8.3	0.77
1983	Tanga Region		50.1		1983.8	(10.4)	2462	238	9.67	0.97
1983-87	(18 Area weighted average)				1985.6	(10.3)	30982	...	10.9	1.11
1979[b]	Shinyanga Region, except Shinyanga Distr.	Sample survey	50.9	RT23 2TU, 10mm+	1979.5	6-14 (10.0)	1817	356	19.59	2.16
1978[d]	Dodoma Region	Sample survey	63.3	RT23 2TU, Mode=17	1978.9	6-14 (10.2)	1329	166	12.49	1.30
1977[g]	Tanga Town and nearby rural area	Sample survey of schools	79.0	RT23 2TU, Mode=17	1977.1	7-14 (9.7)	383	33	8.62	0.92

II. WHO Region of the Americas - Region des Ameriques de l'OMS

Year	Area Represented	Survey design	BCG (%)	Antigen and Infection Criterion	Survey Year Midpt.	Age (midpt.)	Tested N	Infected N	Prevalence (%)	Risk/year (%)
Argentina - Argentine										
1974-78[ab]	Whole country	Sample survey	...	RT23 2TU, 10mm+	1976.5	6- 7 (6.5)	26902	970	3.61	0.56
1983[c]	Areas around	Sample survey	81.6	..., 10mm+	1983.5	5- 8 (7.0)	325	...	1.8	0.26
1979-80[c]	Santa Fe City		63.7	..., 10mm+	1980.0	6- 7 (7.0)	443	...	2.0	0.29
1967-68[c]			31.6	..., 10mm+	1968.0	5- 8 (7.0)	1221	...	8.8	1.31
1979-80[c]	Santa Fe City	All schools	57.7	..., 10mm+	1980.0	6- 7 (7.0)	2125	...	1.6	0.23
1974-75[c]			12.9	..., 10mm+	1975.0	6- 7 (7.0)	3590	...	1.6	0.23
1967-68[c]			...	..., 10mm+	1968.0	6- 7 (7.0)	3196	...	3.9	0.57
1960-61[d]	Resistencia Province	Sample survey	Rare	RT25 1TU, 10mm+	1961.0	5- 9 (7.5)	1259	49	3.89	0.53
Brazil - Bresil										
1983[a]	Rio Grande Do Sol Province	Sample survey of school enterers	0	RT23 2TU, 10mm+	1983.5	7- 8 (7.3)	11880	333	2.80	0.39
	By Provincial zone:									
	Metropolitan				1983.5	6- 7 (7.0)	3507	...	3.88	0.56
	Southern rural						4163	...	3.17	0.46
	Northern rural						3670	...	1.31	0.19
1980[b]	Capitals of States and Territories by Region:	All school enterers	...	...	1980.5	... (7.7)				
	North						...	...	...	1.95
	Northeast						...	...	...	1.56
	Southeast						...	...	...	1.17
	Sao Paulo State						...	...	...	0.94
	South						...	...	...	0.78
	East Central						...	...	...	0.78
1970-73[b]	Capitals of States and Territories by Region:	All school enterers	...	RT23 2TU, 10mm+	1972.0	... (7.7)				
	North						...	...	16.9	2.38
	Northeast						...	...	14.2	1.97
	Southeast						...	...	8.3	1.1
	Sao Paulo State						...	...	...	1.2
	South						...	...	6.7	0.90
	East Central						...	...	7.9	1.1

III. WHO South-East Asia Region - Region de l'Asie du Sud-Est de l'OMS

Year	Area Represented	Survey design	BCG (%)	Antigen and Infection Criterion	Survey Year Midpt.	Age (midpt.)	Tested N	Infected N	Prevalence (%)	Risk/ year (%)
India - Inde										
1979[a]	Dodballapur in	Sample survey	14.1	RT23 1TU, 12mm+	1979.5	0- 4 (2.5)	5203	128	2.46	0.99
1974-75[de]	Bangalore District	repeated in same villages	36	RT23 1TU, 10mm+	1974.8		3805	98	2.58	1.04
1977-78[b]	3 Subdistricts in	Repeated	...	RT23 1TU, 10mm+	1977.9	0- 4 (2.5)	1492	36	2.41	0.97
1961-63[a]	Bangalore District	sample surveys	1.5		1962.2		7981	166	2.08	0.84
1972-73[f]	Tumkur District in	Sample survey	...	RT23 1TU, 10mm+	1973.0	0- 4 (2.5)	4277	115	2.69	1.08
1960-61[cfi]	South India	repeated in same 62 villages	...		1960.9		3788	155	4.09	1.66
1978[g]	Kashmir Valley	Sample survey	0.2	PPD-S 3TU, 12mm+	1978.7	0- 4 (2.5)	2448	56	2.29	0.92
1972[h]	Villages in:	Selected for	<5	PPD-S 5TU, 12mm+	1972.8	1- 4 (3.0)				
	Kashmir	altitude contrast					679	...	4.0	1.4
	Kulu Valley						503	...	5.2	1.8
	Lohaghat						381	...	3.1	1.0
	Pithoragarh						290	...	4.1	1.4
	Agra						530	...	5.2	1.8
	Haryana						612	...	4.4	1.5
	Rajasthan						76	...	1.3	0.4
1968-71[h]	Northern Chingelput	Selected for BCG trial	<5	PPD-S 5TU, 12mm+	1969.9	1- 4 (3.0)	27520	...	5.1	1.7
Indonesia - Indonesie										
1983[aefgh]	Tangerang Regency	Sample survey	18.5	RT23 2TU, 10mm+	1983.6	7-10 (8.8)	1549	286	18.46	2.29
1978	in West Java	repeated in	22.1		1978.4	7-10 (8.8)	1649	440	26.68	3.47
1972		same schools	1.9		1972.2	7-10 (9.3)	1371	497	36.25	4.73
1986[bh]	Sambas in West	Selected as	0	RT23 2TU, 10mm+	1986.8	7-10 (8.8)	3839	576	15.00	1.83
1981	Kalimantan	BCG-free area			1981.8	7-10 (8.6)	2181	310	14.21	1.77
1976					1976.9	7-10 (8.6)	1655	391	23.63	3.09
1986[bh]	Padang Pariaman in	Selected as	0	RT23 2TU, 10mm+	1986.9	7-10 (8.7)	1986	472	23.77	3.07
1981	West Sumatra	BCG-free area			1981.7	7-10 (8.9)	2501	363	14.51	1.75
1976					1976.5	7-10 (8.6)	1124	193	17.17	2.17
1984[gh]	Malang in East Java	Selected as	0	RT23 2TU, 10mm+	1984.5	7-10 (8.3)	1406	75	5.33	0.66
1979[cgh]		BCG-free area			1979.5	7-10 (8.9)	1122	86	7.66	0.89
1985[cgh]	Ogan Kamering Ilir in	Selected as	0	RT23 2TU, 10mm+	1985.8	7-10 (8.9)	4840	1309	27.05	3.48
1980	South Sumatra	BCG-free area			1980.2	7-10 (8.5)	4839	1358	28.06	3.80
1975					1975.6	7-10 (8.9)	2425	701	28.91	3.76

III. WHO South-East Asia Region - Region de l'Asie du Sud-Est de l'OMS (continued)

Year	Area Represented	Survey design	BCG (%)	Antigen and Infection Criterion	Survey Year Midpt.	Age (midpt.)	Tested N	Infected N	Prevalence (%)	Risk/year (%)
1985[cgh]	Gowa in South	Selected as	0	RT23 2TU, 10mm+	1985.5	7-10 (8.9)	4001	1198	29.94	3.92
1980	Sulawesi	BCG-free area			1980.5	7-10 (8.7)	3573	1076	30.11	4.03
1975					1975.8	7-10 (8.2)	1429	429	30.02	4.26
1983[cgh]	Stabat Langkat	Selected as	0	RT23 2TU, 10mm+	1983.2	7-10 (8.5)	1894	196	10.35	1.28
1978	in North Sumatra	BCG-free area			1978.4	7-10 (8.9)	1125	165	14.67	1.77
1982[cgh]	Hulu Sengai Tengah	Selected as	0	RT23 2TU, 10mm+	1982.8	7-10 (9.0)	1577	424	26.89	3.42
1977	in South Kalimantan	BCG-free area			1977.3	7-10 (8.7)	1199	352	29.36	3.92
1984[gh]	Pati in	Selected as	0	RT23 2TU, 10mm+	1984.5	7-10 (8.5)	2938	403	13.72	1.72
1979	Central Java	BCG-free area			1979.5	7-10 (8.9)	2197	381	17.34	2.12
1974					1974.5	7-10 (8.1)	1070	143	13.36	1.76
1983[g]	Langsa in	Selected as	0	RT23 2TU, 10mm+	1983.5	7-10 (9)	...	...	24.4	3.06
	D.I. Aceh	BCG-free area								
1964-65[dn]	Rural area in	Sample survey	...	RT23 2TU, 10mm+	1965.0	5- 9 (7.5)	1633	191	11.70	1.64
	East Java									
Thailand - Thailande										
1977-79[a]	Whole country	Sample survey	39.1	...	1978.5	0-14 (7.5)	...	...	15.2	2.17
1960-64[bd]	Bangkok and	Sample survey	...	...	1962.5	10-14 (12.5)	...	...	29	2.7
	Chiengmai Province									
1954[c]	6 localities in	Selected	0	... 5TU, 10mm+	1954.9	8-12 (10.5)	1578	371	23.51	2.52
	Chiengmai and	unvaccinated								
	Kanchanaburi Provinces	areas								

IV. WHO Eastern Mediterranean Region (and Algeria) - Region de la Mediterranee Orientale de l'OMS (et Algerie)

Year	Area Represented	Survey design	BCG (%)	Antigen and Infection Criterion	Survey Year Midpt.	Age (midpt.)	Tested N	Infected N	Prevalence (%)	Risk/year (%)
Algeria - Algerie										
	Whole country in 6 economic zones	School survey every 5 years		RT23 2TU, 10mm+		8 (8.5)				
1985[d]	Zone 2 Tizi Ouzou and Tlemcen	Second survey (commencing)	67.2		1985.5		2378	55	2.31	0.27
1984[d]	Zone 5 & 6	First survey	59.1		1984.5		2125	64	3.01	0.36
1983[ab]	Zone 4 incl. Batna	(nearly complete)	68.6		1983.9		1144	51	4.46	0.54
1982[ab]	Zone 3 incl. Guelma		66.3		1982.9		1067	45	4.22	0.51
1981[ab]	Zone 1 incl. Mascara		63.3		1981.9		1334	71	5.32	0.64
1980[ab]	Zone 2 Tizi Ouzou and Tlemcen		44.6		1980.9		1844	71	3.85	0.46
1980-84	(5 Area weighted average)				1982.8		7514	302	4.02	0.48
1981[ab]	Blida	Survey repeated	71.6	IP48 10TU, 6mm+	1981.5	8 (8.5)	1117	...	6.18	0.75
1976[ab]	Blida	in same schools			1976.5	6-10 (8.5)	262	...	8.4	1.03
1949-52[c]	Whole country	Mass BCG Campaign	...	IP48 5TU, 6mm+ IP48 10TU, 6mm+ Moro Patch, 3+ papules	1951.1	8 (8.5)	110547	...	31.2	4.30
	Selected areas									
	Blida								36.5	5.20
	Tizi Ouzou								25.5	3.40
	Tlemcen								24.3	3.22
	Mascara								29.7	4.06
	Batna								35.4	5.01
	Guelma								29.8	4.08
Afghanistan										
1982[ac]	Whole country	Sample survey	...	RT23 1TU, 8mm+	1982.5	5- 9 (7.5)	881	208	23.61	3.53
1963[bc]	Kabul	Selected schools	...	RT23 1TU, 8mm+	1963.5	7-12 (10.0)	19006	4322	22.74	2.55
	Jalalabad					7-12 (10.0)	3492	1083	31.01	3.64
	Mazar-e-Sharif					7-12 (10.0)	3170	1019	32.15	3.80
	Kandahar					7-12 (10.0)	4079	1586	38.88	4.80
	Pulikumry					13-15 (14.5)	1191	384	32.24	2.65
	(5 Area weighted average)					7-15 (10.2)	30938	8394	27.13	3.06
Bahrain - Bahrein										
1981[a]	Whole country	All schools	0	RT23 1TU, 6mm+	1981.4	6- 7 (7.0)	6151	86	1.40	0.20
1969[a]	Whole country	Sample survey	...	RT23 1TU, 6mm+	1969.5	6- 7 (7.0)	897	55	6.13	0.90

IV. WHO Eastern Mediterranean Region (and Algeria) - Region de la Mediterranee Orientale de l'OMS (et Algerie) (continued)

Year	Area Represented	Survey design	BCG (%)	Antigen and Infection Criterion	Survey Year Midpt.	Age (midpt.)	Tested N	Infected N	Prevalence (%)	Risk/year (%)
Kuwait - Koweit										
1981[a]	Whole country	School campaign	0	RT23 ...	1981.5	4- 6 (5.2)	22710	261	1.15	0.22
1980					1980.5	4- 6 (5.1)	16149	101	0.63	0.12
1979					1979.5	4- 6 (5.3)	22674	283	1.25	0.24
1978					1978.5	4- 6 (5.2)	20843	338	1.62	0.31
1977					1977.5	4- 6 (5.3)	17444	266	1.52	0.29
1976					1976.5	4- 6 (5.1)	9018	201	2.23	0.44
1975					1975.5	4- 5 (4.5)	7665	100	1.30	0.29
1974					1974.5	4- 5 (4.2)	6722	55	0.82	0.20
1973					1973.5	4- 5 (4.3)	6363	80	1.26	0.29
1972					1972.5	4- 5 (4.7)	2258	38	1.68	0.36
1972-81	(10 Year weighted average)				1978.4	4- 6 (5.1)	131846	1723	1.31	0.26
1962-63[a]	Whole country	Sample survey	...	...	1963.0	5- 9 (7.5)	...	...	10.74	1.50
Libya Arab Jamahiriyah - Jamihiriyah Arabe Libyenne										
1976-77[a]	Whole country	Sample survey	63.5	RT23 2TU,	1977.0	5- 9 (7.5)	1827	35	1.92	0.26
	East Libya			Mode=16,17			951	...	1.9	0.26
1959[ab]	East Province Cyrenaica	Sample survey	...	RT23 1TU, Mode=18,19	1959.7	5- 9 (7.5)	361	60	16.62	2.39
1954[ac]	Ben Walid	Selected area	0	RT19-20-21 5TU, Mode=18,19	1954.5	5- 9 (7.5)	188	...	24.5	3.68
Pakistan										
1974-78[abd]	Whole country except Baluchistan	Sample survey	7.8	RT23 1TU, 10mm+	1976.5	5- 9 (7.5)	2289	298	13.02	1.84
1961-62[a-d]	Karachi, Rawalpindi, and Lahore	Sample survey	42.7*	RT23 1TU, 10mm+	1962.0	5- 9 (7.5)	769	178	23.15	3.45
1949-54[be]	Provincial capitals	Mass BCG campaign	0	RT22 5TU, 5mm+	1954.1	7-14 (11.0)	...	...	47.5	5.69
	Other urban areas								44.5	5.21
	Rural areas								41.0	4.68
	(3 Area median)								44.5	5.21

IV. WHO Eastern Mediterranean Region - Region de la Mediterranee Orientale de l'OMS (continued)

Year	Area Represented	Survey design	BCG (%)	Antigen and Infection Criterion	Survey Year Midpt.	Age (midpt.)	Tested N	Infected N	Prevalence (%)	Risk/ year (%)
Syrian Arab Republic - Republique Arabe Syrienne										
1983[a]	Aleppo	Survey repeated in some 1978 survey schools	14.1	RT23 2TU, 10mm+	1983.8	6 (6.5)	1586	31	1.95	0.30
1978[ab]	Aleppo	Sample survey of schools	8.5	RT23 2TU, 10mm+	1978.8	6 (6.5)	1845	31	1.68	0.26
1950[ad]	Aleppo	BCG school campaign	0	Moro patch, 3+ papules	1950.3	6 (6.5)	...	...	15.3	2.52
1983[e]	Homs	Sample survey of schools	17.2	RT23 2TU, 10mm+	1983.8	6 (6.5)	1182	11	0.93	0.14
1950[d]	Homs	Mass BCG campaign	0	Moro patch, 3+ papules	1950.6	6 (6.5)	...	...	10.4	1.68
1960[c]	Districts of Homs and Damascus, excluding City of Damascus	Sample survey	9*	RT23 1TU, 10mm+	1960.8	5- 9 (7.5)	387	21	5.43	0.74

V. WHO Western Pacific Region - Region du Pacifique Occidental de l'OMS

Year	Area Represented	Survey design	BCG (%)	Antigen and Infection Criterion	Survey Year Midpt.	Age (midpt.)	Tested N	Infected N	Prevalence (%)	Risk/year (%)
China - Chine										
1979[ab]	Areas without BCG, in whole country except Taiwan	266 of the 888 clusters in the national sample	0	RT23 2TU, 6mm+	1979.5	7 (7.5)	10000*	...	7.3	1.01
Malaysia - Malaysie										
1976-77[a]	Whole country	Sample survey	81-86	RT23 1TU, Mode=15	1977.0	1- 9 (5.5)	1429	29	2.03	0.37
Republic of Korea - Republique de Coree										
1985[ab]	Whole country	Sample survey	65.9	RT23 1TU, 10mm+	1985.5	0- 4 (2.8)	1420	77	5.42	1.97
1980[cd]	Whole country	Sample survey	50.0	RT23 1TU, 10mm+	1980.5	3m- 4 (2.1)	1310	...	4.89	2.36
1975[c]	Whole country	Sample survey	48.2	RT23 1TU, 10mm+	1975.5	3m- 4 (2.1)	1871	...	4.8	2.32
1970[c]	Whole country	Sample survey	...	RT23 1TU, 10mm+	1970.5	3m- 4 (2.1)	...	...	8.5	4.14
1965[cef]	Whole country, 2 strata	Sample survey	6.9	RT23 1TU, 10mm+	1965.5	0- 4 (2.5)	..	..	10.25	4.23
	Urban stratum	at 1 per 1040					994	97	9.76	4.02
	Rural stratum	at 1 per 2220					1383	144	10.41	4.30
Philippines										
1981-83[ab]	Whole country	Sample survey	38.9	RT23 1TU, Mode=14,15	1982.5	2m- 4 (2.1)	2038	78	3.83	1.84
Samoa										
1975[a]	Main island (Upolu)	Sample survey	72.6	RT23 1TU, 10mm+	1975.6	3m- 7 (2.8)	1824	25	1.37	0.49
1966-68[bc]	Whole country	BCG Campaign	...	RT23 1TU, 10mm+	1967.3	0- 9 (5.0)	1710	46	2.69	0.54
1961-63[b]	Whole country	All persons	...	RT23 1TU, 10mm+	1962.5	0- 9 (5.0)	1284	22	1.71	0.35

Symbols: * Estimated .. Not applicable ... Not available

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Tubercle and Lung Disease

Methodological issues in the estimation of the tuberculosis problem from tuberculin surveys

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SUMMARY. Setting: National tuberculin skin test surveys.
Objectives: To review the operating characteristics of the tuberculin skin test, to ascertain the validity of estimating prevalence and risk of infection from tuberculin skin test surveys under various conditions, and to review constraints in the estimation of the magnitude of the tuberculosis problem in the community from such surveys.
Methods: This report utilizes hypothetical and selected real data obtained in regional and national surveys at various points in time to exemplify methodological issues.
Results: Risk of infection, the essence to be abstracted from tuberculin skin test surveys, theoretically allows for a comparison of the extent of transmission of tubercle bacilli in various populations. However, the conduct of tuberculin skin test surveys and the analysis and interpretation of their results are not free from important technical problems. Accurate estimation of infection prevalence is particularly vulnerable to the great variability of the test's specificity under various circumstances. Furthermore, the annual risk of infection has averaging characteristics that preclude a rapid assessment of changes in transmission patterns. Finally, estimates of infection risk do not necessarily provide a standardized parameter to derive incidence of infectious cases, because of variations in the quality of intervention and varying risks of progression from latent infection to overt tuberculosis.
Conclusions: While tuberculin skin test surveys provide the currently most widely used means of assessing tuberculosis transmission patterns over prolonged periods of time in a community, results from such surveys must be interpreted with caution when accurate estimates of the tuberculosis problem are sought.

RÉSUMÉ. Cadre: Enquêtes tuberculiniques nationales.
Objet: Examen des caractéristiques opératoires du test tuberculinique cutané, évaluation de la validité du calcul de la prévalence et du risque d'infection à partir des enquêtes tuberculiniques sous diverses conditions, et finalement revue des contraintes rencontrées dans le calcul de l'ampleur du problème tuberculeux dans la communauté à partir de telles enquêtes.
Schéma: Ce rapport utilise des données hypothétiques ainsi que des données réelles sélectionnées à partir des résultats des enquêtes régionales et nationales effectuées à différentes époques, afin d'illustrer certains problèmes méthodologiques.
Résultats: Le risque d'infection, résultat essentiel des enquêtes tuberculiniques, permet en théorie de comparer l'importance de la transmission des bacilles tuberculeux dans différentes populations. Cependant la réalisation des enquêtes tuberculiniques ainsi que l'analyse et l'interprétation des résultats n'échappent pas à des problèmes techniques importants. Le calcul précis de la prévalence de l'infection est particulièrement soumis aux variations importantes de la spécificité du test dans différentes situations. De plus le risque annuel d'infection reflète une 'moyenne' des évènements passés qui empêche toute évaluation rapide de modifications dans les données de transmission. Finalement, les calculs du risque d'infection ne fournissent pas toujours un paramètre standardisé dont on puisse en extraire l'incidence des cas infectieux, en raison des variations liées à la qualité de l'intervention et à la variabilité du risque de progression de l'infection latente vers une tuberculose maladie.
Conclusion: Bien que les enquêtes tuberculiniques fournissent la méthode la plus utilisée à l'heure actuelle pour évaluer les caractéristiques de transmission de la tuberculose à travers de longues périodes dans une

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communauté, on devrait interpréter les résultats de telles enquêtes avec prudence quand il s'agit d'obtenir une estimation précise du problème tuberculeux.

RESUMEN. Marco de referencia: Encuestas tuberculínicas nacionales.
Objetivos: Revisar las características operativas del test cutáneo de tuberculina, determinar la validez de la estimación de la prevalencia y del riesgo de infección a partir de las encuestas tuberculínicas bajo diversas condiciones, y revisar las dificultades en la estimación de la magnitud del problema de la tuberculosis en la comunidad a partir de tales encuestas.
Método: Este informe utiliza datos hipotéticos y una selección de datos reales obtenidos de encuestas regionales y nacionales en diversos lugares y períodos a fin de ejemplarizar los problemas metodológicos.
Resultados: El riesgo de infección, resultado esencial de las encuestas tuberculínicas, teóricamente permite la comparación de la extensión de la transmisión del bacilo tuberculoso en las diversas poblaciones. Sin embargo, la conducción de las encuestas tuberculínicas y el análisis e interpretación de sus resultados no están exentos de importantes problemas técnicos.

La estimación precisa de la prevalencia de la infección es particularmente vulnerable a la especificidad del test bajo diversas condiciones. Además, el riesgo anual de infección representa un promedio a un momento dado, lo que impide una rápida evaluación de los cambios en los patrones de transmisión. Finalmente, la estimación del riesgo de infección no proporciona necesariamente un parámetro estándar para calcular la incidencia de los casos infeccionsos, a causa de las variaciones de la calidad de la intervención y de la variabilidad del riesgo de progresión de la infección latente a la enfermedad tuberculosa.
Conclusiones: A pesar que las encuestas tuberculínicas constituyen el medio más ampliamente utilizado para evaluar los patrones de transmisión de la tuberculosis en períodos prolongados en una comunidad, los resultados de cada encuesta deben ser analizados con precaución cuando se requiere una estimación precisa del problema de la tuberculosis en una comunidad.

INTRODUCTION

The most desirable method of ascertaining the current extent of transmission of tubercle bacilli in a society would be to measure the incidence of infection with *Mycobacterium tuberculosis* in susceptible persons. Measuring the incidence of infection is, however, a Herculean task. It requires repeat testing of a large enough number of persons to identify with reasonable precision the few who become newly infected over a specified period of time. Furthermore, the incidence of infection varies across various subpopulations, e.g. various age groups in the same calendar year,[1] and when estimates are based on repeat testing of the same individual both boosting reactions[2] and reversion of initially positive tuberculin skin test reactions[3] may greatly affect the accuracy of the estimates. Some of these problems can be partially overcome through approximation by calculating the average probability that a person has become infected over a specified period of time from a tuberculin skin test prevalence survey in a population which has not been subjected to previous tuberculin skin testing or vaccination with BCG. Detailed technical guidelines on how to conduct such a survey have been published.[4,5]

The purpose of this paper is to highlight methodological issues relevant to the analysis and interpretation of tuberculin skin test survey data and their relation to the tuberculosis problem in the community. Many of the problems have been recognized for quite some time,[6] while other aspects challenge existing concepts and are addressed here to further the discussion on how to critically appraise the meaning of data generated in tuberculin skin test surveys.

TEST CHARACTERISTICS

Each test has its own intrinsic operating characteristics. The sensitivity of the test is the proportion accurately identified by a positive test result among persons with a characteristic in question, while the specificity represents the proportion with a negative test result among persons without that characteristic.[7] A multitude of tuberculin skin test techniques has been developed in this century, but the Mantoux technique is the most quantifiable and, in conjunction with other information, theoretically allows the determination of the sensitivity and specificity of the test at different cut-off points.

In the early 1950s the World Health Organization (WHO) collected information on tuberculin sensitivity in over 3600 hospitalized tuberculosis patients in 10 different countries.[8] The combined results closely fit a normal distribution with a mode at 16–17 mm. The sensitivity in identifying infection with *M. tuberculosis* calculated from this survey is 93% for an induration ≥ 10 mm and 78% for an induration ≥ 14 mm. Similar normal distributions were found in healthy persons in areas with a very low frequency of small reactions[6,8,9] and among healthy United States Navy recruits who had a history of exposure to tuberculosis.[10] In the latter survey, a mode was identified at 18–19 mm and the calculated sensitivities for ≥ 10 mm and ≥ 14 mm were 94% and 75% respectively (Table 1).

Thus, the sensitivity of the tuberculin skin test appears to vary relatively little when different populations are compared, except when cellular immunity is seriously compromised. However, as the tuberculin surveys sponsored by the WHO demonstrate,[9] sensitization to envi-

Table 1. Sensitivity and specificity of the tuberculin skin test in United States Navy recruits, using two commonly used cut-off points as indicating the presence of infection (calculated from Tables 1 and 3)[10]

Test criterion	Sensitivity (%)	Specificity (%)
≥ 10 mm	94.2	98.6
≥ 14 mm	74.9	99.5

ronmental mycobacteria apparently varies considerably in different countries, making the specificity of the test unpredictable, and thus the underlying normal distribution attributable to tuberculous infection difficult to ascertain.

Figure 1 shows a hypothetical distribution of tuberculin skin test reaction sizes. Three distributions influence the composite picture that can be ascertained: (1) the distribution among persons without any mycobacterial infection or with skin test anergy, usually not exceeding a few millimeters (thick dotted line); (2) the distribution among persons with tuberculous infection (thin dotted line, shown here with a mode at 17 mm); and (3) the distribution among persons sensitized to mycobacteria other than tubercle bacilli who cross-react with tuberculin PPD (dashed line shown here with a mode at 7 mm). It is apparent that in this example at a cut-off point of 14 mm some true infections will be missed (*c*) and some will be falsely counted (*b*), the latter because they are attributable to non-specific sensitization. In fact, as shown in this example, this observation pertains, albeit to a different degree, to any cut-off point to indicate presence or absence of infection with *M. tuberculosis* between 4 mm and 21 mm. It is thus apparent that cut-off points are compromises to balance false positive and false negative reactions to still obtain the right prevalence, although individuals themselves are misdiagnosed. Tuberculin prevalence surveys in numerous countries have clearly shown that sensitization to environmental mycobacteria is virtually absent in some, but abundant in other countries, and that the relative magnitude of the distribution due to environmental mycobacteria (and/or sensitization due to BCG vaccination) and the magnitude of the distribution due to tubercle bacilli may vary considerably, even within the same country.[6,9-18] Vaccination with BCG itself appears to induce cross-reactivity with tuberculin PPD to a variable extent.[19-23]

Rust and Thomas have developed a model based on tuberculin skin test data in 700 000 United States Navy recruits.[10] By asking about known history of exposure to a tuberculosis case in the same household they separated people into contacts and non-contacts. This allowed a separation of the influences of reactions caused by environmental mycobacteria from those resulting from infection with tubercle bacilli and the development of a model predicting probabilities of tuberculous infection at various cut-off points. These data thus allow the calculation of the specificity of the tuberculin skin test using various cut-off points in the setting of the United States (Table 1).

Even if it is assumed that the frequency of cross-sensitivity reactions is constant (which is clearly not the case),[6,9,12,13] and therefore that the specificity of the tuberculin skin test is unchanged and the information from Rust and Thomas applicable, the predictive value of a significant tuberculin test reaction ($a/(a+b)$ in Fig 1) would be extremely sensitive to variations in prevalence of infection with tubercle bacilli (Table 2). If the inci-

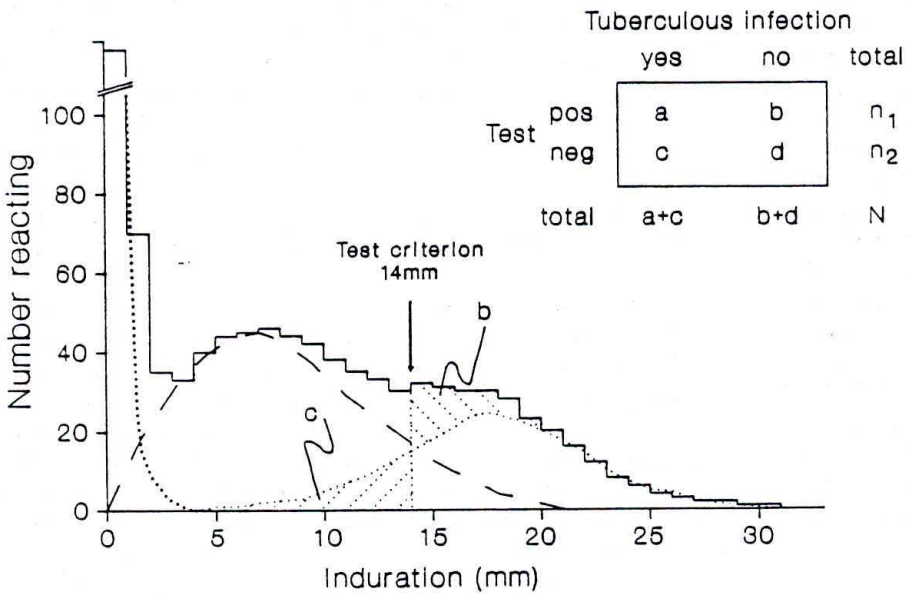

Fig. 1 Example of the distribution of diameters in a tuberculin skin test survey. The distribution of non-specific reactions is shown under the dashed curve, the specific distribution under the dotted curve. The hatched area, labelled *b*, indicates the number of reactions falsely counted as infection using a criterion of ≥ 14 mm to indicate infection, the hatched area, labelled *c*, indicates the infections missed by that criterion. The number of positive reactions (n_1) is found to the left of the test criterion; the number of negative reactions (n_2) is found to its right.

Table 2. Predictive value of a positive test using ≥ 14 mm as indicating infection, assuming (from Table 1) a specificity of 98.6% and a sensitivity of 94.2% with a cut-off of ≥ 10 mm, and specificity and sensitivity of 99.5% and 74.9% respectively using a cut-off of ≥ 14 mm in a population with a prevalence of infection of 0.28% and 10.0% respectively

Prevalence (%)	Predictive value of a positive test result (%)	
	Criterion ≥ 10 mm	Criterion ≥ 14 mm
0.28	15.9	29.6
10.0	88.2	94.3

dence of infection is assumed to be constant at 1% over calendar time and infection risk independent of age, then the expected true prevalence of infection with *M. tuberculosis* in children aged 10.5 years will be 10%. In an industrialized country, where the current risk of infection might be 0.015%, and the decline in risk of infection has been in the order of 10% per year, the expected prevalence of infection in children of the same age is 0.28%. Using these examples, in a country with a low prevalence of infection, a cut-off point of 10 mm indicating infection with *M. tuberculosis* would falsely classify 84.1% of children thus identified as 'infected', with a reduction in mis-classifications to only 70.4% using a cut-off point of 14 mm and more. In a country with a high infection prevalence, the test would falsely classify only 11.8% or 5.7%, using 10 mm or 14 mm induration respectively to indicate infection. It is thus apparent that tuberculin skin test surveys in low infection prevalence countries will almost always preclude meaningful interpretation, unless environmental mycobacteria are of such little importance that the specificity of the test approximates 100% even at low cut-off points. It seems nevertheless that information may be useful in countries with an elevated prevalence of infection.

The commonly used cut-off points of 10 mm and 14 mm, the latter customarily corrected by dividing by 0.82,[11,24] take the sensitivity into account, assuming that with a 10 mm cut-off point virtually all true infections are included, but only about 82% with a cut-off point of 14 mm. The sensitivity of 82% for a cut-off of ≥ 14 mm to indicate infection is a slight overestimation, because in the tuberculin survey in Tanganyika that produced this figure it was assumed that all reactions ≥ 10 mm were 100% specific in two areas with relatively few cross-reactions, which was nevertheless not quite the case.[11] Applied to areas with any non-specific cross-reactions, these criteria have the disadvantage that they do not account for the loss of specificity, a loss that increases the further one moves from the mode of the distribution from tuberculous infection towards the left into increasing contamination by non-specific reactions. Thus, the correction for sensitivity alone will invariably overestimate the prevalence. This is shown in Figure 1, where, to enumerate the infected among those with ≥ 14 mm induration, instead of using $(a+c)$, $(n_1)/[a/(a+c)]$ or $(n_1)/(0.82)$ is erroneously calculated by this technique. Unfortunately, without *a priori* knowledge of both sensitivity and specificity, the proportion of mis-classifications can not be known.

Another technique to estimate prevalence assumes an underlying normal distribution of reactions due to infection with *M. tuberculosis*. This mirror technique attempts to identify the mode, multiplies the number of reactors above the mode by two and adds the number of reactors at the mode to arrive at the number of infected persons. Although the mirror technique partially circumvents the problem of test specificity, the precision of the estimate is by necessity poorer and requires the testing of a much larger number of persons to improve the estimate. Furthermore, using the mirror technique approach, the calculation of infection prevalence is very sensitive to the selection of the location of the mode. If, for example, in Figure 1 the mode is selected to be at 17 mm then the calculated prevalence of infection is 13.7%; if the mode is selected to be at 18 mm, the estimated prevalence of infection is 10.9%, or 20% less.

If the sensitivity (denoted as x) and the specificity (denoted as y) are both known for a certain cut-off point then the calculation of the prevalence is easily done. There are four unknowns (a, b, c and d, see Fig. 1) that can be solved with the four following equations, because n_1 (denoted as the number with a positive test result, i.e. $a+b$) and n_2 (denoted as the number with a negative result, i.e., $c+d$) are defined:

$$a = n_1 - b \qquad \text{eq. (1)}$$

$$b = d/y - d \qquad \text{eq. (2)}$$

$$c = a/x - a \qquad \text{eq. (3)}$$

$$d = n_2 - c \qquad \text{eq. (4)}$$

These equations can be used to solve, e.g., for a:

$$a = \frac{(n_1 + n_2)\,xy - n_2 x}{(x + y - 1)}$$

or any other cell.

EXAMPLES OF TUBERCULIN SKIN TEST SURVEYS

A large tuberculin skin test survey is being carried out in Tanzania under the auspices of the Tuberculosis Surveillance Research Unit of the International Union Against Tuberculosis and Lung Disease. This survey is conducted in 5-year cycles; it encompasses the entire country and is carried out by professional staff, trained by the International Tuberculosis Surveillance Centre. Figures 2 and 3 show the survey data from 1991 from 3 regions (chosen for convenience) combined (Dodoma, Mbeya, and Morogoro) of children with and without BCG scar respectively (reproduced with the permission of the Tanzania National Tuberculosis/Leprosy Programme).[25] Clearly, neither distribution allows rapid identification of the proportion of the proportion infected with tubercle bacilli.

In Figure 3, a mode is proposed (arbitrarily) at 18 mm, allowing for construction of a mirror image of the suspected underlying distribution. Although the mirror image technique accounts for the loss in sensitivity at this

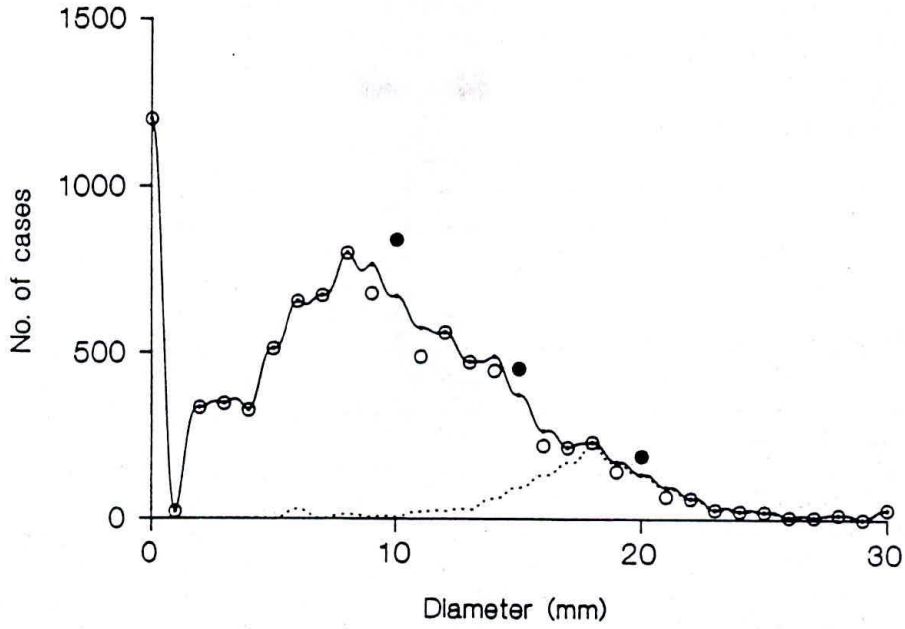

Fig. 2 Measured distribution of tuberculin skin test reaction size diameters in Tanzania 1991 (Dodoma, Mbeya, and Morogoro regions) among children with BCG scar. Large circles are recorded data, filled circles emphasize digit preferences at 10 mm, 15 mm and 20 mm. Points are values linearly adjusted for digit preference (one neighbour only to each side). Line is fitted through adjusted values by inverse squared distance smoothing. Area under dotted line indicates probable true infection with *Mycobacterium tuberculosis*. For better display, the number with 0 mm reaction (10 240 children) has been cut off. (reproduced with the permission of the Tanzania National Tuberculosis/Leprosy Programme).[25]

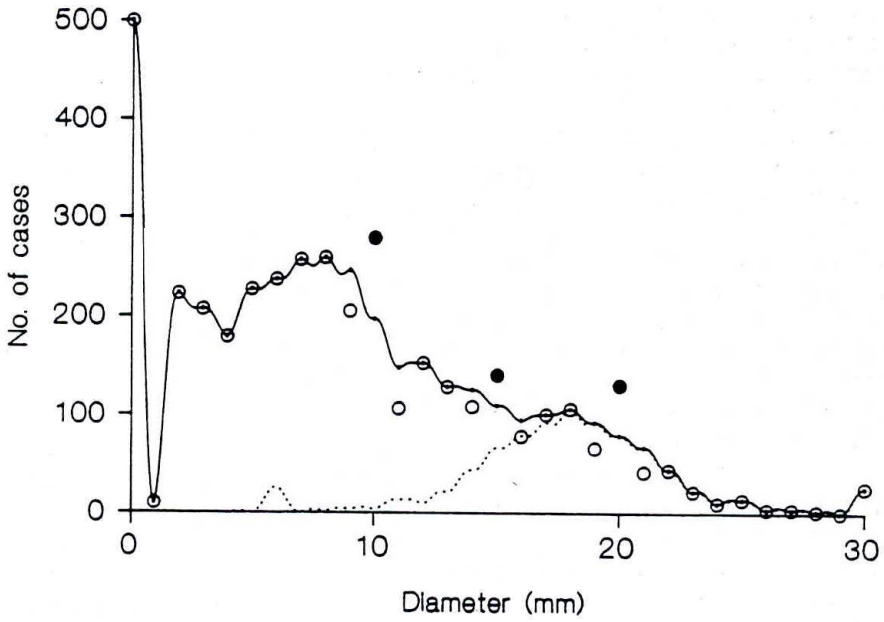

Fig. 3 Measured distribution of tuberculin skin test reaction size diameters in Tanzania 1991 (Dodoma, Mbeya, and Morogoro regions) among children with no apparent BCG scar. Large circles are recorded data, filled circles emphasize digit preferences at 10 mm, 15 mm and 20 mm. Points are values linearly adjusted for digit preference (one neighbour only to each side). Line is fitted through adjusted values by inverse squared distance smoothing. Area under dotted line indicates probable true infection with *M. tuberculosis*. For better display, the number with 0 mm reaction (7210 children) has been cut off. (reproduced with the permission of the Tanzania National Tuberculosis Leprosy Programme).[25]

diameter, the figure suggests that even at this diameter some reactors are still likely to be falsely classified as being infected. Here, the mode was assumed to be at 18 mm and the calculated infection prevalence was 7.9%. Had a mode been selected at 17 mm, the prevalence calculated with the same technique would be 9.8%, 24% higher than with a mode at 18 mm.

Figures 2 and 3 also demonstrate that even experienced readers clearly have a preference for certain digits (shown as full circles at 10 mm, 15 mm, and 20 mm). It would thus be difficult to use a cut-off point of 20 mm or an immediately neighboring value and account algebraically for the loss of sensitivity for the sake of gaining specificity.

Figure 4 shows the results of two tuberculin surveys in Korea conducted 25 years apart with the same technique utilizing 1 TU PPD RT23 in children aged 0–9 years.[26] It demonstrates that a large decrease in infection prevalence fundamentally changes the interpretability of a tuberculin survey in a country even if it has a relatively small contribution from sensitization with environmental mycobacteria. In 1965, the relative contribution of non-specific sensitization was negligible and did not preclude a clear dichotomization between those infected with tubercle bacilli and those not. While the absolute magnitude of non-specific reactions in 1990 was apparently similar to that in 1965, their relative contribution to the overall distribution had become very important by 1990, because true prevalence had declined to very low levels, making it exceedingly difficult to separate the infected from the non-infected. The ratio of reactions attributable to environmental mycobacteria to those resulting from infection with *M. tuberculosis* had inverted to an extent that the mode had shifted to the left (Fig. 4).

CALCULATING THE RISK OF INFECTION FROM PREVALENCE DATA

Assuming that the prevalence of infection with *M. tuberculosis* has been satisfactorily estimated, the essence to be extracted from the data is the estimation of the average annual risk of infection. The annual risk of infection refers to a risk at a specified calendar time $b+x$, where b indicates the calendar time at which the cohort in the survey was born and x is a number between 0 and a, where a is the age of the cohort at calendar time $b+a$, the time when the survey was conducted. It cannot be known at exactly what calendar time this risk existed without inferences from serial surveys.[1,27] Because the risk may change over calendar time, x has been approximated to lie at the midpoint between the year the cohort was born and the year the survey was conducted, if data from a single survey only are available:[1,28]

$$R_{b+a/2} \approx 1 - (1 - P_{b+a})^{1/a},$$

where $R_{b+a/2}$ denotes the annual risk of infection at the midpoint in calendar time between the year the cohort was born and the year of the survey, and P_{b+a} the prevalence of infection at the time of the survey, where both risk and prevalence are expressed as fractions. Thus, if the prevalence of infection among 10.5-year-old children is found to be 10% at the midpoint of the survey (assumed to be in, for example, the end of June 1993, i.e. 1993.5) then the risk of infection is:

$$R_{1988.25} \approx 1 - (1 - 0.1)^{1/10.5} = 0.010,$$

i.e. 1% at the approximated calendar time the end of March 1988. The estimate of $b+x$ can be improved from the first approximation of $b+a/2$ only if serial surveys are available.[27] Serial estimates, only if closely fitting a calculated regression, allow extrapolation to current infection risk.

Two sequential surveys alone a few years apart will not necessarily provide information on the change in infection risk because of the problems associated with the comparison of cross-sectional data across time. If it is assumed that an earlier survey, e.g. conducted in 1988, had also provided an estimated average annual risk of infection of 1% (approximated at calendar time 1983), then the conclusion is not necessarily warranted that the risk of infection has remained unchanged over calendar time up to the time of the second survey in 1993. It may well be that the risk decreased in the first years after the birth of the second cohort, perhaps because an efficient programme for identifying and curing cases spreading infection was implemented, but subsequently the number of infectious cases began to increase because

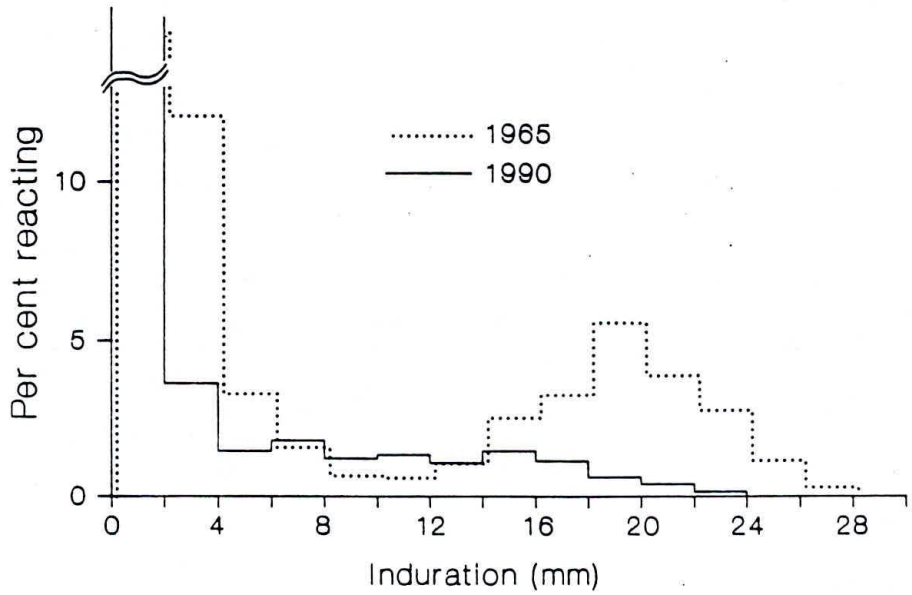

Fig. 4 Frequency distribution of tuberculin skin test reaction sizes among children aged under 10 years, Korea 1965 and 1990. Reproduced with permission.[26]

of increasing prevalence of infection with the human immunodeficiency virus (HIV) among persons with tuberculous infection, leading to an increasing number of transmitters and thus an increased risk of infection in the community. It may just be that the net effect of an initial decline, followed by an increase in infection risk, resulted in no change in infection prevalence.

RISK OF INFECTION AND INFECTIOUS CASES

It is apparent that the rate of transmission of tubercle bacilli is related to the number of sources of infection in a society. The number of successful transmissions by infectious cases to a susceptible population over a defined period of time (usually one year) at a certain calendar time defines the risk of infection in the community during that period. Utilizing the results from a series of WHO sponsored surveys in low income countries and the results of surveys in the Netherlands before chemotherapy, Murray et al correlated annual risk of infection to incidence of tuberculosis by linear regression and obtained an estimate of approximately 50 incident sputum smear-positive cases for each 1% of annual risk of infection.[29] This correlation must be interpreted with caution. The authors performed least squared regression and were thus unable to account for changes in the variance with sample size. More importantly, the authors assume that for areas where information on the incidence was lacking, the incidence was half the prevalence.[29] This is, however, precisely the hypothesis that has to be proven, if a relation between infection risk and incidence rather than person-time of infectiousness is to be demonstrated.

Infection risk is intrinsically coupled to duration of undiagnosed, untreated transmissible tuberculosis, thus with person-time of infectiousness in the community. Intervention with chemotherapy has as its epidemiological aim to reduce the rate of transmission, and where this form of intervention encompasses effectively and efficiently a large proportion of the population, the average duration of infectiousness connecting prevalence and incidence becomes fundamentally changed. Prevalence of infectious tuberculosis thus might correlate better with infection risk than incidence. Nevertheless, it has been pointed out that in countries without a structured programme, the number of infectious (sputum smear-positive) patients remains essentially the same after 2 years with or without such intervention, because the main gain with such intervention lies with a reduction of case fatality at the expense of keeping infectious cases alive.[30] Conversely, in countries where intervention effectively cuts the chain of transmission, the number of transmissions caused by one case will be reduced. Thus, to produce a 1% risk of infection, a larger number of incident cases is required, because the person-time of infectiousness is reduced. This has been shown, for example, for the United States before HIV noticeably affected tuberculosis. In that country, extrapolation would have required some 400 incident cases per 100 000 population to result in 1% risk of infection in the early 1980s,[31] some 8 times the number predicted by the model outlined above.[29]

Furthermore, the risk of tuberculosis following infection with *M. tuberculosis* may vary in different populations. It is certainly increased in persons with HIV infection compared to immunocompetent hosts. Thus, the epidemiological balance usually observed between host and bacillus is no longer present under these circumstances where each case of tuberculosis may produce more than one new infectious case in the HIV-infected segment of the population.

SUMMARY AND CONCLUSIONS

Theoretically, the incidence of infection is epidemiologically the most informative parameter, because it identifies the extent of current transmission in the community. It is usually not feasible to measure infection incidence, and the derivation of the average annual risk of infection from a tuberculin prevalence survey as a proxy has become one of the most cherished tools in tuberculosis epidemiology. Unfortunately, tuberculin skin testing is fraught with problems of a technical nature, including selection of standardized tuberculin, the technique of administration, and reading of the test result. Even if all of these barriers are overcome, it is in many circumstances exceedingly difficult to arrive at an estimate of the prevalence of infection. Sensitization to environmental mycobacteria and *M. bovis* BCG results in cross-reactions with the standard tuberculin. The higher this sensitization is and the lower the prevalence of true infection with tubercle bacilli, the more difficult it becomes to disentangle the truth from confounding factors. It is clear that techniques must be developed to address the problems of interpretation that arise in so many countries which have completed a tuberculin skin test survey. It remains to be determined whether simultaneous testing with different antigens, algebraic manipulation or other approaches can help to overcome some of the apparent shortcomings of tuberculin skin test surveys. Because sensitivity is already largely known for various cut-off points, it appears that the most promising approach would lie with an attempt to determine the specificity of the tuberculin test at a given cut-off point in a country planning a tuberculin skin test survey using different antigens.[14–18] This would help greatly in improving the validity of the results of a tuberculin skin test survey.

The calculation of the risk of infection (should the determination of infection prevalence be successful) from a single or even two sequential surveys provides only information on the extent of transmission at some point in the past, determined by the age of the children that have been tested. The tool is not sensitive to short-term changes, because of its 'averaging' characteristic.

The knowledge of risk of infection cannot precisely

provide information on the number of expected incident cases of tuberculosis; it can only state to what extent such cases are capable of transmitting tubercle bacilli within the community, which is a function of the number of infectious cases, the number of case-contact interactions, the duration of infectivity, and characteristics of exposure.

The determination of the risk of infection has nevertheless been regularly used to compare the extent of the tuberculosis problem in various populations. It is, if technically interpretable, the only available means of measuring the extent of transmission that has occurred, on average, over specified periods of time in the past. The common underlying technical problems will often undermine the precision in estimating the size of the tuberculosis problem in a community from a single survey. It can be useful for global estimates of the level of the tuberculosis problem in a community and of trends over relatively long periods of time. The observation of trends in prevalence or risk of infection over time is by far more informative than a single survey, because the change in slope might be freer from bias than the level of the intercept. A consistent recession of age prevalence curves, as observed for example in the 6 five-yearly Korean prevalence surveys,[26] is enough to convince that the risk of infection has been declining. However, any formal estimation of a change in the risk of infection within a certain precision may be impossible to assure.

To move forward in gaining a better understanding of the intricacies in estimating the tuberculosis problem in a community from tuberculin skin test survey data requires a concerted effort on the part of researchers in the field to address the various issues and problems encountered in the conduct of such surveys and the interpretation of their results.

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Re-examining the Annual Risk of Infection as a Monitoring Tool

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Tuberculosis has now been widely appreciated as one of the most important causes of ill health and mortality in the developing world. WHO is spearheading a global effort to combat tuberculosis using short-course chemotherapy which has been adopted by an increasing range of countries. Monitoring the epidemiological trends in tuberculosis has become increasingly essential. While tuberculosis kills more than 2 million a year, the clinical disease is relatively uncommon in the population. Typical developing countries experience incidence rates of 100 cases per 100,000 per year. Measuring the prevalence of such an uncommon disease requires large sample sizes which are perforce costly. Even if the effort is made to survey prevalence, programs require information or estimates of incidence to monitor the evolution of the disease because treatment programs can radically alter the relationship between prevalence and incidence.

While disease is rare, infection is extremely common. WHO estimates that 32.8 percent of the world is infected (Sudre et al. 1992). Skin testing with PPD has been providing information on the prevalence of infection for nearly 90 years. The interpretation of these prevalences, however, was limited (Sutherland 1976). In the 1960's, the Tuberculosis Surveillance Research Unit (TSRU) refined methods of estimating the annual risk of becoming infected with tuberculosis based on the prevalence of past infection from skin test data (Styblo et al. 1969) . This major breakthrough in tuberculosis epidemiology has become the mainstay of epidemiological monitoring in developing countries and Europe (Styblo 1976, ten Dam 1985, Bleiker 1991). Recently, a number of individuals and events have challenged the dominance of ARI as a tool for monitoring the epidemiology of tuberculosis (e.g.Reider 1995).

The objective of this paper is to review the basis for the TSRU method of estimating the ARI and the relationship between ARI and other epidemiological indices of tuberculosis. The method of estimating the ARI from PPD skin test prevalence data and estimating the incidence of tuberculosis on the basis of the ARI is founded on four key premises. First, one can distinguish the infected from the non-infected at the population level using induration size. Second, when the ARI is changing, it declines or increases exponentially overtime. Third, the ARI does not vary with age or at least does not vary over the ages 0-14. Fourth, there is a close relationship between the ARI and incidence of smear-positive tuberculosis. In this paper, we will re-examine the evidence supporting each of these four premises, explore some new findings and speculate on the impact of other changes on this approach to monitoring tuberculosis.

Distinguishing Infected from Non-infected Using PPD Skin Tests

The ARI method depends critically on the ability to estimate the prevalence of past infection in a given population using PPD skin test results. Measuring the prevalence of past infection is complicated by several issues: skin test reversion, the sensitivity and specificity of different cutoffs of induration size used to define infection, and the impact of BCG on skin test interpretation. Each of these issues will be addressed in turn.

Sutherland (1971;1976) argued that if skin test positives will revert to being skin test negative at a low rate, 1-2% per year, this would not have a significant effect on the estimation of the risk of infection based on the prevalence of positive skin test reactions. Felten and Van Der Merwe (1989) showed that children with skin test reactions greater than 15mm had an average decrease in induration size of 3.6mm on the second test given an average of 262 days later. Such variability on skin test response may mean that reversion rates could be substantially higher than 1-2% per year. If skin test reversion occurs at higher rates then risk estimated from the prevalence of positive skin tests is likely to be underestimated.

For any test, the starting point for discussing the test should be its sensitivity and specificity. Sensitivity of PPD skin tests for detecting infection with M.tuberculosis has been studied by examining characterics of the test in patients with clinical tuberculosis who are therefore knwon to be infected. Depending on what dose of PPD and type that is used and where it is given, those infected with M.tuberculosis develop an induration that is normally distributed with a mode between 14 and 20mm. The sensitivity of the PPD skin

test for detecting M.tuberculosis infection, therefore, depends on the induration size used to define infection. Table 1 summarizes the sensitivity of a 5TU dose of PPD in ten populations included in a collaborative WHO study in the 1950s (WHO Tuberculosis Research Unit 1955) and two other large studies (Edwards and Edwards 1960; Palmer and Bates 1952)using an induration cutoff of 10mm.

In population surveys where exposure to atypicals is low, there is usually a mode somwhere between 14 and 20 mm representing the infected population (Nyboe). Figure 1 illustrates the distribution of induration size in Korea in the 1965 prevalence survey for those that are BCG scar-negative. There is a clear mode at 18 and antimode at 9-11mm. In such cases, the proportion of the population with an induration greater than the antimode will be a reasonable estimate of the prevalence of infection, even without making an estimation of the sensitivity of the antimode as a cutoff because the small number of false negatives are likely to be balanced by a small number of false positives.

In environments such as the South of the United States where individuals are exposed to atypical mycobacteria, many individuals develop a non-specific reaction to PPD which is larger than the small reaction that some have to the trauma of the Mantoux test. Unfortunately, the induration size of this non-specific reaction may overlap with the induration size of those with a specific reaction due to past exposure to M.tuberculosis. Figure 2 shows the distribution of induration size for white male Navy recruits resident in the United States throughout their life aged 17-21 during the years 1961 to 1968. In this population, the mode at 4 mm is due to non-specific reactions to PPD and there is no clear mode above 10 mm due to specific reactions. In essence, this population is a mixture of three groups, those who are uninfected with M.tuberculosis or atypicals, those exposed to atypical mycobacteria and those infected with M.tuberculosis.

The problem of determining the prevalence of infection in a population made up of these three groups is much more difficult because the proportion with an induration size above a certain cutoff will be a function of 5 factors: the sensitivity of the cutoff to detecting tuberculosis infection, the sensitivity of the cutoff to detecting past exposure to atypical mycobacteria, the specificity of the cutoff for those uninfected and unexposed to aytpical mycobacteria, the prevalence of exposure to atypicals and the prevalence of M.tuberculosis infection. Even if the sensitivities and specificities were known, the results of the test cannot be used to simoultaneously estimate the prevalence of atypical exposure and the prevalence of infection without supplemental information.

Four alternatives have been proposed to try and estimate the prevalence of infection even in settings where the prevalence of exposure to atypicals is moderate to high and/or BCG coverage is high (see below) so that false positives may exceed false negatives when using an arbitrary cutoff. Rust and Thomas (1975) developed a method to estimate the proportion of the Navy recruits skin tested from 1958-1969 that are infected making use of the information collected on a history of a known contact with a case if tuberculosis. In their method, they take advantage of having two.populations, contacts and non-contacts, where the proportion of infected and non-infected are likely to be quite different but the prevalence of exposure to aytpicals is likely to be the same to estimate the prevalence of infection.[1] The only critical

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[1] Rust and Thomas use the following equations to find the infection prevalences among contacts and noncontacts:

$$P = \frac{f_n(f'_0 - f_0)}{f_n f'_0 - f'_n f_0},$$

$$P' = \frac{f'_n(f'_0 - f_0)}{f_n f'_0 - f'_n f_0},$$

assumption required for their method is the induration size above which everyone is infected with tuberculosis which they assume is 22 mm. Table 2 shows the results of applying their method to data for different ethnic groups using induration sizes above which everyone is presumed infected from 16 to 26mm. Estimated prevalence ranges from 2.2% to 1.8% for this range of induration sizes in this population. The method proposed by Rust and Thomas could be generalized to any situation where two groups in whom the prevalence of atypical exposure will be similar but the prevalence of M.tuberculosis infection will differ. Such information whether by contact status or some other differentiating variable such as socio-economic status is at present rarely available in most skin test surveys.

Second, various investigators have tried to test individuals with other sensitins, PPD like products derived from other mycobacteria (e.g. Edwards et al. 1969). These efforts, however, have not been successful at increasing the ability to distinguish true infection with M.tuberculosis with non-specific reactions due to aytpical mycobacteria (ten Dam 1985).

Third, other efforts at using second PPD tests with or without concomitant BCG have been proposed and applied in in few situations (Raj Narain et al. 1966, Lotte et al. 1971, Liard et al 1989, ten Dam and Hitze 1980). While these methods are interesting they require repeat surveys at an interval between 2 months to 12 months and thus are much more costly to deploy. These methods have not been widely applied.

Fourth, Bleiker et al. (1989) suggest that the mode of those with a specific reaction will lie between 14 and 18mm. As the distribution of those with a specific reaction to PPD are often normally distributed, a reasonable estimate of the prevalence of infection can be obtained by doubling the proportion with an induration over the expected mode of those with a specific reaction. In the USA Navy recruit data, using 18mm instead of 16mm as a cutoff, lowers prevalence for white resident male Navy recruits 1961-1968 from 3.13% to 2.18%. Using results from 30 PPD skin test surveys, Figure 3 compares the prevalence of infection estimated using the two times mode method with the antimode method in the age-group 0-14. In this dataset, the two times mode method gives higher estimates of prevalence than the antimode method. This results may be because the mode of the specific reactions may not be the median of specific reactions because of small sample sizes.

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where

P = prevalence of infection in contacts,

P' = prevalence of infection in noncontacts,

f_0 = proportion of contacts with zero reaction,

f'_0 = proportion of noncontacts with zero reaction,

and

f_n = proportion of contacts in category n,

f'_n = proportion of noncontacts in category n,

for reaction size category n in which all individuals are assumed to be infected.

The combined prevalence for contacts and noncontacts is found by taking the weighted average of P and P'.

In communities where the mode of the specific reactions to PPD cannot be derived from the distribution of induration size, estimated prevalence will be sensitive to the arbitrarily chosen 'mode' (14-20 mm) used. On the other hand, when serial observations are made of prevalence are made in the same population, it may be safe to assume that the mode is stable. It can be shown with simulations (not shown here) that the estimated time trend in the ARI will not be very sensitive to the arbitrary mode chosen for doubling.

The impact of BCG on the Estimation of the Prevalence of Infection

Because BCG immunization can cause an induration with PPD that is difficult to distinguish from M.tuberculosis infection, the rising global prevalence of BCG -- UNICEF estimates coverage exceeds 80% in all regions-- poses a serious challenge to using PPD skin surveys to estimate the ARI. Faced with a large proportion of children that are BCG immunized, there are two strategies for estimating the prevalence of infecteds. The first is to calculate prevalence only in those children that are BCG scar-negative. This method suffers from four problems. First not all children given BCG may develop a scar. Second, BCG scars have been found to wane; the National Tuberculosis Insititure of India (1992) found that of 49 3-4 year olds found to have a BCG scar, 11 or 22.4% had no scar on examination 21.6 months later. Thus, with rising BCG vaccination rates, the BCG scar-negative group may include increasing numbers that have received BCG and thus are more likely to have an induration greater than some arbitrary cutoff. It remains to be seen if scar waning rates are this high in other populations. Third, as BCG coverage has risen over 90% in many countries, there is an ever growing likelihood that the BCG scar-negative children are not representative of the entire population. Fourth, as BCG coverage increases the number of children that must be screened to find a large enough sample to test will increase raising the costs of surveys. Despite these difficulties, the method remains the standard approach.

The effect of BCG on subsequent PPD skin tests is a complex function of the age at which BCG was received, the number of times the individual has been PPD tested in the past, the time since immunization, the strain of BCG used and other factors (Al-Kassimmi et al. 1991;Capewell and Leitch 1986; Friedland 1990; Guled et al. 1968; Joncas et al. 1975; Menzies and Bissandjee 1992; Shaaban et al. 1990; Snider 1985). Most of these studies show that the effect on skin test positivity can be exceedingly hard to predict in settings where BCG is given over a wide range of years and individuals are often PPD tested. On the other hand, Menzies and Vissandjee (1992) show that in Quebec when BCG is given at birth or at least before 1 and individuals have not been PPD tested before, the effect of BCG on induration size is negligible after 7 years or less. Because the strain of BCG used in Quebec is local, it is unclear if this result can be generalized. Despite extensive study, it is difficult at this point to generalize on how skin test reactions in the BCG scar positive population can be meaninfully interpreted.

The restesting methods discussed above can also be used to try and distinguish true infection from BCG induced induration but they have not been widely applied. Another possibility is the recent developmental work has yielded new antigens that may be allow one to distinguish M.tuberculosis infection from BCG infection. MPB64 is one of the more promising that is now being tested (Nagai et al. 1991, Li et al. 1993). The development of new or improved skin tests with greater specificity would allay many concerns about the interpretation of skin test data.

Review of ARI Equations

Styblo et al. (1969) developed a model whereby prevalence of infection in a given age group could be used to calculate the ARI. In the technical appendix, these equations are re-derived in detail and only the summary results presented in this section. Styblo et al.(1969) argued based on logic and empirical observations of the prevalence of infection in Dutch military recruits that the ARI changes exponentially overtime. To further simplify their model, they assumed that ARI is not a function of age, thus:

$$\lambda(t) = R e^{rt} \qquad \text{(equ. 1)}$$

where R is the annual risk at time period zero and r is the rate of decline in the annual risk of infection. The notation used here is not the same as used by Styblo et al. (1969). It has been changed to make the meaning of the parameters more intuitively clear. In addition, the derivation of the equations presented in this paper does not depend on the their approximation that λ is equivalent to $-\ln(1-\lambda)$.

Solving the differential equation, the prevalence of infection at each age a is:

$$P(a) = 1 - e^{\frac{R}{r}\left[e^{rt}\left(e^{-ra}-1\right)\right]}, \text{ for } r \neq 0 \qquad \text{(equ 2)}$$

The equation can be rearranged to get the ARI as a function of prevalence:

$$\lambda = \frac{r * \ln(1-P(a))}{e^{-ra}-1}, \quad \text{for } r \neq 0 \qquad \text{(equ 3)}$$

When r is zero, the equations are much simpler:

$$P(a) = 1 - e^{-Ra} \qquad \text{Equ.4}$$

and

$$\lambda = \frac{-\ln(1-P(a))}{a} \qquad \text{Equ5.}$$

When two surveys are available, we can directly estimate r. Based on equation 3, one can show that:

$$r = \frac{\ln\left[\frac{\ln S(a,t_1)}{\ln S(a,t_2)}\right]}{t_1 - t_2} \qquad \text{equ 6}$$

where t1 is the time of the first survey and t2 is the time of the second survey. S(a,t1) is the prevalence of susceptibles at age a at time t1.

The basic equations for ARI as a function of prevalence of infection at a given age and time are based on the assumption that ARI is uniform across ages in any given time period. Direct observations of skin test conversion rates have mostly shown that the ARI increases with age at least in the first two decades of life (Narain eta. 1966, Nyboe and Christenson 1966, Olakowski 1972) Sutherland and Fayers (1975) explored the possible relationship between ARI and age. They assumed that the ARI might rise exponentially with age such that:

$$\lambda(t) = R\, e^{rt + va} \qquad \text{equ 7}$$

where v is the rate at which the ARI increases with age. Using data from 7 communities where more than one skin test survey had been undertaken, they used to non-linear regression methods to estimate v from the data. Their estimates for the percent increase in ARI with each year of age varied from 1% to 18%.

Confidence intervals for these estimates, however, were not estimated so that they were not able to reject the null hypothesis that there is no relationship between age and ARI.. Sutherland and Fayer also experimented with other forms of the relationship between ARI and age but found they gave similar fits to the exponential curve.

While we do not know if the ARI is definitely a function of age, we can derive equations for the relationship between prevalence of infection and the annual risk of infection for a given v. Based on equation 7, we can derive formulas for prevalence and ARI with the approach used to derive equations 3 and 4:

$$\lambda(a,t) = \frac{(r+v)\ln\left(1-P(a)\right)}{e^{-a(r+v)}-1}, \quad \text{for } r \neq 0 \qquad \text{equ 8}$$

where R and r are as in equations 1-4, and v is the same as in equation 5. This equation will be used below in exploring the statistical properties of different estimators of ARI.

Estimating the ARI from Survey Data

Estimating ARI from a Single Survey

There are three distinct analytical situations that we discuss seperately: one survey, two surveys and three or more surveys. When the results of only one skin test survey are available, the difficulty of estimating the ARI is estimating the annual trend in ARI or r. There are three options for estimating r. First, we can assume that is is zero and use equation 5. In effect, we will be calculating the average risk of infection over a number of years prior to the survey depending on the age-group examined. For example, if the ARI is calculated based on the prevalence in the population 0-14 assuming no trend in ARI, it will be an approximation of the ARI 3-5 years before the survey (Table 3). Second, we can try to estimate r based on circumstantial evidence such as the performance of the tuberculosis control program or trends in the ARI measured in neighboring or similar communities. While this method may be appropriate in certain situations, it can always be challenged as non-objective. Third, we can impute r from the pattern of prevalence in different age-groups -- a method first proposed by Mori (1971). To impute r, first calculate the ARI for the age-groups 0-4, 5-9 and 10-14 using equation 5. If r is negative so that ARI is declining, the estimated ARI using equation 5 will be higher for the older age-groups. Estimates of r can be derived by comparing the estimated ARI from equation 5 for two different age-groups. For example, the formula based on comparing the age-groups 0-4 and 5-9 for r is:

$$\frac{-\ln\left(\frac{ARI_{0-4}}{ARI_{5-9}}\right)}{2.5} \qquad \text{equ. 9}$$

where 2.5 represents the average difference in exposure duration between the two age-groups. A more robust estimate of r can be derived from averaging estimates of r based on pairwise comparisons of 0-4 and 5-9, 5-9 and 10-14, and 0-4 and 10-14.

These three methods for estimating r can be combined with using data on the prevalence of infection from the age-groups 0-4, 5-9, 10-14 or 15-19. Using younger age-groups has the advantage that prevalence is a

function of recent risk and is less sensitive to time trends in risk. Using older age-groups or pooled data from several age-groups increases the number of positives and reduces the confidence interval around estimates of prevalence of infection and therefore the confidence interval around the annual risk of infection.

To investigate the bias and efficiency of different estimators of ARI we have used a simulation approach. We have identified the three leading candidate methods for calculating risk of infection: calculate ARI using the prevalence in the age-group 0-4 and assume no trend in ARI (0-4 Method), calculate the ARI using the average prevalence in the age group 0-14 and assume no trend in ARI (0-14 Method) and calculate the ARI by first estimating r from a pairwise comparison of the ARI with no time trend calculated from 0-4 with 5-9, 5-9 and 10-14 and 0-4 and 10-14, then using this estimated r calculate ARI using the prevalence 0-14 and equation 3 (Imputed r Method). To evaluate these three methods, we have first specified the true level and trend in risk. Then we have simulated surveys of different sample sizes ranging from 250 to 1000 children per age group and applied the three methods for estimating ARI. Figure 4 illustrates the bias and efficiency of the different methods. The 0-4 Method gives estimates with very wide confidence intervals because of the small number of positives that will be present in that age-group but the estimates are only milldy biased, the 0-14 Method gives estimates with very narrow confidence intervals because many more observations are included but the estimates can be very biased. The degree of bias is greater if the time trend in risk is greater. Finally, the Imputed r Method is essentially unbiased but gives unacceptably high confidence intervals.

Estimating ARI from Two Surveys

When two sequential cross-sectional surveys are available, r can be estimated directly from the data. Using equation 6, there are two estimators. Method A would be to calculate r using the data for 0-14 for each survey assuming an average age of 7.5 for the interval and Method B would be to first calculate three estimates of r one for 0-4, one for 5-9 and one for 10-14 and then average the three estimates of r. Simulations summarized in Figure 5 show that Method A is unbiased and more efficient -- in other words, the confidence interval for r is narrower. Of note, Bleiker et al. (1992) recommend calculating r from two surveys by estimating the annual rate of change in prevalence. Estimates of r using this method are inaccurate; for plausible ranges of ARI (0.5-3.0%) and trends in ARI (-0.5 to -6.0%), the estimates will be 3-12% too low.Once r has been estimated from the prevalences 0-14 in the two surveys, ARI can be calculated using equation 3. Estimates of ARI for the second survey using this method are unbiased and efficient.

Estimating ARI from Three or More Surveys

When more than two surveys are available, more powerful statistical techniques can be used to estimate r or ARI directly. With non-linear regression software, a maximum liklihood approach can be used to fit R and r from equation 1 to the available data using a number of solution methods that are available in commercial software. If such sophisticated programs are not available, an unbiased estimate of r can be derived from the coefficient in an ordinary least squares regression of the form:

$$\text{Ln}(-\ln(S(a,t)) = rt + C \qquad \text{equ 10}$$

where a is particular age at which the prevalence is measured at each survey. This relationship can be derived by rearranging equation 3 and noting that overtime holding the age examined constant the complex expression C will not change only the term rt. Once r is estimated from this equation, ARI can be estimated for each year using equation 3.

ARI, Incidence and Prevalence

Styblo (1985) postulated that there was an approximate relationship between ARI and the incidence of smear-positive tuberculosis such that an ARI of 1% mapped to an incidence of smear-positive tuberculosis of 50/100,000. This relationship is widely used by many developing countries to estimate case incidence. In turn these estimates are often used in the denominator to evaluate the performance of the case detection system. Estimated incidence is also frequently used in planning for case load when a program is being expanded into a new area or made freely available in an existing area. ARI based estimates of incidence are also the basis for the current global estimates of tuberculosis incidence and mortality (Murray et al. 1989, Sudre et al., Raviglione et al etc.). The dominance of ARI as a monitoring tool is closely linked to this putative relationship between incidence of infection and the incidence of disease.

Styblo derived this relationship using data from three types of situations: first, where ARI and incidence had been measured, second, where ARI and detected cases are known in communities with high case detection and third where ARI and prevalence were known. He used the latter data sources by postulating that prevalence equals 2 times incidence because of an extensive literature showing a case-fatality rate of tuberculosis of 50% (Styblo 1991). It is interesting to note that the relationship between ARI and prevalence has also been used to estimate the infection parameter, K, or the number of infections caused by an infectious source in one year (Styblo 1991). They are all approximately related as follows:

$$\frac{\lambda}{\kappa} = p = id \qquad \text{equ. 11}$$

where λ is ARI, K is the infection parameter, I is incidence and p is prevalence. The relationship shown should only hold true at the population level if all parameters are constant over age and the population is not growing. Often cited rules of thumb illustrate the basic relationships: an ARI of 1% and a K of 10 are consistent with a prevalence of 100 cases of smear-positive tuberculosis per 100,000 which in turn are consistent with an incidence of 50 cases of smear-positive tuberculosis per 100,000 and a duration of 2 years.

We can rewrite equation 11, to give a formula for incidence as a function of the other parameters:

$$\frac{\lambda}{\kappa d} = \frac{p}{d} = i \qquad \text{equ 12.}$$

Clearly, if K is roughly constant we must expect the relationship between ARI and incidence to change if average duration changes. The widespread use of treatment has substantially altered the average duration of treatment. In developed countries, prompt diagnosis and treatment will have reduced prevalence to be substantially less than 1 year while in some Asian countries poor treatment may have lowered mortality and raised the duration of smear-positive cases to be 3-5 years. Table 4 gives the possible range of incidence rates consistent with a 1% ARI for plausible ranges of the transmission parameter and duration.

Table 5 summarizes the three types of data used by Styblo including his observations and a variety of other studies. The only two true incidence studies, Chingleput and Bangalore, found an incidence rate of 51 and 53 per 1% risk. In both of these studies, however, smear-positives were not distinguished from culture-positive smear-negatives. Styblo had to assume that in both studies 50% of bacilliary cases were smear-positive. Studies based on case incidence data show that the relationship between ARI and incidence was 37 per 1% risk in the Netherlands 1951-1976 but 175 per 1% risk in the USA 1961-1969. The latter finding fits with the fact that average duration in the United States is likely to be quite short. The direct studies of risk and incidence are not convincing for a strong relationship between risk and incidence of the nature proposed by Styblo.

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Technical Appendix

The basic approach is general to other areas in infectious disease modeling where the relationship between the proportion of the population susceptible to new infection at each age and the annual risk of infection is:

$$\frac{\delta S(a,t)}{\delta a} + \frac{\delta S(a,t)}{\delta t} = -\lambda(a,t)S(a,t)$$

where S(a,t) is the prevalence of susceptible at age a and time t, $\lambda(a,t)$ is the annual risk of infection or more precisely the instantaneous risk of infection denominated as an annual rate which is a function of time and age. This formula simply states that the population that is susceptible at each age a to infection changes with age as a function of the risk of infection. This equation is general, it does not specify the relationship between the ARI and time or age.

Styblo et al assume that ARI is declining exponentially overtime:

$$\lambda(t) = \mathrm{R}\,e^{rt}$$

Thus:

$$\frac{\delta S(a,t)}{\delta a} + \frac{\delta S(a,t)}{\delta t} = -\mathrm{R}\,e^{rt}\,S(a,t)$$

Time and age are related such that::

$$t = b + a$$

where t is time, b is year of birth and a is age. This simply means that the current year is equal to the year of birth for a cohort plus their current age. The formula for the annual risk of infection can then be rewritten:

$$\lambda = \mathrm{R}\,e^{r(b+a)}$$

so then we can rewrite the equation for rate of change of susceptibles with age to be:

$$\frac{dS(a)}{da} = -\mathrm{R}e^{r(b+a)}\,S(a)$$

In addition, we know that at birth everyone is susceptible so that S[0]=1. By integrating both sides of this equation, and solving for the constant of integration using S[0]=1 and finally substituting t-a for b, the proportion of susceptibles at any age and time becomes:

$$S(a) = e^{\frac{R}{r}\left[e^{rt}\left(e^{-ra}-1\right)\right]}$$

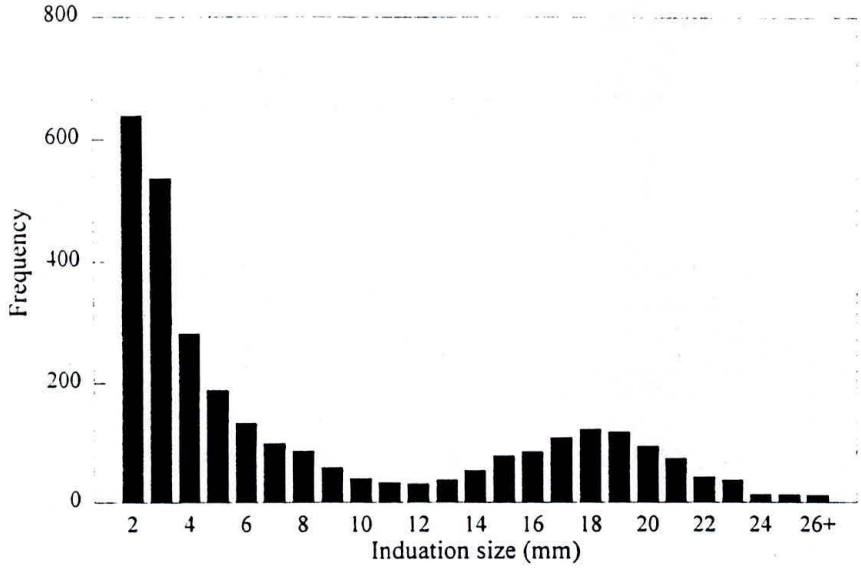

Figure 1. *Frequency distributions of tuberculin reactions, Basutoland, Bechuanaland, and Swaziland, 1958.*

WHO Tuberculosis Research Office, Copenhagen, (April 1958).

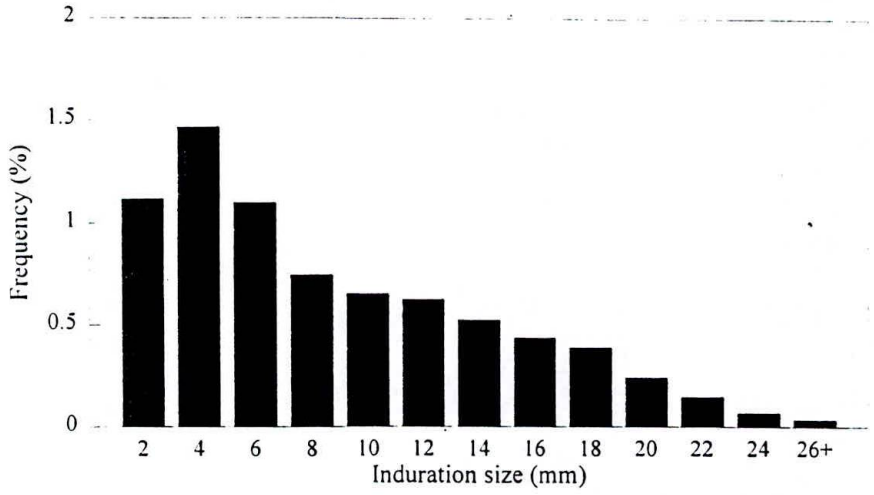

Figure 2. *Frequency distributions of tuberculin reactions, U.S. Navy Recruits, 1961-1968.*

Rust and Thomas (1975)

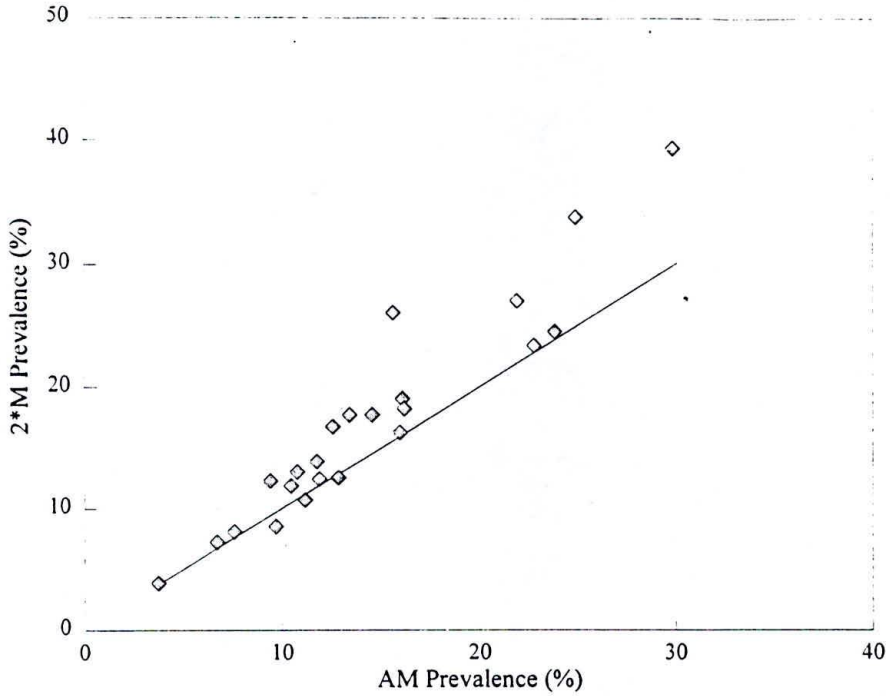

Figure 3. *Prevalence of infection, ages 0-14, calculated from skin test results from twenty-three tuberculosis surveys, using two different methods of determining prevalence. The x-axis shows prevalence calculated from all reactions above a determined induration size. The y-axis shows prevalence calculated by doubling the number of reactions above the mode of the distribution of induration sizes. The tuberculosis surveys were conducted in: Basutoland (1956-57), Bechuanaland (1956-57), Cambodia (1967-68), Ghana (1957), Ibadan, Nigeria (1957-58 and 1962-63), Iraq (1961), Kenya (19 Kiambu, Kenya (1959), Korea (1965 and 80), Liberia (1959-60), Cyrenaica, Li (1959), Libya (1976-77), Machakos, Kenya (1959), Mahe Island, Seychelles (19 Mozambique (1961), Nigeria (1955-56), Pakistan (1987-88), Swaziland (1956-5 Tanginikya (1957), Tumkur, South India (1960-61), and Uganda (1958).*

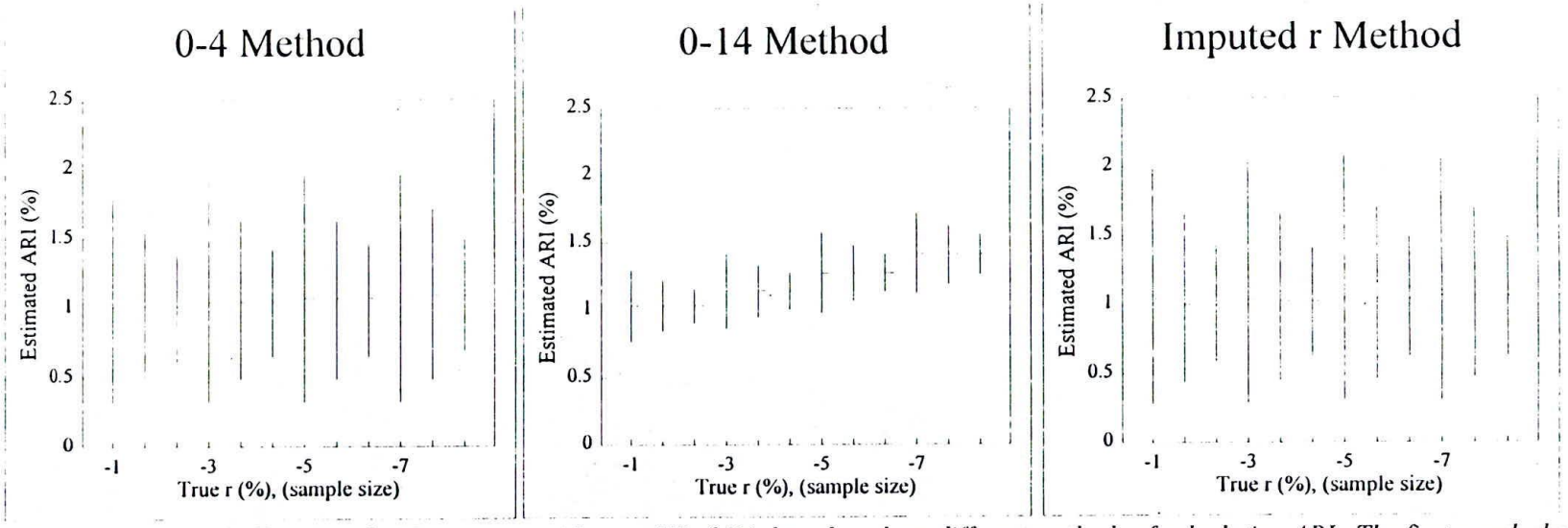

Figure 4. *Bias and efficiency of ARI estimates, with true ARI of 1%, based on three different methods of calculating ARI. The first graph shows the estimate calculated for ages 0-4. The second graph shows calculations of ARI for ages 0-14. The third graph incorporates the trend over time, using an imputed value for r. Each diagram shows the results from twelve different simulations, in which the true value of r and the sample size were varied. Each r-value along the x-axis was tested with sample sizes of 250, 500 and 1000 (not shown on axis).*

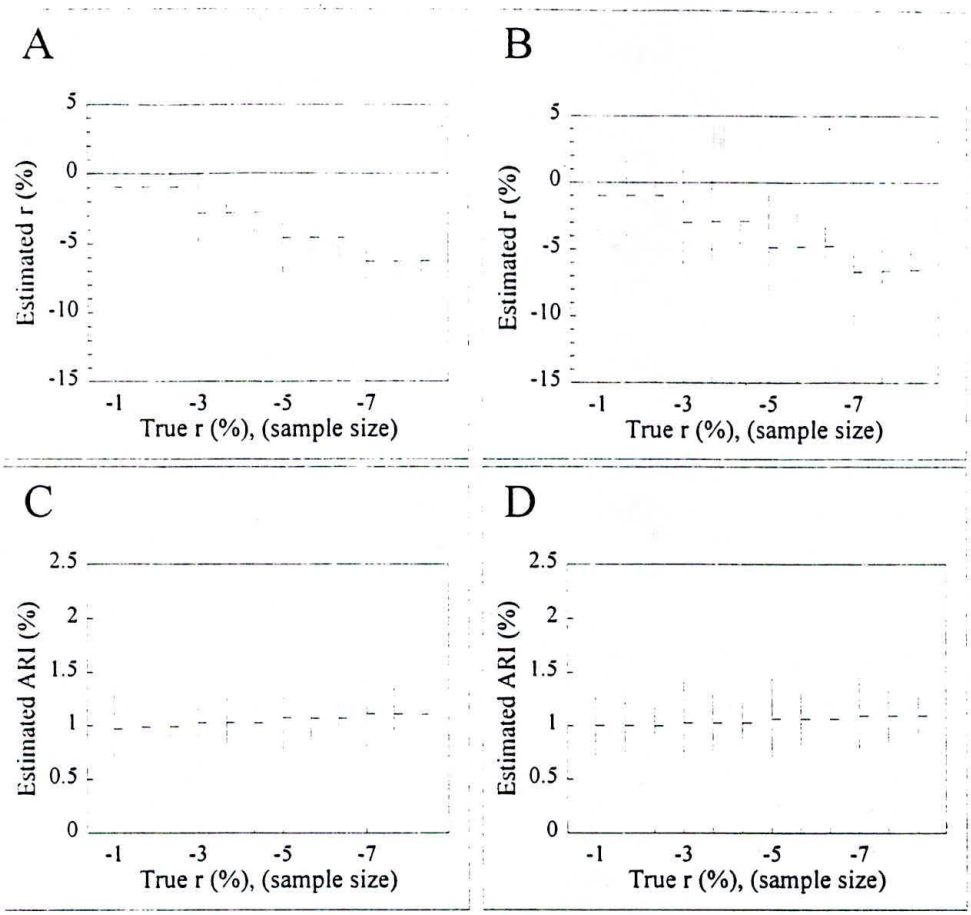

Figure 5. *Graphs show bias and efficiency of estimates of r and ARI based on two different methods of estimating r. Graph A shows estimates of r calculated for ages 0-14. Graph B shows estimates of r calculated as an average of the r-values f age groups 0-4, 5-9, and 10-14. Graph C shows the ARI estimate using the 0-14 method of calculating r, with a true ARI of 1%. Graph D shows the ARI estimate u the average r. Each graph presents the results of twelve different simulations, usin varying true values of r and varying sample sizes. Each of the r-values along the x-axis were tested for sample sizes of 250, 500, and 1000 (not shown on axis).*

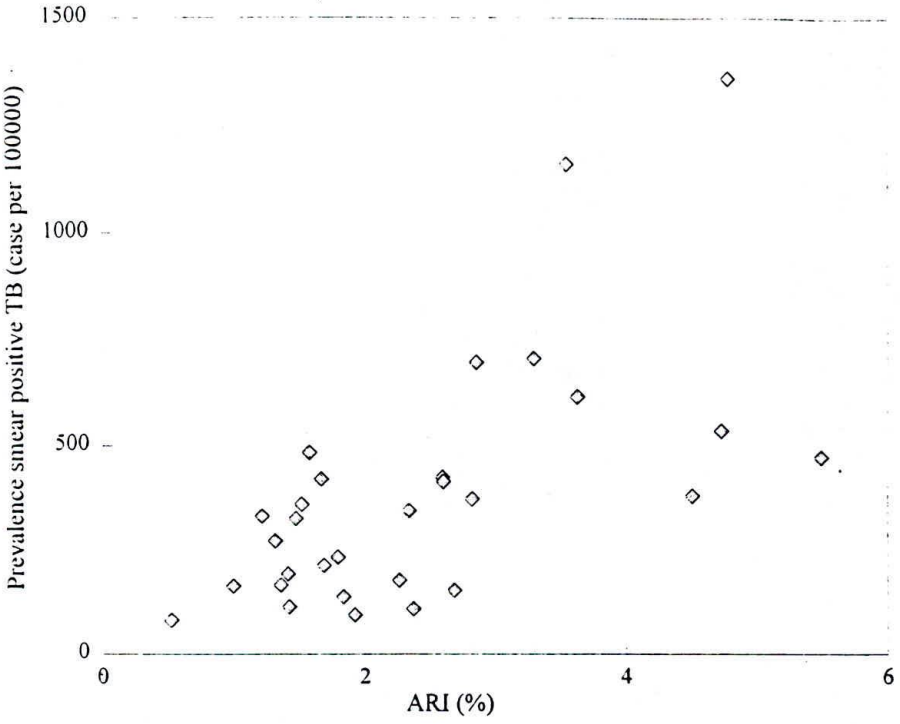

Figure 6. *ARI and prevalence of smear-positive TB, from thirty tuberculosis surveys: Basutoland (1956-57), Bechuanaland (1956-57), Cambodia (1967-68), Chingleput, India (1968), Ghana (1957), Ibadan, Nigeria (1957-58 and 1962-6 Iraq (1961), Kenya (1958-59), Kiambu, Kenya (1959), Korea (1965, 70, 75, 80, 90), Liberia (1959-60), Cyrenaica, Libya (1959), Libya (1976-77), Machakos, K (1959), Mahe Island, Seychelles (1962), Mozambique (1961), Nigeria (1955-56) Pakistan (1987-88), Philippines (1981-83), Swaziland (1956-57), Tanginikya (1 Transkei, South Africa (1977), Tumkur, South India (1960-61), and Uganda (19*

Table 1. Sensitivity of tuberculin skin testing using varying induration sizes to define infection.

	Induration (mm)		
	8	10	12
5TU PPD *			
Denmark	96.0	90.1	87.1
England	100.0	99.4	98.1
North India	97.6	95.9	92.4
South India	88.2	76.9	64.6
Pakistan	98.3	97.6	91.7
Phillipines	95.1	94.3	91.7
South USA - Negro	98.0	96.0	91.0
South USA - White	98.1	96.3	90.4
Sudan	99.4	98.1	98.1
Vietnam	96.0	95.3	94.7
1TU RT †			
Oresund (Denmark)	90.6	84.1	70.6
Kanchrapara (India)	93.8	86.4	75.7
Mehalla (Egypt)	97.3	93.2	85.1
Glen Lake (USA)	89.6	81.0	72.0
1TU PPD-S †			
Charity Lake (USA) - white	90.9	72.7	53.5
Charity Lake (USA) - negro	90.0	83.1	71.5
Battley (USA) - white	85.9	78.0	63.8
Battley (USA) - negro	94.0	87.6	75.4

* WHO Tuberculosis Research Office, 1955.

† Palmer and Bates, 1952

Table 2. *Prevalence of TB Infection among U. S. Navy Recruits, Ages 17-21. 1960-1969. Two methods of calculating prevalence of infection are compared. The Rust and Thomas method is shown using varying values of n, the category in which all individuals are assumed to be infected. The doubling method is shown for three different modes.*

	Rust and Thomas						Doubling		
	15	17	19	21	23	25	15	17	19
White	2.53	2.38	2.35	2.37	2.25	2.58	3.42	2.46	1.59
Nonwhite	10.88	9.34	8.31	7.35	7.23	7.35	18.69	13.69	9.13
ALL RACE	3.26	3.04	2.96	2.94	2.84	3.21	4.52	3.27	2.13

Table 3. The number of years prior to the survey at which point the annual risk of infection equals the average risk of infection calculated from the age group 0-14 using Equation 5.

ARI at the Time of the Survey	Trend in ARI				
	-1%	-3%	-5%	-7%	-9%
1.0%	3.67	4.62	4.9	5.08	5.23
2.0%	2.27	4.05	4.47	4.7	4.86

Note: The number of years prior to the survey at which point the average risk calculated for the age-group 0-14 equals ARI was estimated assuming that within the age-group 0-14, the population was equal at each age. The average prevalence 0-14 was calculated by taking the definite integral of equation 2. The ARI estimated using this average prevalence and Equ 5 was then used to calculate the years prior to the survey when this average annual risk equaled annual risk.

Table 4. Incidence of Smear-Postitive Tuberculosis Expected When the Annual Risk of Infection Equals 1%.

Transmission Parameter	Average Duration of a Smear-Positive Case (Years)													
	0.25	0.5	0.75	1	1.25	1.5	1.75	2	2.25	2.5	2.75	3	3.25	3.5
5	800	400	267	200	160	133	114	100	89	80	73	67	62	57
6	667	333	222	167	133	111	95	83	74	67	61	56	51	48
7	571	286	190	143	114	95	82	71	63	57	52	48	44	41
8	500	250	167	125	100	83	71	63	56	50	45	42	38	36
9	444	222	148	111	89	74	63	56	49	44	40	37	34	32
10	400	200	133	100	80	67	57	50	44	40	36	33	31	29
11	364	182	121	91	73	61	52	45	40	36	33	30	28	26
12	333	167	111	83	67	56	48	42	37	33	30	28	26	24
13	308	154	103	77	62	51	44	38	34	31	28	26	24	22
14	286	143	95	71	57	48	41	36	32	29	26	24	22	20
15	267	133	89	67	53	44	38	33	30	27	24	22	21	19
16	250	125	83	63	50	42	36	31	28	25	23	21	19	18
17	235	118	78	59	47	39	34	29	26	24	21	20	18	17
18	222	111	74	56	44	37	32	28	25	22	20	19	17	16
19	211	105	70	53	42	35	30	26	23	21	19	18	16	15
20	200	100	67	50	40	33	29	25	22	20	18	17	15	14

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World Health Organization
Global Tuberculosis Programme

Report
of the Fourth Meeting of the
Technical Research and Advisory Committee (TRAC)
(Geneva, 2-3 May 1996)

The meeting opened with a welcoming overview by Dr. Ralph Henderson (Assistant Director General). The Chairman of the Co-ordination Advisory and Review Committee (CARG), Dr. Elzinga, took the chair for the first items of business (agenda attached).

He welcomed the sixteen members of TRAC, who had been selected by a working sub-group of CARG to represent, in their personal capacities, the range of disciplines relevant to public policy development for tuberculosis control. In view of the differing backgrounds and experiences of members a briefing day was held immediately prior to the meeting to ensure that all members shared a common core knowledge of the principles and mechanisms of TB control and the structure and functioning of GTB.

Dr Elzinga reviewed the recommendations coming from the CARG 1995 meeting and the environment which CARG 1995 had set for better functioning of the GTB (chart attached) including adoption of a business-like structure and specific follow up of recommendations. He linked this to the need for changes in the terms of reference of the TRAC. Specifically, TRAC was to focus on technical review and advice to the Programme and to the CARG on the soundness of the Programme's TB control work and research activities. Functions of TRAC which had previously duplicated the functions of CARG, in particular the review of the Programme's budget and non-technical or non-scientific policy matters, should be reserved to the CARG. TRAC members reviewed the previous terms of reference for TRAC and made several suggestions. These will be incorporated in the overall terms of reference for the Programme's advisory bodies and reviewed within WHO and by the CARG.

As the last item of business under Dr. Elzinga's chair, a chairperson for TRAC was elected by secret ballot of TRAC members in their first session. Upon election, Dr. Jaap Broekmans took the chair.

The secretariat explained that the agenda for this meeting was guided by the recommendations made by CARG 1995. It was agreed that TRAC members would be able in future to contribute to setting the agenda, either through recommendation to CARG, or by suggesting items to be included in future meetings.

Presentation of first agenda item. Monitoring and Surveillance. The monitoring and surveillance project was developed in response to the request of CARG for better information on the state of the global epidemic and the performance of control programmes in order to

monitor the progress towards achievement of the year 2000 targets. In the six months since the project's inception, the data collection system has been strengthened, and interpretation methods improved. A preliminary analysis of country control programmes showed that 20 countries (11%) are implementing WHO control strategies routinely throughout, while another 62 (33%) have accepted the WHO strategy and partially implemented it.

Discussion. TRAC members supported the approach that had been developed, and advocated that the project should be sufficiently resourced and staffed to ensure its routine functioning. The proposed new data collection forms were endorsed, but several suggestions were made for possible additions, e.g. outcome of smear negative cases, data on HIV prevalence, mortality, and country-specific surveillance projects. These additions will be considered for the data collection forms to be used in subsequent years.

The issue of developing new and better ways of estimating incidence stimulated considerable debate. A practical way to estimate incidence is needed if progress towards the target of 70% case detection is to be more accurately monitored. However, no consensus emerged on the method to use and questions on the appropriateness of the target emerged. It was suggested that, given the high costs and opportunity costs of attempting to measure incidence by approaches such as prevalence surveys, resources would be better used to improve effectiveness of TB control programmes.

Recognizing that this will still leave room for confusion, and noting that TRAC needs to provide advice to the CARG on the year 2000 goals, TRAC members agreed to establish a task force together with the secretariat. The task force will assist the Programme to determine whether, with existing knowledge and diagnostic tools, new methods of measurement of incidence were feasible to develop and, if yes, whether they would be worth the cost and effort of their application. The task force should also provide advice to the Programme on whether the case detection target remains appropriate. If not, the task force should recommend specific alternative targets and provide advice on their use, both within and outside the WHO system. It was agreed that the task force will complete its draft report in time for the 1996 CARG meeting.

From a different perspective, however, there was a need for better country-based data for estimates of the global burden, and the impact of control measures on it, as well as for effective advocacy and informed debate about the global situation.

A TRAC member noted that the GTB still continues to have two different estimates of TB deaths and cases circulating in various publications. (Note, this is true within the WHO system for most causes of death and morbidity - one estimate representing bottom-up country-specific, cumulative results, without any global constraint on total number of deaths; the other being the result of the Global Burden of Disease exercise which constrains total deaths and then apportions their cause. Until the overall policy within WHO is clarified, the GTB will have to continue to use the two sets of numbers for different purposes. It was noted that groups outside WHO were developing other estimates and this would add to confusion among policy makers.

To avoid further confusion in proliferation of estimates TRAC suggested that the Programme should, for use during the rest of the decade, make a new, estimate of TB

incidence and mortality based on the best, currently available, country-by-country information. The Programme will do this.

National Programme Support Activities.

Presentation of agenda item. Overview, GTB's National Programme Support Activities. The Programme offers technical support and advice to countries. These activities are concentrated upon those countries which have the highest case load, and the greatest need for support. The focus of this work is gradually shifting from Geneva towards a Programme presence with tuberculosis control advisers in the regions and in high priority countries. In addition, the Programme is also involved in the development and co-ordination of training, preparation of guidelines for good practice and development of strategies to prevent drug resistance. The main problem presently faced by the Programme is the demand for assistance to an increasing number of countries in an accelerated expansion of the DOTS strategy. The Programme recognised the need for inclusion of many more partners (non-governmental organisations, private corporations and private practitioners and their associations) in adoption and implementation of the DOTS strategy. This required new thinking within the Programme (to become more client-oriented) and new products and knowledge (more user-friendly guidelines and materials, new forms of drug products which could be simpler to administer and help to avoid malpractice) and a new approach to expanding the knowledgeable manpower to deal with TB at all levels. Overall these country support activities had to help create a public environment favourable to all segments of the health sector, public and private, to work effectively to control tuberculosis.

The Programme had chosen three topics related to country support to present to TRAC for its reaction and advice at this meeting, based on CARG's 1995 recommendations and areas of interest: revision of the WHO treatment guidelines, rational and more effective use of tuberculosis drugs and human resource development strategy.

Discussion. In overview discussions TRAC members noted that only 20 countries had adopted the DOTS strategy fully, and that progress in many others was slow, due to the difficulty of changing policy, public perceptions and the allocation of adequate resources in member countries. The strategy therefore proposed by the secretariat of focusing and decentralising technical assistance to priority countries was endorsed by TRAC members. They also agreed that quicker expansion of DOTS coverage and maintenance of high cure rates could be only achieved by involving other partners such as NGOs and the private sector.

One TRAC participant raised a question concerning the priority of smear negative TB within the overall DOTS strategy. In discussion, another TRAC participant focused on the increased incidence of smear negative TB among HIV positive persons and asked for clarification of the DOTS strategy in such settings.

The programme staff clarified that the DOTS strategy was fully articulated in the document entitled "Framework for Effective Tuberculosis Control". Good treatment and rigorous recording and reporting of the process and the outcomes for all forms of TB was part of the DOTS strategy, as set out in that document. Some countries gave priority in their programmes to applying the DOTS approach mainly to smear positive cases. The Global Tuberculosis Programme's technical advice and policy orientation was to advocate the more comprehensive approach as outlined in its policy documents.

Presentation 1: Treatment guidelines were published in 1993 (*Treatment of Tuberculosis: Guidelines for National Programmes*), these were reviewed by a working group in October 1995. Some of the recommendations of this meeting are being incorporated into the second edition of the treatment guidelines that will be published in 1996. The new edition includes more specific case definitions and refinements to the suggested regimens and thus will help to provide clarity compared to the 1993 edition.

Discussion. One TRAC participant expressed concern about some aspects of the new guidelines, specifically that some regimens in the continuation phase had not been proven in clinical trials, another participant noted his worry that regimens advocated for smear negative cases, especially in HIV prevalent settings, may provide inadequate treatment.

The Programme noted that the evidence upon which the new guidelines were based reflected practical experience at country level rather than outcomes of clinical trials. The comments made by various TRAC members were understandable and accurate in the context of their particular country and regional experiences, but did not reflect experience and conditions in other countries and regions. To help TRAC members to gain the alternative perspectives to provide better advice to the Programme the secretariat undertook to invite selected members to join in work in countries/regions with which they were less familiar. The Programme fully agreed on the need for further research on regimens and on a practical response to the management of smear negative patients in HIV prevalent settings. It proposed a correspondence group among key TRAC members (knowledgeable about treatment regimens) to explore these issues further and advise the secretariat appropriately. The group was established subsequent to the meeting.

Presentation 2. Rational and more effective use of tuberculosis drugs. In response to CARG guidance, the Programme had succeeded to establish closer co-operation with the Division of Drug Management and Policies (DMP) in late 1995 and to interest them in the problems of drug resistance caused by inappropriate use of anti-TB drugs. As a consequence, the Programme and DMP succeeded to have the WHO Expert Committee on the use of essential drugs (December 1995) agree to inclusion of combined, fixed dose forms of anti-TB drugs (double and triple combinations) in the Essential Drugs List. More widespread use of these drug forms would not only have eventual impact on efficiency of TB programmes and emergence of drug resistance, but would also begin to alleviate the risks posed by thiacetazone.

Nonetheless, resistance to the main antituberculosis drugs was seen to be a growing problem that will compromise the efficacy of TB programmes, and result in even more deaths from the disease. Good programme management is essential to prevent resistance, but as so much TB care is carried out in the private sector and in other institutions operating outside the national TB programmes, the Programme recognised that other innovations are required. Fixed dose combination drugs can simplify the administration of effective TB treatment and reduce the risk of developing secondary drug resistance. Such products have the potential to unify private sector and non-governmental organisations' treatment practices if these products are seen to be the treatment of choice. Ideally, development of a quadruple, combination product (pill containing all four drugs) for TB treatment would make this approach extremely attractive.

However, the bioavailability of rifampicin in some combination products now available in the market is low (and this problem would be equally important in eventual development of a quadruple combination). GTB thus recognises the need to develop a system for monitoring of product quality, to promote the use of good quality products and ultimately establish systems by which TB patients, physicians and national TB programmes can safely use combination products. Once such a system is working, fixed dose combinations are likely to become accepted as the treatment of choice in both private and public sectors and more easily supported in bilateral and multilateral financed projects.

Discussion. TRAC endorsed the importance and feasibility of this approach noting that where good TB programmes with high cure rates already exist, combination products need not necessarily be introduced or promoted. TRAC also noted that there will be a limited continuing use of individual drug dosage forms to meet the needs of some patients. TRAC agreed that for countries where good TB treatment was not established, or could not easily be maintained because of health system weaknesses or poor co-ordination with the private or voluntary sectors, combinations products (especially quadruple) offered a major step forward.

Discussion yielded support for the directions already taken by the Programme in six areas in order:

1. to finalise and promulgate standardised quality test methodologies;
2. to develop and promulgate specification for combination products suitable for use in public tenders;
3. to specify the added value of combination products which could be used for the purpose of deciding when the (higher) prices of such products were a better buy than single product forms;
4. to develop, in consultation with the World Bank and other development assistance agencies, the conditions of tender by which bidders would be obliged to include in their sales price the fees to operate the standardised testing procedure for each batch delivered;
5. to develop, promulgate and maintain a list of laboratories which could reliably and independently perform such testing;
6. to advocate private sector development of quadruple combination products as soon as possible.

The Programme will report on further progress at the 1996 CARG meeting.

Presentation 3. Training and Human Resources. Despite much progress in training national and district level TB programme staff in the last three years, the Programme recognizes that additional trained, appropriately skilled people at all levels are needed if the DOTS strategy is to be adopted and effective tuberculosis control achieved by the year 2000 in much of the world. In many programmes that are in the expansion phase of DOTS, shortages of qualified staff are perceived to be a major constraint. In order to address these needs, training materials and normative guidelines have been developed and disseminated by the Programme, and training courses have been established. These are so far limited in focus to public sector programmes and do not take into account the needs of non-governmental organisations or private sector practitioners. The Programme recognised the need to substantially broaden its efforts but had uncertainties about strategy, techniques and channels.

Discussion. The Programme was advised to address training needs in their broadest sense, including not only staff involved in TB control activities, but private physicians and general health workers, lay people and policy makers. The scarce resources provided by developing country governments and external donors to invest in human resources in connection with TB was perceived as a major problem, as was the relatively low appeal to health professionals of involvement in tuberculosis control. The Programme undertook to discuss the topic more widely within WHO and to seek outside advice as the first steps in preparing a better descriptive analysis of the specific issues and alternatives to be considered, which might then lead to practical next steps to discuss at the CARG 1996 meeting or at the next TRAC meeting..

Tuberculosis Research Strategy and Activities

Presentations 1 and 2. The research programme of GTB has undergone major restructuring since 1995, to develop a more comprehensive, unified and less narrowly biomedical approach, that complements the overall Programme strategy. While links are being developed with other agencies and institutions, WHO is concentrating its efforts in areas where it has a comparative advantage.

The three main areas of research are the following:

1. To develop methods to increase the dissemination of the DOTS strategy (DOTS More Widely);
2. To improve the efficiency of the DOTS strategy by developing and testing innovations (DOTS More Easily);
3. To promote the development and new tools to facilitate TB control and to bring TB elimination nearer (Beyond DOTS).

Research was prioritised according to the magnitude of the benefit that would result if the research were successful, the certainty that it would achieve such a result, and the duration of the research and its costs. The DOTS strategy is already averting some of the future burden of death and disease due to TB. Expanding the coverage and efficiency of the DOTS strategy could avert the majority of the remaining burden, but new tools would be essential for the complete control of TB.

Discussion. TRAC supported the concept that the future of the Programme depends on good research and good guidelines for research, but requested that the Programme articulate better the match between the needs of tuberculosis control programmes and the research strategy which GTB has adopted a clearer statement of why research is needed. Based on discussion, four hypotheses (aside from lack of financial resources and inappropriate TB control strategies) were offered by the TRAC chair as to why better global TB control was not being achieved: first, current programmes are failing because of a lack of human resources (insufficient people addressing the problem, and insufficient skills in those that are) secondly, NTPs are currently failing because patients bypass them and go directly to the private sector; thirdly, some societies appear willing to tolerate a high burden of disease from tuberculosis. Lastly, many governmental systems of TB control are dysfunctional.

TRAC Members felt the Programme did not have a sufficiently clear picture of the demand for TB care, and particularly of the profile of TB patients. The financial, physical

and social barriers affecting access to care needed to be more clearly described. Institutions that already address TB research, especially those in the public sector, need to be in a dialogue with GTB so that the Programme is aware of all forms of TB research in progress, and of the networks of research that exist in both biomedical and operational spheres. To do this the Programme needs to make its own research strategy and efforts better known, to acquire additional staff with strong leadership experience in global research initiatives and excellent networking skills.

The chairman summarised the following four main deficiencies in high quality TB control throughout the world, together with the research needed to address them:

1. Insufficient countries are implementing the DOTS strategy, and the WHO year 2000 targets may therefore not be achievable if the current pace continues. Research should develop methods for increasing the number of countries accepting the DOTS strategy.

2. Operational problems exist even in countries accepting the DOTS strategy, and operational research should be aimed at resolving these.

3. Even in countries accepting the DOTS strategy and succeeding with it, there is a need to increase the coverage of the population. Research should develop methodologies, such as community-based management of TB, to address this issue.

4. Better tools are needed which can only be obtained from research into new diagnostic agents, new drugs and new vaccines. The wide range of these activities emphasises the need for prioritisation.

Discussions of this summary emphasised that although the DOTS strategy was only launched in 1995 to encapsulate the more complex approach outlined in the WHO "Framework for TB Control", it needed much more marketing and dissemination. Adoption of and support for the DOTS strategy at the regional and country levels required acceleration and expansion. The need to develop innovative and sustainable methods, particularly with the private sector involved in delivery of patient care, was emphasised. With regards to prioritisation of research topics, TRAC suggested that GTB should clearly identify priorities both for the world at large, and for GTB within and between these four major areas of research and report on this to CARG 1996. In addition, GTB should collect information and experience on working with the private sector, and develop prototypes for ways in which the DOTS strategy can be adopted by the sector.

The meeting agreed on the necessity to continue to state clearly to the outside world that DOTS is the best current strategy for TB control and that it works, whilst internally acknowledging the potential deficiencies of the DOTS strategy and implementing a research agenda aimed at improving it. This approach will entail considerable tension in the Programme and staff will be needed who can effectively question established practice, whilst managers will need to encourage and support both those who question, and those who defend current strategies.

Presentation 3. Community based management of tuberculosis. In many countries the primary health care system is unable to cope with the burden of TB or to deliver DOTS effectively. However, existing community structures, such as community-based care organisations, may be involved in TB care and, in some areas, already are. The aim of this project is to explore how TB management can be better integrated with community based organisations to deliver the DOTS strategy effectively. This approach will be piloted through the community care network for HIV patients in Africa.

Discussion. TRAC members supported the operational research project, but suggested that the best chances of success are where well developed community networks already exist and national tuberculosis programmes are well established. It was observed that the project should still depend upon the health system for diagnosis of patients and for supervision of community workers. Concern was expressed about the sustainability of such initiatives, (due to the external support currently provided to most community projects), and their limited population coverage of community projects relative to the national populations affected by TB.

Presentation 4. Elimination of TB - concept development. Health systems and management research concepts were presented to provide a framework for strategic thinking aimed at the ultimate goal of TB elimination.

Discussion. TRAC warned that, given the current poor state of global TB control, excessive efforts in this direction would be premature. There is also a risk that the impact of economic analysis of the benefits of elimination may not be great and may not be credible in the current environment. Nevertheless, the concept of elimination remains a relevant eventual Programme pursuit because of the need to a) establish a long-term vision, and b) use the concept to change the donor environment in order to increase TB research funding.

Presentation 5. Elimination of TB - tools required. The development of new tools for diagnosis, treatment and prevention is necessary to overcome limitations in the application, efficiency and sustainability of the current TB control strategy. The Programme proposed a "diagnostics initiative" based on a situation analysis and the establishment of a coalition (WHO/public and private sector/donors) aimed at developing low cost, easily applied, robust diagnostic tests. The Programme would manage the co-ordination of multicentre clinical trials of the new long-acting rifamycin, rifapentine, and a renewed dialogue with the research community and pharmaceutical companies to stimulate the development of new drugs. The Programme would also advocate funding for targeted and more fundamental research aimed at, for example, new vaccine development. Finally, GTB will collaborate with UNAIDS in the testing and formulation of recommendations for preventive therapy among HIV-infected people.

Discussion. With respect to research on the development of new tools, TRAC supported the continuing GTB involvement in new tool development. There was a discussion concerning the advantages and disadvantages of targeted versus more wide-based fundamental research. With the current level of understanding, targeted research is likely to produce new diagnostic tools based on detection of the organism. TRAC endorsed GTB involvement in an initiative in diagnostics and suggested GTB should make use of the OECD supported analysis on TB diagnostic agents. Regarding the development of new vaccines, TRAC suggested GTB should develop advocacy efforts aimed at fundamental research

needed for vaccine development. TRAC also agreed GTB should encourage the pharmaceutical industry to develop new TB drugs.

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TUBERCULOSIS - A GLOBAL EMERGENCY:
CASE NOTIFICATION UPDATE

February 1996

Global Tuberculosis Programme
World Health Organization, Geneva

Introduction

Surveillance of tuberculosis is a feasible undertaking if a country has an effective National Tuberculosis Programme (NTP). In the absence of such a programme, diagnostic skills are lacking, case definitions are not standardized, and case recording and reporting are weak or non-existent.

Under a well established NTP, on the other hand, suspected cases are detected, diagnosed, and recorded and reported, based on standard registers and quarterly reports. In such a situation, the number of cases notified by district officers to the regional and national levels represent a reasonable estimate of the incidence of tuberculosis in the country.

The World Health Organization (WHO) has been collecting case notification data since 1984 from all of its Member States and other countries and territories to assess the burden of tuberculosis and its trend worldwide. The Case Notification Update, a report published annually by the Global Programme on Tuberculosis, was started in 1992.

Methodology

In mid 1995, WHO sent a data collection form to all Member States and other countries and territories to obtain information on the burden of tuberculosis in 1994. These forms were returned to WHO for data analysis. Additional information was obtained from reports by the International Union Against Tuberculosis and Lung Diseases (IUATLD), the Royal Netherlands TB Association (KNVC), other organizations involved in tuberculosis control and published literature. Prior to finalization of the report, the data were sent to all WHO Regional offices for verification and updating.

For the 1994 case notification update, 141 out of 214 countries (66%) responded to the WHO inquiry. Data for another 17 countries were obtained from other sources. These 158 countries make up 90% of the global population.

Data are reported in three tables per WHO Region, listing absolute numbers of cases notified, case notification rates, and pulmonary smear positive cases respectively (see tables 2.1 to 7.3).

Not all countries provided WHO with data on 1994. In order to obtain a realistic yet up-to-date assessment of the global tuberculosis burden, the latest reports available between 1990 and 1994 were therefore used in generating a global picture of the disease.

Data Interpretation

The data shown in this report should be interpreted with caution for a number of reasons:

1. the information for the most recent years was sometimes missing or incomplete,

2. in several countries the performance of the NTP, including their reporting system, is poor, and

3. case definitions vary between countries. Besides non-standard definitions for pulmonary and extrapulmonary tuberculosis, not all countries distinguish between new TB cases and relapses. For this reason, the first two tables per Region show data on all cases (new and relapses) while the third table, which is being included here for the first time, provides information on sputum smear positive cases only, i.e., the infectious cases whose trend is of crucial significance in the TB epidemic.

Global Tuberculosis Situation

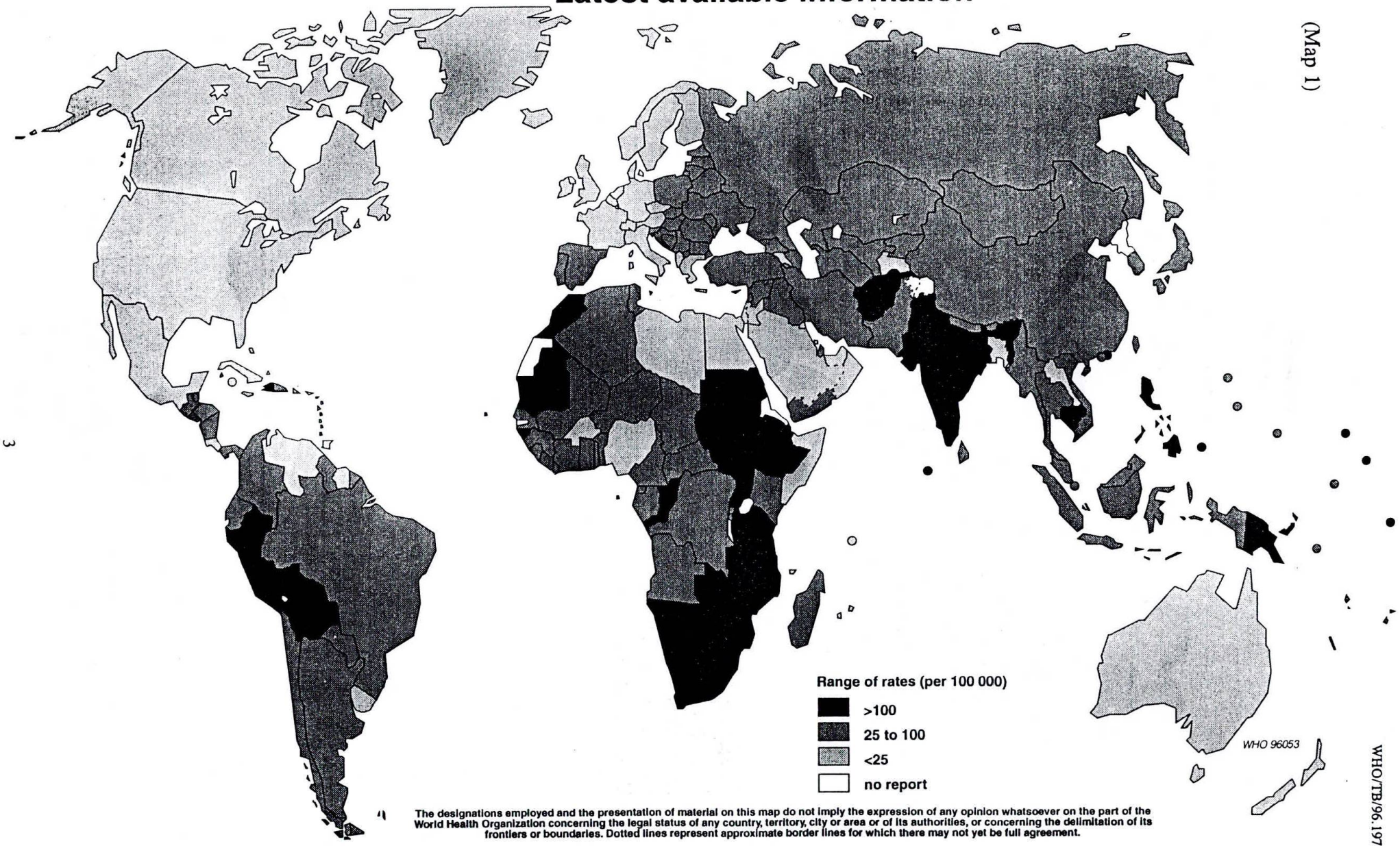
Discrepancies between reported case rates and incidence estimates are evident in maps 1 and 2. Map 1 shows the latest available case notification rates for all countries, categorized by low (<25), medium (25-100), and high (>100) levels of notifications. Map 2 shows estimates of incidence in 1990 using the same scale, according to the 1993 World Bank Development Report[1] and WHO.

[1] *World Development Report 1993. Investing in Health*, World Bank. Oxford University Press, New York, 1993

Tuberculosis notification rates

Latest available information

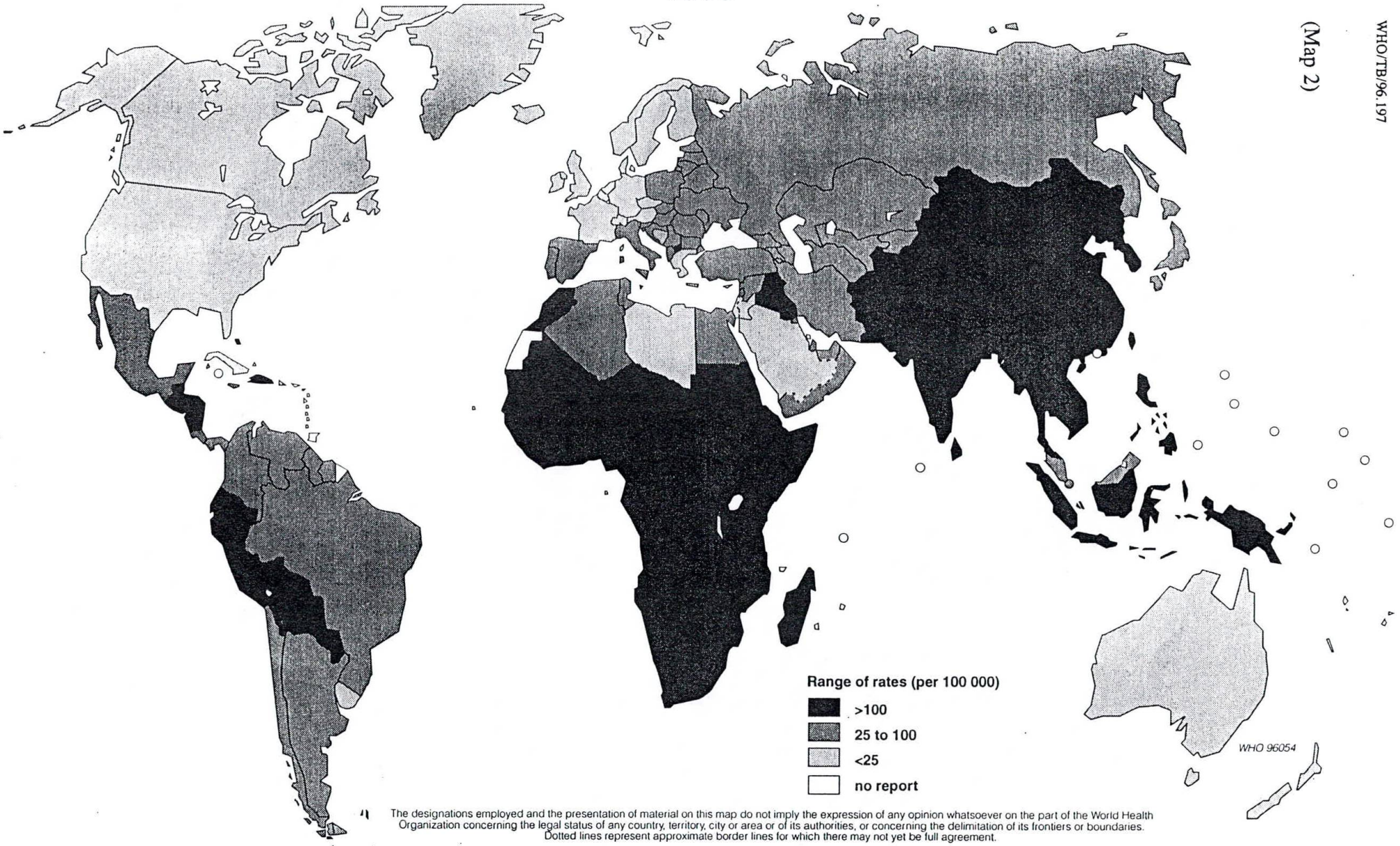
(Map 1)



The designations employed and the presentation of material on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines represent approximate border lines for which there may not yet be full agreement.

WHO/TB/96.197

Estimated tuberculosis incidence rates
1990



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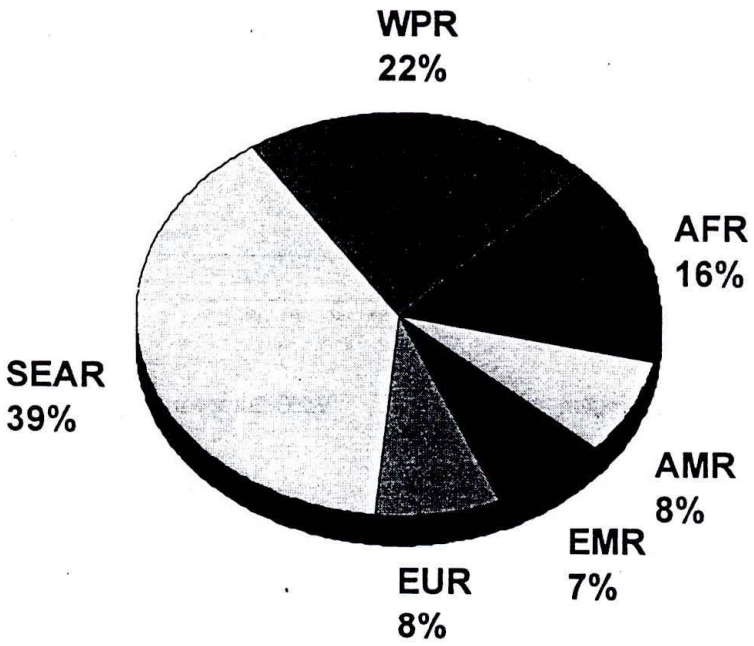
(Map 2)

WHO/TB/96.197

Table 1. TB cases notified in the world, latest reports between 1990 and 1994

WHO Region	No. of cases notified	Rate (per 100,000 pop)
Africa	541,360	96.8
Americas	264,221	34.9
Eastern Mediterranean	237,937	55.2
Europe	286,608	33.3
South-East Asia	1,298,999	94.4
Western Pacific	725,014	45.5
GLOBAL	**3,354,139**	**60.1**

Figure 1 Distribution of notified tuberculosis cases by WHO Region



Regional Tuberculosis Situation

The figures shown below illustrate the trend of tuberculosis over the past 10 years for each WHO Region.

In the African and European Regions, the disease is on the increase.

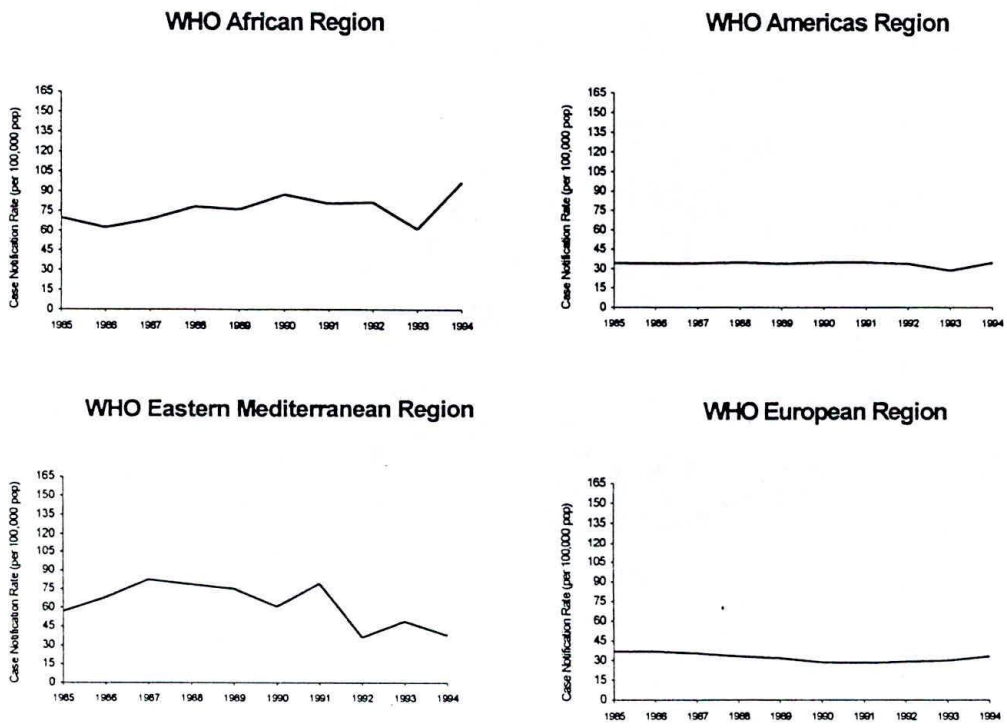
In the African Region, HIV, malnutrition, urbanization and to some extent improvement in NTPs, may be the underlying factors.

In the European Region, population movements, social upheaval, and HIV in some countries have resulted in the re-emergence of a disease which until a few years ago had virtually disappeared.

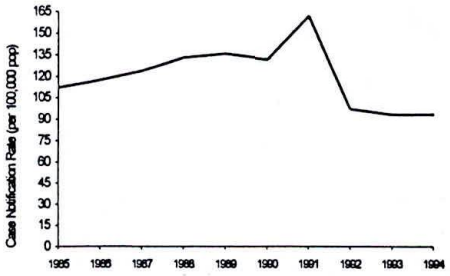
In the American and Western Pacific Regions, case notification rates have remained relatively stable, indicating no significant improvements in tuberculosis control.

In the Eastern Mediterranean and South-East Asian Regions, an apparent decrease in the case notification rates occurred during the past four years. This phenomenon is most likely an artifact, reflecting marked fluctuations in reporting activities of some large countries.

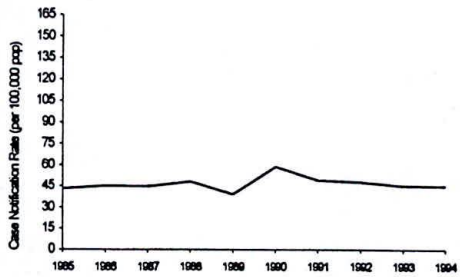
Figure 2 Case notification rates in different WHO Regions, 1985 - 1994



WHO South East Asian Region



WHO Western Pacific Region



NTP Performance

A new addition to this report is table 3 which provides information on new pulmonary smear positive cases. "Proportion of new smear positive cases to all cases" is one of the indicators used for measuring the performance of an NTP, i.e., the ability of the national TB programme to detect tuberculosis. This indicator allows countries to be classified according to three criteria:

1. >50% = good NTP performance or a reporting system which does not include pulmonary smear negative or extrapulmonary cases,

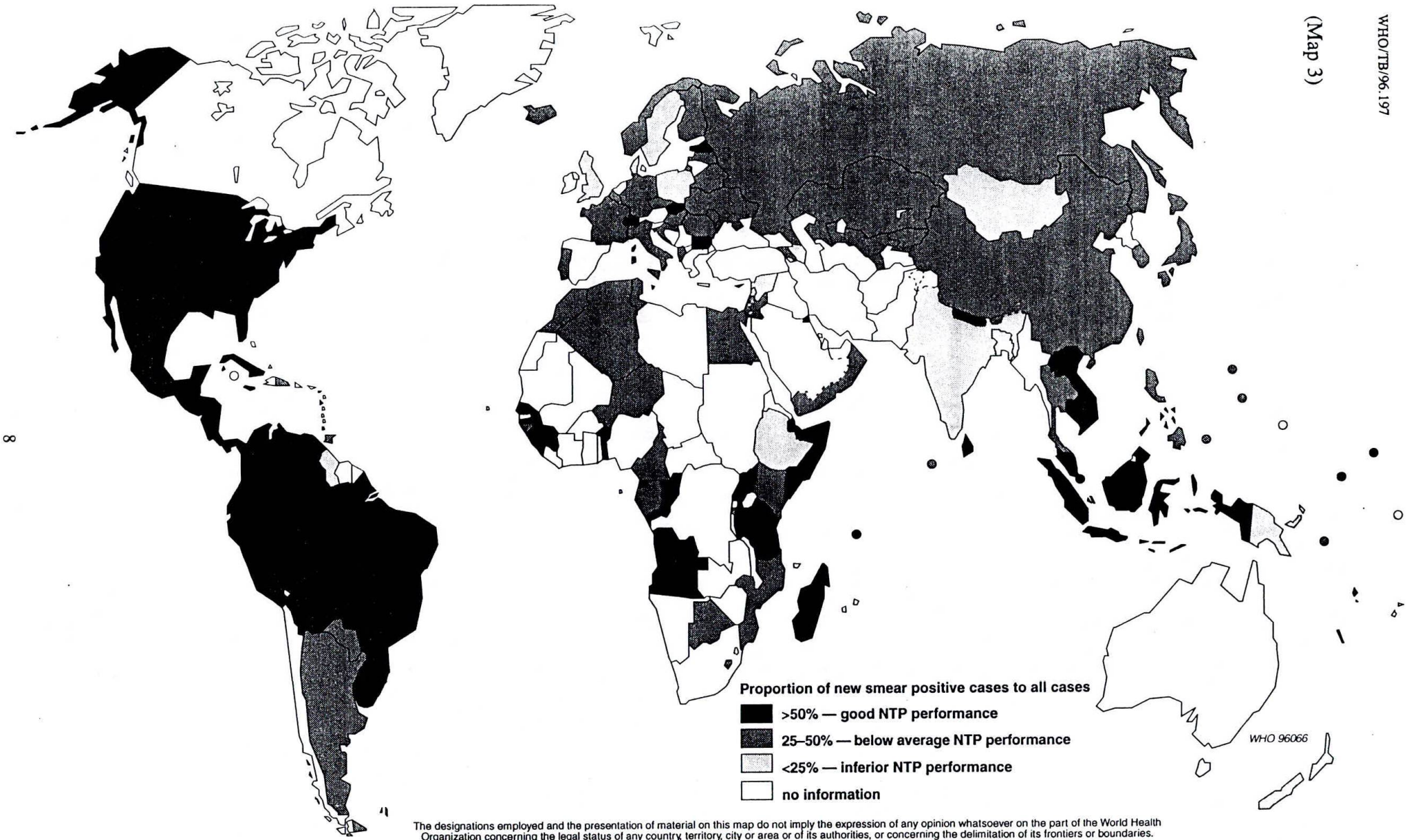
2. 25 - 50% = below average NTP performance, and

3. <25% = inferior NTP performance.

Performance status of National Tuberculosis Programmes, 1994

(Map 3)

WHO/TB/96.197



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Table/Tableau 2.1: African Region - Number of tuberculosis cases notified/Région de l'Afrique - Nombre de cas de tuberculose notifiés, 1975-1994

COUNTRY / PAYS	1975	1976	1977	1978	1979	1980	1981	1982	1983	1984	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994
Algeria/Algérie					2,362	2,702		13,916	13,681	13,133	13,832	12,917	11,212	11,325	11,039	11,607	11,332	11,487	13,382	13,725
Angola	1,542	1,959	6,990	9,375	7,202	10,117	7,501	7,911	6,625	10,153	8,653	9,363	8,510	8,184	9,587	10,288	10,628	10,639	7,318	7,157
Benin/Bénin	1,400	1,576	1,597	1,613	1,688	1,835	1,862	1,793	1,804	1,913	2,041	2,162	1,901	2,027	1,941	2,074	2,162	2,420	2,340	2,119
Botswana	3,534	2,797	2,598	2,662	2,850	2,662	2,605	2,705	2,883	3,101	2,706	2,627	3,173	2,740	2,532	2,938	3,274	4,179	4,654	4,756
Burkina Faso		1,047	2,437	1,060	480	2,577	2,391	2,265	3,061	877	4,547	1,018	1,407	949	1,616	1,497			1,443	
Burundi	1,062	667	902	975	460	789	643	951	1,053	1,904	2,317	2,569	2,739	3,745	4,608	4,575	4,883		4,677	3,840
Cameroon/Cameroun				512	1,037	2,434	2,236	3,765	3,445	3,338	3,393	2,138	3,878	4,982	5,521	5,892	6,814	6,803	7,064	7,312
Cape Verde/Cap Vert		173	246	289	427	516	344	393	230	285	259		285	276	210	221				
Cent. Afr. Rep./Rép. Centrafricai	1,657	805	599	559	463	651	758	1,475	1,686	468	520	779	499	814	64	2,124	2,045			
Chad/Tchad	1,950	2,421	2,509	2,889	512	220	286	127	1,977	1,430	1,486	1,285	1,086	2,977	2,572	2,591	2,912			
Comoros/Comores		725	725											212	139	140	119	108	129	115
Congo	1,026	1,276	1,055	1,453	1,085	742	1,214	3,716	4,156	2,776	2,648	3,120	3,473	3,878	4,363	591	618	1,179	1,976	3,080
Ivory Coast/Côte d'Ivoire	2,862	2,946	2,936	3,991	3,995	4,197	4,418	5,000	6,000	6,062	5,729	6,072	6,422	6,556	6,982	7,841	8,021	9,093	9,563	
Equat. Guinea/Guinée Equat.										181	17	1	11	20	157	260	331	262	309	356
Eritrea/Eritree																				
Ethiopia/Ethiopie	30,454	33,174	26,596	26,022	30,880	40,096	42,423	52,403	56,824	65,045	71,731	80,846	85,867	95,521	80,795	88,634	60,006			99,329
Gabon	516	549	535	699	758	865	796	761	752	654	855	769	864	721	912	917	906	926	972	1,034
Gambia/Gambie	343	188	294	294	289	239	58													
Ghana	6,355	8,452	5,250	5,000	4,479	5,207	4,041	4,345	2,651	1,935	3,235	3,925	5,877	5,297	6,017	6,407	6,732	7,044	7,569	8,894
Guinea/Guinée		138	65	83	131		1,884	1,469	832	1,203	1,317	1,128	1,214	1,740	1,869	1,388	2,274	2,867	3,300	3,241
Guinea/Guinée-Bissau		715	599	802	770	645	465	205	376	368	530	1,310	752	778	1,362	1,163	1,246	1,059	1,558	1,647
Kenya	5,086	5,731	7,208	6,345	10,223	11,049	10,027		11,966		10,460	10,022	10,515	10,957	12,592	11,788	12,320	14,599	20,451	22,930
Lesotho	2,795	1,948	2,498	2,236	2,861	4,082	3,830	4,932	3,443	2,923	2,927	21	225	2,346	2,463	2,525	2,994	3,327	3,384	4,334
Liberia/Libéria	133	1,454	1,366	562	660	774	1,002	835	885		425	232	384	894				1,948	1,766	1,764
Madagascar		1,653	1,595	6,016	3,160	9,082	7,464	3,573	3,588	8,673	3,220	3,717	4,007	4,393	5,417	6,261	6,015	8,126	9,855	10,671
Malawi		4,679	4,170	4,318	4,652	4,758	5,033	4,411	4,707	4,404	5,334	6,301	7,581	8,247	9,431	12,364	14,322	15,183	17,105	
Mali		2,037	1,408	1,164	877	839	933	187	532	1,872	1,621	1,851	2,534	2,578	1,626			1,876	3,309	3,076
Mauritania/Mauritanie	5,320	4,826	3,319	2,784	1,997	7,576	9,427	2,327	2,333	3,977	4,406	2,257	3,722	3,928	4,040	5,284	3,064	4,316	3,996	
Mauritius/Maurice	222	198	191	195	182	132	157	121	152	118	111	119	117	114	129	119	134	130	159	149
Mozambique	2,142	2,916	5,267	5,953	6,561	7,457	6,984	5,787	5,937	5,204	5,645	8,263	10,996	13,863	15,958	15,899	16,609	15,085	16,588	27,885
Namibia/Namibie											4,840	4,427	3,640	2,815	3,703	2,671	2,500	1,756	5,500	
Niger	1,189	2,500	780	3,100	3,600	717	2,871	754	673	665	698	570	556	631	608	5,200			626	3,784
Nigeria/Nigéria	18,498	15,334	14,750	14,292	13,587	9,877	10,838	10,949	10,212	11,439	14,937	14,071	19,723	25,700	13,342	20,122	19,626	14,802	11,601	8,449
Rwanda		1,759	2,493	1,447	1,653	1,495	1,386		1,364	1,419	1,327	2,460	3,287	4,145	4,741	6,387	3,200			
Sao Tome & Prin.				191	108	131	37	40	59	49	40	8	55	13		17	120		97	
Senegal/Sénégal	2,691	2,527	2,605	2,967	2,654	2,014	2,573	1,612	2,417		1,065	927	6,145	5,611	5,965	4,977	5,025	5,038	6,487	6,913
Seychelles		0			3	16	0	16	16	10	10	24	14	10	6	41			5	
Sierra Leone		17	4	2	199	750	847	889	293	816	865	358	130	120		666	1,466	1,664	2,691	2,564
South Africa/Afrique du Sud	64,794	57,506	52,502	53,710	54,476	55,310	59,943	64,115	62,556	62,717	59,349	55,013	57,406	61,486	68,075	80,400	77,652	82,539	89,786	90,292
Swaziland	802						143	3,059	1,955				1,098	1,352	1,394		1,531		1,458	
Togo	305	234	498	385	144	208	126	204	174	343	745	596	1,184	1,071	940	1,324	1,243	1,223	1,005	1,137
Uganda/Ouganda	8,478	928	720	957	163	1,058	1,170	497	2,029			1,392	1,464	3,066	1,045	14,740	19,016	20,662	21,579	26,994
U.R. Tanzania/R.U. Tanzanie		4,419	374	318	7,594	5,103	6,964	11,748	11,783	12,089	14,292	15,477	16,920	18,254	19,516	22,544	25,449	28,711	31,827	34,799
Zaire/Zaïre				4,715	3,710	5,122	8,929					5,043	6,343				21,135	31,400	34,319	
Zambia/Zambie	4,726	4,672	6,137	4,903	5,243	5,342	6,070	6,519	6,948	6,500	6,747	7,909	11,525	12,876	14,239	22,902	23,373	25,732	36,889	
Zimbabwe	3,715	3,832	3,539	3,139	3,494	4,057	4,051	4,577	3,881	5,694	4,759	5,233	5,848	6,002	6,822	9,132	11,710	16,237	20,125	
Other territories:																				
Reunion/Réunion	275	244	246	183	217	153	174	175	167	118	146	173	130	159	131	114	122	136		
St Helena/Ste Hélène		1																		
Total	**173,872**	**179,023**	**167,603**	**178,160**	**187,886**	**213,596**	**224,904**	**230,527**	**246,106**	**243,856**	**269,785**	**278,493**	**314,719**	**343,373**	**334,469**	**396,625**	**392,929**	**352,556**	**406,862**	**402,346**
No. of countries/No. de pays	*28*	*40*	*38*	*40*	*42*	*41*	*42*	*39*	*41*	*38*	*41*	*42*	*44*	*44*	*41*	*41*	*39*	*34*	*39*	*29*
% of countries reporting	*58*	*83*	*79*	*83*	*88*	*85*	*88*	*81*	*85*	*79*	*85*	*88*	*92*	*92*	*85*	*85*	*81*	*71*	*81*	*60*

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Table/Tableau 2.2: African Region - Case notification rates (per 100 000 population)/Région de l'Afrique - Taux de notification des cas (pour 100 000 habitants), 1975-1994

COUNTRY / PAYS	1975	1976	1977	1978	1979	1980	1981	1982	1983	1984	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994
Algeria/Algérie					13.0	14.4		69.7	66.4	61.8	63.2	57.4	48.5	47.7	45.4	46.5	44.4	44.0	50.1	50.2
Angola	25.2	31.3	108.7	141.7	105.8	144.7	104.4	107.3	87.5	130.7	108.5	114.4	101.2	94.7	107.7	111.9	111.6	107.6	71.2	67.1
Benin/Bénin	46.2	50.7	50.0	49.2	50.1	53.1	52.4	49.0	47.9	49.4	51.2	52.6	44.9	46.5	43.2	44.8	45.2	49.1	46.0	40.4
Botswana	465.6	355.4	318.8	315.0	325.7	293.8	277.7	278.6	286.9	298.2	251.3	235.6	275.0	229.5	205.0	230.3	248.6	307.5	332.2	329.6
Burkina Faso		16.5	37.6	16.0	7.1	37.0	33.5	31.0	40.9	11.4	57.7	12.6	17.0	11.1	18.5	16.7			14.8	
Burundi	28.9	17.8	23.6	24.9	11.4	19.1	15.2	21.8	23.5	41.3	48.8	52.5	54.4	72.2	86.3	83.1	86.1		77.6	61.8
Cameroon/Cameroun				6.3	12.3	28.1	25.1	41.1	36.6	34.5	34.0	20.8	36.7	45.8	49.3	51.1	57.5	55.8	56.4	56.8
Cape Verde/Cap Vert		61.8	87.2	101.8	149.3	178.5	117.8	132.8	76.7	93.4	83.5		89.1	84.7	63.1	64.8				
Cent. Afr. Rep./Rép. Centrafricai	80.6	38.2	27.8	25.3	20.5	28.1	32.0	60.9	68.0	18.5	20.0	29.3	18.3	29.2	2.2	72.6	68.1			
Chad/Tchad	48.4	58.9	59.8	67.4	11.7	4.9	6.2	2.7	41.2	29.1	29.6	25.1	20.8	56.0	47.4	46.7	51.2			
Comoros/Comores		221.0	212.6											42.0	26.5	25.8	21.1	18.5	21.3	18.3
Congo	70.9	85.7	68.9	92.2	66.9	44.5	70.7	210.4	228.9	148.5	137.7	157.5	170.2	184.6	201.5	26.5	26.9	49.7	80.9	122.4
Côte d'Ivoire	42.4	41.9	40.2	52.6	50.7	51.2	51.9	56.5	65.2	63.4	57.7	58.8	59.9	58.9	60.5	65.5	64.6	70.7	71.8	
Equat. Guinea/Guinée Equat.										61.6	5.4	0.3	3.3	5.9	45.5	73.9	91.9	71.0	81.5	91.5
Eritrea/Eritree																				185.9
Ethiopia/Ethiopie	94.5	100.6	78.7	75.1	87.0	110.3	113.9	137.3	145.4	162.3	174.4	191.3	197.6	213.6	175.5	186.9	122.8			
Gabon	81.0	81.9	76.1	95.0	98.3	107.3	94.5	86.7	82.2	68.8	86.8	75.5	82.3	66.6	81.9	80.0	76.8	76.3	77.9	80.6
Gambia/Gambie	62.6	33.2	50.3	48.8	46.5	37.3	8.8													
Ghana	64.6	84.5	51.7	48.6	42.7	48.5	36.5	37.9	22.2	15.6	25.2	29.6	42.9	37.5	41.3	42.7	43.5	44.1	46.0	52.5
Guinea/Guinée		3.3	1.5	1.9	3.0		41.4	31.6	17.5	24.7	26.4	22.0	23.0	32.1	33.5	24.1	38.3	46.9	52.3	49.9
Guinea/Guinée-Bissau		108.3	86.1	109.6	100.5	81.1	56.9	24.6	44.4	42.8	60.7	147.4	83.0	84.1	144.3	120.6	126.6	105.3	151.6	156.9
Kenya	37.0	40.2	48.6	41.2	63.8	66.4	58.1		64.5		52.6	48.7	49.4	49.8	55.3	49.9	50.3	57.4	77.5	83.9
Lesotho	235.5	160.5	201.1	175.9	219.6	304.9	277.7	346.6	234.4	192.8	187.3	1.3	13.6	138.1	141.2	140.9	162.6	175.9	174.2	217.1
Liberia/Libéria	8.3	87.6	79.9	31.9	36.3	41.3	51.8	41.8	42.9		19.3	10.2	16.4	37.0				70.8	62.1	60.0
Madagascar		20.6	19.3	70.7	36.0	100.2	79.8	37.0	36.0	84.3	30.3	33.8	35.2	37.4	44.5	49.8	46.3	60.6	71.1	74.6
Malawi		86.3	74.4	74.4	77.6	77.0	79.1	67.5	70.0	63.3	73.6	82.8	94.5	97.3	105.6	132.0	146.5	149.4	162.6	
Mali		32.3	21.9	17.7	13.1	12.2	13.2	2.6	7.1	24.4	20.5	22.7	30.2	29.8	18.2			19.1	32.6	29.4
Mauritania/Mauritanie	388.0	343.5	230.6	188.7	132.1	488.5	592.5	142.5	139.1	231.1	249.5	124.6	200.3	206.2	206.9	263.8	149 2	204.8	184.9	
Mauritius/Maurice	24.9	21.8	20.7	20.8	19.1	13.7	16.1	12.2	15.2	11.7	10.9	11.6	11.3	11.0	12.3	11.3	12.6	12.0	14.6	13.5
Mozambique	20.4	27.0	47.5	52.1	55.8	61.7	56.2	45.4	45.5	39.1	41.7	60.3	79.7	99.8	113.9	112.1	115.1	102.4	109.8	179.6
Namibia/Namibie											410.9	365.9	292.8	220.3	282.0	198.0	180.5	123.4	376.5	
Niger	24.9	50.9	15.4	59.3	66.6	12.8	49.7	12.6	10.9	10.4	10.6	8.4	7.9	8.7	8.1	67.3			7.3	42.8
Nigeria/Nigéria	29.5	23.8	22.3	21.0	19.4	13.7	14.6	14.4	13.0	14.2	18.0	16.5	22.4	28.4	14.3	20.9	19.8	14.5	11.0	7.8
Rwanda		38.8	53.3	29.9	33.1	29.0	26.0		24.0	24.2	21.9	39.4	51.2	62.7	69.7	91.4	44.6			
Sao Tome & Prin.				217.0	118.7	139.4	38.5	40.4	58.4	47.6	37.7	7.4	49.5	11.5		14.3	99.2		76.4	
Senegal/Sénégal	56.0	51.1	51.2	56.7	49.3	36.4	45.2	27.5	40.1		16.7	14.1	91.1	80.9	83.6	67.9	66.8	65.4	82.1	85.3
Seychelles					4.8	25.4		25.0	25.0	15.4	15.4	36.4	20.9	14.7	8.7	58.6			6.9	
Sierra Leone		0.6	0.1	0.1	6.3	23.2	25.7	26.4	8.5	23.3	24.1	9.8	3.5	3.1		16.7	35.8	39.7	62.6	58.2
South Africa/Afrique du Sud	252.4	218.3	194.2	193.7	191.5	189.6	200.4	208.9	198.8	194.4	179.6	162.6	165.8	173.6	187.9	216.9	204.8	212.9	226.4	222.6
Swaziland	166.4						24.8	514.1	318.9				160.1	191.8	192.5		200.1		180.2	
Togo	13.3	10.0	20.7	15.6	5.7	8.0	4.7	7.4	6.1	11.7	24.6	19.1	36.8	32.3	27.5	37.5	34.1	32.5	25.9	28.4
Uganda/Ouganda	75.8	8.0	6.0	7.8	1.3	8.1	8.7	3.6	14.2			8.9	9.1	18.3	6.0	82.1	102.3	107.3	108.2	130.9
U.R. Tanzania/R.U. Tanzanie		27.0	2.2	1.8	42.2	27.5	36.3	59.3	57.7	57.3	65.6	68.7	72.7	76.0	78.7	88.1	96.4	105.5	113.6	120.6
Zaire/Zaire				18.6	14.2	19.0	32.0					15.4	18.7				54.6	78.6	83.2	
Zambia/Zambie	97.6	93.5	118.7	91.7	94.7	93.1	102.1	105.8	108.8	98.2	98.3	111.2	156.5	168.9	180.5	281.0	277.9	296.7	412.8	
Zimbabwe	60.5	60.6	54.3	46.8	50.6	56.9	55.1	60.3	49.5	70.2	56.7	60.3	65.1	64.6	71.0	92.2	114.9	155.1	187.4	
Other territories																				
Reunion/Réunion	56.9	50.2	50.2	37.0	43.4	30.2	33.9	33.6	31.5	21.9	26.5	30.9	22.8	27.3	22.1	18.9	19.9	21.8		
St Helena/Ste Hélène		20.0																		
Total	**77.7**	**62.8**	**57.2**	**53.3**	**51.9**	**58.0**	**61.7**	**67.3**	**65.3**	**70.6**	**70.1**	**62.7**	**68.6**	**78.5**	**75.3**	**87.9**	**80.7**	**80.0**	**85.0**	**90.6**

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Table/Tableau 2.3: African Region - New Smear Positive Cases/Région de l'Afrique - Frottis Positif Nouveaux

COUNTRY / PAYS	No. of cases 1993	No. of cases 1994	Rate (per 100,000 pop) 1993	Rate (per 100,000 pop) 1994	Proportion of new smear + cases to all cases 1993	Proportion of new smear + cases to all cases 1994
Algeria/Algérie		6,793		24.9		49%
Angola	4,874	4,337	47.4	40.6	67%	61%
Benin/Bénin	1,653	1,618	32.5	30.8	71%	76%
Botswana	1,508	1,668	107.6	115.6	32%	35%
Burkina Faso	1,203		12.3		83%	
Burundi	1,861	1,527	30.9	24.6	40%	40%
Cameroon/Cameroun	2,316	1,883	18.5	14.6	33%	26%
Cape Verde/Cap Vert						
Cent. Afr. Rep./Rép. Centrafricain						
Chad/Tchad						
Comoros/Comores		82		13.0		71%
Congo		1,691		67.2		55%
Côte d'Ivoire	7,012		52.7		73%	
Equat. Guinea/Guinée Equat.		274		70.4		77%
Eritrea/Eritree						
Ethiopia/Ethiopie		5,752		10.8		6%
Gabon		395		30.8		38%
Gambia/Gambie						
Ghana						
Guinea/Guinée	2,082	2,158	33.0	33.2	63%	67%
Guinea/Guinée-Bissau	1,059	800	103.0	76.2	68%	49%
Kenya	10,149	11,324	38.5	41.4	50%	49%
Lesotho	1,405	1,330	72.3	66.6	42%	31%
Liberia/Libéria	1,547		54.4		88%	
Madagascar	6,881	7,366	49.7	51.5	70%	69%
Malawi						
Mali						
Mauritania/Mauritanie						
Mauritius/Maurice						
Mozambique	9,526	9,677	63.1	62.3	57%	35%
Namibia/Namibie						
Niger	463	1,865	5.4	21.1	74%	49%
Nigeria/Nigéria	1,723		1.6		15%	
Rwanda						
Sao Tome & Prin.	28		22.0		29%	
Senegal/Sénégal		4,599		56.8		67%
Seychelles	2		2.8		40%	
Sierra Leone		1,408		32.0		55%
South Africa/Afrique du Sud						
Swaziland						
Togo	545		14.0		54%	
Uganda/Ouganda	11,949	14,763	59.9	71.6	55%	55%
U.R. Tanzania/R.U. Tanzanie	15,569	17,164	55.6	59.5	49%	49%
Zaire/Zaïre	14,924		36.2		43%	
Zambia/Zambie						
Zimbabwe	5,331		49.6		26%	
Other territories:						
Reunion/Réunion						
St Helena/Ste Hélène						
Total/Total Average	**103,610**	**98,474**	**21.7**	**22.2**	**25%**	**24%**

WHO/TB/96.197

Table/Tableau 3.1: American Region - Number of tuberculosis cases notified/Région des Amériques - Nombre de cas de tuberculose notifiés, 1975-1994

COUNTRY / PAYS	1975	1976	1977	1978	1979	1980	1981	1982	1983	1984	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994
Antigua & Barbuda	2	3	6	8	2	8	3	0	1	3	2	7	0	3	3	1	0	6		
Argentina/Argentine	14,311	18,808	17,197	16,267	16,569	16,406	16,693	17,292	17,305	16,359	15,987	14,681	13,368	13,267	12,636	12,309	12,185	12,606	13,887	13,683
Bahamas	57	44	33	26	56	70	67	54	58	53	63	52	43	51	52	46	53	63	60	
Barbados/Barbade	26	16	14	16	23	64	3	30	17	14	12	7	3	4	5	5	5	6		
Belize	29	52	28	13	34	21	33	44	140	35	25	23	41	28	30	57	89	65	80	59
Bolivia/Bolivie	2,594	2,965	3,637	3,852	4,062	4,412	5,072	4,777	5,178	4,131	7,679	6,837	8,960	10,664	12,563	11,166	11,223	9,520	8,614	9,431
Brazil/Brésil	53,419	51,301	54,552	56,484	64,734	72,608	86,411	87,822	86,617	88,365	84,310	83,731	81,826	82,395	80,048	74,570	84,990	85,955		87,280
Canada	3,551	3,143	3,194	2,940	2,761	2,885	2,554	2,515	2,186	2,345	1,980	2,046	1,952	2,032	1,982	1,964	2,043	2,091	2,012	
Chile/Chili	8,289	9,482	9,312	8,257	8,105	8,523	7,337	6,941	6,989	6,561	6,644	6,854	6,280	6,324	6,728	6,151		5,304	4,598	
Colombia/Colombie	12,424	11,878	11,569	10,725	10,924	11,589	11,483	12,126	13,716	12,792	12,024	11,639	11,437	11,469	11,329	12,447	12,263	11,199	11,043	8,901
Costa Rica	433	389	371	383	462	396	521	459	479	393	376	418	434	442	311	230	201	118		325
Cuba	1,326	1,270	1,257	1,261	1,133	1,133	833	815	762	705	680	656	630	628	581	546	514	410	790	1,681
Dominica/Dominique	10	14	20	11	5	20	26	18	16	5	8	35	27	7	13	6	14	13	7	12
Dominican Rep./Rép. Domin.	1,468	1,424	1,287	1,387	2,093	2,174	1,778	2,457	2,959	3,100	2,335	2,634	2,459	3,081	3,145	2,597	1,837	3,490	4,033	3,783
Ecuador/Equateur	2,790	2,647	2,858	2,617	3,149	3,950	3,966	3,880	3,985	4,301	4,798	5,687	5,867	5,497	5,480	8,243	6,879	7,313	7,050	9,685
El Salvador	2,875	3,181	2,658	2,449	2,281	2,255	2,091	2,171	2,053	1,564	1,461	1,659	1,647	2,378	617	2,367	2,304	2,495	3,347	3,901
Grenada/Grenade	8	1	11	0	10	17	1	1	6	4	2	1	2	0	4	0	1	3	0	3
Guatemala	6,335	6,208	6,695	5,353	5,307	5,624	6,641	7,277	6,013	6,586	6,570	4,806	5,700	5,739	4,900	3,813	3,755		2,646	2,976
Guyana	137	160	120	110	71	124	117	135	149	165	215	190	117	150	120	168	134	182	91	266
Haiti/Haïti	5,361	4,897	1,110	610	1,390	8,306	6,550	3,337	6,839	5,803	4,959	8,583	8,514	8,054	8,100		10,237			
Honduras	1,793	1,421	1,435	1,323	1,414	1,674	1,696	1,714	1,935	2,120	3,377	4,213	4,227	3,962	4,026	3,647	4,560	4,155	3,745	4,291
Jamaica/Jamaique	348	368	349	365	255	176	178	153	157	160	130	88	133	65	86	123	121	111	115	109
Mexico/Mexique	11,417	11,332	10,713	10,158	26,931	31,247	32,572	24,853	22,795	14,531	15,017	13,180	14,631	15,371	15,489		15,216	8,897	15,145	16,353
Nicaragua	1,160	1,937	1,741	1,932	1,132	1,300	3,723	3,082	2,773	2,705	2,604	2,617	2,983	2,737	3,106	2,944	2,797	2,885	2,798	2,750
Panama	965	1,021	909	888	750	643	580	580	429	413	614	709	765	770	672				1,146	827
Paraguay	1,031	1,075	1,087	1,014	1,317	1,354	1,388	1,415	1,800	1,718	1,931	1,628	1,502	1,438	2,270	2,167	2,283	1,927	2,037	1,850
Peru/Pérou	16,668	22,257	17,660	15,506	15,616	16,011	21,925	21,579	22,753	22,792	24,438	24,702	30,571	36,908	35,687	37,905	40,580	52,552	51,675	48,601
St Kitts & Nevis	13	8	3	1	1	7	4	6	2	3	0	0	0	0	0	0	1	4	6	2
St Lucia/Ste Lucie	54	33	37	50	42	41	39	37	48	55	21	34	25	32	28	13	25	26		24
St Vincent	54	33		21	19	78	11	14	4	23	14	9	3	6	3	2	1	4	13	0
Suriname	63	9	104	71	69	78	81	56	78	76	50	60	77	77	70	70	33	50		53
Trinidad & Tobago/Trinité & Tob.	85	168	157	125	88	80	82	62	112	108	112	119	122	108	124	120	141	142	112	129
USA/Etats Unis	33,989	32,105	30,145	28,521	27,669	27,749	27,373	25,520	23,846	22,255	22,201	22,768	22,517	22,436	23,495	25,701	26,283	26,673	25,287	24,361
Uruguay	1,706	1,635	1,654	1,709	1,850	1,874	1,699	1,450	1,359	1,389	1,201	1,082	1,023	951	987	886	759	699	689	666
Venezuela/Venézuela	4,395	4,222	4,019	4,167	4,161	4,233	4,093	4,159	4,266	4,737	4,822	4,974	4,954	4,557	4,524	5,457	5,216	5,444	5,169	4,877
Other territories:																				
Anguilla		5	0	1	0	0	0	4	0	0	1	0	0	0	0	0	0	0		
Bermuda/Bermudes	6	6	0	3	3	1	2	5	10	3	3	6	2	1	2	0	3	4		
Cayman Islands/Iles Caïman	0	1		0	1	0	2	0	1	1	4	1	0	0	2	2	3	3	2	
French Guiana/Guyane Fran.	137	160	120	110	71	124	117	135	125	171	219	30	53	52	15				91	
Guadeloupe	46	49	0	28	41	82	32	129	50	70				21	8				31	
Martinique	72	67	77	50	74	40		63	61	41	54	40	45	47	11	24	13		33	
Montserrat				4	1	1	0	0	1	7	9	5	13	6	5	1	1	0		0
Neth. Antilles/Antilles Néer.																				
Puerto Rico/Porto Rico	524	457	363	395	310	686	521	473	452	418	338	363	303	275	314	159	241		257	
Turks & Caicos Is./Iles T. & C.		3	0	0	0	2	0	2	5	0	4	2	12			0	0	0	0	
Virgin Is./Iles Vierges (UK)	0	0	0	0	0	0	0	0	1	0	0	0	1	0	1	0	1	0		0
Virgin Is./Iles Vierges (USA)	9	6	2	5	4	0	1	1	2	3	1	1	2	6	4	4	4			
Total	**189,980**	**196,261**	**186,504**	**179,216**	**204,990**	**228,066**	**248,299**	**237,643**	**238,533**	**227,083**	**227,295**	**227,177**	**233,271**	**242,039**	**239,576**	**215,911**	**247,009**	**244,415**	**166,609**	**246,879**
No. of countries/No. de pays	*43*	*45*	*43*	*46*	*46*	*46*	*45*	*46*	*46*	*46*	*45*	*45*	*45*	*45*	*45*	*41*	*42*	*38*	*34*	*32*
% of countries reporting	*91*	*96*	*91*	*98*	*98*	*98*	*96*	*98*	*98*	*98*	*96*	*96*	*96*	*96*	*96*	*87*	*89*	*81*	*72*	*68*

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Table/Tableau 3.2: American Region - Case notification rates (per 100 000 population)/Région des Amériques - Taux de notification des cas (pour 100 000 habitants), 1975-1994

COUNTRY / PAYS	1975	1976	1977	1978	1979	1980	1981	1982	1983	1984	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994
Antigua & Barbuda	3.4	5.1	10.0	13.3	3.3	13.1	4.9		1.6	4.8	3.2	11.3		4.8	4.8	1.6		9.2		
Argentina/Argentine	54.9	71.1	64.0	59.6	59.8	58.4	58.5	59.7	58.8	54.8	52.7	47.7	42.8	41.9	39.3	37.8	37.0	37.8	41.1	40.0
Bahamas	30.0	22.8	16.8	12.9	27.2	33.3	31.2	24.5	25.8	23.1	26.9	21.8	17.7	20.6	20.6	18.0	20.4	23.9	22.4	
Barbados/Barbade	10.6	6.5	5.7	6.5	9.3	25.7	1.2	12.0	6.8	5.6	4.7	2.8	1.2	1.6	2.0	1.9	1.9	2.3		
Belize	21.6	38.2	20.3	9.3	23.8	14.4	22.1	28.8	89.2	21.6	15.1	13.5	23.4	15.6	16.3	30.2	45.9	32.7	39.2	28.1
Bolivia/Bolivie	54.5	60.8	72.8	75.2	77.5	82.4	92.8	85.8	91.3	71.5	130.3	113.6	145.8	169.8	195.6	169.9	166.8	138.1	122.0	130.3
Brazil/Brésil	49.4	46.4	48.2	48.7	54.6	59.9	69.7	69.3	66.9	66.8	62.4	60.8	58.3	57.6	54.9	50.2	56.2	55.9		54.8
Canada	15.3	13.4	13.4	12.2	11.3	11.7	10.3	10.0	8.6	9.1	7.6	7.8	7.3	7.5	7.2	7.1	7.3	7.3	7.0	
Chile/Chili	80.2	90.4	87.4	76.4	73.8	76.5	64.8	60.4	59.8	55.2	55.0	55.8	50.3	49.7	52.0	46.8		39.0	33.3	
Colombia/Colombie	52.3	48.9	46.6	42.3	42.1	43.7	42.4	43.8	48.5	44.3	40.8	38.7	37.3	36.8	35.7	38.5	37.3	33.5	32.5	25.8
Costa Rica	22.0	19.2	17.8	17.8	20.8	17.3	22.1	18.9	19.2	15.3	14.2	15.4	15.5	15.4	10.5	7.6	6.5	3.7		9.7
Cuba	14.2	13.5	13.2	13.2	11.8	11.7	8.5	8.3	7.7	7.0	6.7	6.4	6.1	6.0	5.5	5.2	4.8	3.8	7.3	15.3
Dominica/Dominique	13.9	19.2	27.4	15.1	6.8	27.0	35.1	24.7	21.9	6.8	11.1	48.6	37.5	9.7	18.1	8.5	19.7	18.3	9.9	16.9
Dominican Rep./Rép. Domin.	29.1	27.5	24.3	25.5	37.6	38.2	30.5	41.2	48.5	49.7	36.6	40.4	36.9	45.2	45.2	36.5	25.3	47.2	53.5	49.2
Ecuador/Equateur	40.4	37.2	39.1	34.8	40.7	49.6	48.5	46.1	46.1	48.5	52.7	61.0	61.4	56.1	54.6	80.3	65.5	68.1	64.2	86.3
El Salvador	70.4	76.1	62.1	56.0	51.2	49.8	45.7	47.0	44.2	33.4	30.8	34.5	33.7	47.8	12.2	45.8	43.6	46.2	60.7	69.2
Grenada/Grenade	8.7	1.1	12.2		11.2	19.1	1.1	1.1	6.7	4.4	2.2	1.1	2.2		4.4		1.1	3.3		3.3
Guatemala	105.2	100.3	105.2	81.8	78.9	81.3	93.4	99.5	79.9	85.1	82.5	58.6	67.6	66.1	54.8	41.5	39.7		26.4	28.8
Guyana	18.7	21.7	16.2	14.7	9.4	16.3	15.3	17.5	19.1	21.0	27.2	24.0	14.8	18.9	15.1	21.1	16.7	22.5	11.2	32.2
Haiti/Haïti	109.0	97.9	21.8	11.8	26.4	155.2	120.2	60.2	121.1	100.9	84.6	143.5	139.5	129.3	127.5		154.7			
Honduras	59.4	45.6	44.5	39.6	41.0	46.9	46.0	45.0	49.2	52.3	80.7	97.5	94.9	86.3	85.0	74.7	90.7	80.2	70.2	78.1
Jamaica/Jamaïque	17.3	18.1	16.9	17.5	12.1	8.3	8.2	6.9	7.0	7.0	5.6	3.8	5.7	2.8	3.7	5.2	5.1	4.6	4.8	4.5
Mexico/Mexique	19.4	18.7	17.2	15.9	41.2	46.6	47.4	35.3	31.6	19.7	19.9	17.1	18.5	19.0	18.7		17.6	10.1	16.8	17.8
Nicaragua	47.8	77.5	67.7	73.0	41.6	46.4	129.0	103.8	90.7	86.0	80.6	79.1	88.0	78.9	87.1	80.1	73.5	72.9	68.0	64.3
Panama	56.0	57.7	50.1	47.7	39.4	33.0	29.1	28.5	20.6	19.5	28.3	32.1	33.9	33.4	28.6				45.2	32.0
Paraguay	38.4	38.9	38.2	34.5	43.4	43.2	42.8	42.3	52.0	48.1	52.3	42.7	38.2	35.4	54.2	50.2	51.4	42.1	43.3	38.3
Peru/Pérou	109.9	142.8	110.3	94.3	92.5	92.4	123.4	118.5	122.0	119.4	125.2	123.9	150.2	177.8	168.6	175.6	184.3	234.1	225.8	208.3
St Kitts & Nevis	28.9	17.8	6.7	2.2	2.3	15.9	9.1	13.6	4.5	7.0							2.4	9.5	14.3	4.9
St Lucia/Ste Lucie	50.0	30.0	33.3	44.6	36.8	35.7	33.3	31.1	40.0	45.1	16.9	27.0	19.5	24.8	21.4	9.8	18.5	19.0		17.0
St Vincent	58.1	35.1		21.9	19.6	79.6	11.1	14.0	4.0	22.8	13.7	8.7	2.9	5.7	2.8	1.9	0.9	3.7	11.8	
Suriname	17.3	2.5	29.1	19.9	19.4	22.0	22.7	15.5	21.3	20.5	13.3	15.7	19.9	19.7	17.7	17.5	8.1	12.2		12.7
Trinidad & Tobago/Trinité & Tob.	8.4	16.4	15.2	11.9	8.3	7.4	7.5	5.6	9.9	9.4	9.7	10.1	10.2	8.9	10.1	9.7	11.3	11.2	8.8	10.0
USA/Etats Unis	15.7	14.7	13.7	12.8	12.3	12.2	11.9	11.0	10.2	9.4	9.3	9.5	9.3	9.2	9.5	10.3	10.4	10.5	9.8	9.3
Uruguay	60.3	57.6	57.9	59.5	63.9	64.3	57.9	49.1	45.7	46.5	39.9	35.8	33.6	31.1	32.1	28.6	24.4	22.3	21.9	21.0
Venezuela/Venézuela	34.5	32.0	29.4	29.4	28.4	28.0	26.4	26.1	26.1	28.3	28.1	28.3	27.4	24.6	23.8	28.0	26.1	26.6	24.7	22.8
Other Territories:																				
Anguilla		83.3		16.7				57.1			14.3									
Bermuda/Bermudes	11.3	11.3		5.6	5.6	1.9	3.7	9.1	18.2	5.5	5.4	10.5	3.4	1.7	3.3		4.8	6.5		
Cayman Islands/Iles Caiman		6.7			5.9		11.1		5.0	5.0	19.0	4.5			8.0	7.7	11.1	10.7	6.9	
French Guiana/Guyane Fran.	240.4	271.2	196.7	174.6	109.2	182.4	162.5	177.6	154.3	198.8	240.7	31.3	52.5	49.1	13.5				67.4	
Guadeloupe	14.0	14.9		8.6	12.6	25.1	9.7	38.5	14.7	20.1				5.6	2.1				7.5	
Martinique	21.9	20.4	23.5	15.3	22.7	12.3		19.1	18.3	12.2	15.8	11.6	12.9	13.4	3.1	6.7	3.6		8.9	
Montserrat				33.3	8.3	8.3			9.1	63.6	81.8	45.5	118.2	54.5	45.5	9.1	9.1			
Neth. Antilles/Antilles Néer.																				
Puerto Rico/Porto Rico	17.5	15.0	11.8	12.6	9.8	21.4	16.1	14.5	13.7	12.5	10.0	10.7	8.8	7.9	9.0	4.5	6.8		7.1	
Turks & Caicos Is./Iles T. & C.		42.9				28.6		25.0	55.6		44.4	20.0	120.0							
Virgin Is./Iles Vierges (UK)									7.7				6.7		6.3		5.9			
Virgin Is./Iles Vierges (USA)	9.5	6.2	2.0	5.1	4.1		1.0	1.0	2.0	3.0	1.0	1.0	2.0	5.9	4.0	3.9	3.9			
Total	**34.0**	**34.5**	**32.2**	**30.4**	**34.2**	**37.4**	**40.0**	**37.7**	**37.2**	**34.8**	**34.3**	**33.8**	**34.1**	**34.8**	**33.9**	**34.7**	**34.7**	**34.1**	**28.5**	**34.9**

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Table/Tableau 3.3: American Region - New Smear Positive Cases/Région des Amériques - Frottis Positif Nouveaux

COUNTRY / PAYS	No. of cases 1993	No. of cases 1994	Rate (per 100,000 pop) 1993	Rate (per 100,000 pop) 1994	Proportion of new smear + cases to all cases 1993	Proportion of new smear + cases to all cases 1994
Antigua & Barbuda						
Argentina/Argentine	5,937	5,696	17.6	16.7	43%	42%
Bahamas	41		15.3		68%	
Barbados/Barbade						
Belize	50	36	24.5	17.1	63%	61%
Bolivia/Bolivie	6,833	6,905 [3]	96.7	95.4	79%	73%
Brazil/Brésil		44,687		28.1		51%
Canada	542		1.9		27%	
Chile/Chili	2,629	2,199 [3]	19.0		57%	
Colombia/Colombie	6,987	6,532	20.6	18.9	63%	73%
Costa Rica		230		6.9		71%
Cuba	565	914	5.2	8.3	72%	54%
Dominica/Dominique	6	8	8.5	11.3	86%	67%
Dominican Rep./Rép. Domin.	2,297	1,762	30.5	22.9	57%	47%
Ecuador/Equateur	5,325	6,674 [3]	48.5	59.5	76%	69%
El Salvador	2,471	2,144	44.8	38.0	74%	55%
Grenada/Grenade	0	3		3.3		100% [4]
Guatemala	2,128	2,012	21.2	19.5	80%	68%
Guyana	51	61	6.3	7.4	56%	23%
Haiti/Haiti						
Honduras	2,016	2,385	37.8	43.4	54%	56%
Jamaica/Jamaique	83	61	3.4	2.5	72%	56%
Mexico/Mexique	8,164	9,726	9.1	10.6	54%	59%
Nicaragua	1,714	1,615	41.7	37.8	61%	59%
Panama	1,046	748	41.2	28.9	91%	90%
Paraguay	985	873	21.0	18.1	48%	47%
Peru/Pérou	35,646	33,925	155.8	145.4	69%	70%
St Kitts & Nevis	2	2	4.8	4.9	33%	100% [4]
St Lucia/Ste Lucie						
St Vincent	11	0	10.0		85%	
Suriname						
Trinidad & Tobago/Trinité & Tob.		55		4.3		43%
USA/Etats Unis	16,046	14,346	6.2	5.5	63%	59%
Uruguay	388	381	12.3	12.0	56%	57%
Venezuela/Venézuela	2,849	2,736 [3]	13.6	12.8	55%	56%
Other territories:						
Anguilla						
Bermuda/Bermudes						
Cayman Islands/Iles Caiman	2		0.5		100% [4]	
French Guiana/Guyane Fran.						
Guadeloupe	27				87%	
Martinique	16		8.2		48%	
Montserrat		0				
Neth. Antilles/Antilles Néer.						
Puerto Rico/Porto Rico	117		3.2		46%	
Turks & Caicos Is./Iles T. & C.	0					
Virgin Is./Iles Vierges (UK)						
Virgin Is./Iles Vierges (USA)						
Total	**104,974**	**146,716**	**18.0**	**20.7**	**63%**	**59%**

[3] includes relapses
[4] only new smear + cases notified

Table/Tableau 4.1: Eastern Mediterranean Region -Number of tuberculosis cases notified/Région de la Méditerranée Orientale- Nombre de cas de tuberculose notifies, 1975-1994

COUNTRY / PAYS	1975	1976	1977	1978	1979	1980	1981	1982	1983	1984	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994
Afghanistan	1,788	2,262	36,134	63,364	115,032	71,685	71,554	41,752	52,502	18,784	10,742	14,351	18,091	16,051	14,386	4,332	23,067			
Bahrain/Bahrein	152	189	208	209	214	219	262	156	232	208	194	156	120	142	122	117	142	140	114	
Cyprus/Chypre	195	89	85	62	40	69	69	86	73	39	61	48	35	39	23	29	43	39	37	37
Djibouti	1,825	1,949	1,807	1,547	2,297		2,265	671		1,489	2,262	1,864	1,978	2,030	2,040	2,100	2,900	2,884	3,489	3,311
Egypt/Egypte	1,076	1,361	1,237	1,963	1,933	1,637	1,306	1,805	1,932	1,572	1,308	1,209	22,063	1,378	1,492	2,142	3,634	8,876	3,426	3,911
Iran	16,547	4,357	3,712	28,102	37,798	42,717	11,728	9,509	8,589	10,493	8,728	8,032	10,034	9,967	12,005	9,255	14,246	14,121	20,569	
Iraq	20,273	23,462	19,043	17,203	15,525	11,809	10,614	7,741	6,970	6,807	6,485	6,846	6,517	6,504	8,032	14,684			18,553	
Jordan/Jordanie	469	415	352	304	300	298	646	860	856	672	769	592	537	553	484	439	390	504	427	443
Kuwait/Koweit	905	860	890	900	939	847	819	880	855	812	717	611	540	480	468	277	330	282	217	237
Lebanon/Liban							67	75	284	410	1,943	2,257	2,478				884	884		940
Libya/Libye	1,245	1,136	911	837	766	718	481	512	610	357	325	276	331	416	265	442	239	1,164		
Morocco/Maroc	17,768	24,772	25,889	28,757	24,795	24,878	28,637	28,095	26,944	22,279	26,790	27,553	27,159	25,717	26,756	27,658	27,638	25,403	27,626	30,316
Oman	6,894	3,078	3,513	2,528	2,396	1,872	928	897	802	843	861	1,265	616	477	478	482	442	367	281	304
Pakistan	92,687	95,930	66,083	88,652	263,842	316,340	324,576	326,492	117,739	91,572	111,419	149,004	179,480	194,323	170,562	156,759	194,323		73,175	
Qatar	257	220	160	147	162	257	213	172	206	203	250	220	248	223	191	184	195		200	
Saudi Arabia/Arabie Saoudite	38,012	58,506	31,117	18,584	12,808	10,956	8,263	8,529	7,551	7,163	3,966	3,696	3,029	2,433	2,583	2,415	2,221	2,016	2,386	2,518
Somalia/Somalie				1,211					2,838	2,719	2,722	3,079	7,322	2,728	1,323					2,023
Sudan/Soudan		13,924	25,820	27,754	20,866	32,971	47,431				1,509	2,460	800	693	701	212	16,423	19,503	37,516	
Syria/Syrie	1,552	1,888	1,744	1,542	1,645	1,689	1,908	1,838	1,867	2,111	2,163	3,942	4,290	4,952	5,504	6,018	5,651	5,437		5,127
Tunisia/Tunisie	2,810	2,736	2,585	2,587	2,959	2,504	2,316	2,554	3,062	2,501	2,510	2,487	2,272	2,309	2,403	2,054	2,064	2,164	2,565	2,376
Un. Arab Emirates/E. Arab Unis	243	295	188	389	528	522	638	597	507	534	568	464	818	339	308	285	234	227		426
Yemen/Yémen	2,705	5,173	9,744	14,063	12,641	27,627	17,088	20,167	34,634	34,438	7,241	8,366	9,822	19,993	36,984	4,457	6,643		9,899	11,464
Other territories:																				
UNRWA	119	141	163	141	164	191	139	136	136	123	113	63	82	85	145	64	89	97	72	146
Total	**207,522**	**242,743**	**231,385**	**300,846**	**517,650**	**549,806**	**531,948**	**453,524**	**269,189**	**206,129**	**193,646**	**238,841**	**298,662**	**291,832**	**287,255**	**234,405**	**301,798**	**84,108**	**200,552**	**63,579**
No. of countries/No. de pays	*20*	*21*	*21*	*22*	*21*	*20*	*22*	*21*	*21*	*22*	*23*	*23*	*23*	*22*	*22*	*21*	*21*	*18*	*17*	*20*
% of countries reporting	*87*	*91*	*91*	*96*	*91*	*87*	*96*	*91*	*91*	*96*	*100*	*100*	*100*	*96*	*96*	*91*	*91*	*78*	*74*	*87*

WHO/TB/96.197

Table/Tableau 4.2: Eastern Mediterranean Region - Case notification rates (per 100 000 population)/Région de la Méditerranée Orientale - Taux de notification des cas (pour 100 000 habitants), 1975-1994

COUNTRY / PAYS	1975	1976	1977	1978	1979	1980	1981	1982	1983	1984	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994
Afghanistan	11.6	14.4	227.3	394.3	713.1	446.3	451.3	268.8	346.5	127.0	74.0	100.1	126.8	112.0	98.6	28.8	146.6			
Bahrain/Bahrein	55.9	66.1	69.1	65.9	64.5	63.1	72.6	41.7	59.9	52.0	46.9	36.4	27.1	30.9	25.7	23.9	28.1	26.9	21.3	
Cyprus/Chypre	32.0	14.6	13.8	10.0	6.4	11.0	10.8	13.4	11.2	5.9	9.2	7.1	5.1	5.7	3.3	4.1	6.1	5.4	5.1	5.0
Djibouti	890.2	894.0	778.9	626.3	870.1		752.5	209.0		406.8	578.5	447.0	444.5	430.1	411.3	406.2	543.1	528.2	626.4	585.0
Egypt/Egypte	2.8	3.4	3.0	4.7	4.5	3.7	2.9	3.9	4.1	3.2	2.6	2.4	42.2	2.6	2.7	3.8	6.3	15.0	5.7	6.3
Iran	49.6	12.7	10.5	76.9	100.0	108.8	28.7	22.2	19.2	22.4	17.8	15.8	18.9	18.1	21.0	15.7	23.4	22.6	32.1	
Iraq	184.0	206.0	161.7	141.3	123.4	90.8	79.0	55.8	48.6	46.0	42.3	43.2	39.7	38.3	45.8	81.2			95.4	
Jordan/Jordanie	18.0	15.7	13.1	11.1	10.7	10.2	21.0	26.3	24.6	18.3	20.1	15.0	13.4	13.6	11.7	10.3	8.8	10.8	8.7	8.5
Kuwait/Koweit	89.9	80.1	77.6	73.5	72.2	61.6	56.8	58.5	54.7	49.7	41.7	33.4	27.7	23.2	21.9	12.9	15.9	14.6	12.2	14.5
Lebanon/Liban							2.5	2.8	10.6	15.3	72.8	85.5	95.4				33.9	32.8		32.2
Libya/Libye	50.9	44.5	34.2	30.1	26.3	23.6	15.1	15.4	17.5	9.8	8.6	7.0	8.1	9.8	6.0	9.7	5.1	23.9		
Morocco/Maroc	102.7	139.9	143.0	155.3	130.9	128.4	144.3	138.2	129.4	104.5	122.8	123.5	119.1	110.3	112.3	113.7	111.2	100.0	106.5	114.5
Oman	813.9	346.6	375.3	255.6	229.3	170.0	80.1	73.8	63.0	63.2	61.6	86.5	40.2	29.8	28.5	27.5	24.2	19.2	14.1	14.6
Pakistan	124.0	125.3	84.2	110.2	319.0	370.9	367.8	356.8	123.9	92.8	108.7	140.1	162.8	170.2	144.4	128.6	154.6		55.0	
Qatar	150.3	121.5	83.8	73.5	76.1	112.2	85.2	62.8	68.4	61.5	69.8	57.0	60.0	50.7	41.2	37.9	38.8		37.8	
Saudi Arabia/Arabie Saoudite	524.2	764.4	384.5	217.0	141.2	114.1	81.3	79.4	66.5	59.8	31.4	27.7	21.5	16.4	16.7	15.0	13.5	12.0	13.9	14.4
Somalia/Somalie				19.6					38.1	35.5	34.6	38.2	88.8	32.4	15.5					22.3
Sudan/Soudan		84.3	151.5	157.8	115.1	176.5	246.7				7.0	11.2	3.5	3.0	2.9	0.9	65.0	75.2	140.8	
Syria/Syrie	20.9	24.6	22.0	18.9	19.5	19.4	21.2	19.7	19.4	21.1	20.9	36.8	38.6	43.0	46.2	48.7	44.2	41.1		36.2
Tunisia/Tunisie	50.1	47.6	43.9	42.8	47.6	39.2	35.3	37.9	44.3	35.3	34.6	33.5	29.9	29.8	30.3	25.4	25.0	25.7	29.9	27.2
Un. Arab Emirates/E. Arab Unis	48.1	49.4	26.8	48.0	57.6	51.4	57.9	50.6	40.6	40.6	41.2	32.2	54.4	21.7	19.0	17.1	13.6	12.8		22.9
Yemen/Yémen	38.7	71.9	131.1	182.9	159.0	336.1	201.4	230.2	383.3	369.7	75.4	84.7	96.6	190.8	340.8	39.4	56.0		75.0	82.6
Other territories:																				
UNRWA	10.6	11.8	12.7	10.4	11.4	12.6	8.7	8.3	7.8	6.8	6.1	3.3	4.1	4.3	7.0	2.6	3.9	3.7		
Total	**91.1**	**96.9**	**89.9**	**111.1**	**190.0**	**196.0**	**181.9**	**160.8**	**90.2**	**66.7**	**56.9**	**68.0**	**82.4**	**78.6**	**75.0**	**60.7**	**79.2**	**36.0**	**52.9**	**38.2**

Table/Tableau 4.3: Eastern Mediterranean Region - New Smear Positive Cases/Région de la Méditerranée Orientale- Frottis Positif Nouveaux

COUNTRY / PAYS	No. of cases 1993	1994	Rate (per 100,000 pop) 1993	1994	Proportion of new smear + cases to all cases 1993	1994
Afghanistan						
Bahrain/Bahreïn	82		15.3		72%	
Cyprus/Chypre	10	10	1.4	1.4	27%	27%
Djibouti	1,668	1,743	299.5	308.0	48%	53%
Egypt/Egypte		1,811		2.9		46%
Iran						
Iraq	5,240		26.9		28%	
Jordan/Jordanie	173	161	3.5	3.1	41%	36%
Kuwait/Koweit	148	155	8.3	9.5	68%	65%
Lebanon/Liban		148		5.1		16%
Libya/Libye						
Morocco/Maroc	13,168	14,650	50.8	55.3	48%	48%
Oman	123	135	6.2	6.5	44%	44%
Pakistan	11,020		8.3		15%	
Qatar						
Saudi Arabia/Arabie Saoudite	800		4.7		34%	
Somalia/Somalie		1,168		12.9		58%
Sudan/Soudan						
Syria/Syrie		1,175		8.3		23%
Tunisia/Tunisie	1,006	983	11.7	11.3	39%	41%
Un. Arab Emirates/E. Arab Unis						
Yemen/Yémen	2,896	3,351 [3]	21.9	24.2	29%	29%
Other territories:						
UNRWA						
Total	**36,334**	**25,490**	**9.6**	**15.3**	**18%**	**40%**

[3] includes relapses

Table/Tableau 5.1: European Region - Number of tuberculosis cases notified/Région de l'Europe - Nombre de cas de tuberculose notifiés, 1975-1995

COUNTRY / PAYS	1975	1976	1977	1978	1979	1980	1981	1982	1983	1984	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994
Albania/Albanie	1,899	1,527	1,352	1,152	1,075	1,050	954	978	891	975	916	989	915	759	695	653	628			707
Armenia/Arménie	952	868	851	826	829	756	924	759	702	774	768	832	766	651	649	590	741	235	590	753
Austria/Autriche	2,366	2,506	2,311	2,240	2,200	2,191	2,061	1,942	1,825	1,765	1,442	1,377	1,390	1,402	1,334	1,521	1,426	1,354	1,267	1,264
Azerbaijan/Azerbaïdjan	3,219	3,065	2,784	2,665	3,031	3,080	3,180	3,217	3,176	3,506	3,772	3,804	3,677	3,340	2,989	2,620	2,771	2,821	3,036	2,839
Belarus	7,147	7,002	6,514	6,059	6,361	5,954	6,198	5,468	5,509	5,065	4,873	4,128	3,911	3,769	3,708	3,039	3,745	2,414	4,134	4,348
Belgium/Belgique					2,959	2,687	2,837	2,652	2,190	2,149	1,956	1,893	1,772	1,588	1,648	1,577	1,462	1,335	1,503	1,521
Bosnia-Herz./Bosnie-Herz.																600	3,546	600	680	1,595
Bulgaria/Bulgarie	4,273	4,179	3,745	3,575	3,396	3,280	3,007	2,999	2,892	2,856	2,555	2,530	2,352	2,387	2,301	2,256	2,606	3,096	3,213	5,296
Croatia/Croatie	4,407	4,593	4,468	4,660	4,183	3,999	4,021	3,718	3,632	3,612	3,605	3,355	3,326	2,973	2,861	2,576	2,158	2,189	2,279	2,217
Czech Republic/Rép. tchèque	6,085	5,804	5,684	5,248	4,915	4,962	4,312	4,146	4,016	3,653	3,117	2,553	2,196	2,047	1,905	1,937	2,079	1,986	1,864	1,960
Denmark/Danemark	619	548	514	438	459	430	394	378	348	302	312	299	322	304	328	350	334	359	411	494
Estonia/Estonie	826	777	677	582	608	614	560	563	587	546	541	522	446	471	422	332	406	403	532	645
Finland/Finlande	3,497	3,095	3,027	2,757	2,508	2,247	2,204	2,170	1,882	1,791	1,819	1,546	1,419	1,078	970	772	771	700	542	539
France	25,024	22,911	20,087	18,924	17,341	17,199	16,459	15,425	13,831	12,302	11,290	10,535	10,241	9,191	9,027	9,030	8,510	8,605	9,551	9,093
Georgia/Géorgie	2,819	2,700	2,868	2,681	2,388	2,098	2,124	2,168	1,881	1,855	1,822	1,833	1,810	1,598	1,609	1,537		2,130	3,741	
Germany/Allemagne	40,233	38,599	36,605	34,334	32,034	29,991	27,083	24,865	22,977	20,243	20,074	17,906	17,102	16,282	15,385	14,653	13,834	14,113	14,161	12,982
Greece/Grèce	7,955	8,101	7,981	8,160	8,022	5,412	7,334	5,193	3,880	1,956	1,556	1,566	1,193	907	1,068	877	762	920		
Hungary/Hongrie	6,333	5,790	5,431	5,509	5,120	5,412	5,322	5,181	5,028	4,472	4,852	4,522	4,125	4,016	3,769	3,588	3,658	3,960	4,209	4,163
Iceland/Islande	40	58	23	27	24	25	23	25	24	26	13	13	12	16	18	18	15	16		18
Ireland/Irlande	1,154	1,061	1,145	1,151	1,099	1,152	1,018	975	924	837	804	602	581	534	672	624	640	604		
Israel/Israël	416	306	266	239	242	249	227	232	222	257	368	239	184	226	160	234	505	345	419	395
Italy/Italie	4,070	4,782	4,128	4,063	3,936	3,311	3,182	3,850	4,253	4,008	4,136	4,037	3,839	3,262	4,068	4,185	4,147	4,685	4,734	5,816
Kazakhstan/Kasakhstan	16,135	15,179	14,914	14,910	14,255	14,442	13,876	13,808	13,357	12,563	12,423	13,090	13,286	13,501	13,307	10,969	10,821	10,920	10,425	10,519
Kyrgyzstan/Kyrgisizstan	2,037	1,985	2,110	1,964	1,915	1,973	2,085	2,051	1,981	2,022	2,094	2,122	2,088	2,159	2,132	2,306	2,515	2,582	2,427	2,726
Latvia/Lettonie	1,532	1,427	1,313	1,225	1,167	1,194	1,140	1,077	1,072	1,054	1,223	982	948	938	857	906	943	955	994	1,470
Lithuania/Lituanie	2,236	2,042	1,916	1,693	1,610	1,636	1,599	1,495	1,477	1,420	1,453	1,412	1,372	1,339	1,381	1,471	1,556	1,598	1,895	2,135
Luxembourg	104	226	107	62	98	71	45	41	41	46	42	45	48	16	45	48	48	25	35	33
Malta/Malte	53	38	28	24	31	24	26	13	24	15	11	14	14	12	16	13	26	30	26	
Moldova	3,921	3,946	3,399	3,275	3,033	2,781	2,852	3,197	2,858	2,554	2,732	3,022	2,810	2,510	2,281	1,728	1,910	1,835	2,426	2,626
Monaco	0	0	0	1	0	1	0	0	0	0	1	2	2	1	1	1	0	1		1
Netherlands/Pays Bas	2,230	2,081	1,974	1,911	1,765	1,701	1,734	1,514	1,423	1,400	1,362	1,238	1,227	1,341	1,317	1,369	1,345	1,465	1,587	1,811
Norway/Norvège	499	654	579	458	489	499	461	448	396	373	374	343	307	294	255	285	290	288	256	242
Poland/Pologne	26,255	25,070	26,796	26,801	26,857	25,807	24,087	23,685	23,411	22,527	21,650	20,603	19,757	18,537	16,185	16,136	16,496	16,551	16,828	16,653
Portugal	9,442	7,710	7,498	7,651	6,635	6,873	7,249	7,309	7,052	6,908	6,889	6,624	7,099	6,363	6,664	6,214	5,980	5,927	5,447	5,619
Romania/Roumanie	23,363	20,078	17,814	14,841	14,385	13,553	13,602	13,588	13,570	12,952	12,677	12,860	13,361	14,137	14,676	16,256	15,482	18,097	20,349	21,422
Russia/Russie	86,779	78,577	80,062	76,267	65,565	74,270	73,369	72,236	73,280	74,597	64,644	71,764	70,132	67,553	62,987	50,641	50,407	53,148	63,591	70,822
San Marino/Saint Marin																1	1		3	2
Slovakia/Slovaquie	3,130	3,035	2,761	2,614	2,511	2,465	2,304	2,263	2,252	2,152	1,989	2,022	1,830	1,651	1,501	1,448	1,620	1,733	1,799	1,760
Slovenia/Slovénie	1,161	1,225	1,293	1,238	1,092	1,085	939	982	925	896	923	816	792	760	768	722	583	640	646	526
Spain/Espagne	3,063	3,396	3,685	3,639	4,165	4,853	5,552	7,961	8,987	10,078	10,749	13,755	9,468	8,497	8,058	7,600	9,007	9,703	9,441	
Sweden/Suède	1,446	1,307	1,105	1,127	991	926	875	784	832	754	702	640	545	536	595	557	521	610	616	537
Switzerland/Suisse	2,091	1,823	1,648	1,575	1,447	1,160	1,193	1,167	1,097	946	961	881	1,018	1,201	1,104	1,278	1,134	987	930	924
Tajikistan/Tadjikistan	2,746	3,395	2,963	2,880	2,910	2,647	2,631	2,628	2,509	2,427	2,485	2,610	2,727	2,474	2,621	2,460	2,116	1,671	652	892
TFYRM*																		1,602	1,712	728
Turkey/Turquie	20,314			100,808	39,927	36,716	39,992	26,457	28,634	27,589	30,960	31,029	30,531	27,884	26,669	24,468	25,166	25,455		
Turkmenistan	1,922	1,827	1,918	1,795	1,713	1,677	1,625	1,559	1,541	1,604	1,607	1,614	1,956	1,904	2,169	2,325	2,358	2,074	2,751	
Ukraine	31,835	29,600	29,112	27,111	27,073	26,095	25,646	24,710	24,216	24,356	24,058	22,946	22,145	20,744	20,182	16,465	16,713	18,140	19,964	20,622
United Kingdom/Royaume-Uni	12,620	11,781	11,156	11,204	10,722	10,488	9,290	8,436	7,814	7,026	6,666	6,841	5,732	5,793	6,059	5,908	6,088	6,411	6,481	6,196
Uzbekistan/Ouzbekistan	11,195	10,723	9,555	9,518	9,767	9,163	9,682	8,697	8,817	8,544	8,717	9,427	9,794	10,134	10,632	9,414		9,370	9,774	14,890
Yugoslavia/Yougoslavie	15,092	13,540	13,427	12,932	12,426	11,561	11,754	12,106	11,744	12,119	11,876	11,720	11,526	10,534	9,977	8,477	4,502	3,771	3,843	
Other territories:																				
Andorra/Andorre															12	23	24	21	15	24
Liechtenstein						14	14	7	10	3	2	7	14	10	4	9	2	2		
Total	**404,535**	**358,937**	**347,594**	**432,814**	**355,279**	**349,774**	**347,046**	**325,123**	**319,990**	**309,875**	**299,861**	**303,510**	**292,108**	**277,624**	**268,041**	**243,067**	**232,398**	**248,482**	**241,779**	**239,825**
No. countries/No. de pays	*46*	*45*	*45*	*46*	*47*	*48*	*48*	*48*	*48*	*48*	*48*	*48*	*48*	*48*	*49*	*51*	*49*	*50*	*45*	*43*
% countries reporting	*88*	*87*	*87*	*88*	*90*	*92*	*92*	*92*	*92*	*92*	*92*	*92*	*92*	*92*	*94*	*98*	*94*	*96*	*87*	*83*

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Table/Tableau 5.2: European Region - Case notification rates (per 100 000 population)/Région de l'Europe - Taux de notification annuelles des cas (pour 100 000 habitants), 1975-1994

COUNTRY / PAYS	1975	1976	1977	1978	1979	1980	1981	1982	1983	1984	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994
Albania/Albanie	78.3	61.7	53.6	44.8	41.0	39.3	35.0	35.2	31.4	33.6	30.9	32.6	29.5	23.9	21.5	19.9	18.8			20.7
Armenia/Arménie	33.7	30.1	29.0	27.7	27.4	24.6	29.7	24.1	22.1	24.1	23.8	25.6	23.4	19.8	19.6	17.6	21.8	6.8	16.9	21.2
Austria/Autriche	31.2	33.1	30.5	29.6	29.1	29.0	27.3	25.8	24.2	23.4	19.1	18.2	18.3	18.4	17.4	19.7	18.4	17.3	16.1	16.0
Azerbaijan/Azerbaïdjan	56.6	53.0	47.4	44.7	50.0	50.0	50.8	50.6	49.2	53.4	56.6	56.3	53.7	48.1	42.5	36.8	38.4	38.7	41.1	38.0
Belarus	76.3	74.3	68.8	63.7	66.5	61.8	64.0	56.1	56.1	51.2	48.9	41.2	38.8	37.2	36.4	29.8	36.6	23.6	40.6	42.8
Belgium/Belgique					30.0	27.3	28.8	26.9	22.2	21.8	19.8	19.2	17.9	16.0	16.6	15.8	14.6	13.3	15.0	15.1
Bosnia-Herz./Bosnie-Herz.																13.9	85.2	15.2	18.3	45.2
Bulgaria/Bulgarie	49.0	47.7	42.6	40.6	38.4	37.0	33.8	33.7	32.4	31.9	28.5	28.2	26.2	26.5	25.6	25.1	29.1	34.7	36.2	60.1
Croatia/Croatie	103.4	107.2	103.7	107.6	96.1	91.4	91.4	84.1	81.8	81.1	80.6	74.8	74.0	66.0	63.4	57.0	47.8	48.5	50.5	49.2
Czech Republic/Rép. tchèque	60.9	57.7	56.2	51.5	48.0	48.3	41.8	40.2	38.9	35.4	30.2	24.8	21.3	19.9	18.5	18.8	20.2	19.3	18.1	19.0
Denmark/Danemark	12.2	10.8	10.1	8.6	9.0	8.4	7.7	7.4	6.8	5.9	6.1	5.8	6.3	5.9	6.4	6.8	6.5	7.0	8.0	9.5
Estonia/Estonie	57.7	53.9	46.7	39.9	41.4	41.5	37.6	37.5	38.8	35.8	35.2	33.7	28.6	30.0	26.8	21.1	25.8	25.8	34.3	41.9
Finland/Finlande	74.2	65.5	63.9	58.0	52.7	47.0	45.9	45.0	38.8	36.7	37.1	31.4	28.7	21.8	19.5	15.5	15.4	13.9	10.7	10.6
France	47.5	43.2	37.7	35.4	32.3	31.9	30.4	28.4	25.3	22.4	20.5	19.0	18.4	16.4	16.0	15.9	14.9	15.0	16.6	15.7
Georgia/Géorgie	57.4	54.7	57.8	53.7	47.6	41.6	41.8	42.3	36.4	35.6	34.7	34.6	34.0	29.8	29.8	28.4		39.1	68.7	
Germany/Allemagne	51.1	49.0	46.5	43.7	40.8	38.3	34.7	31.9	29.6	26.1	25.8	23.0	21.9	20.7	19.5	18.5	17.3	17.6	17.5	16.0
Greece/Grèce	87.9	88.5	86.0	86.7	84.1	56.1	75.4	53.1	39.4	19.8	15.7	15.7	11.9	9.0	10.5	8.6	7.4	8.9		
Hungary/Hongrie	60.1	54.7	51.1	51.7	47.9	50.5	49.7	48.5	47.2	42.1	45.9	42.9	39.3	38.4	36.2	34.6	35.5	38.6	41.2	41.0
Iceland/Islande	18.3	26.4	10.4	12.1	10.6	11.0	10.0	10.7	10.2	10.9	5.4	5.3	4.9	6.4	7.1	7.1	5.8	6.2		6.8
Ireland/Irlande	36.3	32.9	35.0	34.7	32.7	33.9	29.6	28.0	26.3	23.7	22.6	16.9	16.4	15.1	19.1	17.8	18.3	17.2		
Israel/Israël	12.0	8.6	7.3	6.4	6.4	6.4	5.7	5.8	5.4	6.2	8.7	5.6	4.2	5.1	3.5	5.0	10.5	6.9	8.0	7.2
Italy/Italie	7.3	8.6	7.4	7.2	7.0	5.9	5.6	6.8	7.5	7.1	7.3	7.1	6.7	5.7	7.1	7.3	7.3	8.2	8.3	10.2
Kazakhstan/Kasakhstan	114.1	106.1	103.2	102.1	96.6	96.9	92.1	90.6	86.6	80.6	78.7	82.0	82.2	82.6	80.5	65.8	64.5	64.7	61.5	61.8
Kyrgyzstan/Kyrgyzistan*	61.7	59.0	61.6	56.3	53.9	54.5	56.5	54.5	51.6	51.7	52.5	52.2	50.4	51.2	49.7	52.9	56.7	57.2	52.9	58.4
Latvia/Lettonie	61.9	57.4	52.5	48.8	46.3	47.1	44.7	42.0	41.6	40.6	46.8	37.3	35.8	35.2	32.1	33.9	35.5	36.2	38.1	56.9
Lithuania/Lituanie	67.6	61.2	57.0	50.1	47.3	47.7	46.2	42.8	41.9	39.9	40.5	39.0	37.6	36.4	37.4	39.6	41.9	43.0	51.1	57.6
Luxembourg	28.7	62.1	29.3	17.0	26.9	19.5	12.4	11.3	11.2	12.6	11.4	12.2	12.9	4.3	11.9	12.6	12.5	6.4	8.9	8.2
Malta/Malte	17.4	12.4	9.0	7.6	9.7	7.4	7.9	3.9	7.1	4.4	3.2	4.0	4.0	3.4	4.5	3.7	7.3	8.4	7.2	
Moldova	102.1	101.8	86.9	83.1	76.3	69.3	70.4	78.1	69.1	61.2	64.8	71.1	65.6	58.2	52.6	39.6	43.6	41.8	55.0	59.4
Monaco				3.8		3.7					3.6	7.1	6.9	3.4	3.3	3.3		3.2		3.2
Netherlands/Pays Bas	16.3	15.1	14.2	13.7	12.6	12.0	12.2	10.6	9.9	9.7	9.4	8.5	8.4	9.1	8.9	9.2	8.9	9.7	10.4	11.8
Norway/Norvège	12.5	16.2	14.3	11.3	12.0	12.2	11.2	10.9	9.6	9.0	9.0	8.2	7.3	7.0	6.0	6.7	6.8	6.7	6.0	5.6
Poland/Pologne	77.2	73.0	77.4	76.7	76.2	72.5	67.1	65.3	64.0	61.0	58.2	55.0	52.4	49.0	42.6	42.3	43.2*	43.3	43.9	43.4
Portugal	103.8	83.8	80.3	80.5	68.7	70.4	73.7	73.9	71.2	69.7	69.6	66.9	71.7	64.3	67.4	63.0	60.7	60.2	55.4	57.2
Romania/Roumanie	110.0	93.6	82.3	67.9	65.3	61.0	60.9	60.5	60.2	57.2	55.8	56.3	58.2	61.2	63.3	70.0	66.8	78.3	88.4	93.5
Russia/Russie	64.6	58.2	58.9	55.8	47.6	53.6	52.6	51.5	51.9	52.5	45.2	49.8	48.3	46.1	42.8	34.2	34.0	35.9	43.0	48.1
San Marino/Saint Marin																4.3	4.3		12.5	8.0
Slovakia/Slovaquie*	66.1	63.4	57.1	53.5	50.9	49.5	45.9	44.8	44.3	42.1	38.7	39.1	35.3	31.7	28.7	27.5	30.7	32.7	33.9	33.0
Slovenia/Slovénie	66.6	69.6	72.7	68.9	60.1	59.2	50.9	52.9	49.6	47.8	49.1	43.2	41.8	39.9	40.2	37.6	30.3	33.1	33.4	27.1
Spain/Espagne	8.6	9.4	10.1	9.9	11.2	12.9	14.7	20.9	23.5	26.3	27.9	35.6	24.4	21.8	20.6	19.4	22.9	24.6	23.9	
Sweden/Suède	17.6	15.9	13.4	13.6	11.9	11.1	10.5	9.4	10.0	9.0	8.4	7.6	6.5	6.3	7.0	6.5	6.1	7.1	7.1	6.1
Switzerland/Suisse	33.0	28.8	26.0	24.9	22.9	18.4	18.8	18.3	17.1	14.6	14.7	13.4	15.3	17.9	16.3	18.7	16.4	14.1	13.2	13.0
Tajikistan/Tadjikistan	79.8	95.8	81.3	76.9	75.6	66.9	64.7	62.8	58.3	54.8	54.5	55.6	56.4	49.6	51.1	46.5	38.9	29.8	11.3	15.0
TFYRM*																		76.5	80.8	34.0
Turkey/Turquie	50.8			236.8	91.9	82.6	87.9	56.7	59.8	56.1	61.5	60.2	58.0	51.8	48.5	43.6	44.0	43.6		
Turkmenistan	76.3	70.6	72.2	65.8	61.3	58.6	55.4	51.9	50.1	51.0	49.8	48.8	57.7	54.7	60.8	63.6	63.0	54.1	70.2	
Ukraine	64.9	60.1	58.9	54.6	54.4	52.2	51.1	49.1	47.9	48.0	47.3	44.9	43.2	40.3	39.1	31.9	32.4	35.1	38.7	40.1
United Kingdom/Royaume-Uni	22.4	20.9	19.8	19.9	19.0	18.6	16.5	15.0	13.8	12.4	11.8	12.1	10.1	10.2	10.6	10.3	10.6	11.1	11.2	10.7
Uzbekistan/Ouzbekistan	80.1	74.6	64.7	62.8	62.9	57.5	59.2	51.8	51.2	48.4	48.1	50.8	51.5	52.0	53.3	46.1		43.8	44.7	66.6
Yugoslavia/Yougoslavie*	166.1	147.6	144.9	138.2	131.6	121.4	122.5	125.2	120.7	123.8	120.6	118.4	115.9	105.5	99.2	83.5	43.8	36.1	36.2	
Other territories:																				
Andorra/Andorre															24.0	44.2	44.4	36.2	24.6	36.9
Liechtenstein						56.0	56.0	26.9	38.5	11.5	7.4	25.9	50.0	35.7	14.3	31.0	6.9	6.9		
Total	**53.6**	**49.9**	**48.0**	**56.1**	**45.2**	**44.2**	**43.6**	**40.6**	**39.7**	**38.2**	**36.8**	**37.0**	**35.3**	**33.4**	**32.0**	**28.7**	**28.2**	**29.1**	**30.9**	**33.0**

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Table/Tableau 5.3: European Region - New Smear Positive Cases/Région de l'Europe - Frottis Positif Nouveaux

COUNTRY / PAYS	No. of cases 1993	No. of cases 1994	Rate (per 100,000 pop) 1993	Rate (per 100,000 pop) 1994	Proportion of new smear + cases to all cases 1993	Proportion of new smear + cases to all cases 1994
Albania/Albanie		250		7.3		35%
Armenia/Arménie		319		9.0		42%
Austria/Autriche						
Azerbaijan/Azerbaïdjan	499	513	6.8	6.9	16%	18%
Belarus	1,493	1,775	14.7	17.5	36%	41%
Belgium/Belgique	484	427	4.8	4.2	32%	28%
Bosnia-Herz./Bosnie-Herz.						
Bulgaria/Bulgarie		3,096		35.1		58%
Croatia/Croatie	1,147	1,083	25.4	24.0	50%	49%
Czech Republic/Rép. tchèque	548	524	5.3	5.1	29%	27%
Denmark/Danemark	243	120	4.7	2.3	59%	24%
Estonia/Estonie	303	347	19.5	22.5	57%	54%
Finland/Finlande	123	176 [3]	2.4	3.5	23%	33%
France	4,455	3,196	7.7	5.5	47%	35%
Georgia/Géorgie						
Germany/Allemagne	4,730	4,177 [3]	5.8	5.1	33%	32%
Greece/Grèce						
Hungary/Hongrie	1,905	1,357	18.7	13.4	45%	33%
Iceland/Islande		6		2.3		33%
Ireland/Irlande						
Israel/Israël	150	129	2.9	2.4	36%	33%
Italy/Italie		1,441		2.5		25%
Kazakhstan/Kasakhstan	3,207	3,022	18.9	17.7	31%	29%
Kyrgyzstan/Kyrgisizstan		681		14.6		25%
Latvia/Lettonie	470	451	18.0	17.5	47%	31%
Lithuania/Lituanie	688		18.5		36%	
Luxembourg						
Malta/Malte	13		3.6		50%	
Moldova	615	704	14.0	15.9	25%	27%
Monaco						
Netherlands/Pays Bas	1,063		7.0		67%	
Norway/Norvège		86		2.0		36%
Poland/Pologne	7,606	4,000	19.9	10.4	45%	24%
Portugal		2,072		21.1		37%
Romania/Roumanie	9,339	10,385	40.6	45.3	46%	48%
Russia/Russie		30,389		20.6		43%
San Marino/Saint Marin						
Slovakia/Slovaquie	882	409	16.6	7.7	49%	23%
Slovenia/Slovénie	361	294	18.6	15.1	56%	56%
Spain/Espagne						
Sweden/Suède	312	106	3.6	1.2	51%	20%
Switzerland/Suisse	528	507	7.5	7.1	57%	55%
Tajikistan/Tadjikistan						
TFYRM*						
Turkey/Turquie						
Turkmenistan	472		12.0		17%	
Ukraine	8,314	8,471	16.1	16.5	42%	41%
United Kingdom/Royaume-Uni	283	270	0.5	0.5	4%	4%
Uzbekistan/Ouzbekistan		7,487		33.5		50%
Yugoslavia/Yougoslavie						
Other territories:						
Andorra/Andorre	15	24	24.6	36.9	100% [4]	100% [4]
Liechtenstein						
Total	**50,248**	**88,294**	**6.4**	**12.1**	**21%**	**37%**

* The Former Yugoslav Republic of Macedonia/Ex-République yougoslave de Macedoine
[3] includes relapses
[4] only new smear + cases notified

Table/Tableau 6.1: South East Asian Region - Number of tuberculosis cases notified/Région de l'Asie du Sud-Est - Nombre de cas de tuberculose notifiés, 1975-1994

COUNTRY / PAYS	1975	1976	1977	1978	1979	1980	1981	1982	1983	1984	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994
Bangladesh	11,549	6,517	25,943	26,941	34,377	39,774	42,644	49,870	52,961	45,679	41,802	45,599	45,355	44,280	45,191	48,673	56,052	31,400	54,001	48,276
Bhutan/Bhoutan				976	1,159	1,539	2,657	720	1,017	904	1,073	1,582	608	1,126	1,525	1,154	996	140	108	1,159
DPR Korea/RPD Corée																				
India/Inde	675,508	589,768	610,531	668,794	662,600	705,600	769,540	923,095	1,075,098	1,109,310	1,168,804	1,279,536	1,403,122	1,457,288	1,510,500	1,519,182	1,555,353	1,121,120	1,081,279	1,114,374
Indonesia/Indonesie	17,402	19,913	19,374	19,517	21,924	25,235	32,461	33,000	31,809	32,432	17,681	16,750		97,505	105,516	74,470	469,832	98,458	62,966	49,647
Maldives	173	185	139	126	106	73	112	111	143	123	91	111	115	85	203	152	123	92	175	249
Myanmar	10,585	9,935	10,156	10,215	11,846	12,744	12,461	12,069	11,012	11,045	10,506	10,840	11,986	9,348	10,940	12,416	14,905	17,000	19,009	15,583
Nepal/Népal		1,235	1,975	959	1,264	1,020	337	1,459	700	190	52	252	1,012	1,603	11,003	10,142	8,983		13,161	15,572
Sri Lanka	7,324	6,823	5,994	6,360	6,152	6,212	6,288	7,334	6,666	6,376	5,889	6,596	6,411	6,092	6,429	6,666	6,174	4,026	6,573	6,372
Thailand/Thailande		2,195	7,066	10,584	13,297	45,704	49,452	48,553	65,413	69,240	77,611	52,152	51,835	50,021	44,553	46,510	43,858	47,697	49,668	47,767
Total	**722,541**	**636,571**	**681,178**	**744,472**	**752,725**	**837,901**	**915,952**	**1,076,211**	**1,244,819**	**1,275,299**	**1,323,509**	**1,413,418**	**1,520,444**	**1,667,348**	**1,735,860**	**1,719,365**	**2,156,276**	**1,319,933**	**1,286,940**	**1,298,999**
No. countries/No. de pays	*6*	*8*	*8*	*9*	*9*	*9*	*9*	*9*	*9*	*9*	*9*	*9*	*8*	*9*	*9*	*9*	*9*	*8*	*9*	*9*
% of countries reporting	*60*	*80*	*80*	*90*	*90*	*90*	*90*	*90*	*90*	*90*	*90*	*90*	*80*	*90*	*90*	*90*	*90*	*80*	*90*	*90*

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Table/Tableau 6.2: South East Asian Region - Case notification rates (per 100,000 population)Région de l'Asie du Sud-East - Taux de notification des cas (pour 100 000 habitants), 1975-1994

COUNTRY / PAYS	1975	1976	1977	1978	1979	1980	1981	1982	1983	1984	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994
Bangladesh	15.1	8.3	32.0	32.2	40.0	45.1	47.2	53.9	56.0	47.3	42.4	45.4	44.3	42.5	42.6	45.0	50.8	27.9	46.9	41.0
Bhutan/Bhoutan				82.2	95.6	124.4	210.4	55.9	77.3	67.2	78.0	112.2	42.0	75.9	100.6	74.7	63.6	8.8	6.8	71.8
DPR Korea/RPD Corée																				
India/Inde	108.8	93.0	94.3	101.2	98.2	102.4	109.3	128.3	146.2	147.5	152.2	163.1	175.2	178.3	181.1	178.6	179.3	126.8	119.9	121.3
Indonesia/Indonesie	12.8	14.4	13.7	13.5	14.8	16.7	21.1	21.0	19.8	19.8	10.6	9.8		55.2	58.7	40.7	252.9	52.2	32.9	25.5
Maldives	126.3	131.2	95.9	84.6	68.8	46.2	68.7	66.1	82.7	69.1	49.5	58.7	58.7	42.1	97.1	70.4	55.2	39.8	73.5	101.2
Myanmar	34.8	31.9	32.0	31.5	35.8	37.7	36.1	34.2	30.6	30.0	28.0	28.3	30.6	23.3	26.7	29.7	34.9	38.9	42.6	34.2
Nepal/Népal		9.2	14.4	6.8	8.7	6.9	2.2	9.3	4.3	1.1	0.3	1.4	5.7	8.8	58.6	52.7	45.5		63.2	72.9
Sri Lanka	53.8	49.3	42.6	44.4	42.2	41.9	41.7	47.8	42.7	40.2	36.5	40.3	38.7	36.3	37.8	38.7	35.4	22.8	36.7	35.2
Thailand/Thailande		5.2	16.2	23.7	29.1	97.8	103.8	100.0	132.4	137.8	151.8	100.2	97.9	92.8	81.3	83.7	77.9	83.7	86.3	82.1
Total	**76.1**	**65.6**	**68.7**	**73.5**	**72.7**	**79.2**	**84.7**	**97.4**	**110.3**	**110.6**	**112.4**	**117.6**	**124.0**	**133.4**	**136.2**	**132.4**	**162.9**	**97.9**	**93.7**	**94.4**

Table/Tableau 6.3: South East Asian Region - New Smear Positive Cases/Région de l'Asie du Sud-Est - Frottis Positif Nouveaux

COUNTRY / PAYS	No. of cases 1993	No. of cases 1994	Rate (per 100,000 pop) 1993	Rate (per 100,000 pop) 1994	Proportion of new smear + cases to all cases 1993	Proportion of new smear + cases to all cases 1994
Bangladesh	18,993	1,710	16.5	1.5	35%	4% [5]
Bhutan/Bhoutan		352		21.8		30%
DPR Korea/RPD Corée						
India/Inde	225,256	226,543	25.0	24.7	21%	20%
Indonesia/Indonesie	62,966	49,647	32.9	25.5	100% [4]	100% [4]
Maldives	126	125	52.9	50.8	72%	50%
Myanmar						
Nepal/Népal	6,679	10,442	32.1	48.9	51%	67%
Sri Lanka	3,335	3,405	18.6	18.8	51%	53%
Thailand/Thaïlande		20,260		34.8		42%
Total	**317,355**	**312,484**	**23.1**	**22.7**	**25%**	**24%**

[4] only new smear + cases notified
[5] data for project areas only

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Table/Tableau 7.1: Western Pacific Region - Number of tuberculosis cases notified/Région du Pacifique Occidental - Nombre de cas de tuberculose notifies, 1975-1994

COUNTRY / PAYS	1975	1976	1977	1978	1979	1980	1981	1982	1983	1984	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994
Australia/Australie	1,347	1,387	1,251	1,292	1,542	1,457	1,386	1,270	1,219	1,299	1,088	906	907	954	952	1,016	950	1,011	991	1,020
Brunei Darussalam/Brunéi Darus		336		230	216	196	285	245	276	256	238	212	189	126	128	143		180	160	
Cambodia/Cambodge						2,576	1,980	8,158	7,572	10,241	10,145	10,325	9,106	10,691	7,906	6,501	10,903	16,148	13,270	15,172
China/Chine								98,654	117,557	151,564	226,899	265,095	251,600	304,639	310,607	375,481	345,000	320,426	344,218	363,804
Cook Islands/Iles Cook	55	20	15	36	30	37	10	19	29	20	36	17	16	20	1	1	8	12	6	4
Fiji/Fidji	268	259	257	187	205	210	180	163	185	165	230	199	173	162	218	226	247	240	183	280
Japan/Japon	108,088	97,924	89,245	80,629	76,455	70,916	65,867	63,940	62,021	61,521	58,567	56,690	56,496	54,357	53,112	51,821	50,612	48,956	48,461	44,590
Kiribati	279	278	97	40	94	146	187	193	127	111	103	129	110	208	121	68	91	100	99	253
Laos	1,806	1,132	999	1,028		7,630		4,706	4,700	6,528	4,258	1,514	3,468	7,279	2,952	1,826	1,951	994	2,093	1,135
Malaysia/Malaisie	11,692	11,098	10,264	10,441	11,094	11,218	10,970	11,944	11,634	10,577	10,569	10,735	11,068	10,944	10,686	11,702	11,059	11,420	12,285	11,708
Marshall Islands/Iles Marshall	0	17	8	6	4	6	7	12	15	12	15	37	32	11	7		26	52	61	
Micronesia/Micronésie								67	73	75	66	60	98	77	68	367	350	111	151	173
Mongolia/Mongolie	1,116	1,122	1,075	1,103	1,123	1,161	1,094	1,340	1,512	1,651	2,992	2,818	2,432	2,541	2,237	1,577	1,611	1,502	1,433	1,730
Nauru			7	4	2	0	2	8	0	0	0	8	6	8	0	7				4
New Zealand/Nouvelle-Zélande	663	611	608	595	542	474	448	437	415	404	359	320	296	295	303	348	335	317	274	352
Niue	16	0	0	0	0	1	0	2	3	1	0	5	0	3		0		2	1	2
Palau	20	5	7	14	9	17	10	17	14	20	26	13	38	17	3		6	4	25	41
Papua N.Guinea/Pap.N.-Guinée		1,782	2,212	2,446	2,232	2,525	2,508	2,742	2,955	3,505	3,453	2,877	2,251	4,261	3,396	2,497	3,401	2,540	7,451	5,335
Philippines	133,537	148,057	107,108	118,587	108,813	112,307	116,821	104,715	106,300	151,863	151,028	153,129	163,740	183,113	217,272	317,008	207,371	236,172	178,134	180,044
Republic of Korea/Rép. Corée	121,735	121,735	153,334	107,819	81,910	89,803	98,532	100,878	91,572	85,669	87,169	88,789	87,419	74,460	70,012	63,904	57,864	48,070	46,999	38,155
Samoa	51	79	36	59	58	59	49	43	41	37	43	65	29	29	37	44	44	26	49	45
Singapore/Singapour	3,097	2,813	2,760	2,964	2,800	2,710	2,425	2,179	2,065	2,143	1,952	1,760	1,616	1,666	1,617	1,591	1,841	1,778	1,830	1,677
Solomon Islands/Iles Salomon	261	307	355	411	455	266	313	324	302	337	377	292	334	372	488	382	309	364	367	332
Tonga	90	67	79	89	71	64	49	45	50	54	49	35	24	14	36	23	20	29	33	23
Tuvalu		17	5	15	7	33	18	12	23	9	32	27	22	24	26	23	30	30	28	19
Vanuatu	214	214	150	131	184	178	92	173	196	188	124	131	90	118	144	140	230	193	114	152
Viet-Nam	19,514	56,272	170,878	68,659	11,821	43,062	43,506	51,206	43,185	43,875	46,941	47,557	55,505	52,463	52,270	50,203	59,784	56,594	52,994	51,763
Other territories:																				
American Samoa/Samoa am.	12	12	7	8	2	2	6	6	8	12	5	8	9	13	5	9	3	1	4	4
French Polynesia/Polynésie fran.	134	110	95	78	81	76	66	65	78	80	78	85	80	63	73	59	49	83	82	89
Guam	49	46	67	64	71	55	41	49	48	54	37	49	34	41	75			60	70	94
Hong Kong	8,192	7,928	7,191	6,623	7,903	8,065	7,729	7,527	7,301	7,843	7,545	7,432	7,269	7,021	6,704	6,510	6,283	6,545	6,537	6,319
Macau/Macao	1,383	1,088	120	1,017	442	1,101	585	233	455	671	571	420	389	320	274	343	329	294	285	
Mariana Islands/Iles Mariannes							26	75	74	58	64	16	56	27	28	28		67		46
New Caledonia/Nouvelle-Caléd.	163	155	155	108	68	108	128	120	171	144	104	98	74	111	128	143	184	140		132
Tokelau	0		0	0	10	0	1	0	0	0	2	0	9	1	0	1	1	1		0
Wallis & Futuna	4	34	44	6	1	23	24	5	17	14	14		34	1	30		22	4	11	11
Total	**413,786**	**454,905**	**548,429**	**404,689**	**308,245**	**356,482**	**355,345**	**461,572**	**462,193**	**541,001**	**615,179**	**651,853**	**655,019**	**716,450**	**741,916**	**893,992**	**760,914**	**754,466**	**718,699**	**724,508**
No. countries/No. de pays	*28*	*30*	*31*	*32*	*31*	*33*	*33*	*36*	*36*	*36*	*36*	*35*	*36*	*36*	*35*	*32*	*31*	*35*	*32*	*33*
% of countries reporting	*78*	*83*	*86*	*89*	*86*	*92*	*92*	*100*	*100*	*100*	*100*	*97*	*100*	*100*	*97*	*89*	*86*	*97*	*89*	*92*

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Table/Tableau 7.2: Western Pacific Region - Case notification rates (per 100 000 population)/Région du Pacifique Occidental - Taux de notification des cas (pour 100 000 habitants), 1975-1994

COUNTRY / PAYS	1975	1976	1977	1978	1979	1980	1981	1982	1983	1984	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994
Australia/Australie	9.7	9.9	8.8	9.0	10.7	10.0	9.4	8.5	8.0	8.4	7.0	5.7	5.6	5.8	5.7	6.0	5.5	5.8	5.6	5.7
Brunei Darussalam/Brunéi Darus		201.2		127.8	116.1	101.6	142.5	118.9	129.6	116.4	105.3	91.0	79.1	51.4	51.0	55.6		66.9	58.4	
Cambodia/Cambodge						39.6	30.1	120.6	107.9	140.5	134.2	132.1	112.8	128.5	92.2	73.5	119.6	171.8	137.0	152.2
China/Chine								9.6	11.3	14.4	21.2	24.4	22.8	27.2	27.3	32.5	29.5	27.1	28.8	30.1
Cook Islands/Iles Cook	289.5	105.3	78.9	200.0	166.7	205.6	55.6	111.8	170.6	117.6	211.8	100.0	94.1	111.1	5.6	5.6	42.1	63.2	31.6	21.1
Fiji/Fidji	46.5	44.1	43.0	30.7	33.0	33.1	27.8	24.6	27.4	23.9	32.9	28.1	24.3	22.7	30.3	31.1	33.6	32.2	24.1	36.3
Japan/Japon	96.9	86.8	78.4	70.2	66.0	60.7	56.0	53.9	52.0	51.2	48.5	46.7	46.3	44.3	43.1	41.9	40.8	39.4	38.9	35.7
Kiribati	507.3	487.7	167.2	67.8	156.7	239.3	301.6	306.3	198.4	168.2	153.7	189.7	159.4	297.1	170.4	94.4	123.0	133.3	130.3	328.6
Laos	59.7	36.9	32.3	32.9		238.1		141.3	137.9	186.7	118.5	40.9	90.8	184.7	72.5	43.5	45.0	22.2	45.5	23.9
Malaysia/Malaisie	95.4	88.5	80.0	79.5	82.6	81.5	77.7	82.5	78.3	69.3	67.4	66.7	66.9	64.4	61.3	65.4	60.3	60.8	63.8	59.4
Marshall Islands/Iles Marshall		54.8	25.0	18.2	11.8	17.1	19.4	32.4	39.5	30.8	37.5	90.2	76.2	25.0	15.6		54.2	106.1	122.0	
Micronesia/Micronésie								19.9	21.2	21.3	18.2	16.0	25.3	19.2	16.3	85.5	79.4	24.6	32.8	36.7
Mongolia/Mongolie	77.1	75.4	70.3	70.1	69.4	69.8	64.0	76.2	83.7	88.9	156.7	143.6	120.6	122.6	105.2	72.4	72.4	66.1	61.8	73.2
Nauru			100.0	57.1	28.6		25.0	100.0				88.9	66.7	88.9		70.0				36.4
New Zealand/Nouvelle-Zélande	21.5	19.7	19.6	19.2	17.5	15.2	14.3	13.8	13.0	12.5	11.1	9.8	9.0	8.9	9.1	10.4	9.9	9.2	7.9	10.0
Niue	400.0					33.3		66.7	100.0	33.3		250.0		150.0				100.0	50.0	100.0
Palau	181.8	45.5	63.6	116.7	75.0	141.7	83.3	130.8	107.7	153.8	185.7	92.9	271.4	113.3	20.0		37.5	25.0	156.3	241.2
Papua N.Guinea/Pap.N.-Guinée		63.7	77.1	83.2	74.1	81.8	79.4	85.0	89.6	104.0	100.3	81.8	62.6	116.0	90.4	65.0	86.6	63.2	181.3	126.9
Philippines	310.5	336.1	237.6	257.2	230.6	232.4	235.9	206.2	204.1	284.4	276.3	273.9	286.7	314.1	365.0	521.6	334.0	372.4	274.9	272.0
Republic of Korea/Rép. Corée	345.0	339.2	420.5	291.2	218.0	235.6	254.7	257.1	230.1	212.5	213.6	215.2	209.8	177.0	164.9	149.1	133.7	110.0	106.5	85.6
Samoa	33.3	51.3	23.1	37.6	36.7	37.1	30.8	26.9	25.6	23.1	26.9	40.4	18.0	18.0	22.8	27.2	26.8	15.8	29.3	26.6
Singapore/Singapour	136.9	122.5	118.6	125.8	117.4	112.2	99.3	88.1	82.6	84.7	76.3	68.0	61.8	63.0	60.4	58.8	67.3	64.3	65.5	59.4
Solomon Islands/Iles Salomon	137.4	155.8	174.0	194.8	207.8	117.2	133.2	133.3	119.8	129.1	139.6	104.7	115.6	124.4	157.4	119.4	93.4	106.1	103.7	90.7
Tonga	102.3	75.3	87.8	97.8	78.0	69.6	53.3	49.5	54.9	59.3	53.8	38.0	25.8	14.9	37.9	24.0	20.6	29.9	33.7	23.5
Tuvalu		242.9	71.4	214.3	100.0	412.5	225.0	150.0	287.5	112.5	400.0	337.5	275.0	300.0	288.9	255.6	333.3	333.3	311.1	211.1
Vanuatu	209.8	203.8	138.9	118.0	161.4	152.1	76.7	140.7	155.6	145.7	93.9	96.3	64.7	83.1	98.6	94.0	150.3	122.9	70.8	92.1
Viet-Nam	40.6	114.5	340.0	133.6	22.5	80.2	79.2	91.2	75.3	74.8	78.4	77.7	88.8	82.2	80.1	75.3	87.7	81.2	74.3	71.0
Other territories:																				
American Samoa/Samoa am.	40.0	40.0	23.3	25.8	6.3	6.3	18.2	17.1	22.2	31.6	12.8	19.5	21.4	29.5	11.1	19.1	6.3	2.0	7.8	7.5
French Polynesia/Polynésie fran.	103.1	82.1	68.8	54.9	55.1	50.3	42.3	40.6	47.3	47.3	44.8	47.5	43.7	33.5	37.8	29.9	24.3	40.3	38.9	41.4
Guam	51.6	47.4	67.0	62.7	68.3	51.4	37.6	43.8	42.1	46.2	31.1	40.2	27.2	32.0	57.3			42.9	48.6	63.9
Hong Kong	186.4	175.4	154.6	138.3	160.7	160.1	150.3	143.8	137.3	145.5	138.3	134.7	130.5	124.9	118.4	114.1	109.4	113.3	112.5	108.2
Macau/Macao	591.0	463.0	51.1	430.9	184.9	455.0	235.9	91.4	172.3	245.8	201.1	142.9	127.5	100.9	83.0	100.3	92.4	79.5	74.2	
Mariana Islands/Iles Mariannes							162.5	468.8	462.5	341.2	336.8	69.6	200.0	79.4	71.8	65.1		142.6		97.9
New Caledonia/Nouvelle-Caléd.	122.6	114.0	112.3	77.1	48.2	75.5	88.3	81.6	114.0	94.7	67.1	62.4	46.3	68.5	77.6	85.1	108.2	80.9		74.2
Tokelau					500.0		50.0				100.0		450.0	50.0		50.0	50.0	50.0		
Wallis & Futuna	44.4	377.8	440.0	60.0	9.1	209.1	218.2	41.7	141.7	116.7	116.7		261.5	7.7	230.8		157.1	28.6	78.6	78.6
Total	**147.7**	**158.1**	**187.6**	**136.3**	**103.3**	**114.0**	**113.1**	**34.2**	**33.8**	**39.0**	**43.7**	**45.6**	**45.1**	**48.6**	**49.6**	**58.9**	**49.5**	**48.5**	**45.7**	**45.5**

Table/Tableau 7.3: Western Pacific Region - New Smear Positive Cases/Région du Pacifique Occidental - Frottis Positif Nouveaux

COUNTRY / PAYS	No. of cases 1993	No. of cases 1994	Rate (per 100,000 pop) 1993	Rate (per 100,000 pop) 1994	Proportion of new smear + cases to all cases 1993	Proportion of new smear + cases to all cases 1994
Australia/Australie	557		3.2		56%	
Brunei Darussalam/Brunéi Darus	68		24.8		43%	
Cambodia/Cambodge		11,058		110.9		73%
China/Chine	84,898	104,729	7.1	8.7	25%	29%
Cook Islands/Iles Cook	4	1	21.1	5.3	67%	25%
Fiji/Fidji	58	60	7.7	7.8	32%	21%
Japan/Japon	17,890	16,770	14.4	13.4	37%	38%
Kiribati	99	184	130.3	239.0	100% [4]	73%
Laos	765	752	16.6	15.9	37%	66%
Malaysia/Malaisie	6,954	6,861	36.1	34.8	57%	59%
Marshall Islands/Iles Marshall	12		24.0		20%	
Micronesia/Micronésie	8	15	1.7	3.2	5%	9%
Mongolia/Mongolie	86	145	3.7	6.1	6%	8%
Nauru		2		18.2		50%
New Zealand/Nouvelle-Zélande	91	61	2.6	1.7	33%	17%
Niue	0	0				
Palau	8	11	50.0	64.7	32%	27%
Papua N.Guinea/Pap.N.-Guinée	1,653	573	40.2	13.6	22%	11%
Philippines	92,279	87,401	142.4	132.0	52%	49%
Republic of Korea/Rép. Corée	16,630	13,266	37.7	29.8	35%	35%
Samoa	21	18	12.6	10.7	43%	40%
Singapore/Singapour	513	861	18.4	30.5	28%	51%
Solomon Islands/Iles Salomon	155	114	43.8	31.1	42%	34%
Tonga	16	17	16.3	17.3	48%	74%
Tuvalu	2	1	22.2	11.1	7%	5%
Vanuatu		62		37.6		41%
Viet-Nam	36,534	35,813	51.2	49.1	69%	69%
Other territories:						
American Samoa/Samoa am.	1	4	2.0	7.5	25%	100% [4]
French Polynesia/Polynésie fran.	39	38	18.5	17.7	48%	43%
Guam		40		27.2		43%
Hong Kong	2,429		41.8		37%	
Macau/Macao	108		28.1		38%	
Mariana Islands/Iles Mariannes		22		46.8		48%
New Caledonia/Nouvelle-Caléd.		42		23.6		32%
Tokelau		0				
Wallis & Futuna	2	2	14.3	14.3	18%	18%
Total	**261,880**	**278,923**	**16.6**	**17.5**	**36%**	**38%**

[4] only new smear + cases notified