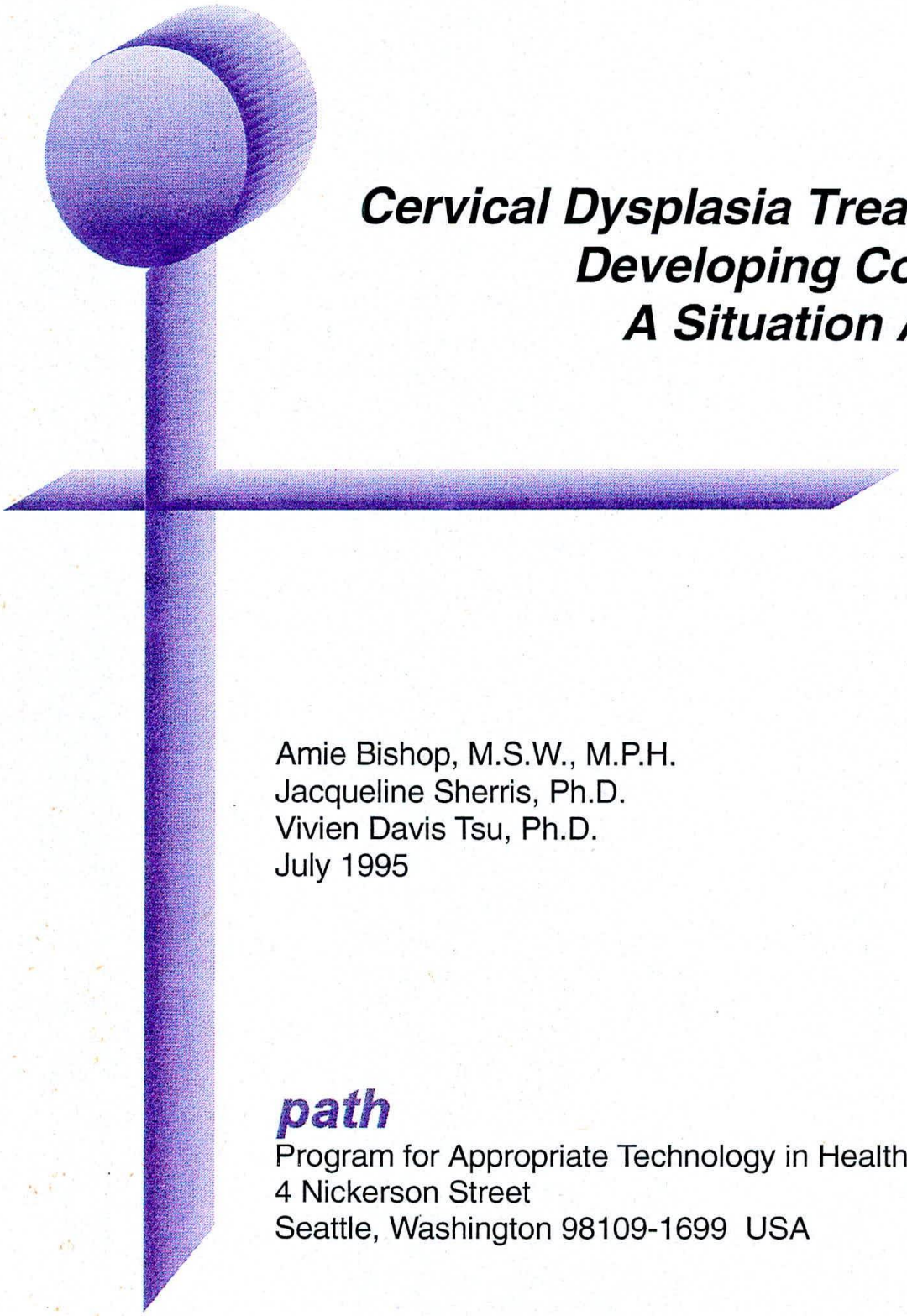

Cervical Dysplasia Treatment in Developing Countries: A Situation Analysis

Amie Bishop, M.S.W., M.P.H.
Jacqueline Sherris, Ph.D.
Vivien Davis Tsu, Ph.D.
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path
Program for Appropriate Technology in Health
4 Nickerson Street
Seattle, Washington 98109-1699 USA

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path
Program for Appropriate Technology in Health
4 Nickerson Street
Seattle, Washington 98109-1699 USA
Tel: (206) 285-3500
Fax: (206) 285-6619
Internet: info@path.org
WWW: http://www.path.org

This document was prepared for the World Bank Population, Health, and Nutrition Department's FY94 program to support Safe Motherhood.

ACKNOWLEDGMENTS

We would like to thank the Population, Health, and Nutrition Department of the World Bank for supporting the research and preparation of this document. In particular, we would like to thank Ms. Kirrin Gill and Ms. Anne Tinker for their helpful feedback and encouragement. Thanks are due as well to our many colleagues at PATH who provided input on content and presentation of the document. We also would like to express our special thanks to the following expert reviewers, whose input was greatly appreciated: Beverly Barnett, MB, MS, DM, MPH (PAHO, Bridgetown, Barbados); Peter Blake, MD, FRCR (The Royal Marsden NHS Trust, London, England); Paul Blumenthal, MD, MPH (JHPIEGO, Baltimore, USA); Z.M. Chirenje, MRCOG (University of Zimbabwe, Harare, Zimbabwe); Beatrice Guyard-Boileau, MD (Ob/Gyn consultant, Seattle, USA); Khama O. Rogo, MD, PhD (University of Nairobi, Nairobi, Kenya); Ralph Richart, MD (Columbia University, New York, USA); Robert Scott, MD (Swedish Medical Center, Seattle, USA); Jan Stjernswärd, MD, PhD and Saloney Nazeer, MD (WHO, Geneva, Switzerland); and Franklin White, MD (PAHO, Washington, D.C., USA). The assistance of these reviewers was invaluable in ensuring that the document was accurate and appropriate. Any errors in the text remain the responsibility of the authors. Finally, we would like to thank NanCee Sautbine for her production assistance.

Amie Bishop
Jacqueline Sherris
Vivien Tsu

July 1995

- Treatment of preinvasive cervical disease is more cost-effective than treatment of invasive disease.
- Integrated services are more cost-effective than vertical ones and are more likely to achieve broad population coverage.
- General physicians and non-physician providers should be trained to perform simple outpatient CIN treatment (and screening). Non-clinicians also could be trained to do history-taking and counseling of women being treated for CIN.
- More limited, outpatient treatment methods (like cryotherapy and LEEP) are highly effective, less expensive, safer, and more acceptable than inpatient methods such as cold-knife conization and hysterectomy.
- First priority should be given to treating all women with high-grade lesions.
- Women, health care providers, key community leaders, and policymakers must understand and support the cervical cancer control program for it to be effective.

With these principles in mind, a planning group should be established to develop a plan of action with the input of key decision-makers, clinicians, and women and women's health advocates.

Conclusion

The survey undertaken for this report suggests that existing outpatient modalities such as cryotherapy and LEEP are not sufficiently available in many developing country settings, and clinicians still must rely primarily on cone biopsies and hysterectomies to treat CIN. Since these inpatient methods are much more costly and require more infrastructure than outpatient techniques, many women do not have access to them. In addition, reliance on these methods makes inefficient use of scarce resources. Survey results also suggest that existing practices involving treatment of all CIN must be reevaluated to ensure that the most rational, appropriate, and cost-effective CIN treatment protocols are being used.

Certainly, in some countries, the resources simply do not exist to initiate a comprehensive cervical cancer screening and treatment program. Although requiring further study, alternative strategies such as use of an inexpensive magnification device to facilitate treatment (and screening), however, may enhance the feasibility and cost-effectiveness of expanding detection and treatment of preinvasive conditions. Furthermore, the strategy of screening only higher-risk women (35 to 50 years old) and treating only high-grade lesions may reduce the burden on health care facilities, while still achieving significant public health benefit.

INTRODUCTION

Cervical cancer is a leading cause of death from cancer among women in developing countries. About 437,000 new cases of cervical cancer occur worldwide per year, nearly 80 percent of which are in developing countries (Parkin et al, 1993). In several East African countries, cervical cancer accounts for up to 80 percent of all gynecologic cancer admissions (Machoki and Rogo, 1990). As populations from developing countries age during the coming decades, the number of cervical cancer cases is likely to increase significantly.

Unlike many other cancers, cervical cancer can be prevented through screening at-risk women and treating preinvasive disease. Cervical cancer generally develops slowly (over a period of up to 10 years) and has readily detectable and treatable precursor conditions known as cervical intraepithelial neoplasia (CIN), or as squamous intraepithelial lesions (SIL) under the new Bethesda system terminology. These precursor conditions have been classified according to severity. Most low-grade SIL, which comprises CIN I and cellular atypia related to human papillomavirus (HPV) infection, is known to regress spontaneously (or does not progress) and generally does not require treatment, while high-grade SIL (CIN II and particularly CIN III/carcinoma *in situ*) is more likely to progress to invasive cancer and generally requires intervention.

Many countries in the developing world face obstacles in implementing successful cervical cancer control programs due to a variety of financial, technical, and logistical constraints. In Brazil in the early 1980s, for instance, screening and treatment programs for preinvasive conditions were able to cover only two percent of women at risk (WHO, 1986). In addition, in many countries, women often do not seek medical services until the advanced stages of disease, when chances of successful treatment are slim and treatment is expensive. Efforts are being made in various countries to strengthen cytology services and to identify simple, low-cost alternative screening strategies that may improve early CIN detection. For example, visual inspection currently is being evaluated as a screening approach in some settings. Any real gains in reducing the incidence and mortality of cervical cancer, however, will come not only through detecting but also effectively treating women with preinvasive disease. (For more information on cervical cancer screening strategies in developing countries, see Appendix A.)

In industrialized countries over the last decade, CIN management has shifted toward more conservative, outpatient approaches. This is due to several factors, including the introduction of colposcopy, increased knowledge about the natural history of cervical dysplasia, and availability of outpatient technologies such as cryotherapy, loop electrosurgical excisional procedure (LEEP), and laser surgery (Chamberlain, 1986; Giles and Gafar, 1991; Wright, Richart et al, 1992). In many developing countries where diagnosis and treatment are being performed, however, clinicians still must rely primarily on invasive, inpatient methods to treat CIN such as cone biopsy and hysterectomy, resulting in over-treatment of many women. Although appropriate for certain circumstances, these approaches are associated with significant complications and side effects and, therefore, put women who could be treated with less invasive methods unnecessarily at risk of morbidity and mortality. In addition, conization and hysterectomy are very costly procedures, requiring significant infrastructural support.

They are usually provided through tertiary or university hospitals in urban settings, which are beyond the reach of many women who need them. Effective cervical cancer programs, then, must reach more at-risk women with simple screening methods that are coupled with low-cost, easy-to-use, and effective diagnostic and treatment methods, as well as appropriate follow-up protocols.

Clearly, treatment of preinvasive cervical cancer is essential to any cervical cancer control strategy. Identifying and introducing low-cost, outpatient CIN treatment methods, therefore, could make a major positive impact on service delivery, both financially and from a public health perspective.

As part of an effort to establish rational, cost-effective, and appropriate treatment strategies for settings with limited resources, this document addresses the following questions:

- What grades of CIN (or SIL) should be treated?
- Which treatment techniques are most appropriate for the conditions being treated?
- How are preinvasive lesions and/or cervical cancer currently being managed in low-resource settings, and how could new approaches be integrated into existing services?
- How do current policies affect cervical cancer screening and treatment programs?
- Which CIN management strategies are most cost-effective? How is cost-effectiveness determined for CIN treatment?
- What key steps can be taken to expand access to treatment services in low-resource settings?

Answers to these questions were derived from literature reviews, interviews with key international cervical cancer experts and clinicians, and survey responses from over 100 developing country providers with experience in cervical cancer detection and treatment (see box below).

A Survey of Current CIN Treatment Practices in Developing Countries

As part of an overall effort to expand access to CIN screening and treatment in developing countries, PATH sent questionnaires to 238 clinicians and women's health experts throughout the world who may have had some experience in cervical cancer/dysplasia detection and treatment. Selected recipients further disseminated the survey to their local contacts, thereby increasing overall distribution. The survey data also were supplemented by guided interviews conducted in several countries. No attempt was made to send the survey to a respresentative sample of practitioners by region or by facility. Therefore, survey results provide a picture of prevailing CIN treatment practices only in the facilities represented by respondents.

The purpose of the survey was to gather information on current CIN treatment practices in developing countries as a basis for identifying low-cost, simple treatment alternatives that may be appropriate for low-resource settings and could be used with simplified screening strategies. Information also was gathered on current screening practices, costs of screening and treatment interventions, perceived barriers to screening and follow-up care, personnel requirements, and other logistics concerns. One hundred-ten surveys were received from over.30 countries, representing a 46 percent return rate.

CIN MANAGEMENT: CURRENT STATUS

In industrialized countries, aggressively treating all grades of CIN, as defined by cytology, was standard practice until the 1960s. For many years, hysterectomy, and even radiotherapy, were considered necessary to treat CIN; later, large cone biopsies, which remove a cone-shaped section of the cervix including the entire transformation zone, replaced hysterectomy as part of standard CIN management (Chamberlain, 1986). Hysterectomy still is indicated for some conditions, such as adenocarcinoma *in situ*, as well as for selected cases of microinvasion and for all invasive cases. It also may be selected for women who have completed childbearing and who may be unlikely to return for follow-up. In general, however, hysterectomy is unnecessarily radical for the treatment of CIN and carcinoma *in situ* (CIS) and is clearly unacceptable for women who wish to retain their fertility.

Similarly, although cone biopsy is relatively effective in both diagnosing and eradicating high-grade SIL (CIN II and III/CIS), it is no longer generally indicated as an initial diagnostic procedure because of significant morbidity such as immediate and prolonged bleeding, cervical stenosis, and increased incidence of spontaneous miscarriage and obstructed labor in subsequent pregnancies. In women with a suspicion of invasive disease, cervical gland involvement, or an unsatisfactory colposcopy, however, cone biopsies still may be recommended. Cone biopsy also may be indicated if colposcopy is not available and invasive cancer cannot be ruled out by random biopsies or other means (WHO, 1986).

The introduction of colposcopy played an important role in the shift from radical treatment to more conservative approaches by enhancing the ability of clinicians to visualize abnormal cytology and to pinpoint the location, extent, and degree of diseased cervical tissue (Giles and Gafar, 1991). Colposcopy (which uses a special scope to magnify the cervix) primarily is used to further evaluate cervical abnormalities, guide diagnostic punch biopsies, and facilitate local treatment of histologically confirmed lesions. Endocervical curettage also is sometimes used to facilitate diagnosis of endocervical lesions, particularly in the United States (U.S.). The procedure involves scraping the cervical canal to collect endocervical cells that are then examined to ensure that invasive cancer has not been missed by biopsies or colposcopy. It is not practiced widely outside of the U.S. as it adds time, expense, and requires the use of a special curette. In addition, its added value to the diagnostic process may not always be significant, particularly if the lesion or transformation zone is completely visible.

Current diagnostic and treatment protocols in industrialized countries dictate that women with abnormal smears requiring further evaluation must return to the health care facility for colposcopy. During this visit, the woman's cervix is assessed visually, a cervical smear may be repeated, and colposcopically directed punch biopsies are taken. The biopsy samples are then sent to a pathology laboratory for analysis, and several weeks may pass before results are available. If the CIN diagnosis is confirmed histologically, the woman is then asked to return again for treatment. Recently, clinicians, particularly in Europe, have begun to adopt the "See and Treat" approach to treating preinvasive lesions, whereby excision of tissue for diagnosis and treatment is performed immediately following a colposcopic evaluation. This

approach bypasses the diagnostic biopsy stage and may have important implications for developing countries since it reduces the number of visits a woman must make to receive proper care (see page 20).

An increased understanding of the etiology and natural history of cervical cancer over the years also has changed CIN management. Although it was once believed that preinvasive lesions progressed through mild, moderate, and severe stages before developing into cancer (as reflected in the traditional Pap smear classification system using CIN I, II, and III), research now indicates that most mild dysplasia, classified as low-grade SIL, will spontaneously revert to normal without therapy (Nasiell et al, 1986). Further, preinvasive cervical lesions appear to be caused by the human papillomavirus, a sexually transmitted disease (STD) (Schiffman et al, 1993). A variety of HPV types exist and are classified according to oncogenic risk and DNA base pair sequence. Low-grade SIL is associated with both high- and low-risk HPV types, whereas high-grade lesions are associated only with certain high-risk HPV types (e.g., HPV 16 and 18). High-grade SIL (CIN II and CIN III/ CIS) is considered a clear precursor to invasive cancer; up to 70 percent of untreated CIS lesions, in particular, progress to invasive cancer within ten years (Richart, 1995) (see diagram on CIN natural history, page 5).

This view of cervical cancer's natural history has important implications for establishing appropriate CIN treatment strategies. For example, since the majority of low-grade lesions are likely to regress, these lesions could be monitored (if possible), while reserving local destructive or excisional therapy for high-grade lesions only. (For more details on cervical cancer natural history, see *Cervical Cancer in Developing Countries: A Situation Analysis*, Sherris et al, World Bank, 1993.)

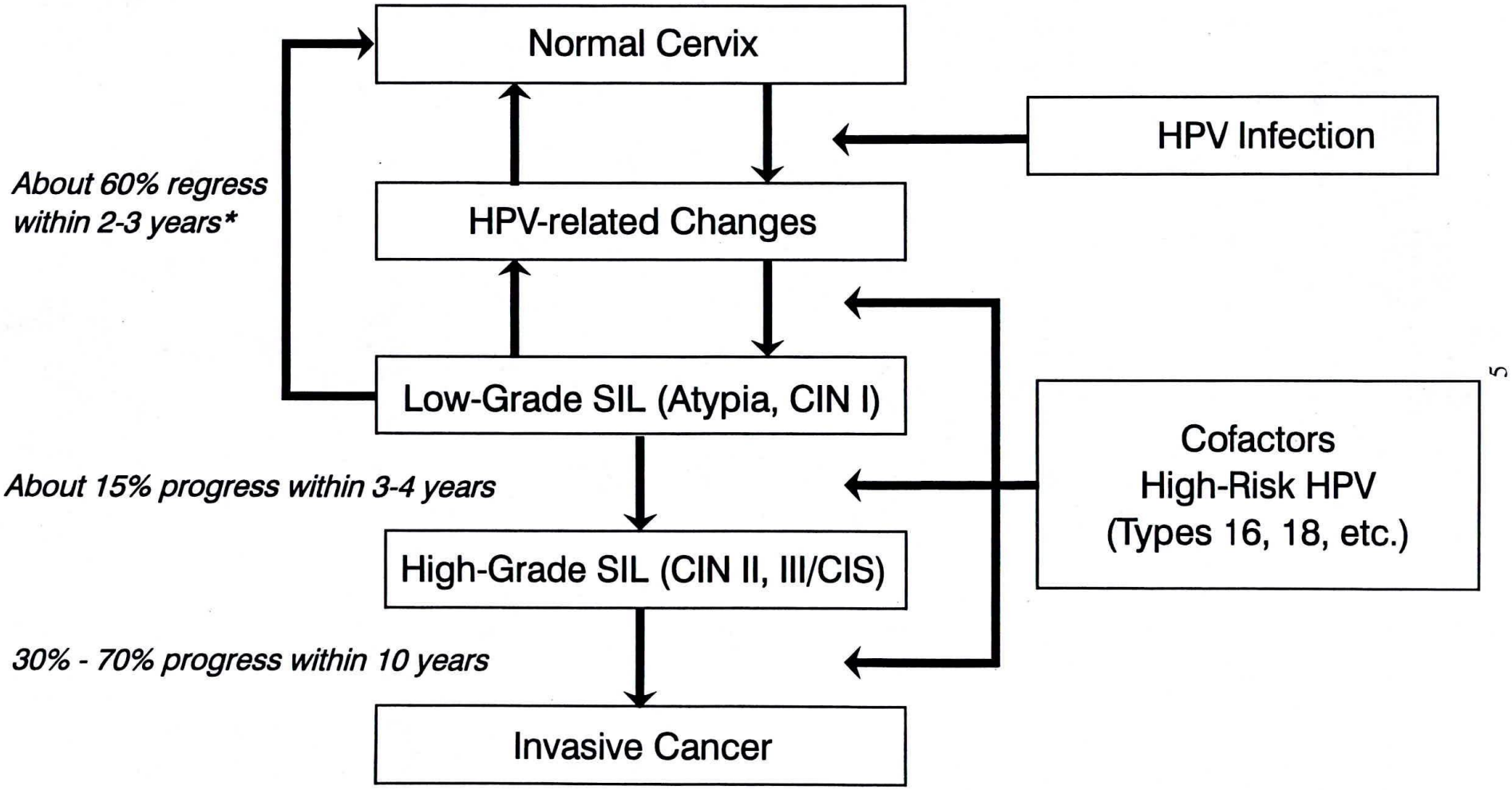
DEVELOPING TREATMENT STRATEGIES: WHICH CIN GRADES SHOULD BE TREATED?

The main goal of any cervical cancer screening program is to identify women at high risk for developing cervical cancer and to treat those who clearly require intervention. Efforts to reach as many high-risk women as possible should not result in compromised quality of care, however.

As knowledge has increased regarding the natural history of CIN and the role of HPV, the standard treatment strategy used in most industrialized countries suggests that only CIN II and III should be treated. Of course, individual country strategies will depend on assessments of local capability to treat or monitor women, local epidemiology, and cost factors, among others.

For example, additional factors may need to be considered in determining the need for CIN treatment among women infected with the Human Immunodeficiency Virus (HIV), since some evidence suggests that the coexistence of HIV may alter the natural history of CIN. Some studies indicate that HIV-positive women may have higher prevalence rates of HPV and CIN, higher CIN grades, and higher recurrence rates than uninfected women after

Natural History of Cervical Cancer: Current Understanding



*NOTE: Prevalent cases will have a lower regression rate than incident cases, on which this estimate is based.

standard therapies (Warren and Duerr, 1993; Maiman et al, 1993; Spinillo et al, 1994). In addition, HIV-positive women may have more frequent involvement of the vagina, vulva, and other portions of the anogenital area than uninfected women (Fruchter et al, 1994). Failure to identify high-grade lesions early, therefore, could have serious consequences, which suggests that HIV-positive women with CIN should be treated promptly and monitored closely, if possible.

Several specific treatment approaches are described below.

Standard Approach

Treat women with high-grade lesions (CIN II, CIN III/CIS)

Limiting treatment to women with high-grade lesions is considered standard in many countries where adequate services are available. It is reflected in the Bethesda system of terminology, which classifies CIN II and CIN III/CIS as high-grade SIL.

Rationale and advantages: Increasing evidence suggests that a significant proportion of low-grade SIL does not progress or regresses spontaneously (about 60 percent regresses after an average of 39 months of follow-up), with only about 15 percent progressing to high-grade lesions after an average of 48 months of follow-up (Nasiell et al, 1986). In addition, progression from low-grade conditions to cancer is sufficiently slow that the risk of developing cancer in a brief period is slight; therefore, low-grade conditions can be monitored at appropriate intervals to ensure the lesion regresses without increasing a woman's risk of cancer. American College of Obstetrics and Gynecology (ACOG) recommendations suggest monitoring women with low-grade conditions every four to six months (ACOG, 1993); however, this is quite costly and evidence suggests that annual follow-up screening of women with mild lesions may be sufficient. Treating only high-grade lesions can reduce costs and lessen the stress on health care systems that otherwise might be overwhelmed by women with low-grade cervical abnormalities.

Disadvantages: This approach requires an ability to monitor women with low-grade conditions, which may be beyond the capabilities of some facilities. Monitoring also may be difficult where women are rarely in contact with the health care system. In addition, since some low-grade lesions do progress, these women may be lost to follow-up. Also, untreated women with low-grade SIL are more likely to transmit HPV infection to sexual partners than those who are treated (Richart and Wright, 1993). Finally, in largely unscreened populations, low-grade lesions are likely to have existed for several years prior to detection (prevalent cases). These lesions, therefore, may regress at much lower rates than newly developed low-grade lesions among well-screened populations (incident cases) (Richart, 1995).

Alternative Treatment Approaches

The following approaches are more controversial but may be practical and appropriate in some settings as first steps towards expanding CIN treatment services.

Treat women with severe lesions (CIN III/CIS) only

A variation of the standard approach, this strategy relies on the CIN classification system, which distinguishes between CIN II and CIN III, and proposes that CIN II could be monitored instead of treated.

Rationale and advantages: In regions with very scarce resources, programs may opt to refer and treat only women with severe dysplasia to lessen the health care burden but still achieve significant public health impact. Evidence suggests that CIN II can regress, although at a significantly lower rate than CIN I (Richart and Wright, 1993). The appropriateness and cost-effectiveness of this approach, therefore, will depend in part on the proportion of cases in which CIN II, in fact, regresses among the population being screened and treated, and the proportion of women left untreated who return for follow-up screening before invasive disease develops.

Disadvantages: Again, this strategy requires an ability to monitor women identified with CIN I and II, which could be difficult and expensive in some settings. In addition, it assumes that CIN grades can be accurately differentiated cytologically. Like the previous strategy, it also carries the risk that women whose conditions do progress (which may be more likely in previously unscreened than regularly screened populations) may be lost to follow-up. Finally, a decision to monitor rather than treat preinvasive disease may cause considerable anxiety to the woman, reducing the acceptability of this approach.

Treat women with low-grade as well as high-grade lesions

Rationale and advantages: Where cervical cancer rates are high, but where monitoring and follow-up of women is difficult or unlikely, this approach could be appropriate, particularly since no practical and affordable method yet exists to predict with certainty which CIN lesions will progress to cancer and which will not. Proponents of this approach also argue that outpatient treatment is now simple, fast, effective, inexpensive, and has very few complications (Richart and Wright, 1993). In particular, the introduction of LEEP, an outpatient excisional method to treat CIN, has made outpatient treatment even more efficient since LEEP permits simultaneous diagnostic tissue sampling and treatment (see page 20).

Disadvantages: The principal drawback to this approach is that it could lead to unnecessary treatment or overtreatment, possibly resulting in side effects or complications associated with treatment that could have been avoided. The benefits of treating all lesions, therefore, need to be weighed against the risks of unnecessary treatment for some women. This approach also may place a heavy burden on the health care system as well as on providers, and potential costs to the system could be high. Women also may find this approach unacceptable if they feel that treatment may be unnecessary.

Prophylactic ablation of the transformation zone: a controversial approach

A fourth, more controversial strategy suggests that prophylactic ablation of the transformation zone, most likely using cryotherapy, be performed on all at-risk women in a

given area, even when they have no evidence of CIN. The theory behind this approach has been likened to that of immunization, whereby all individuals (for example, children under five years old) are immunized against particular diseases regardless of whether they are truly at risk.

Early studies in the U.S. indicated that ablating the transformation zone provides long-term protection against or at least delays subsequent development of cervical neoplasia. This approach essentially eliminates the need to screen as frequently as is generally recommended, and it addresses the difficulties in following-up women who are rarely in contact with the health care system. Specific protocols would need to be developed for special conditions such as pregnancy, STD infection, and pelvic inflammatory disease (Bosch and Castellsagúe, 1994).

Because of the risk of unnecessarily exposing women to side effects and complications, however, this approach raises serious ethical questions and likely would make recruiting women for a study difficult. In fact, the only scenario in which this approach might be appropriate would be in high prevalence settings where screening services have never been available and are unlikely to become available in the near future. As with previous strategies, the possibility of reducing cervical cancer mortality using this approach must be weighed against the risks of possible side effects and complications from unnecessary treatment. Acceptability of this strategy to women also would be a major concern.

OUTPATIENT TREATMENT TECHNIQUES: A TECHNICAL REVIEW

Determining which outpatient treatment techniques are most appropriate for a particular setting is an important part of establishing a cost-effective and feasible cervical cancer control program. Outpatient therapy is appropriate for visible lesions on the ectocervix when invasive cancer and endocervical involvement have been ruled out. Over the past several decades, numerous ablative and excisional methods to treat preinvasive cervical disease have been used. Ablative methods, which destroy the abnormal tissue, include cryotherapy, cold coagulation, laser vaporization, and electrosurgery. Excisional methods include cone biopsy (an inpatient procedure) and, most recently, loop electrosurgical excision procedure. Excisional methods have the advantage of providing tissue specimens for histopathologic diagnosis (if available), which sharply reduces the possibility of overlooking invasive cancer. (Table 1a reviews key outpatient treatment techniques, while, for comparison, Table 1b provides information regarding hysterectomy and cone biopsy.) Since all treatment techniques are associated with recurrence rates of up to 10 percent, post-treatment cytologic follow-up at approximately three-month intervals for one year and then annually thereafter is generally recommended, although some clinicians believe that longer follow-up intervals are acceptable (except in the case of CIS). Given the natural history of CIN, however, determining the true effectiveness of treatment is problematic (see box on page 11). In this document, unless otherwise noted, effectiveness refers to the ability of a particular treatment technique to completely eliminate high-grade lesions without recurrence.

Table 1a: Outpatient CIN Treatment Approaches

	Ablative Methods[1]			Excisional Methods
	Cryotherapy[2]	*Cold Coagulation*	*Electrocautery*	*Loop Electrosurgical Excision Procedure (LEEP)*
Effectiveness	70-90% for CIN III	92% for CIN III	85-89% for CIN III	90-95% for CIN III
Potential side effects	Watery discharge for 2 weeks, infection risk, receded transformation zone	Bleeding, pain, uterine cramping, vaginal discharge	Uterine cramping, pain, bleeding, cervical stenosis, receded transformation zone	Bleeding, infection risk
Training requirements	Low	Low	Moderate	Moderate-high
Anesthesia requirements	None, though some women may prefer local anesthesia	None, though some women may prefer local anesthesia	None	Local anesthesia
Supply requirements	Refrigerant-i.e., liquid nitrogen or carbon dioxide, local anesthesia, needles, syringes, Lugol's solution	Probes, needles, syringes, local anesthesia, Lugol's solution	Ball-type and return electrodes, needles, syringes, local anesthesia, Lugol's solution	Needles, syringes, local anesthesia, loop and ball-type electrodes, return electrodes, suture set, Lugol's solution, vasoconstrictive agent, Monsel's paste
Equipment requirements	Cryotherapy unit, cryoprobes, colposcope or low-power magnification device, speculum, examination table, light source	Electrosurgical generator (Semm Cold Coagulator), colposcope or low-power magnification device, speculum, examination table, light source	Electrosurgical generator, non-conductive speculum, colposcope or low-power magnification device, examination table, light source	Electrosurgical generator, colposcope or low-power magnification device, non-conductive speculum, smoke evacuator
Personnel requirements	Physicians, nurse-midwives, or nurse-practitioners	Physicians, nurse-midwives, or nurse-practitioners	Physicians, nurse-midwives, or nurse-practitioners	Physicians
Infrastructure requirements	Record keeping, counseling, follow-up, reliable source of refrigerant	Power supply, record keeping, counseling, follow-up	Power supply, record keeping, counseling, follow-up	Power supply, record keeping, counseling, follow-up
Costs	Initial cost: US$1,000-$3,000; low recurrent costs	Initial cost: US$1,000-$2,000; low recurrent costs	Initial cost: US$1,000-$2,000	Initial cost: US$4,000-$6,000; US$15-$60/loop

[1]Other methods, such as laser vaporization, are not described in this table because their technical requirements and high cost make them less suitable for low-resource settings.
[2]Cryotherapy is the only method that does not require electricity.

Table 1b: Treatment Approaches for Early and Advanced Cervical Cancer		
	Early Cancer	**Advanced Cancer**
	Cone biopsy/hysterectomy	*Hysterectomy plus radiation/ chemotherapy/palliative care (depending on stage of cancer)*
Effectiveness	Varies with extent of cancer	Often not successful; 5-year survival rates less than 35%
Training requirements	High	Very high
Potential side-effects & complications	Bleeding, cervical stenosis, spontaneous miscarrage, obstructed labor, infection, and other side effects and complications of surgery	Side effects and complications of surgery and radiation/chemotherapy
Anesthesia requirements	Local, spinal, or general anesthesia (depending on technique used[1])	General or spinal anesthesia
Supply requirements	Surgical supplies, anesthesia	Extensive
Equipment requirements	Colposcope, surgical equipment	Extensive
Personnel requirements	Gynecologists	Medical specialists (surgeons, radiologists)
Infrastructure requirements	Well-equipped hospital; ability to recall women post-treatment	Well-equipped hospital; ability to recall women post-treatment
Costs	High	Very high

[1]New cone biopsy techniques using CO_2 lasers may be performed under local anesthesia in some cases.

Ablative Methods

Cryotherapy

Procedure: Cryotherapy destroys abnormal cells by using a low-temperature probe (-60° C to -90° C) to freeze the transformation zone. Cryoprobes varying in size and shape may be used depending on the size and grade of the lesion as well as on the shape of the cervix. Carbon dioxide (CO_2), liquid nitrogen, or nitrous oxide are generally used as refrigerants. Cryotherapy can be done without anesthesia, although one study indicated that using local anesthesia reduced discomfort significantly (Sammarco et al, 1993).

Measuring Treatment Effectiveness: Methodological Issues

Treatment effectiveness, usually expressed as cure rates (or failure rates) can be defined in several ways and may be misleading when applied to CIN treatment. A major difficulty in evaluating CIN treatment effectiveness is separating the spontaneous regression of CIN lesions from the impact of a treatment modality: lower grades of dysplasia often regress spontaneously, therefore it is not surprising that "cure rates" are higher for these conditions than for high-grade conditions. Since studies suggest that about 60 percent of CIN I regresses in screened ("incidence") populations, a "cure rate" of 90 percent among women with CIN means that the treatment modality contributed to only 30 percent of cures. (In unscreened, "prevalence" populations, regression rates are much lower.) Because of this fundamental difficulty, treatment studies that report only overall cure rates (for CIN I, II, and III combined) are not as helpful in evaluating a given treatment modality than studies that report cure rates separately for low- and high-grade preinvasive disease. In addition, most studies are descriptive rather than randomized evaluations.

Another difficulty in evaluating treatment studies is that the literature often is inconsistent in how effectiveness is expressed. Some studies distinguish between persistence rates (the proportion of CIN that persists despite treatment) and recurrence rates (the proportion of CIN that recurs after complete eradication of lesions). Many studies, however, combine persistence and recurrence rates to measure effectiveness and may consider repeat treatment in their calculations. Similarly, complications and side effects may be defined differently, depending on the study.

Another important factor in calculating effectiveness is length of follow-up. Many studies calculate effectiveness based on examination three months post-treatment (often referred to as the initial cure rate). A minimum of one year (or longer, if possible), however, may be necessary to accurately assess effectiveness.

In this document, wherever possible, studies that distinguish treatment effectiveness for high-grade disease from effectiveness for all CIN are highlighted. Also, emphasis has been placed on studies that report longer follow-up; ideally one year or more. Readers should remain aware, however, of the limitations of reported "cure rates" for various treatment methods.

Effectiveness: Overall cure rates for this method range from 84 to 96 percent for all grades of CIN (see Table 2, page 12). Several studies indicate that effectiveness increases significantly using a "double-freeze" (instead of "single-freeze") technique (Schantz and Thormann, 1984; Bryson et al, 1985). For this technique, the cervix is frozen for three minutes, thawed for five minutes, and refrozen for another three minutes. A ball of ice four- to five-millimeters in diameter must form past the edge of the lesion with each freezing to ensure adequate tissue destruction. (Large lesions may require multiple applications to ensure that this occurs.) In one study, the recurrence rate after one year for all grades following double-freeze treatment was 8.8 percent, compared to 6.3 percent using the single-freeze method. Failure rates were highest among women with severe lesions treated with the single-freeze technique (Schantz and Thormann, 1984).

Effectiveness also is affected by the severity and size of the lesion treated (Creasman et al, 1981; Creasman et al, 1984). Reported cure rates range from about 70 to 90 percent in women with CIN III. Most researchers suggest that cryotherapy is appropriate for CIN III provided that patients are able to adhere to rigorous follow-up.

Other studies suggest that the apparent association between lesion grade and treatment success rate may be due, in fact, to the association between lesion size and grade (Townsend, 1979; Richart et al, 1980; Bryson et al, 1985). One study showed that when controlling for lesion size, the grade of dysplasia did not influence the cure rate. Lesion size, however, was significantly associated with cure rate regardless of grade (Arof et al, 1984). Another study indicated that treatment failure was significantly associated with large, high-grade cervical lesions, particularly those containing high-risk HPV types (Guijon et al, 1993).

One descriptive study suggested that cryotherapy may be more effective in women under 30 years old. Researchers found that the cure rate for this group for all grades was 88 percent after five years, compared to 77 percent for women over 30. This may be because older women are more likely to have high-grade, aggressive disease. Also, women over 30 are more likely to have lesions that extend into the cervical channel where it is difficult to achieve adequate freezing (Hemmingson et al, 1981).

Table 2

Cryotherapy for Treatment of CIN:
Key Studies with at Least 1 Year of Follow-up

Author	*Year*	*Number of Women*	*Overall Cure Rate (Percent)*	*CIN III Cure Rate (Percent)*	*Follow-up*
Andersen & Husthe	1992	261	83.5	77.8	7 years (mean)
Olatunbosun et al.	1992	70	90	80.8	5 years
Berget et al.	1991	93	96	90.5	2 years
Draeby-Kristiansen et al.	1991	96	92	86	10 years
Ferenzcy	1985	147	93.2	71	1 year
Bryson et al.	1985	422	--	92.9	1 year
Creasman et al.	1984	770	89.9	82.3	2 years
Townsend & Richart	1983	100	93	88	1 year
Monaghen et al.	1982	159	87.4	85	1 year
Wright	1981	152	85.5	75	12-42 months
Benedet et al.	1981	906	88.2	87.2	1 year
Hemmingson et al.	1981	181	84	82	5-8 years

Side effects: After treatment, the cervix takes about six weeks to heal. The most prominent side effect is profuse, watery discharge for two to four weeks post-treatment. Cryotherapy does not appear to impair subsequent fertility or childbirth, however, and has been performed safely during pregnancy (Benrubi et al, 1984). Another potential problem with cryotherapy is that the transformation zone tends to recede into the endocervix post-treatment, particularly if an inappropriately sized probe is used or if the woman is post-menopausal. Given the high cure rate of cryotherapy, particularly for mild and moderate lesions, however, the inability to visualize the transformation zone in women who may be screened only once or twice in their lives may be offset by the benefit of providing effective treatment.

Equipment and supply requirements and costs: Cryotherapy units generally vary in initial purchase price from about US$1,000 to $3,000 in developing countries. The thermos-like canisters containing refrigerant can be filled and reused and are available in a wide variety of sizes. For example, CO_2 canisters range from 2 kg canisters, which enable treatment of approximately four to five people, to 130 kg canisters or larger. Although each type of refrigerant has different freezing points, all are effective in treating CIN. Liquid nitrogen and nitrous oxide are cleaner than CO_2, leading to fewer mechanical problems related to blockage of the tube from the tank to the probe (Creasman et al, 1984). They are, however, more expensive than CO_2. To avoid blockage problems, only medical grade or "bone dry" CO_2 should be used. It is important that adequate tank pressure be maintained. If tank pressure is low, optimal temperatures may not be reached and tissue destruction can be inadequate. Various sizes of cryotherapy probes also are available. Probes of adequate size to completely cover a lesion must be used for successful treatment.

Cold coagulation

Procedure: Originally invented in the 1960s to treat benign cervical conditions, cold coagulation involves the cervical application of a thermal probe heated to 100° C using the Semm Cold Coagulator. Several 20-second applications are usually necessary to cover the entire transformation zone. Although not required, local anesthesia may be used to reduce discomfort. Cold coagulation has been used primarily in Europe, and several studies have indicated that it is quite effective and is associated with minimal complications.

Effectiveness: Most studies have reported overall success rates of 92 to 97 percent (see Table 3, page 14). One study, spanning 14 years, indicated a 92 percent success rate after five years in treating CIN III (Gordon and Duncan, 1991). Another, spanning 13 years, found that cold coagulation had success rates after five years of 96.5 percent for CIN I and 95.4 percent for CIN II (women with CIN III were not included) (Loobuyck and Duncan, 1993). In both studies, women experienced few complications, and no impairment of future fertility was noted.

Side effects: Though reportedly minimal, side effects may include some pelvic cramping during treatment. In a small percentage of cases, bleeding, vaginal discharge, or some residual pain may occur for several weeks post-treatment. Scarring has not been reported as a problem.

Table 3

Cold Coagulation for Treatment of CIN: Key Studies

Author	*Year*	*Number of Women*	*Efficacy*	*Follow-up*
Loobuyck & Duncan (CIN I & II Only)	1993	1,165	CIN I - 96.5% CIN II - 95.4%	5 years
Williams et al.	1993	125	96.5% (CIN II & III)	18 months
Gordon & Duncan	1991	1,628	92% (CIN III Only)	5 years

Equipment and supply requirements and costs: The equipment necessary to perform cold coagulation, which includes a Semm Cold Coagulator and a variety of probes, is relatively inexpensive (about the same as cryotherapy equipment), and the unit operates on mains electricity. One clinician in Argentina indicated that cold coagulation costs only US$0.28 per application, thus making it an extremely cost-effective intervention in that setting (Vasquez, 1994). Indeed, given this method's effectiveness, cost, and relative lack of serious side effects, it may well be appropriate for low-resource settings, provided electricity is available. (In the absence of mains electricity, the unit may be adaptable to 12-volt battery power or 110-volt generator.) The primary drawback, however, is the limited access to equipment in most countries. Other drawbacks include very limited study and use of the method in current programs outside of Europe. According to the survey, only about five percent of respondents currently use this method.

Ablative electrosurgery

Procedure: Two types of ablative electrosurgery have been used to treat CIN: cauterization (or electrocautery) and electrocoagulation diathermy. Electrocautery uses an electrically heated probe reaching very high temperatures to destroy abnormal tissue. It has been known since the early 1900s and was used for years to treat benign chronic cervicitis and erosion. It also was used in the U.S. in the 1930s and 1940s, before screening methods were available, as a prophylactic measure to prevent cervical cancer. Some early studies indicated that women treated prophylactically had a much lower incidence of the disease than untreated women (Wright, et al, 1992b).

Electrocoagulation diathermy is similar to electrocautery but uses ball-type electrodes to ablate surface tissue and needle electrodes, inserted repeatedly, to destroy deeper tissues. Initially, this method was used with general anesthesia, although a 1989 study indicated that local anesthesia could be used instead without compromising comfort and effectiveness (Chanen, 1989).

Effectiveness: Once Pap smears became available, ablative electrocautery was used as a method to treat all grades of CIN. Studies suggested initial cure rates for CIN III of about 85 to 89 percent (Schuurmans et al, 1984; Deigan et al, 1986). Studies of radical diathermy electrocoagulation reported cure rates up to 98 percent for all grades of CIN (Chanen, 1989).

Side effects: Ablative electrosurgery is rarely used in industrialized countries now because it is associated with significant side effects such as cervical stenosis and recession of the transformation zone into the endocervical canal, which makes future screening difficult. Significant pain and uterine cramping and bleeding, particularly in women 40 or older, also are associated with this method (Chanen, 1989; Wright, et al, 1992b).

Equipment and supply requirements and costs: Required equipment is relatively inexpensive and includes an electrosurgical generator and ball-type and/or needle electrodes. Electrosurgical methods also require electricity.

Local anesthesia is required for radical diathermy electrocoagulation but not for electrocautery.

Laser vaporization

While carbon dioxide laser vaporization is an effective method that allows precise destruction of cervical lesions under local anesthesia, it is generally inappropriate for low-resource settings because it is very expensive (up to US$80,000 for initial purchase of equipment) and requires substantial training and practice. Some randomized, comparative studies have indicated that laser therapy holds little advantage over cryotherapy in terms of cost, side effects, complications, and efficacy (Townsend and Richart, 1983; Wetchler, 1984). Carbon dioxide laser ablation provides a higher cure rate than cryotherapy on initial treatment of CIN, although effectiveness is virtually the same if women with persistent or recurrent lesions after initial cryotherapy are retreated with the same method (Berget et al, 1991). Laser therapy is consistently more effective than cryotherapy in treating large lesions, however (Ferenczy, 1985; Wright, et al, 1992b). Laser ablation's principal side effect is bleeding.

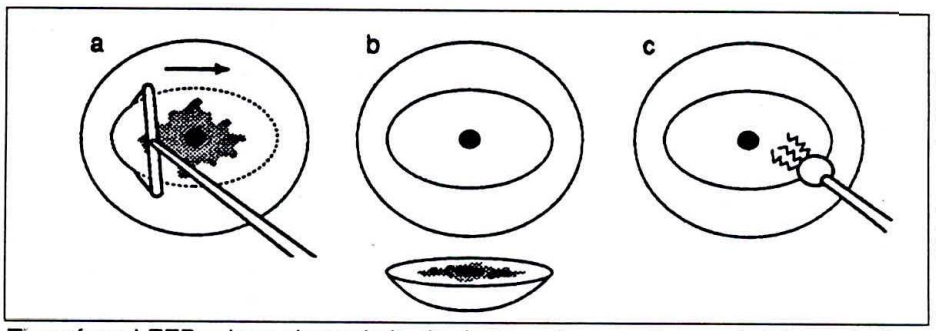
Excisional Methods

The traditional method of surgical excision of the transformation zone to diagnose and treat CIN has been cold knife cone biopsy (conization) under general anesthesia. While effective in eliminating CIN, conization requires hospitalization and is associated with significant morbidity such as bleeding, cervical stenosis, and problems during pregnancy. Other conization methods include laser excision, which can be used to excise shallow cones on an outpatient basis using local anesthesia (although excised tissue may be damaged during the procedure, making specimen analysis difficult), and loop electrosurgical excision procedure.

Loop Electrosurgical Excision Procedure (LEEP)

LEEP, also known as large loop excision of the transformation zone (LLETZ), is a method of outpatient excisional biopsy and treatment that is used to remove the entire transformation zone. LEEP's primary advantage over destructive techniques is that it removes rather than destroys suspicious tissue, thus producing a histologic sample for pathologic review. This allows diagnostic sampling and treatment in the same visit for selected patients (the See and Treat approach–see box, page 20). Since the entire transformation zone is excised for histologic analysis, the presence of invasive disease can be ruled out, which is not possible with ablative therapies.

Procedure: LEEP is performed using a thin wire electrode charged with a low-voltage, high-frequency alternating current (600kHz). The loop electrode, which is attached to an insulated rod, is slowly moved across the cervix so that the current jumps ahead of the wire. A clean cut is produced with only superficial coagulation, so there is little damage to the biopsy specimen. The raw area of the cervix is further coagulated with a ball-type electrode (Editorial, The Lancet, 1991) (see diagram below). The procedure requires local anesthesia and generally takes less than five minutes. Loops are available in a variety of sizes, depending on lesion and transformation zone size. Some researchers have expressed concern that LEEP removes too much tissue; thus, clinicians are now using shallower loops (0.7 cm deep) than those originally recommended (Richart and Wright, 1993). Loop width also may vary. One study indicated women treated with small, narrow loops, which remove the tissue in strips, had a lower cure rate for all CIN (about 80 percent after a mean of 12.4 months) than those treated with wider loop electrodes (90 percent after a mean of 12.4 months), which remove tissue in one or two passes. The wider loops also may be easier to use and may produce a better specimen than the smaller loops (Wright, et al, 1992a). Thermal damage to the excised tissue is generally minimal, although some damage to the edges of the specimen has been reported (Montz et al, 1993).



From Wright, et al, 1992b

To perform LEEP, a loop electrode is slowly moved across the cervix (a), producing a specimen for histologic analysis (b). The cervix is further coagulated using a ball-type electrode (c).

Studies indicate that LEEP may improve the accuracy of histologic diagnosis of CIN over colposcopically directed biopsy (Prendiville et al, 1989; Howe and Vincenti, 1991; Rattray et al, 1993). For example, in one study comparing histologic results of colposcopically directed biopsies and LEEP sampling from the same patients, CIN was underestimated based on biopsy results in 16 percent of cases and overestimated in 41 percent of cases (Chappatte et al, 1991).

LEEP also has been used to perform conization on an outpatient basis. Although loop conization has a somewhat higher complication rate than simple excision, it has far fewer complications and a faster recovery time compared with cold knife cone biopsy. Loop conization may be indicated when CIN lesions extend a limited distance into the endocervical canal (Mor-Yosef et al, 1990; Mayeaux and Harper, 1993; Saidi et al, 1993).

Effectiveness: Efficacy and patient acceptance of LEEP generally compare favorably to other methods (Gunasekera et al, 1990). Average cure rates for all CIN usually range from 90 to 98 percent after three to twelve months; cure rates for CIN III/CIS also are high during the same time frame. Lesion size rather than grade appears to influence results (Wright, et al, 1992a) (see Table 4, page 18).

Side effects: The primary complication is perioperative and postoperative bleeding, which has occurred in up to nine percent of cases (Prendiville et al, 1989; Gunasekera et al, 1990; Bigrigg et al, 1990; Keijser et al, 1992; Wright, et al, 1992b). Use of Monsel's paste may reduce bleeding to one or two percent, however. Perioperative bleeding may be much more significant in patients with acute cervicitis. Infection also has been reported in up to two

Patient Selection is Key to CIN Treatment Success

Regardless of which outpatient treatment technique is used, appropriate selection of patients is key to treatment success as well as to reducing the incidence of side effects. For all outpatient techniques (cryotherapy, cold coagulation, electrocautery, and LEEP), the first step is to rule out (with reasonable probability) the possibility of invasive cancer, which requires more aggressive, hospital-based therapy. It also is important to ensure that lesions do not extend into the endocervical canal (which may be more likely in older women in whom the transformation zone may have receded into the endocervix). These women will require an excisional method. Pap smear, colposcopy, and biopsy results, where available, are helpful in making these decisions.

Another important aspect of ensuring treatment success is selecting the best treatment technique for the size and grade of cervical lesion. Available data clearly suggest that cryotherapy may not be as successful in treating more severe and/or larger lesions as, for example, LEEP. When treating larger, more severe lesions, it is particularly important to ensure that the entire lesion has been either ablated or removed; LEEP, using an appropriate loop size and shape, can be effective in this situation. Also, where histology services are available, it may be especially helpful to have tissue samples from larger lesions evaluated to ensure that all abnormal tissue has been removed. If cryotherapy is the only treatment technology available, larger lesions should be treated with appropriately sized cryoprobes, using the "double freeze" technique (see page 11).

For some women, cervical ablation or excision is contraindicated. These include women with acute cervicitis (which could result in an increase of false-positive identification of CIN, make identifying the treatment area more difficult, and increase the chance of post-treatment infection and bleeding), women who are pregnant, women who are less than six weeks postpartum, and women with bleeding disorders. In most cases, women with cervicitis can be treated after appropriate antimicrobial therapy, and women who are pregnant or postpartum can be treated at a later date unless the lesion is quite advanced. All of these patient selection issues should be addressed through development of appropriate CIN treatment protocols as well as adequate training of providers.

Table 4

LEEP for Treatment of CIN:
Key Studies with at Least 6 Months of Follow-up

Author	*Year*	*Number of Women*	*Overall Cure Rate (Percent)*	*Cure Rate for CIN III/CIS (Percent)*	*Post-op Bleeding (Percent)*	*Follow-up*
Keijser et al.	1992	395	81	--	8	4.8 years (mean)
Wright et al.	1992a	141	94	94	2	6 months
Gunasekera et al.	1990	98	95	94.7	0	6 months
Luesley et al.	1990	557	96.6	95.7	4.3	6 months
Prendiville et al.	1989	102	97	99	4	18 months (mean)

percent of patients, while stenosis occurs in up to one percent of patients (Prendiville et al, 1989). Healing generally takes two to three weeks; during this time, some vaginal discharge can be expected. LEEP appears to have no adverse effect on fertility or subsequent pregnancy (Keijser et al, 1992; Bigrigg et al, 1994), although long-term follow-up of patients has yet to be completed.

Equipment and supply requirements and costs: LEEP requires the following equipment and supplies:

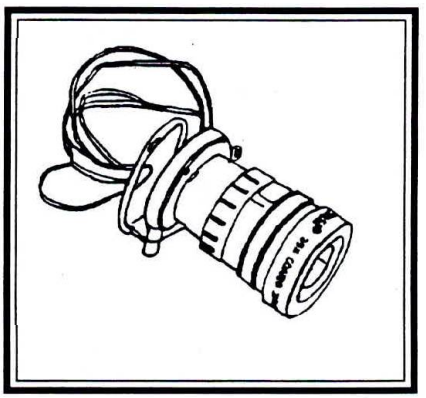
- electrosurgical units (produced by a number of companies at a cost of US$3,000-US$6,000) that run off mains electricity and/or another power source.
- a supply of loops, available in disposable or reusable forms (US$15 to $60 per loop, depending on the country). Programs in countries such as India, Kenya, and South Africa have had loops made locally (using steel wire) at a fraction of the cost of imported loops. If reusable loops (good for 10 to 25 procedures) are preferred, they must be decontaminated, disinfected, and cleaned thoroughly with a scrubbing pad to remove carbonized material, and they must be sterilized before reuse.
- compact smoke evacuator with an adequate filter to remove steam or smoke generated during the procedure. Smoke evacuators are usually separate devices, but some LEEP units now have them built in.
- an insulated non-conductive or special plastic speculum (with a strong locking mechanism) that will not allow transmission of current from the loop electrode to the vagina and that has an outlet for smoke evacuation.

Other necessary supplies include a colposcope, a light source, return electrodes, a suture set, Lugol's solution to delineate the transformation zone prior to treatment, Monsel's paste to control bleeding, local anesthetic and a vasoconstrictive agent such as epinephrine, as well as needles, syringes, and other adjunct equipment associated with administering local anesthesia (Apgar et al, 1992).

Accessory Equipment: Magnification of the Cervix

All of the outpatient treatment methods described above typically require colposcopy to visualize the cervix for pre-treatment assessment and, in most cases, to facilitate the treatment procedure. Colposcopes, however, are very expensive, require substantial training to use, and are not readily available in developing countries. Even central or provincial referral facilities may not be equipped with colposcopes. In the Philippines, for instance, only a few hospitals in Manila are equipped with them and few are available elsewhere in the country.

Since some type of magnification traditionally has been considered necessary to support CIN diagnosis and treatment, identifying and validating an alternative to colposcopy, such as a portable magnifying device, would have significant implications for CIN management in low-resource settings (see diagram). For example, screening might then be based on aided visual inspection (AVI), either as an adjunct to or replacement for cytology, followed by biopsy and/or treatment guided by the same device.* Where cytology and biopsy are not feasible, a one-visit strategy relying on visual inspection to detect and guide treatment of preinvasive lesions might be feasible (see box, page 20).



One version of a low-power magnification device currently being evaluated to facilitate visual inspection of the cervix.

In Kenya, a low-power (2.5x) magnification device was evaluated for its effectiveness compared to colposcopy in confirming CIN and facilitating biopsy sampling. The investigator was a trained colposcopist. Histological grading concurred with grading using the magnifying device in 40 out of 50 women. No severe lesions were missed in any case (Rogo, 1995). Although more extensive research must be conducted, preliminary findings suggest that this method can yield similar results to colposcopy. In addition, given that the alternative device is inexpensive, portable, and does not rely on electricity, it may hold real promise in settings where colposcopes are not available. Recommendations for improving the device include increasing the magnification from 2.5x to 4x or 6x, if possible, and incorporating a light source (Sjamsuddin et al, 1994; Blumenthal et al, 1994).

* A number of researchers are now investigating the potential of various approaches to visual inspection to detect preinvasive lesions. As a result, some confusion has arisen regarding terminology and definition. For the sake of clarity, we adhere to the following definitions in this document:

Unaided visual inspection (UVI): visualization of the cervix without magnification, but with acetic acid.

Aided visual inspection (AVI): visualization of the cervix using a portable, low-power magnification device (as opposed to a colposcope) and acetic acid.

Reducing the Number of Clinic Visits for Treatment: The See and Treat Approach

In many low-resource settings, especially in rural areas, women's access to health services may be limited due to distance from clinics, transportation costs, and family or work responsibilities. Reducing the number of clinic visits for screening and treatment, therefore, may make it easier for women to receive the care they need. One method that has been studied is the See and Treat approach, which eliminates the need for women to wait for the results of directed biopsy before returning for treatment. Instead, this relatively new two-visit strategy has relied on initial Pap smear screening (visit one), followed by colposcopic examination of women with abnormal results and subsequent treatment, if necessary (visit two). In addition to reducing the number of clinic visits, this approach also may decrease patient discomfort and anxiety, reduce service delivery costs, and perhaps most important, reduce the number of patients lost to follow-up who do not receive the treatment they need (Mayeaux and Harper, 1993). Studies evaluating the feasibility of the See and Treat approach, which have taken place largely in Europe, have found a high level of patient acceptance.. In addition, it has been shown to be extremely cost-effective as well as clinically effective (Bigrigg et al, 1990). The See and Treat approach is not appropriate when colposcopic findings are equivocal or suggest invasive cancer.

Most studies of the See and Treat approach have relied on LEEP as the treatment of choice, since in most developed country settings, the histologic sample provided can be analyzed post-treatment to confirm the diagnosis and to assure that invasive cancer was not missed. The See and Treat approach also has been used with an ablative method, however. In two studies, cold coagulation immediately followed colposcopic assessment and directed biopsy (Gordon and Duncan, 1991; Loobuyck and Duncan, 1993). Biopsy results were then analyzed after treatment was performed to assure that the lesions were adequately treated.

According to some studies, approximately 5 to 39 percent of patients could be treated unnecessarily using the See and Treat approach (Chappatte et al, 1991; Luesley et al, 1990; Bigrigg et al, 1990). This may be beneficial to some women, however, since eliminating the transformation zone would reduce the risk for subsequently developing cervical cancer. About 30 percent of low-grade lesions likely contain high-risk HPV types and, therefore, are at risk of progression. Currently, however, it is virtually impossible to determine which lesions are at risk of progressing and which are not (Wright et al, 1992b). Thus, the morbidity and mortality from the possibility of missing more advanced disease must be weighed against the potential morbidity of the procedure itself (Mayeaux and Harper, 1993).

In many developing countries, particularly in non-urban areas, the See and Treat technique as practiced in developed countries (with colposcopic and histologic evaluation available) may be impossible. Given this situation, another approach to reducing the number of clinic visits may be to modify the See and Treat strategy so that only one visit is required. Essential to this strategy would be the use of acetic acid and a portable, inexpensive, low-power magnification device that could be used to detect CIN as well as facilitate outpatient treatment: women would undergo aided magnified visual inspection to detect abnormalities and, if indicated, be treated immediately with a low-cost, outpatient method such as cryotherapy. This one-visit strategy likely would be less accurate than conventional approaches and may result in some women being treated unnecessarily. Further, if cryotherapy is used, there would be some risk in ablating CIN in the absence of a biopsy specimen, since diagnostic procedures have always been considered mandatory before proceeding to treatment (or as part of treatment, as illustrated by the standard See and Treat approach). Still, the benefits in terms of treated disease and prevention of future disease may outweigh the risk of treatment-associated morbidity in many cases, especially in high prevalence areas where screening and treatment currently are not being provided at all. Determining the risks and benefits of these approaches, however, must occur locally. Clearly, more research is needed to determine the effectiveness and acceptability of such an approach, particularly if it involves destruction rather than excision of tissue. For either a one-visit or two-visit strategy, some system of follow-up post-treatment still would need to be developed; nevertheless, these strategies would greatly reduce current cervical cancer prevention service delivery demands.

Guiding CIN Treatment: Future Possibilities

HPV testing for the management of CIN: Now that the causal relationship between HPV and cervical cancer is essentially clear, using HPV diagnosis to predict cervical cancer risk is increasingly being explored. This approach may be particularly useful in some developing countries, where it is believed that HPV prevalence, especially among pre-menopausal women, may be greater than in industrialized countries. Over 70 HPV types have been identified and more than 20 are associated with lesions of the cervix and the genital tract; these are grouped according to low, intermediate, and high oncogenic risk. Studies have shown that the presence of high-risk HPV correlates very closely with the presence of CIN in women referred for abnormal Pap smears, with at least 95 percent of cervical cancers and precursor lesions containing HPV (Richart and Wright, 1993). Studies still are needed to confirm that low-grade CIN lesions associated with high-oncogenic risk HPV types have a higher progression rate than those associated with intermediate risk HPV and, similarly, that lesions associated with low-risk HPV types are more likely to regress (Richart and Wright, 1993). In addition, HPV is not necessarily an independent predictor of progression or regression of untreated CIN lesions, and other factors or co-factors apparently must be present to cause CIN progression. Finally, high-risk HPV types also are found in about 15 percent of cervical specimens from women with normal cervices, with a mean of 25 to 30 percent of women with normal cytology being infected with some HPV type (ACOG, 1993; Koutsky and Kiviat, 1993; Richart and Wright, 1993).

Current HPV tests, based on DNA probe technology, are largely used for research purposes only. These assays are too expensive and complex for routine use in low-resource settings. Currently, the most widely used HPV test is the hybrid capture assay, approved by the U.S. Federal Drug Administration in April 1995.

Despite some remaining technical issues, many experts believe that within the next five to ten years, simple, rapid HPV assays, perhaps costing less than US$4 a test, could play a role in determining appropriate management for women with low-grade CIN or with indeterminate results (Koutsky and Kiviat, 1993; Richart and Wright, 1993). In addition, tests using alternative formats, such as highly accurate and easy-to-use colorimetric assays, are likely to become available within one to two years and may eventually be affordable to programs with limited resources.

Until research and technical issues related to HPV screening issues are better understood and testing costs are reduced, HPV typing cannot be recommended yet as part of routine triage for women who have suspicious results suggesting CIN. Eventually, however, it could improve efficacy as well as cost-effectiveness of screening, colposcopic examinations, and treatment in some developing country settings, since more rational decisions about which women to treat and which to monitor could be made. In addition, HPV testing, possibly used in conjunction with cytology and/or visual inspection, could be beneficial in low-resource situations, as it has the potential to improve the efficacy of the See and Treat approach and obviate the need for more expensive and time-consuming diagnostic procedures without compromising quality of care.

Treatment of Invasive Cancer

Treatment of invasive cervical cancer (stages I-IV) relies on expensive equipment and highly skilled medical experts to perform radiotherapy and/or hysterectomy and administer chemotherapy. In more advanced stages of the disease, treatment options depend on the extent of tumor spread and on patient preference (WHO, 1986). Extensive pelvic surgery and radiation are capable of curing disease that has spread beyond the cervix, although success in the more advanced stages is less likely (Jamison and Moseley, 1990). In fact, five-year survival rates by stage, as found in a descriptive evaluation of 32,000 women in over 120 cancer centers in mostly developed countries, are: 78 percent for stage I, 57 percent for stage II, 31 percent for stage III, and only 8 percent for stage IV (Petterson, 1985). By contrast, preinvasive disease, if adequately treated, has virtually a 100 percent cure rate with simple outpatient procedures (WHO, 1986). When women seek treatment for late-stage cancer, emphasis should shift from curative therapy to pain relief and palliative care (WHO, 1986).

In most developing countries, treatment services for invasive cervical cancer generally are available only at central teaching hospitals or large regional facilities. In some countries, women with invasive cancer must wait up to nine months for treatment, by which time the disease may have progressed too far for treatment success. Primary barriers include lack of affordable, maintainable equipment and lack of trained personnel. For example, Kenya has only one cobalt radiotherapy unit, which is located at Kenyatta National Hospital in Nairobi. The unit serves the whole country as well as neighboring countries, which do not have cancer treatment capability (Rogo et al, 1990). In India, ten institutions are identified as regional cancer research and treatment centers. They are able to handle only about 10 percent of the 500,000 new cases of cancer (all cancers) that are identified in India each year. In addition to these facilities, 77 other institutions are equipped with radiotherapy facilities and treat patients with advanced disease (Luthra and Rengachari, 1993).

Unfortunately, at the start of any new cervical cancer screening and treatment program, a cohort of women inevitably will be identified with invasive disease, which could strain weak health infrastructures in developing countries (Elias, 1991). These women will need to be referred for appropriate therapy or palliative care, where feasible. If women with advanced disease do not have access to some form of treatment, the entire screening and treatment program may be viewed negatively by women, thus discouraging them from seeking the services they need.

Given that treatment for advanced stages of cervical cancer may not be effective and is not readily available in many countries, particularly in rural areas, health programs must maintain a focus on early detection and low-cost management of preinvasive disease, at the same time making appropriate palliative care available to women with incurable invasive disease.

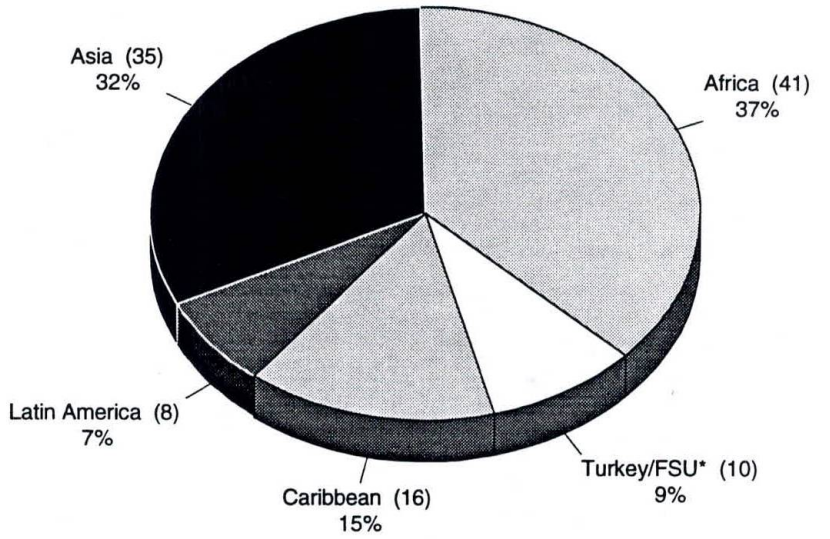
CURRENT CIN TREATMENT PRACTICES AND PREFERENCES IN DEVELOPING COUNTRIES: SURVEY RESULTS

Although the efficacy of low-cost outpatient treatment methods is well-established, these technologies are not widely available in many countries for a variety of reasons. The survey and guided interviews that were undertaken as part of this report sought to evaluate the availability of CIN treatment interventions and to determine current CIN treatment practices and preferences in less developed countries. In addition, the survey identified barriers to delivering treatment services. Unfortunately, very little information was gathered on the

types of diagnostic procedures that are typically used to assess the need for treatment. One hundred-ten responses were received from over 30 countries, representing a 46 percent overall return rate. Regional return rates and a list of countries from which surveys were received are attached as Appendix B.

The geographic and organizational distributions of the respondents are shown in Figures 1 and 2. Information on the respondent's prior experience was not available.

FIGURE 1: Geographic Distribution of Respondents



N=110
*FSU=Former Soviet Union

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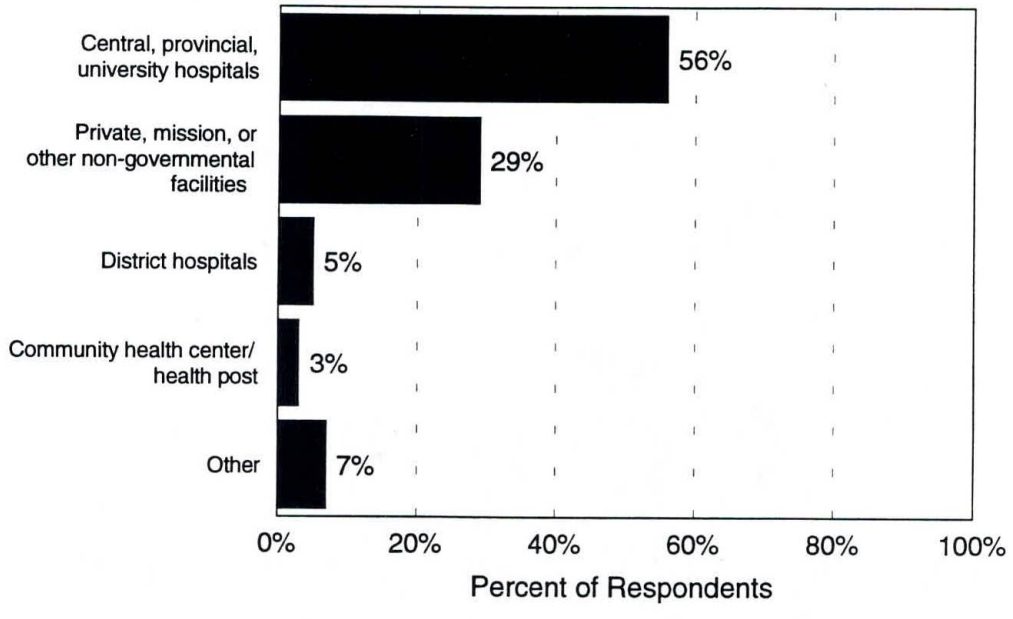
Surveys were sent to clinicians and women's health and public health specialists drawn from professional contacts and the literature. No attempt was made to send the survey to a representative sample of practitioners by region or by facility level. The majority of respondents work in central or provincial facilities, with others in private, mission, or other non-governmental facilities. Survey results, therefore, provide a picture of prevailing CIN treatment practices primarily in those settings in developing countries and in the former Soviet Union (FSU). The results do not provide much information on whether or not CIN treatment is being undertaken at less centralized facilities and, if so, what methods are used, as few respondents represented district-level or peripheral health facilities. It is likely, however, that the majority of treatment occurs at the centralized level, thus accounting for the high response rate from this group. A majority of responses were received from Africa and Asia. The Middle East and Eastern Europe/Former Soviet Union regions, in particular, were not well represented, with surveys being received only from Turkey (8), Armenia (1), and Russia (1). This may be attributed to PATH having fewer contacts in these regions, as well as to the lower rates of cervical cancer in some of these areas.

FIGURE 2: Distribution of Organizations Represented by Respondents

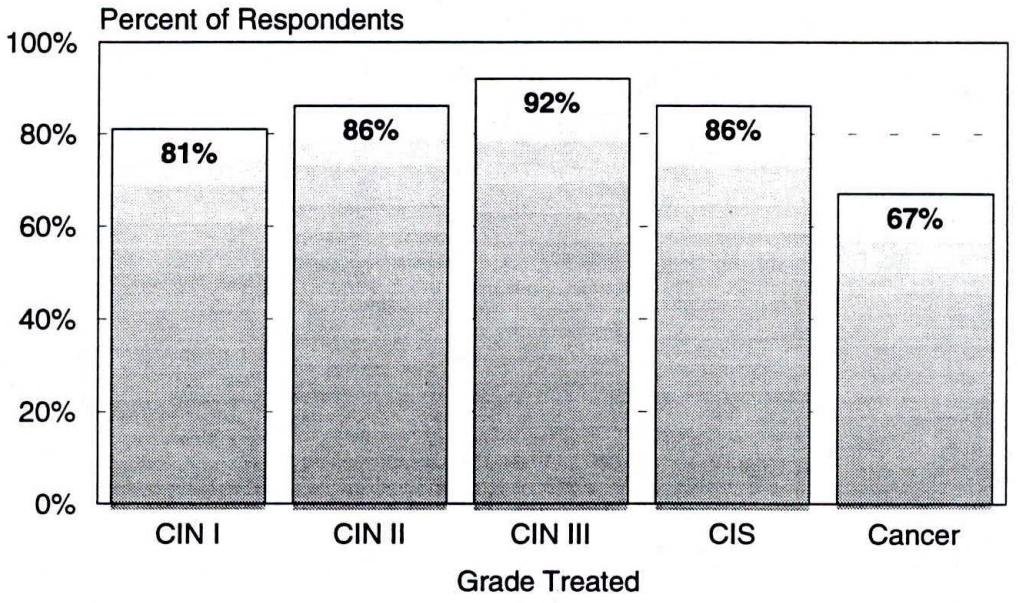


Current treatment practices: These survey results describe a sampling of CIN treatment practices in specific developing country and FSU settings from which some possible trends can be observed, rather than a definitive and comprehensive picture of CIN treatment practices worldwide. Over three-quarters of respondents indicated that their facilities currently provide treatment for CIN, while about two-thirds indicated that their facilities treat cancer (see Figure 3). A vast majority (81 percent) also indicated that they treat women with CIN I, as well as high-grade dysplasia. Most facilities represented in the survey also provide some opportunistic screening.

Survey data strongly suggest that hysterectomy and cone biopsy are predominantly used to treat preinvasive cervical disease in the countries represented, although it was unclear whether all grades or only high-grade lesions were treated with these methods. Figure 4 indicates the types of treatment modalities for CIN that are currently being used by respondents. No information was gathered on the frequency of use.

Several respondents from India and the Philippines indicated that cone biopsy or hysterectomy were preferred for women with CIN who are unlikely to return for proper follow-up as well as for older patients who have completed their childbearing. About 60 percent of respondents currently use cryotherapy, while about 41 percent currently use LEEP. Electrocautery is being used by about 16 percent of survey respondents to treat all grades of CIN. About seven percent of survey respondents, predominantly from Asian countries, indicated that they are currently using laser therapy to treat CIN. Presumably, it is not used more widely because the costs, technical maintenance, training burden, and colposcope

FIGURE 3: Grade of Dysplasia Treated



N=86

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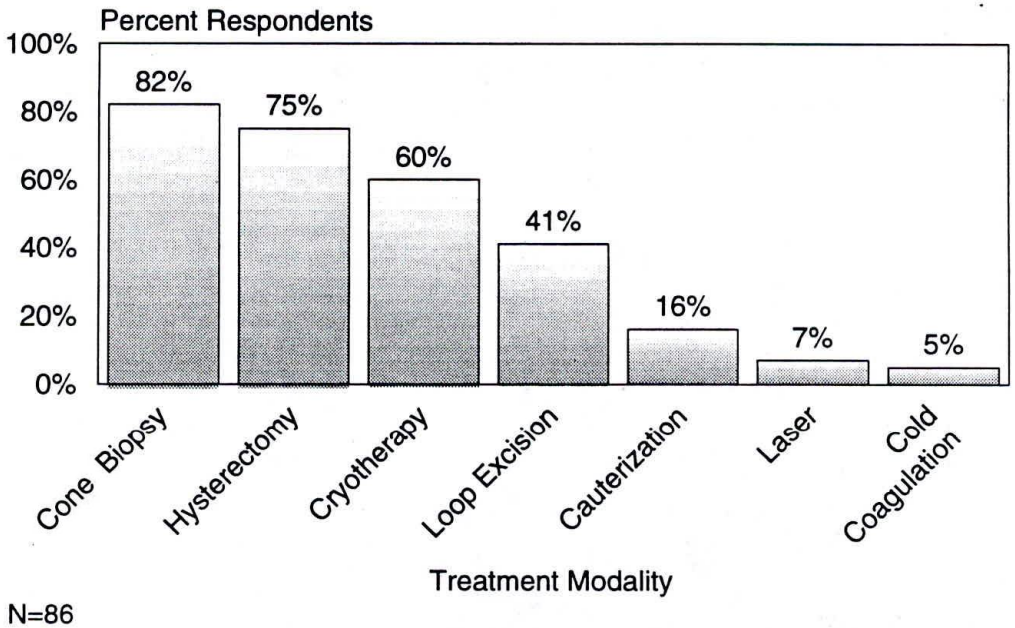
FIGURE 4: CIN Treatment Modalities Currently Being Used by Respondents



N=86

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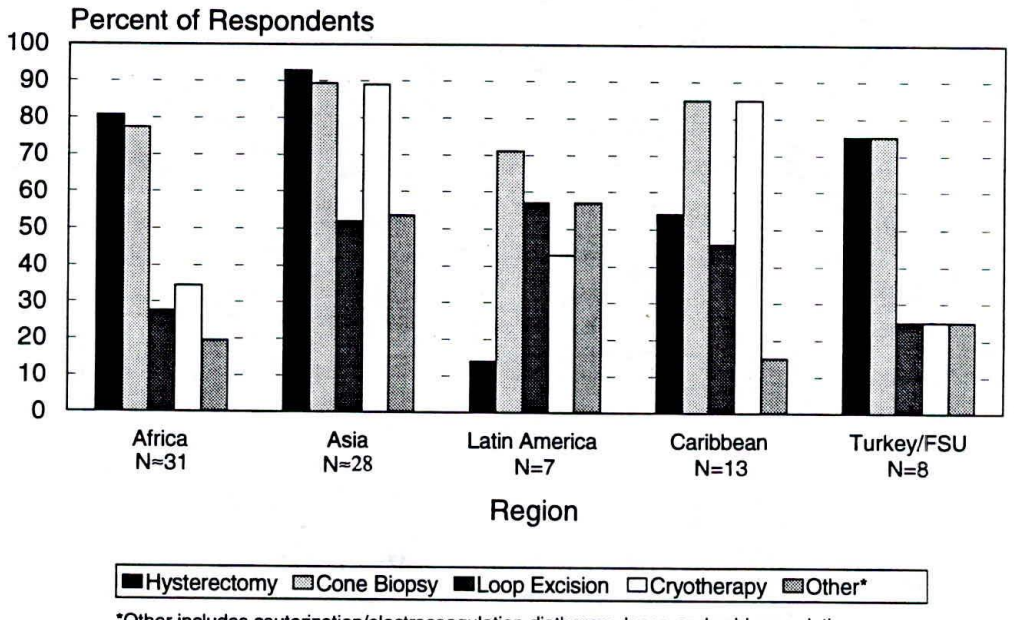
requirements are prohibitive in many developing country settings, particularly in Africa. Just under five percent use cold coagulation, the majority of whom were from Latin America.

By region, it appears that hysterectomy may be used widely to treat CIN in all regions except Latin America, where respondents indicated that cone biopsy is used more widely than other methods (see Figure 5). Respondents from Caribbean countries also indicated that cone biopsy was used more widely than other treatment methods.

FIGURE 5: Type of CIN Treatment Now Being Used by Region



*Other includes cauterization/electrocoagulation diathermy, laser, and cold coagulation.

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Larger differences existed among regions regarding cryotherapy and, to a lesser extent, loop excision. Overall, a greater proportion of respondents from Asia, the Caribbean, and Latin America appear to have access to cryotherapy and, particularly, to loop excision than those from other regions.

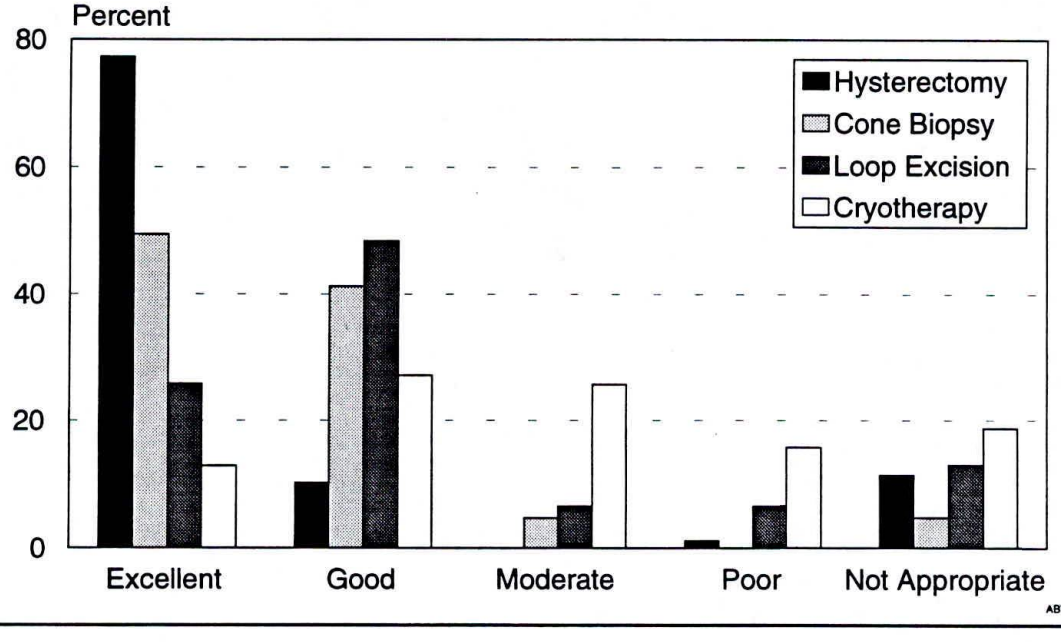
If several treatment modalities were available, respondents indicated that choice of method would depend on the following, in order of importance:

- extent/severity of lesion
- childbearing status/desires of woman/family
- woman's ability to return for follow-up visits
- availability of equipment and trained personnel
- existence of associated medical illness/other gynecological factors
- treatment affordability to patient
- availability of colposcopy
- response to prior treatment
- patient preference

Several respondents indicated that they currently rely on methods such as cryotherapy, electrocoagulation diathermy, or cauterization to treat CIN I and II, and on LEEP, hysterectomy, or cone biopsy to treat CIN III/CIS.

Survey respondents generally perceived hysterectomy and cone biopsy to be more effective than other methods to treat severe dysplasia (CIN III/CIS). This suggests that education of providers will be essential if alternative, outpatient methods are to be adopted. Among the lower-cost, outpatient procedures, loop excision is perceived to be more effective in treating severe CIN, although cryotherapy appears to be used more widely (see Figure 6). This may be because respondents are more familiar with cryotherapy, and therefore, its limitations, than with loop excision. In addition, since LEEP is a relatively new treatment approach, respondents may have assumed that it is better than the older technologies.

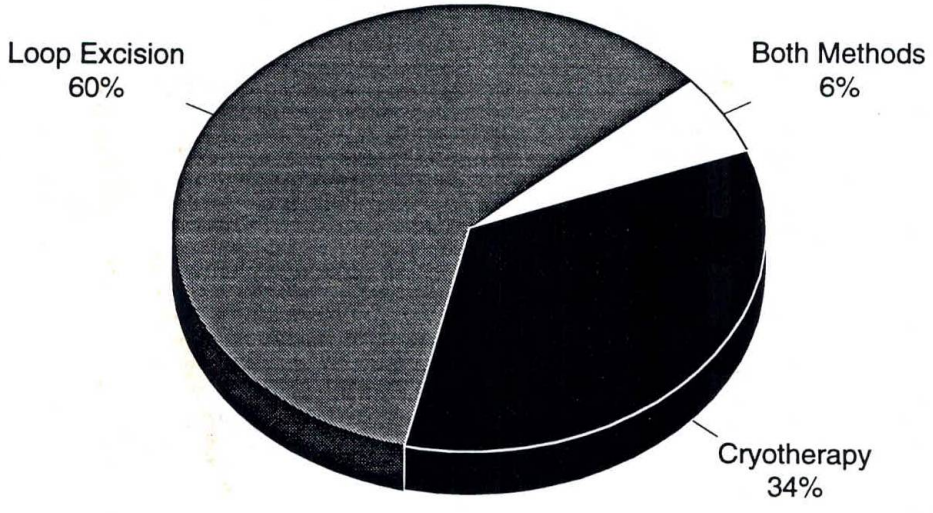
FIGURE 6: Perceived Effectiveness of Treatment for Severe Dysplasia (CIN III/CIS)



In some cases, experience with a particular method seems to be related to its perceived effectiveness. For example, those respondents who have ever used loop excision tended to rate its effectiveness as "excellent" or "good" in treating severe dysplasia (CIN III or above); among those who had never used LEEP, a greater proportion considered it "not appropriate" for treatment of severe CIN. By contrast, there was little difference in responses between those with and without cryotherapy experience. Both groups tended to consider the method only "good" or "moderate" in treating severe dysplasia, with fairly large proportions of each group (20 percent and 14 percent, respectively) considering it "not appropriate" for treatment of severe dysplasia.

CIN treatment method preference: Of the two most effective outpatient treatment procedures (cryotherapy and loop excision), nearly 60 percent of respondents indicated that they would prefer loop excision, while about 34 percent would prefer cryotherapy. A small number would choose both methods, commenting that cryotherapy would be useful for CIN I and II lesions, while loop excision or cone biopsy would be useful for CIN III lesions and for women with unsatisfactory colposcopic results and indeterminate smears (see Figure 7).

FIGURE 7: Outpatient CIN Treatment Method Preference



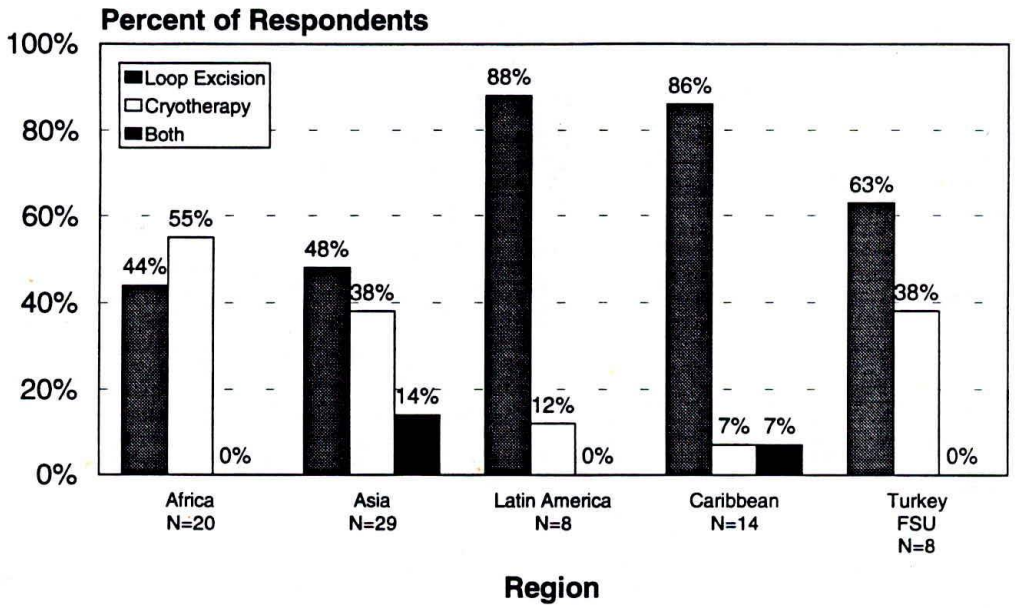
By region, respondents from Africa indicated slightly greater preference for cryotherapy than loop excision. This may be due to limited exposure to and knowledge about LEEP. Respondents from all other regions preferred LEEP, with a much greater proportion of respondents in Latin America and the Caribbean (88 and 86 percent, respectively) than in other regions choosing this method (see Figure 8).

Perceived barriers to providing treatment for CIN/CIS: The following were listed as the main barriers to treatment (N≈97):

- Lack of a comprehensive screening program (66%)
- Cost of equipment (57%)
- Inability to follow-up women (54%)
- Lack of trained personnel (48%)

- Inability to identify women with early, treatable disease (34%)
- Women's resistance to treatment (15%)
- Other* (19%)

FIGURE 8: CIN Treatment Preference Between Loop Excision & Cryotherapy by Region



Regionally, slight differences were noted in these results. For example, fewer respondents from Asia than from other regions listed "cost of equipment" as a key barrier. Rather, an "inability to follow-up women" was cited more frequently by Asian respondents. "Inability to identify women with early, treatable disease" also was cited more often by African respondents than by those from other regions.

A detailed discussion of each barrier and of potential solutions is presented below:

Lack of a comprehensive screening program: About 66 percent of respondents identified this as a barrier to treatment. Survey results indicated that in all regions, screening largely occurs opportunistically, rather than as part of an integrated program, in large, central facilities as well as in selected family planning, maternal and child health, STD, or private clinics.

*Other included: cost of travel to hospital; treatment affordability to patients; lack of patient/public education; lack of political will; insufficient equipment, supplies, and facilities for the large number of women needing treatment; high false-negative rate of Pap smears; crowded conditions; and long waiting time for diagnosis.

Where cytology screening is already in place, respondents expressed concern about Pap smear quality, and specifically, about high rates of false-negative results. Clearly, establishing widespread, reliable screening is essential to reducing cervical cancer morbidity and mortality, and simple and appropriate screening approaches for low-resource settings that can be paired with appropriate treatment technologies must be identified. Because some of the settings that currently provide opportunistic screening already may be providing minor surgical care such as sterilization, they may have the capacity to provide simple, outpatient CIN treatment as well.

Cost and availability of equipment: Nearly 60 percent of respondents indicated that cost of equipment was a key barrier to treatment. Survey results revealed that equipment prices varied widely among countries and presumably depended on local availability of equipment and supplies. Still, investing in lower-cost outpatient methods to treat preinvasive conditions is likely to lead to considerable savings in the long run, since the equipment lasts for many years and the incidence of advanced cases should decrease, thus reducing the demand for more expensive therapy. Finally, survival rates will be much greater, resulting in a lower cost per Discounted Healthy Life Year (DHLY) gained.*

Obtaining supplies for some treatment technologies also is difficult. Anecdotal information gathered in interviews suggests that there are some common problems related to cryotherapy use in low-resource settings. For example, in Kenya, cylinders for refrigerant are in short supply and leakage occurs frequently. This can result in improper application of cryotherapy because of difficulty in attaining appropriately low temperatures. Improper application, of course, likely would lead to higher rates of treatment failure and a loss of confidence in the method.

Inability to follow-up women: Difficulty with following up women was identified as a barrier by over half of respondents. Referral and follow-up systems are essential to developing an effective cervical cancer screening and treatment program. Some strategies, such as the See and Treat approach, could reduce the number of clinic visits required for evaluation and treatment, which can take many weeks (and is also perceived as a barrier to care). Estimates of the percentage of women who actually return for required post-treatment follow-up varied considerably, although about 58 percent of the respondents indicated that they had approximately 75 to 100 percent return rates (see Table 5, page 31). The mean return rate calculated from the survey was about 71 percent. This figure may represent highly motivated women since they were willing to be screened and to return again for diagnosis and treatment. On the other hand, follow-up rates could be increased if specific outreach programs were established to encourage women to return for follow-up care.

Lack of trained personnel: Nearly half of respondents indicated that lack of trained personnel was a major barrier to providing CIN treatment. According to the survey, gynecologists, as opposed to other clinicians, largely perform CIN treatment in all regions.

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*DHLY = number of years between the age at which death would have occurred from cervical cancer and the individual's expected age at death, with years gained discounted at 3 percent each year.

Table 5:
Percentage of Women Returning for Follow-up after Treatment

Return Rate (Percent)	*# of Respondents*	*Percent of Respondents*
0-24	5	6.4
25-49	7	9
50-74	21	27
75-89	23	29.5
90-100	22	25.6
Total	78	100

Only a handful of respondents (all from Africa) indicated that midwives or nurses provide treatment, while a few (two from Africa and one each from Latin America and the Caribbean) indicated that general practice physicians provide it. Since many countries have a shortage of gynecologists, reliance on these physicians to perform all CIN treatment probably has hindered efforts to expand cervical cancer screening and CIN treatment beyond urban areas. If mid-level practitioners, such as nurse-midwives, could be trained to perform screening, and perhaps simple outpatient treatment such as cryotherapy, screening and treatment coverage could be expanded in some settings. For example, nurse practitioners in Jamaica currently are trained to provide cryotherapy. This approach may hold particular promise in African countries, where survey results indicate that a greater variety of clinicians, including nurse-midwives and nurse practitioners, conduct speculum examinations as well as cervical cancer screening. The feasibility of training non-gynecologists, including non-physicians, to perform screening and treatment, however, depends on local policies regarding health care delivery and should be evaluated within the local context; still, this approach warrants further exploration wherever feasible.

Women's resistance to treatment: Only a small proportion of respondents (about 15 percent) cited women's resistance as an important barrier. Perceived resistance by women, however, may be related to lack of education and information for women about cervical cancer, which also was mentioned as a barrier by some respondents.

Other barriers: Travel costs to facilities providing treatment also was cited by respondents. For example, many women diagnosed with CIN III/CIS in a district outside of Nairobi, Kenya, could not afford the transportation to Nairobi for treatment. Treatment cost to patients also is a serious barrier. Costs may vary widely among and within countries

depending on whether health services are subsidized by governmental or other funds. For example, the cost of a colposcopic exam and LEEP in one Kenyan facility is over US$90, making it impossible for most women to afford the service.

Lack of political will also was cited as a barrier in the survey. In many countries, despite high rates, cervical cancer may not be considered a priority due to competing demands for limited resources. Still, if cost-effective and reliable screening and treatment approaches could be identified, some countries might be able to initiate or expand cervical cancer prevention and control programs. Integrating these activities into existing services could result in considerable savings in start-up costs and ultimately in costs associated with treating advanced cancer, since the number of cancer cases would drop. To make appropriate decisions, however, it is essential that policy makers at national, regional, and local levels be informed of potential cost-saving strategies and persuaded of their feasibility.

Availability of Basic Supplies and Equipment

Survey findings suggest that the majority of facilities represented by the respondents are equipped with examination tables, specula, lights, and electricity, although facilities in African countries represented in the survey were not as well-equipped with these items as those in other countries. Most facilities also have access to a pathology laboratory. A majority are equipped with local anesthesia and consumable supplies, although over 30 percent of respondents from Africa (compared to between 7 and 12 percent from other regions) indicated that their facilities experienced shortages. About 82 percent of respondents indicated that their facilities have staff trained in administering general anesthesia, with slightly fewer having the equipment needed to administer general anesthesia. By region, however, over 96 percent of respondents from Asia said that they had facilities and staff to administer general anesthesia, while fewer respondents from other regions (57 to 75 percent) indicated that this was the case.

About three-quarters of respondents indicated that they always have access to antibiotics, while about 22 percent sometimes have access. About 62 percent of respondents indicated that they were equipped with a colposcope, with 38 percent indicating that they only sometimes or never were equipped with one. Regionally, a greater proportion of respondents from Latin America and the Caribbean (87 percent each) indicated that they always were equipped with a colposcope, while only about 35 percent of respondents from Africa indicated that their facilities were always equipped with one. Overall, just over half of respondents indicated that their facilities are equipped with blood transfusion and HIV screening capabilities, with about one-third not being equipped. A greater proportion of respondents from Africa, Latin America, and the Caribbean than from Asia, however, indicated that their facilities were not equipped with these services. For example, 50 percent of respondents from Latin America said their facilities did not have blood transfusion services, while nearly 38 percent did not screen for HIV. For Africa, the figures were 40 percent and 39 percent, respectively, and for the Caribbean, 40 percent and 33 percent.

With regard to supplies specifically for cryotherapy, survey results suggest that carbon dioxide may be used more widely than other refrigerants in all developing country regions except Latin America. Specifically, about 61 percent of survey respondents indicated that their facilities have access to carbon dioxide (and about the same percentage now use it). It is often procured from local sources such as soda factories or private gas companies. About 38 percent have access to liquid nitrogen and now use it. About 11 percent use nitrous oxide. Facilities in Africa may have less access to refrigerants, in general. Of those respondents who perform cryotherapy, over one-third (36 percent) experience delays in resupply of refrigerants or other necessary supplies for cryotherapy.

Although facilities represented in the survey seem to have basic equipment to provide some type of CIN treatment, respondents still indicated that for the numbers of women requiring treatment, insufficient supplies, facilities, and equipment remained a barrier to service delivery. In particular, respondents cited crowded clinic conditions and long waiting times for services and laboratory results as being important deterrents to providing treatment services.

Summary

Despite this survey's limitations, data suggest that in all regions, but particularly in Africa, low-cost, simple, outpatient procedures such as cryotherapy and loop excision may not be sufficiently used. Rather, clinicians still rely heavily on hysterectomy and cone biopsy, even to treat low-grade lesions. This suggests that education of providers to help change their perception of various methods, and ultimately their methods of choice, is crucial. Heavy reliance on inpatient methods also is likely due to limited access to alternative methods such as cryotherapy and loop excision, as well as to lack of resources to support early detection and treatment of preinvasive conditions. For example, "lack of comprehensive screening programs" was listed by a majority of respondents as a key barrier to provision of treatment, further indicating the need to identify simple and appropriate screening approaches for low-resource settings that can be paired with appropriate treatment technologies. Cost and lack of trained personnel were other key barriers to treatment that were identified, thus emphasizing the importance of introducing the most cost-effective and easy-to-use methods available. In addition, inability to follow up women was cited as another important barrier; this highlights the need to address the systems that are essential to developing an effective cervical cancer screening and treatment program.

Regionally, it appears that countries in Asia, Latin America, and the Caribbean may have greater access to cryotherapy and loop excision than African countries, as well as greater capacity to incorporate these methods into their programs. This suggests that strategies for outpatient treatment introduction likely will differ among these regions, and that introduction efforts in Africa, in particular, will need to be carefully considered in the context of limited resources. In all regions, however, introducing outpatient methods and clear guidelines for their use could improve overall quality of care and extend treatment services beyond central facilities, thereby reaching more women who need them.

Although little information was collected regarding CIN treatment capabilities in less centralized facilities, it is unlikely that many peripheral centers are providing treatment, since outpatient methods are not widespread and inpatient methods require substantial infrastructural support. Indeed, interviews with experts in several countries suggest that treatment is not generally provided outside main urban centers. For example, in the Philippines, CIN treatment is generally only available at national, regional, and district public hospitals, or at private hospitals and clinics. No treatment is done in health centers at the local ("barangay") level, although some peripheral facilities may conduct screening. Similarly, in Viet Nam, treatment, which relies on cone biopsy, hysterectomy, or in some cases, electrocautery, is available only at the provincial and central hospital levels. Further, follow-up with women living in non-urban areas is very poor. Interviews in other countries suggested similar conditions.

More information is needed on whether outpatient treatment modalities are being used or could be introduced in less centralized facilities and, more specifically, which methods would be most appropriate for specific settings. These methods would be valuable only if some method of screening were in place, however. Since population-based cytology services are very difficult, if not impossible, to implement in most low-resource settings, evaluating alternative methods such as aided visual inspection is crucial.

Clearly, more research is needed to develop appropriate CIN treatment strategies and interventions.

Research Needs

- Further evaluate which treatment protocols would be most appropriate, cost-effective, and acceptable for various low-resource settings.
- Determine what kinds of support services such as counseling and follow-up care must accompany CIN treatment in low-resource settings.
- Evaluate low-power magnification as a replacement for colposcopy to facilitate outpatient treatment (as well as screening) in certain settings.
- Determine the level of additional infrastructural support necessary to introduce technologies such as loop excision or cryotherapy.
- Evaluate existing services to determine which could best absorb cervical cancer screening and treatment services.
- Investigate the feasibility of training other types of clinicians, such as mid-level practitioners, to provide simple, outpatient treatment (in conjunction with screening).
- Develop strategies to change or influence relevant policies and practices, particularly if alternative screening and treatment methods are proven feasible and effective.

Following up Women: A Key Problem in Delivering Treatment Services

Referral and follow-up systems, after both screening and treatment, are essential to developing effective cervical cancer control programs. In industrialized countries, it generally is recommended that women treated for preinvasive cervical lesions receive cytological follow-up exams every three to four months for one year, and then yearly thereafter (ACOG, 1993). (Some countries, however, suggest longer intervals, i.e., three years between Pap smears.) In many other countries, particularly those with large rural populations, traveling long distances to seek health services and returning for follow-up care may be extremely difficult for many women. Further, cervical cancer screening and treatment programs, if they exist at all, often are limited and may not have the resources to actively recall women requiring follow-up care. For example, in India, one study indicated that only 59 percent of women participating in a large screening program were adequately followed up, and of those, 28 percent had only one follow-up visit post-treatment (Singh et al, 1991).

Some strategies, such as the See and Treat approach, could reduce the number of clinic visits required for evaluation and treatment, as well as eliminate the waiting time for biopsy results. This approach, or other alternatives, may ease the burden on women and on health facilities. Other strategies, such as mobile screening and treatment, also may improve screening coverage and enable women to receive the treatment they need, provided that low-cost, simple treatment methods such as cryotherapy are available. For any strategy to work, however, women, as well as their families and health care providers, must be given information about cervical cancer through community channels so that they understand the importance of screening and treatment.

IMPACT OF CURRENT POLICIES ON CIN TREATMENT STRATEGIES

Whether formal or informal, policies regarding personnel, facilities, cost recovery, and medical protocols have diverse impacts on the coverage, effectiveness, and acceptability of CIN treatment services. Policies can be inscribed in codes of medical practice, in government regulations, or more informally in customary procedure. Often, policies established with one purpose in mind have undesirable effects on other programs that have not been anticipated. Well-designed policies, however, can provide important guidance to programs on how to provide good quality, cost-effective services, especially where resources are limited. The key aspects of CIN treatment service delivery affected by policy are detailed below:

Personnel: Based on the PATH survey results and on other reports, it appears that most countries permit only doctors (primarily gynecologists) to carry out CIN treatment, with a few also allowing nurse-midwives to do so. Given the heavy concentration of physicians in urban areas, this policy clearly limits rural women's access to this care. It also increases the cost of such care, either to the public sector or to the private patient. Since survey respondents cited the lack of trained personnel as one of the key barriers to providing treatment, it is essential that the feasibility of training non-physicians be explored as a means to expand both screening and treatment services.

Facilities: In some countries, only the central referral hospital is equipped to offer conization, cryotherapy, or, perhaps, loop excision, although many countries also may offer such services at large regional hospitals. Few countries make treatment, even for early

preinvasive cervical disease, available at the district level, largely because of financial and technical constraints. The location of treatment services, however, is a significant determinant of a woman's access to care, given the difficulties and costs of transportation and arranging coverage of family responsibilities in her absence. This was confirmed by the survey results, which indicated that women are prevented from seeking services due to high travel costs.

Cost Recovery: While many countries offer CIN treatment as part of public health services (supported by the government), most require some payment by the patient, especially for surgical or inpatient services. This trend is likely to expand as countries face growing pressure to recover health care costs. Survey respondents noted that such fees can be a significant barrier, however, especially for women who are asymptomatic (in the preinvasive stage) and who may not fully appreciate the serious implications of their condition. Effective education and communication messages directed to women at risk may help them understand the importance of screening and early treatment so that they will seek and, if necessary, pay for the services they need, but clearly efforts to reduce costs by adopting more cost-effective screening and treatment technologies and protocols are essential.

Medical protocols: Medical protocols determine how patients are identified, what conditions are treated, what treatments are used, and the steps involved in standard treatment. Which patients are identified for treatment depends on the screening policy (active or opportunistic, targeted at higher-risk women or younger family planning/antenatal care clients), local epidemiology, and the effectiveness of the referral system. Many countries are conducting only limited screening, often among younger women. Therefore, because the highest-risk women are not screened, cases actually discovered tend to be advanced, symptomatic cases, resulting in low demand for early treatment. The demonstrated preference for more invasive or radical treatments noted in the survey may, in fact, partially reflect the lower proportion of early cases detected by screening. While most countries routinely treat high-grade dysplasias, the survey suggests that many developing countries continue to treat all low-grade dysplasias as well, rather than adopting the more conservative "wait-and-see" approach common in developed countries. Treating low-grade dysplasia raises the cost of care (in the form of potentially unnecessary treatment and more women experiencing side effects) but ensures treatment for women who are unlikely to get any further follow-up.

In terms of treatment methods, the predominant use of conization and hysterectomy reported in the survey has serious implications for financial costs to the system and to women and results in unnecessarily invasive procedures in many cases. The requirements for anesthesia, equipment, inpatient care and surgical skills are much greater than would be necessary for cryotherapy or loop excision.

Finally, the standard protocol for managing cervical abnormalities involves multiple steps, an extended timeframe, and often multiple facilities and providers. The protocol usually includes cytology, colposcopically-directed biopsy, histology, treatment, three-month follow-up to confirm cure, and repeated periodic follow-up visits for at least one year. The dropout rate is high at each stage for a variety of reasons, resulting in suboptimal outcomes even

when abnormalities are detected. Indeed, difficulty in following up women both after screening and after treatment was cited in the survey as a major barrier to delivering effective cervical cancer prevention and control services. Even in developed world settings, this multi-step protocol is not always feasible; in resource-limited settings, it often overtaxes the system and seldom results in cost-effective care.

Programs seeking to initiate or expand CIN treatment (and screening) services are encouraged to undertake a review of each of the issues and determine how key policies affecting them could be changed.

IMPACT OF LOW-COST TREATMENT ON COSTS OF CERVICAL CANCER CONTROL

Determining whether to integrate new clinical management strategies often is based on cost factors and availability of necessary equipment and training. Based on the survey results, it is clear that many programs still rely on expensive, invasive, inpatient procedures to treat CIN. Capital and recurrent costs for outpatient procedures (including training), however, are far less than for inpatient methods; furthermore, outpatient procedures should not compromise CIN treatment efficacy.

Calculating cost-effectiveness of various treatment options must be done on a country-specific basis and requires detailed information on several different aspects of service delivery and management. This section focuses on provider costs (public or private) in an effort to guide decision makers on ways to incorporate financial information into cervical cancer control program design and evaluation.

Definitions and Key Considerations

In this document, cost refers to the monetary value of inputs used. While the costs experienced by clients are important, they are hard to quantify, and broader opportunity costs have not been considered. Effectiveness here refers to the prevention of cases of invasive cervical cancer (or "cervical cancer cases averted"), which is the primary goal of CIN treatment.

Clearly, the cost-effectiveness of various CIN treatment regimens is difficult to disentangle from costs associated with screening and with treating more advanced cases of cancer. For example, without information on the costs associated with treating invasive cancer, it is difficult to make a strict comparison between treating many women early and treating only those who develop cancer later. This section focuses on early treatment only, with the understanding that a broader range of costs (such as those associated with screening and treatment of invasive cancer) must be included in any comprehensive country-specific analysis (see box, page 38). For example, it would be expected that at the start of any new cervical cancer control program, a large number of women with CIS or invasive cancer may be identified, which initially may drive up program costs.

Worksheet Explanation: Defining Treatment Costs

The examples in this section and in Appendix B include estimates for cervical cancer screening and treatment program component costs that are attributable *only to the CIN treatment services* included in the program. Other factors affecting overall program costs such as screening accuracy and coverage are considered screening rather than treatment costs and, therefore, are held constant (and set at 100 percent) for the purposes of these exercises. Similarly, it is assumed that the accuracy of detecting persistent or recurring CIN during follow-up evaluation (after initial CIN treatment) also is 100 percent.

These assumptions, although unrealistic in practice, are made so that the costs for varying treatment strategies can be directly compared. (In reality, it might be expected that 85 rather than 100 percent of CIN is accurately detected, which would cause overall costs per CIN case treated and costs per cervical cancer case averted to increase.) Although the worksheet examples attempt to isolate treatment-specific costs, it is critical that in evaluating total costs incurred by a cervical cancer prevention and control program, treatment costs are assessed in conjunction with other major cost factors such as CIN prevalence, screening costs, and screening accuracy.

Despite this somewhat limited focus, it is clear that the most important determinants of CIN treatment cost-effectiveness are screening accuracy, treatment method effectiveness, and CIN stage at treatment. Other variables, such as capital expenditures for equipment, and even staff salaries, may vary widely with little effect on costs per cervical cancer case averted. By contrast, slight shifts in CIN treatment efficacy, for example, have a large impact on costs per cancer case averted. As demonstrated in the following exercise, when a treatment method has a high degree of effectiveness, expensive follow-up treatments are avoided. Likewise, if treatment is limited to high-grade SIL, which has a higher risk of progression to invasive disease, the cost per cancer case averted is much lower than for strategies that treat all grades. This is because the considerable increase in resources necessary to treat all instances of CIN is largely spent on cases with a low risk of progression. The costs of the relatively few additional cases averted when treating all CIN (that is, the additional costs to the program divided by the number of additional cases of cancer prevented) can be enormous.

Calculating the Cost of CIN Treatment

Treatment costs must include both capital costs (for equipment and training) and recurrent costs (labor, supplies, fees for purchased supplemental services such as laboratory work, facility use, transport, and communication). Capital costs are highly sensitive to patient load over which the amounts can be amortized; thus, they depend on variables such as total population, disease prevalence, and screening effectiveness. Because LEEP has multiple surgical uses beyond CIN treatment, costs for this method could be shared over several programs, thus reducing overall capital equipment costs. Some recurrent costs are less sensitive to patient load. Costs of managing side effects and complications, which are a function of the number of procedures performed and the probability and expense of treating associated medical problems, also must be included as recurrent costs.

Example: Classifying costs for cryotherapy

Consider a developing country screening and treatment program that screens 250,000 women a year, 1.5 percent (3,750) of whom have high-grade dysplasia. To calculate the principal costs of providing cryotherapy, estimated capital and recurrent costs must be supplied for the major components of this method. A worksheet for calculating cryotherapy costs is provided in Appendix C, pages C-2 and C-3. Hypothetical estimates of capital and recurrent costs for cryotherapy are listed below:

Capital Costs:	Cryotherapy units	$8,000	(4 units @ $2,000 each)
	Reusable refrigerant canisters	$2,000	(8 canisters @ $250 each)
	Staff training time	$3,000	(8 people)
	TOTAL	$13,000	

These costs include the assumed purchase of one cryotherapy unit at $2,000 and two refrigerant canisters at $250 each for every 1,000 cases of CIN. Note that total capital costs here do not include facilities. Note also that they do not include screening and diagnosis capital costs, which could include colposcopes and other laboratory and clinic equipment.

Recurrent Costs:	Salaries	$24,000	($6,000 x 4 FTEs)
	Consumable supplies	$18,750	($5 x 3,750 treatments)
	Follow-up conizations	$56,300	($100 x 563 conizations)
	Treatment-related complications	$1,900	($50 x 38 complications)
	Hysterectomies	$21,000	($1,500 x 14 invasive Ca)
	TOTAL	$121,950	

Salary costs are based upon the arbitrary assumption of $6,000 per full-time equivalent (FTE) and two FTEs per 1,000 cases. Consumable supply costs include refrigerant (CO_2) needed for each cryosurgical procedure. Conization costs are based on the assumption that about 15 percent of high-grade CIN will persist despite cryotherapy. Hysterectomy costs cover those cases that may progress to invasive cancer despite cryotherapy and follow-up conization.

If capital costs are amortized over five years in a straight-line depreciation, total capital and recurrent annualized costs for cryotherapy are $124,550. This results in an estimated cost per treatment of $33 and a cost per invasive cancer case averted of $67, assuming that 50 percent of high-grade dysplasia would progress to invasive carcinoma without treatment and that high-grade CIN is correctly identified, both initially and during post-treatment follow-up. Therefore, 1,862 cases would be averted due to treatment. If the assumption regarding disease progression is lowered, as would be the case where all grades of CIN are treated, the cost per cancer case averted would be expected to rise considerably, with only a marginal gain in the total number of cases averted. (See Appendix C, pages C-6 and C-7, for completed worksheets on cryotherapy cost calculations based on survey data from urban facilities in Thailand and Zimbabwe.)

Example: Calculating costs for LEEP

LEEP requires many of the same key capital and recurrent cost components used with cryotherapy. LEEP equipment, however, is more expensive than cryotherapy equipment, as are salary, consumable supply, training, and follow-up costs. Hypothetical capital and recurrent costs are listed below:

Capital Costs:	Loop excision unit	$24,000	(4 units @ $6,000 each)
	Staff training time	$3,800	(8 people)
	Other (colposcope)	$80,000	(4 colposcopes @ $20,000 each)
	TOTAL	$107,800	
Recurrent Costs:	Salaries	$32,000	(assumes higher skill)
	Consumable supplies	$93,750	(assumes 5x greater costs)
	Follow-up conizations	$18,800	(assumes fewer conizations)
	Treatment-related complications	$2,800	($50 x 56 complications)
	Hysterectomies	$7,500	($1,500 x 5 invasive ca)
	TOTAL	$154,850	

Based on these calculations, the costs per CIN treatment and per cancer case averted are $47 and $94, respectively. Using these estimates, an additional nine cases of invasive carcinoma are averted by providing loop excision instead of cryotherapy at an additional annualized cost of almost $50,000. This suggests that if these numbers were real, the cost of averting these additional cases is $5,556 per case.

Again, using survey data from urban facilities in Thailand and Zimbabwe and estimating some of the missing costs, a cost per loop excision treatment can be calculated (see completed worksheets in Appendix C, pages C-6 and C-7).

INCREASING THE AVAILABILITY OF TREATMENT IN LOW-RESOURCE SETTINGS: DEVELOPING A SITE-SPECIFIC PLAN OF ACTION

Regardless of the treatment strategy used, reaching higher-risk women, particularly in non-urban areas, will be difficult in resource-poor settings. A coordinated cervical cancer prevention and control plan, preferably national in scope, is the best way to achieve broad screening and treatment coverage, rational allocation and use of limited resources, a uniform standard of care based on the best available scientific information, and an efficient planning and monitoring process. The plan must include short-, medium-, and long-term phases that realistically reflect local resources, priorities, and commitment levels. Education, legislation, and national leadership are essential in developing a national plan (WHO, 1995).

General Principles and Recommendations

Each country must develop its own national plan of action for prevention of cervical cancer; in some cases, subnational strategies may be implemented in advance of the national level.

While each plan must reflect local circumstances, some key principles regarding a cervical dysplasia treatment strategy can be drawn from the available scientific literature, results of the PATH survey, and consensus of expert opinion. These principles are as follows:

- Treatment of preinvasive cervical disease is more cost-effective than treatment of invasive disease.

  Based on the cost information collected in the survey, as well as from other sources, it is clear that treating invasive disease, which, depending on the stage, could include major surgery, chemotherapy, radiation, and/or palliative care, is far more costly than treating preinvasive disease, especially if low-cost, outpatient methods are used.

- Integrated services are more cost-effective than vertical ones and are more likely to achieve broad population coverage.

  Existing programs such as maternal/child health, STD, family planning, or other outpatient services may have some of the same capabilities required for cervical cancer control already in place. These include procuring and transporting equipment and appropriate test media; developing appropriate triage, counseling, follow-up, quality control, and record-keeping systems; and providing staff training and continuing education (Elias, 1991). The 1994 International Conference on Population and Development held in Cairo, Egypt, strongly endorsed developing comprehensive, integrated reproductive health services, of which cervical cancer prevention and management should be an important component (United Nations, 1994). Linkage between reproductive health services and the broader health care system also will be essential; without cervical cancer control programs, some women inevitably will require referral to tertiary facilities for major surgery or palliative care (Elias, 1991).

- General physicians and non-physician providers should be trained to perform simple outpatient CIN treatment (and screening). Non-clinicians also could be trained to do history-taking and counseling of women being treated for CIN.

  Having a broader pool of clinicians who are capable of providing screening and treatment could significantly increase women's access to appropriate and timely care, particularly in non-urban areas. Survey results suggested that lack of trained personnel was a key barrier to service delivery.

- More limited, outpatient treatment methods (like cryotherapy and LEEP) are highly effective, less expensive, safer, and more acceptable than inpatient methods such as cold-knife conization and hysterectomy.

  Cold coagulation also could be considered. Unless clinically indicated, cold-knife cone biopsy and hysterectomy should not be used as initial treatment methods for CIN, although the survey clearly indicated that these are the only methods available in many settings. The use of general anesthesia is usually not necessary for outpatient methods and should be avoided to reduce costs and complication risks.

- First priority should be given to treating all women with high-grade lesions.

  Women with low-grade lesions should not be treated if resources for treating high-grade lesions are not yet adequate (since the clinical benefit is much greater for those with high-grade lesions) or if follow-up and monitoring for low-grade lesions is feasible (since most will regress spontaneously). If follow-up is poor, women with low-grade lesions can be treated as long as the needs of women with high-grade lesions are already being adequately addressed. Survey results indicate that in many settings, all grades of CIN generally are being treated. This may not be the best use of available resources.

- Women, health care providers, key community leaders, and policy makers must understand and support the cervical cancer control program for it to be effective.

  Given the enormous competition for limited resources in many countries, political will to undertake a cervical cancer prevention and control program is essential. Involving women, health care providers, community leaders, and key policy makers in the planning, implementation, and evaluation of the program helps ensure that potential barriers are identified and realistic approaches are advocated.

Local Situation Review

As a first step in developing a plan of action (before national policies are changed and detailed workplans are developed), several factors related to treatment must be reviewed and additional data collected, if necessary. Existing data from health service statistics, cancer registries, and studies such as the Demographic and Health Surveys should be helpful but may need to be supplemented by compilations of various pathology records or other service statistics or by qualitative research with clinicians, women, and other community members to determine perceived need for services and identify important barriers to service delivery. The key factors that must be clearly understood before proceeding with a plan of action fall into three main areas: features of cervical disease; nature of existing health care resources and constraints; and relevant characteristics of local women and their communities. Specific information to be collected for each of these areas is detailed below:

<u>Cervical disease</u>

- Number of CIN cases identified by existing screening services (or projected number, if improvements in screening are being instituted)
- Estimated prevalence of CIN (by grade) and cancer
- Age distribution for CIN (by grade) and cancer
- Regional variations regarding incidence and prevalence of CIN and cancer within the country
- Age-specific cervical cancer mortality rates

Existing health care resources and constraints

- Number, type, and distribution of staff trained in performing screening and CIN treatment
- Type and distribution of health care facilities
- Type of equipment available and capacity to maintain it
- Systems and funding for essential supplies for providing CIN treatment
- Record-keeping capacity; capacity for making and tracking referrals
- Ability to follow up women after being screened or treated
- Local health care costs and income (from budget allocations and/or fees); analysis of competing demands for health funding
- Analysis of existing health care settings (e.g., sterilization services, maternity hospitals) to which cervical dysplasia treatment might be added
- Availability of treatment services and palliative care for advanced cervical cancer

Characteristics of local women and their communities

- Age and geographic distribution of women
- Financial resources available for travel and treatment costs
- Prevalence of known or suspected risk factors (i.e., HPV or other STD infection, smoking, high parity, high number of sexual partners or partner with lifetime high number of partners, poor nutrition, oral contraceptive use)
- Knowledge, attitudes, and practices regarding cervical cancer and reproductive health
- Social constraints on the ability to seek medical care (such as need to seek husband's permission or manage other family responsibilities)
- Additional barriers to services as perceived by women.

Other site-specific issues also may need to be considered, but this general framework should be useful in forming the basis of a plan of action.

The interplay of these various factors determines the uniqueness of each country's situation and will help suggest the appropriate set of options to be considered. For example, where female sterilization services are established and have a high proportion of older clients, there may be good opportunities to integrate cervical cancer screening and CIN treatment into existing services and improve coverage of women at-risk. Worldwide, about six million women per year seek voluntary surgical sterilization, of which 20 to 40 percent are 35 or older, the appropriate age range for screening (AVSC International, 1994). Regions like Latin America and Asia, in particular, both have high sterilization acceptance as well as high cervical cancer rates. Technical and service delivery requirements for both surgical sterilization and for CIN treatment overlap considerably; for example, much of the same equipment and facility needs, as well as consumable supplies required for sterilization, also are needed for outpatient CIN treatment (see chart, page 45). Still, to ensure optimal use of resources, local programs must base their decision to integrate screening and treatment into sterilization (or other) services on assessments of whether women seeking the existing services in their settings are, in fact, at high risk for developing cervical cancer.

Developing and Implementing a Plan

Because of the focus of this document, this section is limited to a discussion of CIN treatment only, but it is understood that any planning process for cervical cancer control must be done in a larger context that includes screening, cancer treatment, and palliative care for advanced cervical cancer. Where feasible, developing pilot projects based on this model would be extremely useful. A diagram of a potential model for developing a comprehensive plan for cervical cancer prevention and control, of which CIN treatment would be an important component, is presented on page 47.

Key Components

Policies: Current policies must be articulated and modified as appropriate, along the lines suggested in the "General Principles and Recommendations" (pages 40-42). Given the survey's findings, in many settings, policies affecting both treatment technologies and diagnostic and treatment protocols should be reevaluated to determine if the most cost-effective approaches are being supported. In countries where new protocols, such as the See and Treat approach based on LEEP, could be adopted, policies regarding cytology, colposcopy, and biopsy may have to be modified. Similarly, using a low-power magnification device (should it prove feasible) instead of a colposcope to facilitate CIN treatment also would require policy change. Policies will not be changed easily, however, unless decision makers fully understand the health benefits and cost savings of introducing new cervical cancer screening and treatment strategies.

Personnel: Any new plan must consider the issues of training existing staff, revising medical and nursing curricula, reallocating staff time, and even redistributing staff geographically, in some cases. Again, the survey points to the need, in particular, to improve training of existing staff as well as expand training to non-physician providers to ensure cost-effective coverage.

Equipment and Supplies: This is perhaps one of the biggest challenges to developing a successful plan of action to improve cervical cancer prevention and control. Key issues that must be addressed include type, number, maintenance and resupply, and distribution of essential equipment and supplies. Cost, of course, is a primary limiting factor, but, as has been demonstrated, selecting low-cost, outpatient methods over more expensive and aggressive forms of treatment can result in considerable savings. Given that many settings represented in the survey, particularly in Africa, are not equipped with colposcopes, exploring alternative approaches to facilitating treatment (and/or screening) is strongly recommended.

Community Involvement: Mechanisms to ensure community involvement, including local government or nongovernment channels, must be included. Women and women's health advocacy groups, in particular, must be involved in developing a feasible and acceptable plan. Without women's support and understanding of the rationale for cervical cancer prevention and control services, even an extremely well-planned program will fail.

Cervical Dysplasia Treatment

	Sterilization Services	
	Already Required	Would Need to be Added
Staff skills:		
speculum exam	✔	
local anesthesia administration	✔	
cryotherapy or loop excision		✔
equipment sterilization	✔	
Facilities:		
clean, private exam room	✔	
Equipment		
exam table	✔	
light	✔	
non-conductive speculum		✔
magnifying device or colposcope		✔
electrosurgical generator and loop equipment		✔
or cryotherapy set		✔
Supplies:		
local anesthesia supplies (needles, syringes, etc.)	✔	
liquid nitrogen or CO_2 (cryo)		✔
electrodes, loops, smoke evacuator (loop excision)		✔
antibiotics	✔	
Systems:		
records	✔	
counseling	✔	
follow-up		✔

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Monitoring and Evaluation: Once a plan is implemented, monitoring and evaluation of key components is essential to help guide the continuing development of these components and to "fine-tune" the plan. In addition, evaluation indicators and mechanisms for ongoing monitoring and impact assessment are essential to maintain political support and to ensure efficient and effective program management. Both quantitative and qualitative indicators should be derived from epidemiological, financial, and service delivery/quality of care data.

Costs: The costs and cost-effectiveness of planned treatment (and screening) interventions must be well understood before a program is launched. Financial implications include capital and recurrent budgets, whether locally or donor-financed, as well as issues of cost recovery through patient fees. Every effort must be made to develop the most cost-effective, yet efficacious program possible, and introducing low-cost CIN treatment methods will be essential to the success of these efforts. In addition, decisions regarding what conditions to treat and who can provide treatment will have profound effects on cost.

Process

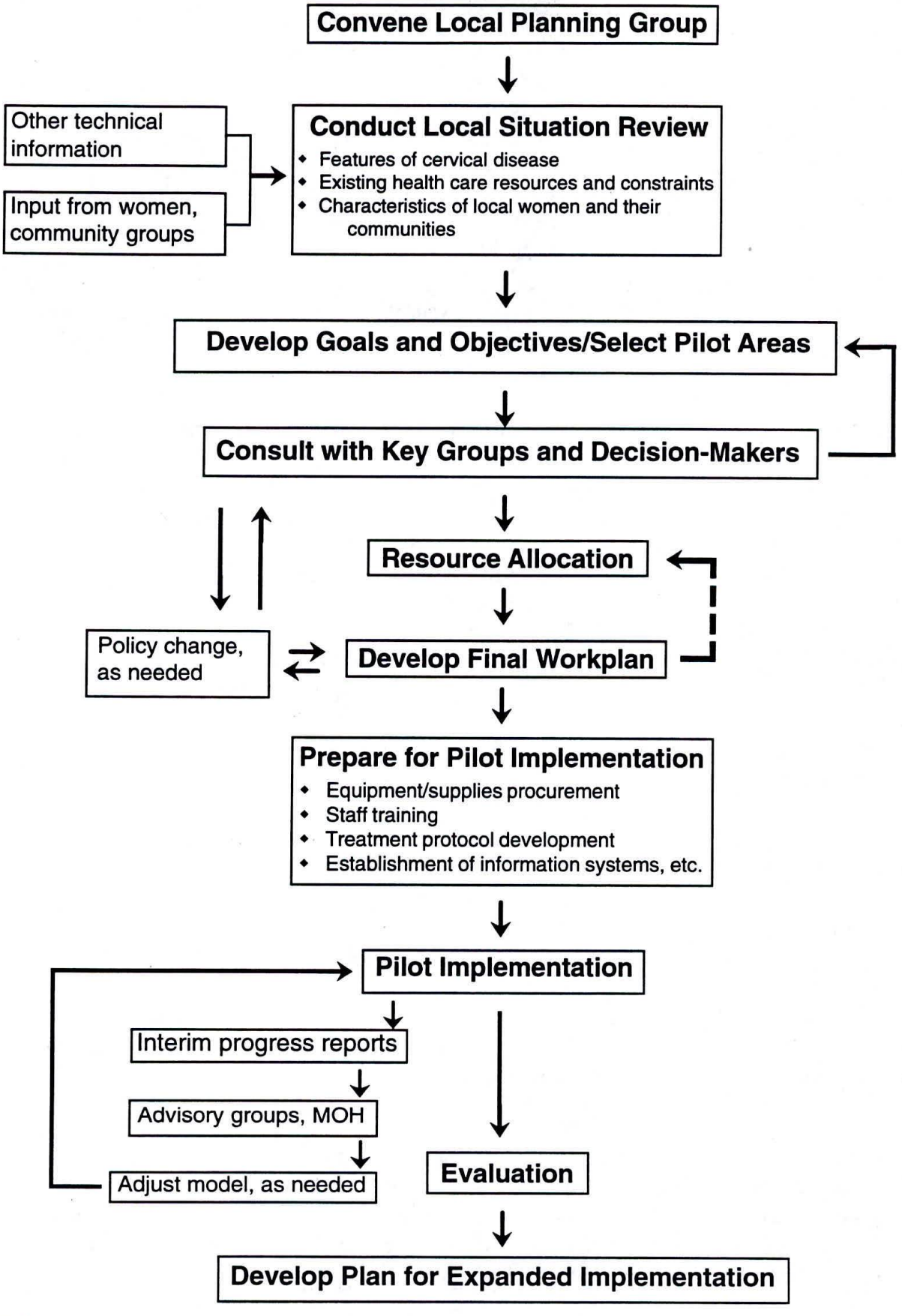
Establishing a planning group: A planning group should be established that includes representatives from at least clinical, epidemiology, health administration and financial planning, and health education disciplines, as well as women and/or representatives from women's groups. Perspectives from medical/nursing education and research, procurement and supplies, and health information systems also would be helpful. The process would start with a consensus-building phase to determine goals and methods of introducing new CIN treatment approaches. The local situation review, draft position papers on various policy issues and strategies, technical information regarding new methods being considered, and small meetings (including clinician and community consultation) should be used during this phase. Considering cost-effectiveness of proposed approaches is essential, particularly if major policy changes are recommended, since such concerns undoubtedly will play a large role in how to allocate the limited resources available for cervical cancer prevention and treatment. The draft plan must include a detailed timeline and budget.

Develop goals and objectives: Based on information from the local situation review and other sources, a set of draft goals and objectives may be developed. This should be considered a working document, which will be revised based on interactive feedback with key groups and decision makers. The goals and objectives should include a proposed geographic site for pilot introduction.

Consultation with key decision makers: Once consensus on a draft plan is achieved, consultation with key decision makers is needed to build broad support for the plan and to secure eventual approval. As part of these consultations, presentations could be made by the planning group that strongly state the rationale for the program and include details about the cost-effectiveness of the interventions proposed.

Consultation with other key groups: This would include a broader array of public- and private-sector clinicians, women's groups, researchers, educators, and other essential parties. Before the plan is approved, consultation with these groups is essential to solicit feedback

Developing a Plan of Action to Control Cervical Cancer



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and to gain their support, and materials appropriate to the particular audience should be provided to contribute to their understanding of the plan being proposed. Based on the feedback and support of these groups, the plan then can be modified, if necessary.

Development of final workplan and preparation for implementation: Based on input from key groups and decision makers, a final workplan can be developed. The workplan must accurately reflect the resources available, and adjustments to the scope of work may be necessary to stay within resource limits. The plan should have a phasing strategy built in that, for example, gradually builds up services or extends them to different regions within the country over a set period of time. A preparation phase for carrying out training, purchasing needed equipment and supplies, and developing appropriate educational materials for clients, care providers, and the community will be needed. Additional research, including operations research to evaluate new strategies (such as the See and Treat approach or use of a low-power magnification device), also may be part of the plan.

Pilot Implementation: Implementing the plan will be most successful if responsibility for it is assigned to an individual or group with a high level of authority and credibility, as well as personal interest in and commitment to the goal of cervical cancer control. Detailed annual workplans, with periodic progress reviews by an advisory group, will help maintain momentum and provide an opportunity to address unexpected obstacles or modify the plan in the face of new information or circumstances. Information exchange between the implementation team and key groups such as clinicians, women's representatives, community leaders, and decision makers will help the team be responsive to concerns as they arise, maintain strong support for its efforts, and determine appropriate revisions to the workplan.

Evaluation: Before proceeding with the next phase of implementation (expansion to other areas or populations), an evaluation of the pilot effort is essential. Issues such as cost-effectiveness, staff training and technical skills, quality of care and health impact, acceptability of new interventions to clients, maintenance of equipment and supplies, and referral and follow-up systems must be carefully analyzed.

Innovative strategies

In addition to the guidelines and recommendations suggested earlier, several specific strategies have been put forward for which additional data may be needed or that may be appropriate only for particular situations. These include using an inexpensive, low-power magnification device instead of a colposcope to facilitate biopsy sampling or LEEP treatment; introducing the one- or two-visit See and Treat approach; using mobile teams relying on aided visual inspection to provide follow-up assessments for women with low-grade lesions, as well as to monitor those who have been treated for high-grade conditions (visual screening also could be done); and using record cards retained by both women and providers that document the date and results of either Pap smears or visual inspection as well as recommended follow-up action. These suggestions are based on survey results and other information that cited the inability to follow-up women, cost of equipment, prohibitive travel

costs for women, and lack of trained personnel, among others, as major barriers to CIN treatment provision. In addition, strategies such as the use of mobile clinics could enable monitoring rather than treatment of low-grade conditions (which seems to be widely practiced and may be unnecessary).

CONCLUSIONS

The information gathered for this situation analysis clearly indicates that simple screening methods must be coupled with low-cost, easy-to-use, and effective diagnostic and treatment modalities to reduce cervical cancer morbidity and mortality and to reach more women at risk. Survey results suggest that many countries do not have the resources to establish effective cervical cancer control programs. Existing outpatient modalities such as cryotherapy and LEEP are not widely available, and clinicians still must rely primarily on cone biopsies and hysterectomies to treat CIN. Yet, women who are unscreened in these countries risk eventually developing cervical cancer, and treatment for invasive conditions is far more expensive than treatment of preinvasive disease. Cost analyses have demonstrated that, depending on the prevalence of CIN, the cost per cervical cancer case averted through appropriate management of preinvasive conditions is quite reasonable.

The survey also indicates that existing practices involving treatment of all CIN must be reevaluated to ensure that the most rational, appropriate, and cost-effective CIN treatment protocols are being used. In some settings, treating all grades, may, in fact, be the most rational approach, but in many other settings, similar health benefits can be achieved at much lower cost by treating only high-grade conditions with low-cost technologies.

Certainly, in some countries, the resources simply do not exist to initiate a comprehensive cervical cancer screening and treatment program. Alternative strategies that match local resources and epidemiology, however, may enhance the feasibility and cost-effectiveness of expanding detection and treatment of preinvasive conditions. For example, should simple screening approaches such as visual inspection prove accurate and feasible, early detection of preinvasive lesions without cytology may become possible. Access to simple treatment also may increase if low-power magnification could be used instead of colposcopy to facilitate treatment. Furthermore, the strategy of screening only at-risk women (35-50 years old) and treating only high-grade lesions may reduce the burden on health care facilities, while still achieving public health benefit. Finally, integrating treatment services into existing programs such as sterilization clinics may reduce costs. In any case, cervical cancer prevention and control strategies must be tailored to local situations and needs, particularly where resources are limited, to ensure that they are cost-effective and successful.

Governmental agencies, donor organizations, as well as program managers should work to initiate and support efforts to determine the prevalence of cervical cancer in their settings. A local situation review, as previously described, is a key first step to developing a plan of action. With the advent of low-cost, effective CIN treatment technologies, as well as ongoing research regarding alternative screening approaches, cervical cancer prevention and control eventually may be within the grasp of even the most financially strapped countries.

Glossary

Adenocarcinoma: A malignant neoplasm primarily consisting of glandular epithelium. Adenocarcinoma accounts for approximately 5 percent of cervical cancer cases worldwide.

Aided visual inspection (AVI): Visualization of the cervix using a portable, low-power magnification device (as opposed to a colposcope) and acetic acid to facilitate cervical cancer screening (and/or possibly to guide biopsy and outpatient treatment of preinvasive lesions).

Acetic acid: A vinegar solution that is applied to cervical tissue to facilitate identification of abnormal tissue. The acetic acid interacts with diseased cells, causing epithelial lesions to turn white.

Bethesda Classification System: Proposed in 1988 by the U.S. National Cancer Institute, this system relies on only two grades for reporting cervical cancer precursor conditions: low-grade squamous intraepithelial lesions (SIL), which include cellular atypia and CIN I, and high-grade squamous intraepithelial lesions, which include CIN II, III and CIS. The system creates uniform terminology, includes a statement regarding the adequacy of the cytological specimen, and uses subcategories to further describe cytologic changes.

Cervical stenosis: A narrowing of the cervical canal.

Cervical Intraepithelial Neoplasia (CIN) Classification System: Introduced in the 1960s, the CIN classification system for reporting cytological (Pap smear) results grades the severity of cervical lesions so that mild cervical dysplasia was categorized as CIN I; moderate cervical dysplasia as CIN II; and severe cervical dysplasia as CIN III.

Carcinoma *in situ* (CIS): Cellular changes in the stratified squamous epithelium associated with invasive cancer but not extending to adjacent structures. CIS is generally a recognizable precursor of invasive squamous cell cancer.

Coagulation: The process of clotting blood and contracting the ends of blood vessels to cause bleeding to stop. Electrosurgically, the type of current that promotes coagulation.

Cold coagulation: The use of a thermal probe heated to 100° C to destroy abnormal cervical tissue.

Colposcopy: Examination of the vagina and cervix using an endoscopic instrument (colposcope) that provides magnification to allow direct observation and study of vaginal and cervical cells *in vivo*.

Cold knife cone biopsy (also known as conization): A surgical procedure to obtain a cone of endocervical tissue with a cold knife blade so as to preserve the tissue's histological characteristics for histopathologic analysis.

Cryotherapy: The use of extremely low temperatures (-60° C to -90° C) to freeze and destroy abnormal tissue.

Cytology: The study of the anatomy, physiology, pathology, and chemistry of the cell, such as those associated with the endo- and ecto-cervix.

Diathermy: The generation of heat resulting from the passage of a high-frequency electric current.

Dysplasia of the uterine cervix: Epithelial abnormality involving part of the cervical squamous epithelium.

Electrode: The terminal of an electric circuit through which electrons pass.

Electrocautery (electrocoagulation): The process of using an electrically heated metal probe reaching very high temperatures to destroy abnormal tissue.

Ectocervix: The external portion of the uterine cervix and os.

Endocervix: The mucous membrane of the cervical canal.

Gynoscope: One version of an experimental, low-power (2.5x) magnification device that may be useful in visual inspection of the cervix (in conjunction with acetic acid) to facilitate cervical cancer screening and, perhaps, to guide biopsy and treatment of preinvasive disease. Further evaluation of the gynoscope or a similar device is necessary to validate these potential applications.

Loop Electrosurgical Excision Procedure (LEEP): Also known as large loop excision of the transformation zone (LLETZ), LEEP is a method of outpatient excisional biopsy and treatment that is used to remove the entire transformation zone using a thin wire electrode charged with a low-voltage, high-frequency alternating current (600kHz), producing a tissue specimen for histologic analysis.

Microinvasion: Invasion of tissue immediately adjacent to a carcinoma *in situ*; the earliest stage of malignant neoplastic invasion.

Punch biopsy: A method by which a small sample of tissue is extracted for histological analysis.

Return electrode (or patient return electrode): The electrode that directs electrical current flow from the patient back to the generator during electrosurgery.

Squamocolumnar junction: The point at which columnar cells meet ectocervical squamous cells on the cervix. This junction is located in the center of the transformation zone and is most vulnerable to abnormal changes in cervical cells.

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Transformation zone: Located at the entrance to the endocervical canal, the transformation zone is surfaced with glandular (columnar) epithelium until the onset of puberty, when the glandular epithelium is gradually replaced by squamous epithelium, similar to the lining of the vagina. Cervical cancer generally originates in the transformation zone.

Unaided visual inspection (UVI): Visualization of the cervix without magnification (but with acetic acid) to screen for cervical cancer.

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CERVICAL CANCER SCREENING: KEY ISSUES

Screening and treatment clearly are interdependent and cannot be addressed in isolation of one another. Below is a brief review of the key issues related to screening:

Screening Strategies

Screen only older women: To be most efficient and effective, cervical cancer screening in low-resource settings should focus on women age 35 and older. Data suggest that the incidence of cervical cancer peaks in women age 40 to 50; therefore, initiating screening among younger women will result in only a slight change in disease incidence but will cause a substantial increase in costs.

Screen infrequently: Screening should be performed relatively infrequently such as once every five to ten years. Indeed, screening women even once in their lifetime prevents many more cases of cervical cancer than screening a small proportion of women every few years.

Use simple screening technologies: Investigations are underway on several innovative approaches to screen for cervical cancer that may be particularly appropriate for low-resource settings. The standard screening approach as well as several innovative approaches are described below.

Screening Technologies

Cytology: The standard approach to cervical cancer screening relies on cytology (the Papanicolaou or "Pap" smear). Cervical cells are scraped from the cervix, fixed on a slide, and analyzed using a microscope to determine the presence or absence of cancerous or precancerous conditions. In many settings, however, cytology-based screening is impossible to implement given clinical, laboratory, financial, and other logistics requirements.

Visual screening: One promising alternative approach to screening is visual inspection of the cervix during a speculum exam. Several variations of visual inspection currently are being evaluated:

- Downstaging: Visual inspection of an untreated cervix to detect signs of early cancer.
- Unaided visual inspection (UVI): Visual inspection of a cervix treated with acetic acid (a vinegar solution which turns lesions white) to detect high-grade dysplasia.
- Aided visual inspection (AVI): Visual inspection of an acetic-acid treated cervix using a small, lightweight, low-power magnifying device to detect high-grade dysplasia.

Cervicography: Currently used in several countries, cervicography relies on a camera to photograph the cervix. These photographs are later projected as slides and examined for abnormalities.

Automated Pap screening: This approach relies on machines, currently being developed and tested, that will evaluate cervical cytology slides. Standard cytology methods then would be used only to confirm positive slides.

HPV screening: Suggested approaches to HPV screening include concurrent HPV and Pap screening to identify women who have both an abnormal Pap smear and are infected with high-risk types of HPV, and HPV screening first to determine which women should receive Pap smears or further evaluation. Currently, however, HPV testing is very expensive and generally is used for research only.

HPV Vaccine: Research currently is underway to develop a vaccine that would prevent infection with HPV (therefore preventing most cervical cancer). Such a vaccine is unlikely to be available for many years, however.

(For more detailed descriptions of these approaches, see *Cervical Cancer in Developing Countries: A Situation Analysis* by J. Sherris et al, World Bank, 1993, which is available from PATH).

REGIONAL RETURN RATES AND LIST OF COUNTRIES REPRESENTED IN THE SURVEY

Return Rate by Region

Region*	Return rate
Africa	43% (41/96)
Asia	60% (35/58)
Latin America	22% (8/36)
The Caribbean	46% (16/35)
Middle East	72% (8/11)
Former Soviet Union	100% (2/2).
TOTAL	46% (110/238)

Countries Represented in the Survey

Africa	Asia	Latin America	Caribbean
Burkina Faso	India	Argentina	Anguilla
Cameroon	Indonesia	Brazil	Antigua
Ethiopia	Philippines	Chile	Barbados
Ghana	Thailand	Costa Rica	Dominican Republic
Kenya	Vietnam	Nicaragua	Jamaica
Malawi			Monserrat
Nigeria	Middle East	Former Soviet Union	Trinidad & Tobago
Sierra Leone	Turkey	Russia	St. Vincent & Grenadines
South Africa		Armenia	
Uganda			
Zambia			
Zimbabwe			

*There was particularly strong representation from Kenya (about 11 percent of the total) as well as from Sierra Leone, Thailand, and the Philippines (9 to 10 percent each of the total). This may be due to the presence of PATH field offices or associates in these countries.

CALCULATING TREATMENT COSTS

Introduction

The following examples are intended to demonstrate a possible approach for calculating costs associated with CIN treatment. Hypothetical examples are included for cryotherapy and LEEP, for which values have been estimated. In addition, country examples (Thailand and Zimbabwe) are included for each of these methods. Since cost information for these countries was incomplete, certain values such as salaries and consumable supplies had to be estimated. In addition, because these examples do not include screening-related costs, which would be required to calculate true costs of cervical cancer prevention and control activities, readers should focus on the *process* of calculating CIN treatment costs rather than on the outcome.

Key Inputs

To calculate treatment-related costs, information on local cervical dysplasia and cancer epidemiology as well as on capital and recurrent treatment costs is needed.

Epidemiology and service provision: In the following examples, several assumptions are made that affect costs per dysplasia case treated or cancer case averted. For instance, calculations are based on treating only those women who were screened and correctly identified as requiring treatment both initially and during post-treatment follow-up. At-risk women who remained unscreened or those who were incorrectly classified are not included. This was done because additional treatment costs resulting from screening inaccuracy (which greatly affect costs per case treated) are really screening rather than treatment costs and are not the focus here. Therefore, in order to limit the focus to treatment costs for this demonstration, it was assumed that 100 percent of at-risk women would be screened and that Pap smears were 100 percent sensitive in detecting dysplasia, both on initial screening and as part of post-treatment evaluation (see box, page 38). The rate of cryotherapy-associated treatment complications was assumed to be 1 percent, while the rate of LEEP-associated complications was assumed to be 1.5 percent.

Several key factors affect treatment cost:

- *Treatment cure rate:* For cryotherapy, the cure rate for high-grade CIN was assumed to be 85 percent, while for LEEP, it was assumed to be 95 percent.
- *Prevalence of high-grade CIN:* In the two country examples, the difference in total program costs is largely attributable to the difference in prevalence, since other costs are quite similar.
- *Progression rate of high-grade CIN to cancer:* In these examples, the progression rate was assumed to be 50 percent, although, in reality, this rate would be greatly influenced by the proportion of the CIN II (versus CIN III/CIS) in the population. In largely unscreened populations, it can be assumed that the progression rate would be higher than in screened populations since CIN III prevalence is likely to be high. As screening coverage expands, the progression rate would begin to decline, while the costs per cancer case averted would begin to rise.

Capital and recurrent costs: Capital costs are spread over the life of the investment, which has been set arbitrarily at five years for these examples. Recurrent costs include consumable supplies, as well as costs associated with follow-up therapy of treatment failures and/or complications.

Hypothetical Example

Cryotherapy Costs

Assumptions

I. Epidemiology and Service Provision

A.	Total population at risk	250,000
B.	Prevalence of CIN II+ in population	1.5%
C.	Proportion of untreated CIN II+ progressing to Ca	50%
D.	Proportion of at-risk population screened/year	100%*
E.	Proportion of CIN II+ detected by screening test	100%*
F.	Proportion of normal cervices classified correctly	100%*
G.	Primary treatment success rate	85%
H.	Proportion of cases of treatment failure detected during follow-up	100%*
I.	Follow-up treatment success rate	95%

II. Expected cases and outcomes

J.	Expected CIN cases–primary treatment	(A x D x B x E) 250,000 x 1.00 x .015 x 1.00 = 3,750
K.	Expected CIN cases–follow-up treatment	(1-G) x J x H (1-.85) x 3,750 x 1.00 = 563
L.	Cancer cases averted	C x [(J x G) + (K x I)] .50 x [(3,750 x .85) + (563 x .95)] = 1,862
M.	Cancer cases missed due to ineffective treatment	J x C x [(1-G) x (1-H) + (1-G) x H x (1-I)] 3,750 x .50 x [(1-.85) x (1-1.00) + (1-.85) x 1.00 x (1-.95)] = 14
N.	Cases of treatment-associated complications	(J x 1%) (3,750 x .01) = 38

III. Cost Calculations

Capital Costs	Costs per 1,000 women treated	Total (for 3,750 cases)	Amortized (5 years)
Equipment	$2,000 (1 cryotherapy unit)	$8,000	$1,600
Training	$750 (2 people)	$3,000	$600
Refrigerant	$500 (2 tanks)	$2,000	$400
TOTAL		$13,000	$2,600

*See box, page 38

Recurrent Costs	Costs per 1,000 women treated	Total (for 3,750 cases)
Salaries *(1 FTE**/1,000 cases)*	$6,000	$24,000
Supplies *($5/case treated)*	$5,000	$18,750
Follow-up of ineffective treatment *($100/cone biopsy x K)*	--	$56,300
Treatment complications *($50/complication x N)*	--	$1,900
Treatment of cancer *($1,500/hysterectomy x M)*	--	$21,000
TOTAL		$121,950

TOTAL ANNUALIZED TREATMENT COSTS	**$121,950 + $2,600 = $124,550**
TOTAL COSTS PER CIN CASE TREATED* **	**Total Costs ÷ J** **$124,550 ÷ 3,750 = $33**
TOTAL COSTS PER CANCER CASE AVERTED* **	**Total Costs ÷ L** **$124,550 ÷ 1,862 = $67**

**FTE = Full-time equivalent

***Not including screening costs.

Hypothetical Example

LEEP Costs

Assumptions

I. Epidemiology and Service Provision

A.	Total population at risk	250,000
B.	Prevalence of CIN II+ in population	1.5%
C.	Proportion of untreated CIN II+ progressing to Ca	50%
D.	Proportion of at-risk population screened/year	100%*
E.	Proportion of CIN II+ detected by screening test	100%*
F.	Proportion of normal cervices classified correctly	100%*
G.	Primary treatment success rate	95%
H.	Proportion of cases of treatment failure detected during follow-up	100%*
I.	Follow-up treatment success rate	95%

II. Expected cases and outcomes

J.	Expected CIN cases–primary treatment	(A x D x B x E) 250,000 x 1.00 x .015 x 1.00 = 3,750
K.	Expected CIN cases–follow-up treatment	(1-G) x J x H (1-.95) x 3,750 x 1.00 = 188
L.	Cancer cases averted	C x [(J x G] + (K x I)] .50 x [(3,750 x .95) + (188 x .95)] = 1,871
M.	Cancer cases missed due to ineffective treatment	J x C [(1-G) x (1-H) + (1-G) x H x (1-I)] 3,750 x .50 x [(1-.95) x (1-1.00) + (1-.95) x 1.00 x (1-.95) = 5
N.	Cases of treatment-associated complications	(J x 1.5%) (3,750 x .015) = 56

III. Cost Calculations

Capital Costs	Costs per 1,000 women treated		Total (for 3,750 cases)	Amortized (5 years)
Equipment	$6,000	(LEEP unit)	$24,000	$4,800
Training	$950	(2 people)	$3,800	$760
Other	$20,000	(colposcope)	$80,000	$16,000
TOTAL	$26,950		$107,800	$21,560

*See box, page 38

Recurrent Costs	Costs per 1000 women treated	Total (for 3,750 cases)
Salaries *(1 FTE**/1,000 cases)*	$8,000	$32,000
Supplies *($25/case treated)*	$25,000	$93,750
Follow-up of ineffective treatment *($100/cone biopsy x K)*	--	$18,800
Treatment complications *($50/complication x N)*	--	$2,800
Treatment of cancer *($1,500/hysterectomy x M)*	--	$7,500
TOTAL		$154,850

TOTAL ANNUALIZED TREATMENT COSTS	**$154,850 + $21,560 = $176,410**
TOTAL COSTS PER CIN CASE TREATED* **	**Total Costs + J** **$176,410 + 3,750 = $47**
TOTAL COSTS PER CANCER CASE AVERTED* **	**Total Costs + L** **$176,410 + 1,871 = $94**

**FTE = Full-time equivalent
***Not including screening costs.

Country Example

Urban Facility in Thailand*

Assumptions

I. Epidemiology and Service Provision		
A. Total population (# of clients) at risk	24,000	
B. Prevalence of CIN II+ in population	0.3%	
C. Proportion of untreated CIN II+ progressing to Ca	50%	
D. Proportion of at-risk population screened/year	100%**	
E. Proportion of CIN II+ detected by screening test	100%**	
F. Proportion of normal cervices classified correctly	100%**	
	Cryotherapy	LEEP
G. Primary treatment success rate	85%	95%
H. Proportion of cases of treatment failure detected during follow-up	100%**	100%**
I. Follow-up treatment success rate	95%	95%
II. Expected Cases and Outcomes		
J. Expected CIN cases–primary treatment	72	72
K. Expected CIN cases–follow-up treatment	11	4
L. Cancer cases averted	36	36
M. Cancer cases missed due to ineffective treatment	0	0
N. Cases of treatment-associated complications	1	1
III. Cost Calculations (annualized costs)		
Capital Costs		
Equipment	$400	$1200
Training (1 person)	$300	$380
Other (refrigerant tanks, colposcope)	$100	$4,000
Recurrent Costs		
Salaries	$8,000	$8,000
Supplies	$2,880	$3,384
Follow-up of ineffective treatment	$660	$240
Treatment complications	$50	$50
Treatment of cancer	0	0
Total Annualized Treatment Costs	**$12,390**	**$17,254**
Total Costs Per CIN Case Treated* **	**$172**	**$240**
Total Costs Per Cancer Case Averted* **	**$344**	**$479**

*The values used in this example are either derived from cost information gathered on the surveys, or they are estimated for the purposes of demonstration. The final calculations, therefore, should be considered only as illustrative.

**See box, page 38.

***Not including screening costs.

Country Example

Urban Facility in Zimbabwe*

Assumptions

I. Epidemiology and Service Provision		
A. Total population (# of clients) at risk	3,000	
B. Prevalence of CIN II+ in population	6%	
C. Proportion of untreated CIN II+ progressing to Ca	50%	
D. Proportion of at-risk population screened/year	100%**	
E. Proportion of CIN II+ detected by screening test	100%**	
F. Proportion of normal cervices classified correctly	100%**	
	Cryotherapy	LEEP
G. Primary treatment success rate	85%	95%
H. Proportion of cases of treatment failure detected during follow-up	100%**	100%**
I. Follow-up treatment success rate	95%	95%
II. Expected Cases and Outcomes		
J. Expected CIN cases–primary treatment	180	180
K. Expected CIN cases–follow-up treatment	27	9
L. Cancer cases averted	90	90
M. Cancer cases missed due to ineffective treatment	1	0
N. Cases of treatment-associated complications	2	3
III. Cost Calculations (annualized costs)		
Capital Costs		
Equipment	$400	$1,200
Training (1 person)	$300	$380
Other (colposcope, refrigerant tank)	$100	$4,000
Recurrent Costs		
Salaries	$6,000	$6,000
Supplies	$7,280	$9,900
Follow-up of ineffective treatment	$1,620	$540
Treatment complications	$100	$150
Treatment of cancer	$200	0
Total Annualized Treatment Costs	**$15,800**	**$22,170**
Total Costs CIN Per Case Treated* **	**$88**	**$123**
Total Costs Per Cancer Case Averted* **	**$176**	**$246**

*The values used in this example are either derived from cost information gathered on the surveys, or they are estimated for the purposes of demonstration. The final calculations, therefore, should be considered only as illustraative.

**See box, page 38.

***Not including screening costs.

TECHNICAL INFORMATION

More than 40% of the women reporting to the Kidwai Memorial Institute of Oncology suffer from a gynaecological cancer.

Cancer of the cervix (one of the gynaecological cancers) is the most common cancer affecting the Indian women. A review of the case records of 6941 women with cancer cervix revealed that majority are from rural areas, they (83.6%) are aged between 35 and 64 years and 97.1% report for treatment with disease that has spread beyond the cervix. Lack of awareness about the symptoms of the disease (57.6%) and lack of adequate advice by medical personnel from whom they had sought assistance (33.7%) was observed to be the reason for women reporting for treatment with advanced disease. We observed that 55.4% did not complete treatment. Noncompliance before the onset of and during therapy was observed in 22.39% and 19.56% respectively. Among those who completed treatment (44.6%), the disease status was unknown in 54%. The internationally accepted 5 year survival rates for stages II, III and IV are 58%, 37% and 8% respectively. Thus the results of therapy of advanced cancer cervix are far from satisfactory. Patients with advanced and recurrent disease suffer from agonising pain, foul smelling vaginal discharge and may develop incontinence of urine and or faeces. Many are abandoned by their families because of the intolerable odour. The final outcome is an undignified death.

These observations at the Department of Gynaecologic Oncology convinced us that the answer is prevention and early detection of cancer cervix, especially as the results of the therapy observed internationally of preinvasive and early stage disease yield 5 year survival rates of 100% and > 82% respectively.

Organised cytology based screening programmes have led to the control of the disease in developed countries. However financial constraints prevent the use of such screening programmes in this country. The World Health Organisation in 1986 suggested the concept of downstaging cancer cervix using visual inspection of the cervix as the test for early detection.

Since 1991 the Department has been involved in two operational field research projects financed by the Indian Council of Medical Research and the World Health Organisation through the Ministry of Health, Government of India, which attempted to assess whether the staff of the health infrastructure in the areas covered by four Primary Health Centres, could be trained to impart health education, perform visual inspection of the cervix and

triage it's appearance into normal, abnormal, and suspicious of malignancy and refer appropriately. The target population comprised of women aged between 35 and 64 years. The results indicated that while the staff could be trained to perform the test for early detection of cancer cervix in rural India, the task of imparting health education and empowering women with knowledge about cancer cervix could not and should not be their responsibility alone. Hence we looked for organisations or individuals who could be involved in imparting health awareness. The existing Mahila Mandals with whom we had already attempted to work was obviously not the answer.

It is well accepted that NGDO's working in rural and semiurban areas have an integrated approach, develop a close contact with the population and along with developmental work many have been working in the area of health. They have experience in empowering the population amidst whom they work. We collaborated with two such organisations. The results indicated that in these areas the staff of the health infrastructure were able to cover a larger number of women when compared to the number that were covered in the initial study.

Thus we were convinced that the strategy could be adopted in the areas where NGDO's work. The attention was next focussed on areas where there were no NGDO's and the aim was to try and develop a strategy that would be successful in such areas.

About 30% of the members of the panchayat system that now exists in the country are women. The women in these local bodies of self government if empowered with knowledge about early detection of cancer cervix could be made responsible to ensure that the women aged between 35 and 64 years who lived in their areas, underwent the test for early detection. Such women panchayat members could also help to ensure accountability of the health infrastructure. Thus they could play the role that the NGDO's would do in their areas. This possibility is at present being assessed in our project areas.

Thus a phase has now been reached when an interaction with experts is imperative in order to draw meaningful conclusions from the experiences of this study. Such an interaction would assist in evolving the direction in which objectives of this study should be modified in order to contribute towards the development of a pragmatic policy for the early detection of this preventable gynaecological cancer.

SPECIFIC OBJECTIVES OF THE WORKSHOP

To create a forum where cancer specialists interact with the Panchayat System, NGDO's (with an interest in health), members of the Health Infrastructure, officials of the Departments of Health and Family Welfare, Women Child and Development and Rural Health & Panchayati Raj and policy planners in order to share experiences and examine strategies with a view to develop a plan of action for the control of cancer cervix and :-

a. To propose that the Departments of Health and Family welfare and the Health infrastructure, Women and Child Development, Rural Development and Panchayati Raj of the Government of Karnataka, NGDO's especially those with an interest in health and the Department of Gynaecologic Oncology, Kidwai Memorial Institute of Oncology work in tandem in order to undertake early detection of cancer cervix.

b. To create an awareness that health workers can be technically equipped to carry out prevention and early detection of cancer cervix.

c. To prepare for launching an all out campaign for early detection of cancer cervix.

PROPOSALS FOR FOLLOW-UP

The expertise of the workshop will be used to :

A. Delineate alternate strategies and policy choices in Karnataka, India.

B. Launch a campaign for the control of cancer cervix on a wider scale within the state of Karnataka, in areas to be identified at the workshop in consultation with the Departments of Health and Family Welfare, Rural Development and Panchayati Raj and Women Child and Development Government of Karnataka and NGDO's.

C. The proceedings of the workshop will be published as a section in the report of the operational field research project that the department has been undertaking which will be entitled " The Community Approach for the Control of Cervical Cancer in India ".

LIST OF PARTICIPANTS UNCONFIRMED

Dr. Amrit Syngle
Survival for Women & Children Foundation
Chandigarh.

Dr. R.S. Arole,
Comprehensive Rural Health Project
Jamkhed

Amal Charles
Mahbubnagar

Alice Joseph
Sumana
Mysore

Dr. Amrit Syngle
Survival for Women and Children Foundation
Chandigarh

Mrs. Annie Chacko
Regional Makers Training School
Dindigal
Tamilnadu

Prof. Amitaverm
WHODSIC
Women House Holds Development
Studies Information Centre
Baroda.

St. Agnes
The Win Centre
Kerala.

Bindu M
'Sthrevedi'
Thiruvambadi,
Thirissur.

Chandrashekar
FEDVORK
Federation of District Voluntary
Organisation Kolar,
Kolar

Dr. R.N. Chakrebarty,
Head Department of Preventive Oncology,
Calcutta.

Dr. Daisy Dharmaraj,
Prepare
India Rural Reconstruction &
Disaster Response Service
Bangalore(NIMHANS)

Dharesh B. Shrimali
Naturopath & Mag Theraphy
Community Health Worker

Sr. Elsey Jeeb
Nava Jyothi
Martamdam

Dr.Gurushant Limbtat
UNESCO Club
Gulbarga.

C.B. George,
India Development Service
Dharwad.

Dr. L.B. Gurushant
A I M S
Gulbarga.

Jyothi Agarwal
Karuna Trust
B.R. Hills
Mysore.

Dr. V. Janardhana Rao
R.D.T. Hospital,
Kalyandurg.

Mr. Jay Maickal
Rural Literacy & Health Programme
Mysore

Kailash Mishra
Awareness
Organisation for Promotion of
Socio-Cultural Awareness &
Preservation of Civil Democratic Morality
ORISSA.

Prof. V.R. Kushtagi
Swami Ramananda Teerth
Research Institute
Gulbarga.

Krishnaswami
170, Pramthi
Banashankari II Stage
Bangalore.

Mr. N. Madhu Sudhana Rao
Social Action for Needy People
Uppal
Andhra Pradesh

Manoj - Bodonaik
FARR, Bolangir Project
Friends Association for Rural Reconstruction
Orissa.

Mr. R.K. Mani,
SAMSKAR
Chelli Nilayam
Varni

Dr. Mira Shiva
V H A K
Bangalore.

P.R. Nawab Mani
The Agency for Rural Developmen
& Consultancy Services
Madras.

E. Narayan Reddy
CASES
Community Action for
Social Education Society
K.G.F.

Nageshwari
Women Resource Centre
Thummapala.

T. Nageshwari
Anakapalle
S.V.D.S.
Andhra Pradesh.

Neena Raina
S W A C H Foundation,
Jaipur.

Dr. Omen Abraham
Hosakote Mission & Medical Centre
Hosakote.

Dr. Patricia Bidinger
Institute for Rural Health Studies
Hyderabad.

Pragathi
Society for Rural Development
Channagiri.

Dr.V.Prakash Kotecha
Jetalpur
Baroda.

Dr. Ravi S. Kittur
Belgaum Integrated Rural
Development Society,
Naganur(Reg)
Belgaum.

Ramachandra Pandith
Harijana Adivasi Shikshana
Prashikshana Kalyana Samstana
Bihar.

Ravindra
People's Development Centre
Bagepalli.

Rani
Jyothis Medical Mission
Kerala.

Mr. Srinivasa
Dhwani
Institute for Rural Development
Mandya.

Sunanda Rosanar,
Shree Sharada Vidyalaya
Bijapur.

Sunita Nigam
Indian Institute of
Health Management Research
Jaipur.

Dr. Sumita G. Limbitat
Sushrut Hospital & Research Centre
Afzalpur
Gulbarga.

Sr. Sally Joseph
Holy Cross Convent
Pomulur
Tamilandu.

Secretary
World Peace Public Health &
Charitable Trust
Afzalpur.

Santhamma G.S.
Santhigram
Pullalvila
Kerala.

M. Siddiqui
C N C I
Calcutta.

Seetha Anagol
(Co-ordinatory Unit Bangalore)
World Conference on Women
Beijing.

Santhosh Vas
JANODAYA
Jayamahal Extension,
Bangalore.

Dr. L.P. Thangavelu
Ashwin Hospital
Coimbatore.

D. Umopani
Bapuji Integrated Rural
Development Society
Huliyur.

Veena Shatrugna
National Institute of Nutrition
Hyderabad.