

Planning Appropriate Cervical Cancer Prevention Programs

2nd Edition

2000

path

Program for Appropriate Technology in Health

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Readers are encouraged to use document sections to educate others about the impact of cervical cancer and potential prevention strategies.



Acknowledgements

The lead authors of *Planning Appropriate Cervical Cancer Prevention Programs, 2nd Edition*, are Cristina Herdman and Jacqueline Sherris, with key contributions from Amie Bishop, Michele Burns, Patricia Coffey, Joyce Erickson, John Sellors, and Vivien Tsu. Support for development of this document was provided by the Bill & Melinda Gates Foundation through the Alliance for Cervical Cancer Prevention.

Planning Appropriate Cervical Cancer Prevention Programs, 2nd Edition, is the revised and updated version of *Planning Appropriate Cervical Cancer Control Programs*, published by PATH in 1997. The original publication was prepared by a team of PATH staff who work on a range of issues related to cervical cancer prevention. The lead author of the original publication was Jacqueline Sherris; key contributions were made by Amie Bishop, Elisa Wells, Vivien Tsu, and Maggie Kilbourne-Brooke.

The authors would like to acknowledge the contributions of individuals who provided information for the project summaries. These individuals are Dr. José Camacho (Cuban National Cancer Control Program, Havana, Cuba); Dr. Carolina Wiesner (National Institute of Cancer, Bogota, Colombia); Dr. Concepción Bratti (Proyecto Epidemiológico Guanacaste, San José, Costa Rica); Dr. Eric Suba (Viet/American Cervical Cancer Prevention Project, San Francisco, California, USA); and Dr. Sharon Fonn (Women's Health Project, Johannesburg, South Africa).

The authors also would like to acknowledge the help of other individuals who reviewed drafts of the document: Dr. Catterina Ferrecchio (Pan American Health Organization, Washington, D.C., USA); Dr. Lynne Gaffikin (JHPIEGO Corporation, Baltimore, Maryland, USA); Dr. Martha Jacobs (AVSC International, New York, New York, USA); Dr. Silvana Luciani (Pan American Health Organization, Washington, D.C., USA); Dr. D. M. Parkin (International Agency for Research on Cancer, Lyon, France); Dr. Raquel Requejo (Pan American Health Organization, Washington, D.C., USA); Dr. Sylvia Robles (Pan American Health Organization, Washington, D.C., USA); and Dr. R. Sankaranarayanan (International Agency for Research on Cancer, Lyon, France). Their comments and advice were key to ensuring the clarity and accuracy of this document. Any inaccuracies that remain are the responsibility of the authors.

PATH welcomes comments on this document, including suggestions for improvements and readers' experience in using the document to educate providers, policy makers, and others. Please send your comments to accp@path.org.

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Summary of Key Recommendations

During the past decade, much has been written about the challenges involved in preventing cervical cancer in low-resource settings and the strategies that are likely to be most effective in these settings. This document summarizes recent research, program experiences, and analyses related to cervical cancer prevention, with a focus on program and policy implications. The document is specifically designed to support program managers and policy makers as they develop new or expanded cervical cancer prevention programs. The publication also can inform health care professionals, administrators, and others about the key concepts related to cervical cancer prevention. Recommendations found throughout this document apply to programs worldwide, with specific considerations outlined for those with limited resources.

To have an impact on cervical cancer incidence and mortality, programs must achieve the minimum program goals listed below:

- ▶ Increase awareness of cervical cancer and preventive health-seeking behavior among women in their thirties and forties, emphasizing the need for cervical cancer screening among women aged 35 to 50. This age range is a reasonable target group for a new cervical cancer prevention program with limited resources.
- ▶ Screen all women aged 35 to 50 at least once before expanding services to other age groups or decreasing the interval between screenings.*
- ▶ Treat women with high-grade dysplasia, refer those with invasive disease where possible, and provide palliative care for women with advanced cancer.
- ▶ Collect service delivery statistics that will facilitate ongoing monitoring and evaluation of program activities and outputs.

As a new or expanded program is designed, it is crucial to ensure strong management of and support for program strategies at all levels of the health care system. To gain this support, it is important to clearly demonstrate the need and demand for a cervical cancer prevention program. Analysis of the estimated costs and impact of suggested program approaches also is important.

Programs should strive to involve potential providers and clients in program design, implementation, and evaluation to ensure that their perspectives are considered and their needs are met. Basing program design and implementation strategies upon substantive research findings

*In countries where resources are limited, the aim should be to screen every woman in the target group once in her lifetime at about the age of 40 years. When resources are available the frequency of screening should be increased to once every 10 years, and then once every 5 years for women aged 35 to 55 years. If resources are high and a large proportion of the target group is being screened, screening should be extended, first to older women (up to age 60) and then to younger women (down to age 25). If additional resources are available and a high proportion of the target group is being screened every 5 years, the frequency of screening should then be increased to once every 3 years for women aged 25 to 60 years.¹



in cervical cancer prevention is critical. Finally, clear program goals and objectives, indicators for measuring progress, and information tracking systems must be developed. These steps allow programs to measure success and identify areas that should be modified.

Activities that are key to achieving minimum program goals in many low-resource settings include:

- ▶ building on strengths in the community's or country's existing health system to increase the likelihood of program sustainability;
- ▶ involving women, their partners, community leaders, and other local stakeholders in program design, implementation, and evaluation;
- ▶ coordinating or integrating cervical cancer prevention services with health programs that offer related services and/or reach older women;
- ▶ identifying and addressing bottlenecks to effective service delivery (for example, inadequate cytology services or inadequate information systems) before initiating a new program;
- ▶ removing regulatory barriers to broadening access to services, such as policies that do not allow nurses to provide screening;
- ▶ ensuring that health care providers at all levels are trained in appropriate cervical cancer prevention measures, including counseling skills;
- ▶ using innovative, culturally appropriate, field-tested strategies to reach underserved women in their thirties and forties;
- ▶ supporting targeted research on new program approaches that may increase access to services and cut program costs.

Through creative service delivery strategies and well-trained, committed staff, cervical cancer prevention programs can address the challenges of providing appropriate screening and treatment, and ultimately have a lasting effect on women's health.

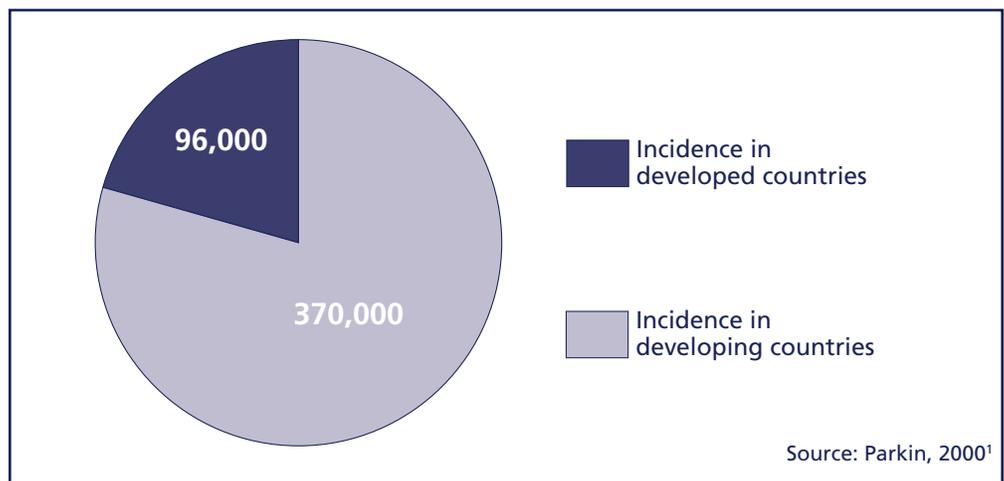
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Cervical Cancer: Magnitude of the Problem

Cervical cancer continues to have a major impact on women worldwide, particularly women in developing countries. The most recent compilation of global data indicates that an estimated 466,000 new cases of cervical cancer occur annually among women worldwide (see Figure 1).¹ Nearly 80 percent of cases are in developing countries, where screening programs are not well established or are minimally effective. In developing countries, cervical cancer incidence is second only to breast cancer, and it is the leading cause of cancer deaths among women. Worldwide, cervical cancer takes the lives of 231,000 women annually, with over 80 percent of these deaths occurring in developing countries.¹

Figure 1. Estimated Number of New Cervical Cancer Cases Worldwide in 2000



Incidence

The highest age-standardized incidence rates of cervical cancer have been reported in Melanesia, Southern Africa, Central America, Eastern Africa, and South America (see Figure 2). In all of these regions, the rates were over 40 per 100,000 women.¹ For example, a study in Zimbabwe found an incidence rate of 54 per 100,000 and rates in Guinea were 46 per 100,000.^{2,3} There is evidence that incidence rates are increasing in some parts of sub-Saharan Africa.⁴

An important reason for the sharply higher cervical cancer incidence in developing countries in comparison to developed countries is the lack of effective screening programs aimed at detecting precancerous conditions and treating them before they progress to invasive cancer. A 1985 estimate indicated that only about five percent of women in developing countries had been screened for cervical neoplasia in the previous five years, compared with some 40 to 50 percent of women in developed countries.⁵ It is unlikely that this disparity has changed significantly. Lack of access to screening compounds the effect of high rates of human papillomavirus (HPV) infection, the primary underlying cause of cervical cancer.



The 2000 estimate of global cervical cancer incidence is over 25 percent higher than the 1990 estimate. Care must be taken when interpreting these estimates, however, because of variability in the availability of data and methodologies used.

Prevalence

A conservative estimate of global prevalence based upon 2000 data suggests that there are nearly 1.4 million cases of clinically recognized cervical cancer (based on the number of patients still alive five years after diagnosis).¹ The vast majority of these cases occurred in developing countries. This estimate reflects the accumulation of cases each year and the fact that few women in developing countries receive treatment. Current knowledge of the natural history of cervical cancer suggests that two to five times as many women may have potential precursor conditions of cervical cancer as have invasive cancer. Therefore, as many as 7,000,000 women worldwide may have high-grade dysplasia that should be identified and treated.

Mortality

It is clear that cervical cancer is taking the heaviest toll on women in developing countries. The age-standardized mortality rate from cervical cancer in these countries is 9.6 per 100,000 women, twice the rate in developed countries.⁶ Nearly 40 percent of cervical cancer deaths in developing countries occur in south central Asia, a heavily populated region that includes India, Pakistan, and Bangladesh.¹

Mortality rates associated with cervical cancer are the most telling indicator of its impact on women, their families, and their communities. Mortality data occasionally are used as substitutes for incidence data in countries with little screening or treatment activity, since cervical cancer is nearly always fatal if not detected and treated. There would be at least a 30 percent reduction in cervical cancer mortality rates in Africa, Asia, and the Pacific Islands if women's access to early detection and appropriate treatment were equivalent to that in developed countries.⁶

Age Distribution

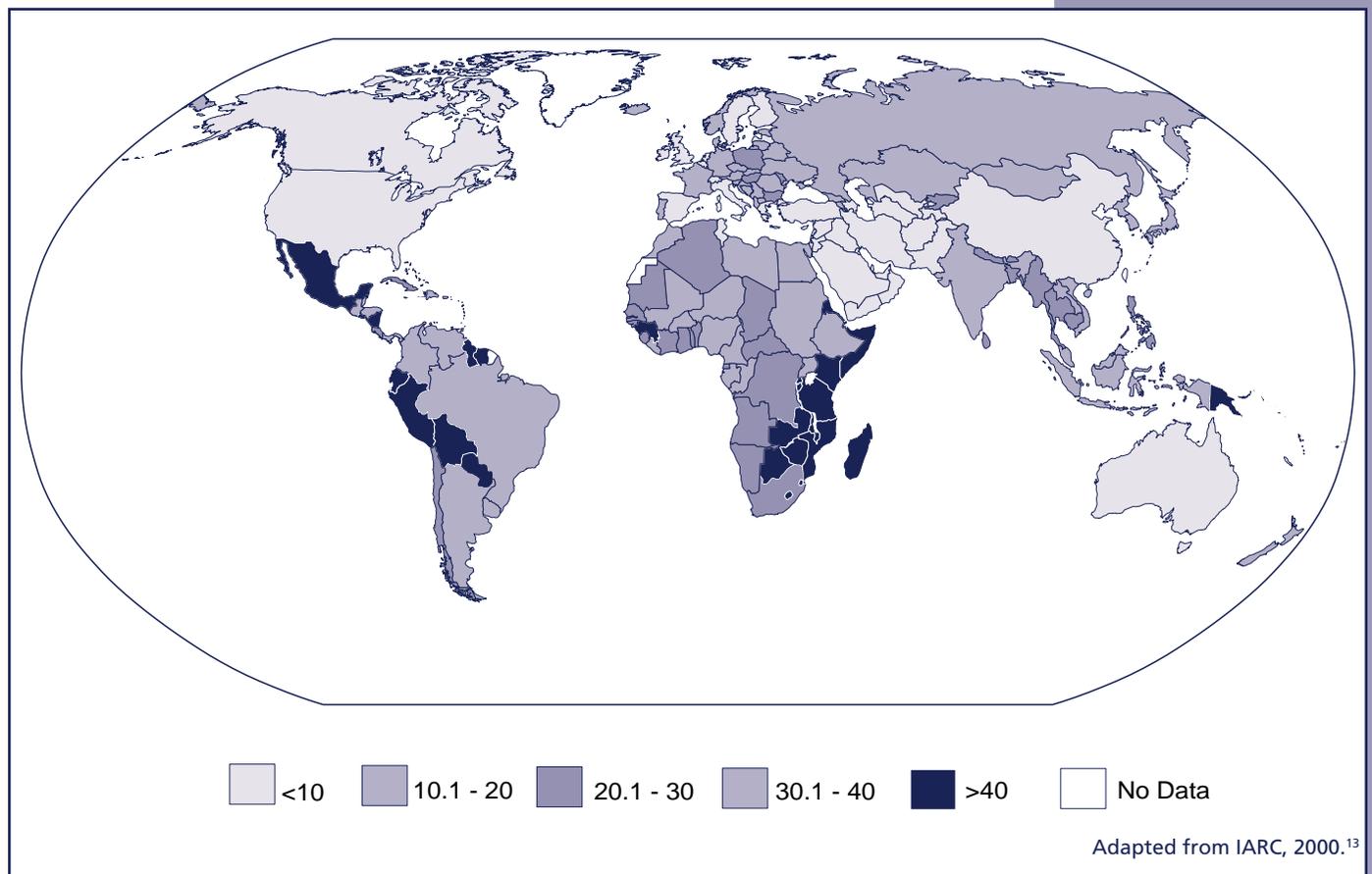
In most countries, the incidence of invasive cervical cancer is very low in women under age 25. Incidence increases at about 35 to 40 years, and reaches a maximum in women in their fifties and sixties.⁷ Data from cancer registries in developing countries indicate that approximately 80 to 90 percent of confirmed cases in these countries occur among women aged 35 or older. Comparative differences in the number of cervical cancer cases in different age groups generally reflect the underlying age structure of the populations, as well as the fact that older women often are not screened.

In a few countries, clinic-based data suggest that age-specific rates have shifted downward from those in developed countries.^{8,9} Due to the bias

inherent to clinic-based studies, however, it is unlikely that similar results would have been observed in a true, population-based sample. Some data suggest that women infected with HIV are at a higher risk of developing precancerous lesions than are women who are not infected.^{10,11} Cervical disease also may progress more rapidly in women infected with HIV, resulting in earlier progression to cancer. For example, one retrospective study in South Africa found that HIV-infected women presented with invasive cervical cancer almost 10 years earlier than HIV-negative women.¹²

Existing estimates of cervical cancer incidence, prevalence, and mortality probably are lower than actual rates, largely because many women with cervical cancer do not receive medical care and thus are not included in cancer registry data. Limitations of diagnostic facilities and their tendency not to reach older women, those with late-stage illness, or those unable to pay for services present further challenges to developing accurate estimates. In addition, the lack of organized health information systems makes recording the number of women with cervical cancer problematic.

Figure 2. Estimated Age-standardized Incidence of New Cervical Cancer Cases, 2000



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Natural History of Cervical Cancer

A clear understanding of the natural history of cervical cancer is key to planning and implementing a rational, cost-effective cervical cancer prevention program. Accepted models of cervical cancer natural history have changed in recent years. Because the natural history of the disease has a direct impact on screening, treatment, and follow-up strategies, program planners should base their cervical cancer prevention strategies on the most current models.

The first cervical cancer prevention programs were based on the premise that the disease developed from precursor lesions (broadly known as dysplasia), progressing steadily from mild to moderate to severe dysplasia to carcinoma *in situ* (CIS), and then to cancer. In fact, it now appears that the direct precursor to cervical cancer is high-grade dysplasia, which can progress to cervical cancer over a period of up to 10 years (See Figure 3). Most lower-grade dysplasia regresses or does not progress, particularly lower-grade incident cases in younger women (aged 34 or less). Prevalent cases are less likely to regress.

Figure 3. Natural History of Cervical Cancer and Program Implications

HPV Infection	Low-grade Cervical Dysplasia	High-grade Cervical Dysplasia	Invasive Cancer
<p>Characteristics: HPV infection is extremely common among women of reproductive age. HPV infection can remain stable, lead to dysplasia, or become undetectable.</p> <p>Management: While genital warts resulting from HPV infection may be treated, there is no treatment that eradicates HPV. Primary prevention through use of condoms offers some protection.</p>	<p>Characteristics: Low-grade dysplasia usually is temporary and disappears over time. Some cases, however, progress to high-grade dysplasia.</p> <p>It is not unusual for HPV to cause low-grade dysplasia within months or years of infection.</p> <p>Management: Low-grade dysplasia generally should be monitored rather than treated since most lesions regress or do not progress.</p>	<p>Characteristics: High-grade dysplasia, the precursor to cervical cancer, is significantly less common than low-grade dysplasia.</p> <p>High-grade dysplasia can progress from low-grade dysplasia or, in some cases, directly from HPV infection.</p> <p>Management: High-grade dysplasia should be treated, as a significant proportion progresses to cancer.</p>	<p>Characteristics: Women with high-grade dysplasia are at risk of developing invasive cancer; this generally occurs slowly, over a period of several years.</p> <p>Management: Treatment of invasive cancer is hospital-based, expensive, and often not effective.</p>

The primary underlying cause of cervical cancer is human papillomavirus (HPV), a common sexually transmitted infection,¹ although it is important to recognize that less than five percent of women infected with HPV ultimately develop cervical cancer if they have no access to treatment. Certain genetic subtypes of HPV are more strongly associated with cervical cancer than others, and persistent HPV infection tends more frequently to lead to high-grade dysplasia and cancer.² Tobacco use may influence whether a woman with dysplasia is likely to develop cervical

The natural history of cervical cancer suggests that screening initially should focus on women at the highest risk of precancerous lesions—women in their thirties and forties—and that screening can take place relatively infrequently and still have a significant impact.

cancer. Immune suppression, particularly related to HIV infection, also is a factor. Some hormonal factors, such as early age at first birth, use of hormonal contraceptives, and high parity have an influence.³ Most other factors identified as associated with cervical cancer—for example, age at first intercourse and number of sexual partners—most likely are indicators of HPV exposure rather than independent risk factors.^{4,5}

Key Considerations for Low-Resource Settings

It is important to take into account the current understanding of the natural history of cervical cancer in deciding:

- ▶ when to initiate screening;
- ▶ how often to screen; and
- ▶ when to recommend treatment and/or follow-up.

The natural history of cervical cancer suggests that screening initially should focus on women at the highest risk of precancerous lesions—women in their thirties and forties. Cervical cancer most often develops in women after age 40 and peaks at around age 50. Dysplasia generally is detectable up to 10 years before cancer develops, with a peak dysplasia rate at about age 35. Unscreened women over 50 remain at relatively high risk of cervical cancer, though women in this age group who have had one or more negative screens in their thirties or forties are at low risk. The benefit of screening post-menopausal women may be reduced by the lower sensitivity of Pap screening due to changes in cervical tissue and difficulty in visualizing the transformation zone, where most cervical cancer originates. Generally, observation of more cases of cervical cancer among younger women reflects a population's age structure or screening patterns rather than a shift in age-specific rates.

Natural history models and clinical data suggest that cervical cancer generally develops slowly from precursor lesions. Therefore, screening can take place relatively infrequently and still have a significant impact on morbidity and mortality. Screening every three years has almost as great an impact as screening every year. Even screening every 10 years can have a significant impact on cervical cancer incidence compared to no screening (see Table 1).⁶ Screening emphasis, then, should be on coverage rather than on frequency.

Current understanding of cervical cancer natural history strongly suggests that, where resources are scarce, treatment of cervical lesions should focus on high-grade dysplasia, with follow-up mechanisms in place for women with low-grade dysplasia. Some studies suggest that about one-third of untreated precancerous lesions will progress to cancer within 10 years; most low-grade dysplasia regresses spontaneously or does not progress.^{7,8}

Table 1. Potential Reduction in Cumulative Cervical Cancer Rates with Different Screening Frequencies

Frequency of Screening*	Percent Reduction in Cumulative Rate†
1 year	93
2 years	93
3 years	91
5 years	84
10 years	64

Adapted from IARC, 1986.⁶

*Screening all women aged 35 to 64 who have had at least one previous negative screen.

†Reductions assume 100 percent screening sensitivity, screening coverage over 80 percent, and effective treatment of every woman in whom high-grade dysplasia is detected.

Policy Implications

As part of efforts to offer services that will have the greatest impact on cervical cancer incidence and mortality, programs should consider the following issues:

- focus initial screening efforts on reaching the maximum number of women at highest risk of cervical cancer precursors (women aged 35 to 50 is a reasonable starting point unless reliable, population-based data support screening younger women). As programs mature and achieve adequate coverage, screening should gradually be expanded to women aged 30 to 60;
- focus treatment on women with test results suggestive of high-grade precancerous lesions, referring those with advanced cancer to hospitals where possible, or for palliative care;
- disseminate summary information and key research papers on cervical cancer natural history to the medical establishment and providers so that they understand the rationale for screening and treatment recommendations;
- ensure that reliable follow-up and tracking procedures are in place and functioning so women with low-grade dysplasia can be screened more frequently than the population as a whole, and that the proportion of women who develop more serious cervical abnormalities can be monitored;
- support targeted research on accurate, inexpensive HPV tests, since identifying a woman's HPV status informs health care providers about the potential course of the infection. Ultimately, HPV testing could be an important addition to targeted screening programs and could help guide treatment decisions.



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Screening: Pap Smears

From a public health standpoint, the purpose of health screening is to provide a low-cost, accessible means of determining who in a population is likely to have a certain disease, and who is not.

From a public health standpoint, the purpose of any type of health screening is to provide a low-cost, accessible means of determining who in a population is likely to have a certain disease, and who is not. Criteria for deciding whether or not screening is appropriate include:

- Is the disease a public health problem?
- Is there an acceptable treatment for the recognized disease?
- Is there a recognizable latent or early symptomatic stage?
- Is the natural history of the disease understood?
- Is there a consensus on whom to treat?
- Are facilities for diagnosis and treatment available and accessible?
- Is there an economic balance between case finding and subsequent medical care?
- Is the program sustainable?

These factors are collectively considered in order to prioritize or determine the need for health screening interventions.

Cervical cancer prevention efforts worldwide have focused on screening women at risk of the disease using Pap smears and treating precancerous lesions. Pap smear screening was developed in the 1930s and named for inventor Dr. George Papanicolaou. Pap smear programs, also known as cytologic screening programs, have achieved impressive results in reducing cervical cancer incidence and mortality in some developed countries. Cervical cancer incidence can be reduced by as much as 90 percent where screening quality and coverage are high.¹ For example, in Finland, a national cervical cancer screening program that was launched in 1963 decreased the cervical cancer rate to 5.5 cases per 100,000 women, a rate that is among the lowest in the world.² In contrast, in developing countries, where some 80 percent of all new cases exist, it has been estimated that only five percent of women have had a Pap smear in the last five years.

A Pap smear is a cytological test designed to detect abnormal cervical cells. The procedure involves scraping cells from the cervix and then fixing them on a glass slide. The slides are then sent to a cytology laboratory and evaluated by a trained cytologist or cytotechnician. Results of this evaluation generally are available within several weeks. In most developed countries, women are advised to have their first Pap smear soon after becoming sexually active and subsequently every one to three years. Many national guidelines are moving to less frequent Pap smears out of recognition that cervical cancer and its precursors usually develop slowly over several years. Most protocols suggest that women with low-grade lesions return for routine follow-up smears. High-grade pre-invasive disease generally is further evaluated via colposcopy (examination of the cervix with a special magnifying scope), biopsy, and subsequent treatment of suspicious areas (through surgical removal or ablation).

Although Pap smear-based screening efforts have been introduced in many developing countries, in general they have achieved limited



Sensitivity and specificity indicate a test's ability to distinguish between those individuals who have a disease and those who do not. *Sensitivity* is the proportion of individuals with disease who are correctly identified by the test as having disease. *Specificity* is the proportion of individuals who are correctly identified by the test as not having disease. *Positive predictive value* refers to the probability of having disease, given a positive test. *Negative predictive value* is the probability of not having disease, given a negative test.

success. For example, in Mexico, where national Pap smear screening programs have been in place since 1974, the mortality rate over 15 years held steady at 16 per 100,000 women.³ This is largely because younger women in urban areas were repeatedly being screened while older “at risk” women were not being reached.

The minimum requirements for establishing an effective Pap smear screening effort include:

- ▶ well-trained Pap smear providers (including non-physicians such as nurses, midwives, and physician’s assistants);
- ▶ access to supplies including swabs, slides, and fixatives;
- ▶ access to equipment such as exam tables, specula, a light source, and lab slips/log books;
- ▶ linkages, including transportation, to a reliable cytology laboratory that employs trained cytologists and cytotechnicians;
- ▶ strategies for ensuring the quality of Pap smear samples and the accuracy of cytological interpretation;
- ▶ proven mechanisms for timely communication of Pap smear results;
- ▶ effective referral systems for diagnosis and treatment.

Health care practitioners in low-resource settings frequently report a lack of access to all the above requirements, thus jeopardizing program success. Furthermore, in many countries, Pap smear-based screening programs tend to be offered only opportunistically and often for a fee to younger, relatively low-risk women. Older women at greatest risk tend to be unaware that cervical cancer is a preventable condition and that having a Pap smear plays an important role in prevention. Additionally, follow-up diagnostic and treatment services are unavailable to most women.

While studies of cytology-based programs have resulted in a broad range of test sensitivity and specificity data,^{4,5} the Pap smear is considered to be specific with regard to detection of high-grade lesions and cancer. This means that a high proportion of individuals who do not have dysplasia is correctly identified by the test as not having dysplasia.

Pap screening has achieved only moderate levels of sensitivity, however, meaning that a low proportion of individuals with dysplasia is correctly identified by the test as having dysplasia. These levels may be even lower among post-menopausal women due to physiological changes of the cervix. A recent meta-analysis found that cervical cytology had an overall sensitivity of 51 percent and a specificity of 98 percent.⁶ As expected, the meta-analysis found that the positive predictive value of the Pap smear was strongly affected by disease prevalence. Higher disease prevalence (meaning a higher positive predictive value) was associated with higher estimates of sensitivity and lower estimates of specificity. A Costa Rica study found that Pap screening had 78 percent sensitivity and 94 percent specificity in identifying atypical squamous cells of unspecified significance.⁷ Several new methods of Pap screening are being investigated to reduce the false-negative rate. In the meantime, the Pap smear is recognized as an important but imperfect screening methodology.

Some New Cytological Screening Technologies

Several new technologies are being explored in an effort to improve the screening accuracy of Pap smears. While these approaches appear promising, they are expensive and heavily reliant upon technology.⁸

Fluid-based, thin-layer processing of cervical samples, such as the ThinPrep™ Pap Test, attempt to reduce sampling errors and improve specimen adequacy by suspending cervical cells in a liquid solution. The solution is filtered to remove mucous, yeast, and bacteria that may interfere with an accurate inspection of the sample. The solution is then applied in a thin layer on a slide, making it easier for a technician to successfully evaluate cervical cells. A Costa Rican study found that use of ThinPrep matched HPV-DNA testing for sensitivity and specificity in detecting high-grade lesions and cancer when performed by an expert cytopathologist. ThinPrep also identified ASCUS more accurately than did conventional Pap smears.⁷

Automated Pap testing, such as PAPNET® and AutoPap®, attempts to reduce laboratory screening errors by utilizing computerized analysis to evaluate Pap smear slides for signs of cervical cancer. These automated technologies, originally developed for secondary screening, highlight potentially abnormal cervical cells for analysis by pathologists. AutoPap was recently approved by the U.S. Food and Drug Administration (FDA) for use in primary screening.

Terminology

Two formal classification systems are used for cytological identification of cervical cancer precursor conditions. In the Cervical Intraepithelial Neoplasia (CIN) system, mild cervical dysplasia is categorized as CIN I, moderate dysplasia as CIN II, and severe dysplasia as CIN III. Carcinoma *in situ* is included in the CIN III category. The Bethesda Classification System includes atypical squamous cells of undetermined significance (ASCUS); low-grade squamous intraepithelial lesions (LSIL), which include CIN I; and high-grade squamous intraepithelial lesions (HSIL), which include CIN II and CIN III.

Policy Implications

In an effort to offer services that will have the greatest impact on cervical cancer morbidity and mortality, individuals planning Pap screening programs should consider the following:

- ensure adequate, ongoing access to all supplies necessary for obtaining good quality Pap smears;
- train non-physicians to successfully perform pelvic examinations and obtain cytological samples to ensure that screening tests are as accessible and accurate as possible;
- build ongoing health care provider training into the program budget to maintain and improve screening skills;
- develop a partnership with a reliable cytological laboratory that provides accurate and prompt test results;
- monitor and support strategies for maximizing the accuracy of all technical phases of Pap screening, specifically as they relate to specimen sampling and laboratory processing;
- support research that explores strategies to maximize the accuracy of cytological or other screening approaches.



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Screening: Visual Approaches

Given the challenges of implementing high-quality cytology-based services, especially in developing countries, there is significant interest in new approaches to screening for precursor lesions. Two approaches of particular interest are visual screening and HPV testing (see *Issue in Brief #4* on Screening: HPV Diagnostics, page 19).

Considerable research has been undertaken recently to explore the accuracy and acceptability of visual inspection as a means of detecting precursor cervical disease and/or cancer. Visual screening is a process of identifying cervical lesions without reliance on cytology (Pap smears). There are several types of visual screening. Early studies utilized visual inspection (VI), which involved simply looking at the cervix with the unaided eye for any signs of early cancer. Also known as “downstaging,” this approach was not accurate in identifying precancerous conditions.¹ Visual inspection with acetic acid (VIA) is considered a more promising screening approach for identifying high-grade precancerous lesions.

Visual Inspection With Acetic Acid (VIA)

This screening approach involves swabbing the cervix with an acetic acid (vinegar) solution prior to visual examination. Differences in precancerous cell structure and absorption rates make abnormal cells temporarily turn white when exposed to this solution. Alternatively, some visual screening approaches have used the application of an iodine-based solution (Lugol’s solution) as a means of staining normal cervical cells brown, leaving the abnormal cells with a yellow or unstained appearance.

Many aspects of VIA make it a promising approach for use in low-resource settings. For example, costs associated with launching and sustaining VIA screening are lower than those associated with other screening methods. VIA also is a relatively simple, low-tech approach that is minimally reliant upon infrastructure for its adequate performance, assuming that treatment services are in place. Non-physicians can perform the procedure, provided that they receive adequate and ongoing training. Furthermore, results of the procedure are available immediately, making it possible, in principle, to provide treatment during the same visit (see *Issue in Brief #5* on Treatment Approaches and Technologies, page 23).

Several studies examining the accuracy of VIA have found that the technique has the potential to be reasonably accurate.² Differences in study protocols, populations studied, and outcomes, make it difficult to summarize results, however. In addition, many studies are subject to verification bias because the reference test was not performed on all study subjects, including women with negative screening test results. This bias tends to inflate the estimated sensitivity of a screening test. Nevertheless, some broad conclusions regarding VIA’s utility in low-resource settings can be made based on results of several studies (see Table 2). In general, the



Table 2. VIA Screening Study Findings

First Author (Year)	Country	Number of Women	Sensitivity*	Specificity*	Level of Provider
University of Zimbabwe/JHPIEGO (1999) ^{3†‡}	Zimbabwe	2,130	77%	64%	Nurse-midwife
Sankaranarayanan (1999) ^{4†}	India	1,351	96%	65%	Nurse
Sankaranarayanan, et al. (1998) ^{5†}	India	2,935	90%	92%	Cyto-technician
Megevand, et al. (1996) ^{6†}	S. Africa	2,426	66%	98%	Nurse
Cecchini (1993) ^{7†}	Italy	2,105	75%	75%	Not specified
Denny, et al. (2000) ^{8‡§}	S. Africa	2,944	67%	88%	Nurse
Belinson, et al. (forthcoming) ^{9¶‡}	China	1,997	71%	74%	Gynecological Oncologist

Adapted from Cullins et al., 1999.¹⁰

*Many of these test performance estimates are subject to verification bias (see text for explanation). The Zimbabwe study is the only published study that actively sought to verify the status of a random sample of test-negative women.

† VIA used to detect HSIL and invasive cancer.

‡ Not subject to verification bias.

§ Positive VIA results confirmed by histology; women were considered free of disease by colposcopy or if results of other tests under evaluation were negative. No random sample of test-negative women was evaluated by colposcopy.

¶ VIA used to detect CIN II and worse.

sensitivity of VIA in detecting high-grade dysplasia is at least equal to that of cytology, while VIA's specificity is somewhat lower.

Lesions viewed by VIA vary in size, thickness, opacity, and border definition (larger, thicker, more opaque lesions with clear border suggest more severe disease). To implement appropriate medical protocols, health care providers must carefully consider the features of a lesion. Clearly, a significant challenge to effective implementation and standardization of VIA is training health providers to recognize the often-subtle characteristics that differentiate degrees of dysplasia. The feasibility of utilizing VIA for wide-scale screening is uncertain, and to a large extent will be determined by the effectiveness of training and monitoring efforts.

The specificity of VIA remains a cause of concern due to the potential for overtreatment of women with false-positive test results. Overtreatment may result in additional health risks to women, as well as overburdening the health care system and increasing costs. VIA also is less effective for screening women in their fifties because of the tendency for the squamocolumnar junction (the point at which columnar cells meet ectocervical squamous cells of the cervix) to recede into the cervical os, making observation of lesions difficult. (Pap smears also are more difficult to obtain in post-menopausal women.) Despite these drawbacks, VIA shows promise as an option for identifying precancerous lesions in many settings, either in conjunction with or as an alternative to other screening approaches.

Visual Inspection With Magnification

VIA with magnification (VIAM) uses the AviScope™—a low-power (4x), hand-held visual inspection device with a built-in light source—to examine the cervix after application of acetic acid. A small Indonesian

evaluation of an earlier version of the device (2.5 magnification) indicated that VIAM may achieve sensitivity and specificity of over 90 percent in identifying pre-invasive cervical lesions.¹¹ Preliminary findings from an ongoing study in Calcutta, India, indicate that VIAM has a sensitivity of 69 percent and specificity of 82 percent.¹² It is not yet known whether use of the AviScope offers a significant advantage over VIA, although the potential for increased specificity is of particular interest. The AviScope, which is not yet available commercially, also may be promising for use in a two-stage screening approach, as a complement to VIA or HPV testing.

Other Approaches to Visual Inspection

One other approach to visual inspection also is noteworthy. Cervicography[®] involves photographing the cervix after application of an acetic acid wash. The developed photographs, called cervigrams, are projected as slides and interpreted by specially trained colposcopists. Like other visual inspection methods, the sensitivity of Cervicography is comparable to cytology, while its specificity appears to be lower. This approach offers the advantage of providing a permanent record of the cervix. Cervigrams can also be helpful as educational tools. Cervicography, however, is relatively expensive and requires a reliable logistics infrastructure.¹³

Other New Screening Technologies

Several new screening technologies using electronic detection are being explored. Methods such as fluorescence spectroscopy, infrared spectroscopy, and the PolarProbe[®] use sensitive electronic detection to highlight and analyze biochemical and physical differences between normal and neoplastic tissues. Electronic detection offers the advantages of providing immediate diagnosis, thus reducing the time from diagnosis to treatment. A recent study found that fluorescence spectroscopy performed better than colposcopy in the diagnosis of lesions. While preliminary results show promise, rigorous studies have been limited, potential clinical roles are unclear, and feasibility in low-resource settings has not been established.

Policy Implications

While more data are necessary to develop conclusions about the strengths and limitations of VIA, it is considered a promising alternative to cytology for identifying precancerous lesions in low-resource settings. Program managers or policy makers considering using VIA screening as part of cervical cancer prevention should:

- broaden guidelines so that non-physician health care providers, such as nurses and midwives, can conduct screening, including VIA, whenever possible;
- ensure that health care providers receive adequate and regular training to maximize their skills in performing VIA and classifying findings;
- monitor the performance of VIA and develop appropriate quality improvement procedures to ensure that it performs adequately and contributes to reduced cervical cancer cases;



- ▶ implement follow-up protocols linking screening, diagnosis, treatment, and monitoring of women with mild dysplasia or treated conditions;
- ▶ explore ways to maximize the accuracy of VIA and identify key factors contributing to its viability as a screening approach;
- ▶ support research to explore use of VIA in low-cost, sequential protocols, such as using VIA as part of a two-stage screening process with VIAM or HPV testing.

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Screening: HPV Diagnostics

Human papillomavirus (HPV) is one of the most common sexually transmitted infections (STIs) and has been established as the primary cause of cervical cancer.¹ Worldwide interest is growing in the potential for HPV testing in cervical cancer prevention programs, both as an adjunct to cytological screening approaches and in primary screening. At the same time, many questions about how HPV tests might be used programmatically remain unanswered, in particular the cofactors that determine which HPV-infected women are most likely to develop cancer. Since the lifetime risk of HPV infection is 70 to 80 percent in many countries, other factors determine the relatively small percentage (less than five percent) of women who ultimately develop cervical cancer.^{2,3}

While there are a variety of laboratory-based approaches for detecting HPV in cervical samples, there currently is only one company—the Digene Corporation—providing a United States Food and Drug-approved commercial kit that detects high-risk HPV types. The corporation's most frequently used test—the Hybrid Capture II kit (HC II)—indicates

whether a person is infected with one or more high-risk HPV viral types (types 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, and 68).

The HC II test already is being incorporated into some screening programs, generally as an adjunct to existing cytological screening approaches.

For detection of high-grade dysplasia, the sensitivity range of the HC II test has been recorded at about 80 to 90 percent; specificity has ranged from 57 to 89 percent.⁵ A

Zimbabwe study found that in screening for high-grade lesions (HSIL), the test sensitivity was 81 percent and specificity was 62 percent. Sensitivity and specificity for low-grade lesions were 64 percent and 65 percent, respectively.⁶

HPV testing generally has a negative predictive value of up to 99 percent, providing useful reassurance to patients. The significance of the test's high negative predictive value on long-term follow-up is not yet known, however. While the test's specificity appears to be higher in older women compared to younger women, in general, the test is not particularly specific. This indicates potential for overtreatment, although some studies currently are exploring the use of a higher cut-off value for positivity to address this problem. The test's objectivity and reproducibility add to its promise as a screening approach.

A study of more than 9,000 sexually active women age 18 and older in Costa Rica found that the HC II test had a sensitivity of 88.4 percent and specificity of 89 percent in detecting high-grade cervical lesions and cancers. When results were calculated by age, specificity was highest (93.2 percent) for women age 41 and older. Overall, HPV testing using the HC II test was more sensitive than conventional Pap testing (88 vs. 78 percent) for detection of high-grade lesions and cancers, but less specific (89 vs. 94 percent).⁴



How Will HPV Testing Ultimately Be Used?

How will HPV testing ultimately be used in cervical cancer prevention programs? The answer to this question is not yet clear, but researchers have suggested various approaches. The most common approaches suggest that HPV testing will be used:

- as a means of triage for women whose Pap smears are “borderline” (ASCUS). Those who test positive for high-risk HPV types would be followed more closely than those who test negative, or referred for colposcopy;
- as a means of surveillance of women treated for HSIL or microinvasive cancer. Those who test positive for high-risk HPV types would be monitored more closely than those who test negative; and
- as a primary screen for HSIL among women aged 30 to 35 or older. Those who test positive for high-risk HPV would undergo diagnosis via colposcopy or some other visualization technique.⁵

In developing countries, available tests likely are too expensive and technologically demanding for widespread use, even though research has

demonstrated their strong potential for identifying high-grade dysplasia in women age 35 and older. Developing-country programs interested in incorporating HPV-DNA testing into cervical cancer prevention activities may have to wait for the development of HPV tests that are less expensive and easier to use in non-laboratory settings (the currently-available test takes at least six hours to process and requires significant laboratory equipment and supplies). Ideally, a field-appropriate HPV diagnostic technology would require minimal supporting equipment and would provide inexpensive, accurate, and rapid detection. At the same time, screening programs based on HPV testing must be carefully designed to maximize their effectiveness in detecting high-grade dysplasia, and ultimately in reducing cervical cancer incidence and mortality.

Self-collected Samples

Several promising studies indicate that women can successfully use vaginal tampons or swabs to obtain self-collected cervical specimens for use in HPV-DNA detection. This has important implications for programs located in countries where cultural and program barriers may limit acceptance of and access to standard gynecologic procedures. A recent South African study evaluating the HC II test found self-collected cervical samples to be less specific, but as sensitive as conventional Pap testing for detecting high-grade cervical disease in women aged 35 or older.⁸ These results indicate that self-collected specimens result in adequate sensitivity and can serve as a satisfactory and culturally acceptable method of collecting samples. Effective self-collection of cervical specimens requires education to ensure that the optimal collection technique is explained effectively by providers and understood by women.

Various approaches to self-collection of samples for HPV testing are being explored in attempts to improve the acceptability of screening. For example, a Canadian study assessed the effectiveness and acceptability of HPV testing comparing physician-obtained samples with self-obtained urine, vulvar, and vaginal samples. The study found that self-collection was acceptable to women and showed sufficient sensitivity to warrant further evaluation.⁷

HPV Testing Information Needs

For most people, finding out that one has a sexually transmitted infection (STI) is cause for concern. Those who are diagnosed with an STI often want to know how they got it, how it can be cured or treated, and how to prevent transmission of the infection to their partner. Women who test positive for HPV, which in some regions will be over 70 percent of all women at some point in their lives, may experience great anxiety about developing cancer despite being at very low risk of developing the disease. Although treatment is available for the genital warts caused by some types of HPV, there currently is no cure or treatment for HPV, prevention is very difficult, and there is no way to clearly predict which women could develop cancer.

Cervical cancer and its association with sexual activity also carries stigma in many parts of the world. Women may be even more reluctant to seek screening if it is associated with taking an STI test. A desire to avoid unnecessary client concern may leave providers grappling with difficult decisions regarding the level of detail they should use in describing the test to women. Some providers may even choose not to explain the linkage between cervical cancer and HPV. These issues must be carefully weighed when considering initiating HPV-DNA testing.

Policy Implications

- ▶ Develop HPV screening strategies that will maximize the identification of women at risk of cervical cancer while minimizing the number of women who are identified as HPV positive but are very unlikely to progress to cervical disease.
- ▶ Ensure that health care systems are capable of responding to the educational, counseling, clinical, and information systems needs that will arise as a result of detecting HPV, precancerous lesions, and cervical cancer.
- ▶ Support research to develop HPV test approaches that are more feasible for use in low-resource settings and that allow providers to interpret a woman's cancer risk based on a variety of risk factors, including HPV status.
- ▶ Evaluate the information needs and counseling messages that are most effective for women at risk of HPV infection and for women diagnosed with HPV infection.



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Treatment Approaches and Technologies

In most developed countries, management of pre-invasive cervical conditions has shifted from use of inpatient surgical methods toward use of less invasive outpatient approaches. This is due to several factors, including the introduction of colposcopy, increased knowledge of the natural history of cervical dysplasia, and availability of low-cost, effective outpatient treatment technologies. Yet in many developing countries where diagnosis and treatment are being performed, clinicians still must rely primarily on inpatient methods such as cone biopsy and hysterectomy to treat dysplasia.¹ Although appropriate for certain circumstances, these approaches can be associated with significant complications and side effects. Use of less invasive treatment methods can minimize women's health risks. In addition, conization and hysterectomy are very costly procedures, requiring significant infrastructural support.²

Outpatient treatment methods traditionally have required colposcopy (a special magnifying scope used to visualize the cervix) for pretreatment assessment to guide diagnostic biopsies, and, in most cases, to facilitate the treatment procedure. Colposcopes, however, generally are very expensive (at least US\$3,000), require substantial training to use, and are not readily available in many developing countries. Identifying and validating alternatives to colposcopy, such as a portable magnifying device, may significantly facilitate management of precancerous conditions in low-resource settings.

What Types of Lesions Should Be Treated?

As knowledge regarding the natural history of cervical cancer, including the role of HPV, has increased, the most common treatment strategy in most developed countries is to treat only high-grade precancerous lesions (HSIL or CIN II-III), and monitor women with low-grade dysplasia (LSIL or CIN I). (See *Issue in Brief #1* on Natural History of Cervical Cancer, page 7). Individual country strategies will vary according to local epidemiological findings, local capability to treat or monitor women, and cost considerations. For example, in cases where clients are unlikely to return for follow-up (due, perhaps, to long distances between their homes and the health facility), it may be appropriate to treat mild dysplasia in older women.

Appropriate Treatment Technologies

Relatively simple, outpatient procedures may be used to destroy or remove precancerous tissue. The specific treatment used depends on the severity, size, and location of the lesion.

Ablative methods, which destroy abnormal tissue, include cryotherapy, cold coagulation, laser vaporization, and electrocauterization. Of these, cryotherapy, which uses a low-temperature probe to freeze abnormal cells and does not require electricity, may be most practical for low-resource settings because of its simplicity and low cost. It is 80 to 90 percent effective in treating high-grade dysplasia.²



Excisional treatment methods have the advantage of providing tissue specimens for histopathologic diagnosis (if available), thereby reducing the possibility of overlooking invasive cancer. A common outpatient excisional method is loop electrosurgical excision procedure (LEEP), sometimes known as large-loop excision of the transformation zone (LLETZ). LEEP utilizes a thin electric wire to remove the entire transformation zone. Other basic equipment required for LEEP includes surgical tables, specula, a light source, sterilization equipment, a smoke evacuator, and antibiotics. LEEP is 90 to 95 percent effective in treating high-grade dysplasia, but is more burdensome than cryotherapy in terms of equipment needs and side effects experienced by the client (see Table 3). At a minimum, LEEP could be made available at central referral sites, while cryotherapy could be made more widely available in peripheral settings.²

Table 3. Two Outpatient Treatment Options for Dysplasia/Carcinoma *in situ**

	Cryotherapy	LEEP
Effectiveness	80 – 90%	90 – 95%
Potential side effects	Watery discharge, infection	Bleeding, infection
Anesthesia required	No	Yes
Tissue sample obtained	No	Yes
Power required	No	Yes
Cost	Relatively low	Relatively high

Source: Bishop, et al., 1995.²

*The specific treatment option used depends on the size, severity, and location of the lesion. Cryotherapy is not suitable for lesions that are not entirely covered by the probe surface and/or are not entirely visible on the ectocervix because of extension into the endocervical canal.

High levels of staff expertise and use of colposcopy to guide the procedure help to ensure the safety and effectiveness of treatment. Since all treatment techniques are associated with dysplasia recurrence rates of up to 10 percent, post-treatment follow-up at approximately three- or six-month intervals for one year and then annually thereafter often is recommended, although some clinicians believe that longer follow-up intervals are acceptable.

The “see-and-treat” approach to managing preinvasive lesions is being investigated as a means of minimizing the numbers of times a woman needs to visit a health center. As initially introduced, the see-and-treat approach meant that, after a Pap referral, the patient was “seen” with a colposcope and then immediately treated with LEEP. The histological sample was then analyzed to ensure an accurate diagnosis and appropriate treatment. The protocol is being used in parts of the United States, Europe, Canada, and elsewhere.

Some programs have begun to adopt a modified see-and-treat approach to managing pre-invasive lesions. The modified see-and-treat approach uses visual inspection with acetic acid (VIA) to highlight lesions that are suspected (but not diagnostically confirmed) to be precancerous, which are

then immediately treated with cryotherapy or LEEP. The modified see-and-treat approach eliminates the usual diagnostic steps of colposcopy and biopsy, thus preventing the delay of waiting for diagnostic biopsy results before treatment and reducing the number of visits a woman must make to receive proper care.^{3,4,5}

Other variations on the modified see-and-treat approach are being explored. For example, a “see, see, and treat” protocol currently being evaluated in Kenya and Peru involves using VIA for primary screening. Those with suspected lesions are referred for VIA with magnification and immediate treatment, if necessary.

The modified see-and-treat approach for identifying and treating women with precancerous lesions shows promise but remains controversial because of the strong likelihood that women will be unnecessarily treated.

Treatment of Invasive Cancer

At a minimum, cervical cancer prevention programs must have some surgical treatment available, such as cone biopsy or hysterectomy, for cases of early cancer. Extensive pelvic surgery and radiation may cure disease that has spread beyond the cervix, although success in the more advanced stages is less likely. In addition, for women with untreatable conditions, palliative care must be available (see *Issue in Brief #7* on Palliative Care for Advanced Cervical Cancer, page 29).

Policy Implications

Planners of cervical cancer prevention programs should consider the following treatment issues:

- ▶ Rely on outpatient treatment technologies as much as possible.
- ▶ Expand access to treatment services by:
 - ▷ making cryotherapy available at the local level, while ensuring that LEEP is available at central or regional referral centers;
 - ▷ broadening provider guidelines so that non-physicians can perform outpatient treatments such as cryotherapy.
- ▶ Treat only high-grade or severe dysplasia instead of all dysplasia, since most low-grade dysplasia regresses spontaneously.
- ▶ Support research to explore alternative treatment protocols and methodologies so that the number of visits required for screening, diagnosis, treatment, and follow-up may be reduced.
- ▶ Support research to explore the clinical and ethical implications of unnecessary treatment that likely will be unavoidable with strategies such as the modified see-and-treat strategy.
- ▶ Offer palliative care at the primary health care level (see *Issue in Brief #7* on Palliative Care for Advanced Cervical Cancer, page 29).



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Follow-up Strategies

Well-functioning information systems are essential to successful client follow-up. Program monitoring and evaluation, quality assurance, and identification of at-risk women also can be strengthened by developing effective information systems.

When screening suggests a cervical lesion, one or more follow-up visits to a health care provider generally are required. Successive visits may be necessary for diagnosis, monitoring, and/or treatment (including post-treatment check-up). In developing countries, however, returning for follow-up care can be challenging for women due to financial, practical, and logistical obstacles. In addition, some clients may not return for follow-up visits because they do not understand the necessity of further evaluation or are afraid of receiving bad news about their condition. Others may not return due to embarrassment or a fear of diagnosis or treatment.

It is important for program planners and policy makers to not only address these barriers, but to also have adequate information systems in place that allow staff to monitor whether a woman has received post-screening care, when needed.

Key Considerations

Program planners and policy makers should consider several key elements that can contribute to the success of a cervical cancer prevention program's follow-up strategies:

Well-designed, functional information systems

Client records should allow programs to track information on individual women over time, including a client's screening results, diagnostic referrals, treatment outcomes, and contact information. These records should be set up so that women can be recalled for screening at appropriate intervals or for repeat screening, diagnosis, and treatment due to abnormal screening results. To do this, a simple registry of the population being serviced can be established using a basic card system. Cards should include the woman's name, identification number, address, date of birth, family contact, date of each screening test, the results, and any treatment referral details. Pathology reports should be filed with the client's card. Because screening, diagnosis, and treatment may be provided by different organizations, it may be necessary to develop formal or informal agreements that permit and facilitate the exchange of information.

In addition to clinical information systems, women also can be given a screening record card (with identification numbers linked to clinic records) detailing their screening visits and results to help remind them of when they must return and to inform new providers of their screening history if they move. Ideally, information from client records should be linked to regional or national databases or cancer registries to allow easy aggregation of data on key indicators. If such a system is not feasible, using sentinel surveillance methods for data collection and monitoring could be a practical alternative.

Reducing the number of post-screening clinic visits

In many low-resource settings, and especially in rural areas, women's access to health services may be limited because of distance from clinics, transportation costs, and family or work responsibilities. Reducing the number of clinic visits for screening, monitoring, and treatment therefore



Alternative cervical cancer screening information systems may be maintained at the community level through women's organizations or mobile health workers, augmenting hospital- or clinic-based information systems. Review of individual screening and follow-up needs can be incorporated into the organization's regular meetings, which can be particularly helpful to low-literate women.

may make it easier for women to receive the care they need. Variations of the see-and-treat approach can eliminate the need for women to wait for the results of biopsy before returning for treatment, although the clinical utility of such approaches is still being studied (See *Issues in Brief #5* on Treatment Approaches and Technologies, page 23).

Integrating services

Integrating cervical cancer prevention with other primary health care services can be an effective strategy for improving the likelihood that women will come for screening services and receive necessary follow-up care. Integrating cervical cancer prevention into existing services will succeed only if the existing services already reach women aged 30 to 35 and older. One Latin American study found that while family planning clinics reach many women, they often reach younger women who are not at high risk for cervical cancer.¹ Programs that provide maternal/child health, sexually transmitted infection treatment, sterilization, hypertension, or other outpatient services may have the capacity to provide cervical cancer screening as well as the established mechanisms to ensure adequate provision of follow-up care.

Educating women

Qualitative research in several countries indicates that many women are not aware that early diagnosis and treatment of cervical lesions can prevent cervical cancer. Furthermore, women also may not understand the importance of returning for follow-up (either for diagnosis, treatment, or repeat screening) when their screening results are abnormal. Health care providers and educators, therefore, must develop skills in counseling and education to ensure that women who need additional services understand their importance.

Policy Implications

To address the challenges of developing feasible follow-up strategies, program planners and policy makers should consider the policy initiatives outlined below:

- ▶ Develop information systems that allow programs to track clients' screening results, diagnostic referrals, treatment outcomes, and contact information.
- ▶ Endorse research to explore alternative screening and treatment approaches that may reduce the number of clinic visits required.
- ▶ Support integration of cervical cancer screening and treatment into existing reproductive health programs that reach or have potential to reach older women and have functioning, effective information systems, where feasible.
- ▶ Ensure that women receive adequate information and counseling about their conditions, the need to return for follow-up, and what they will experience at each stage of intervention (screening, diagnosis, and treatment).

Reference

1. Robles S, White F, Peruga A. Trends in cervical cancer mortality in the Americas. *Bulletin of PAHO* 30(4):290–301 (December 1996).

Palliative Care for Advanced Cervical Cancer

Any cancer prevention program must address the needs of patients with advanced disease. For cervical cancer prevention programs, there always will be women whose disease was not identified until the advanced stage. For new programs, this can be a particular challenge since widespread screening will uncover previously unidentified cases. For programs working with limited resources, it is seldom possible to provide the staff, equipment, medications, and facilities necessary to treat invasive cancer. Therefore, efforts must focus on ensuring that palliative care is available to women with advanced, terminal disease.

Palliative care is the active, total care of patients whose disease is not responsive to curative treatment or for whom curative treatment is not available. Controlling pain and other symptoms, and addressing emotional, psychological, social, and spiritual problems are all part of palliative care; the overall goal is to achieve the best possible quality of life for patients and their families.

While most people would agree that compassionate care should be provided to gravely ill women, in many areas there are major barriers to providing palliative care. Barriers include the absence of national health policies on cancer pain relief or other aspects of palliative care and the lack of training for health care providers and policy makers. Furthermore, many countries impose restrictions on drugs that are effective in controlling severe pain, often because of concern about the legality of certain opioid drugs that are classified as narcotics. In countries where there is legal access to opioids, high costs often place these medications out of the reach of those who need them.

International narcotic regulations have resulted in shortages and/or prohibitive pricing of opiates in some regions. Some of the specific concerns that have resulted from these restrictions may be unfounded. For example, data suggest that medical use of opioids is rarely associated with psychological dependence on the drugs. There also is little evidence to support the concerns that cancer patients develop tolerance to opioids. In fact, dosages generally are increased because pain tends to increase as the disease progresses. Concerns about diversion of drugs for illicit use can be addressed by national drug guidelines that mandate specific uses and distribution requirements.

Palliative Care Supports Patients and Their Caregivers

In many regions, one of the first steps that must be taken to provide palliative care is ensuring that providers discuss the cervical cancer diagnosis and its implications with their clients and the clients' families. It generally is difficult for nurses and physicians to discuss the prognosis of grave disease and death without special training, and cultural norms may dictate against informing the patient about a cancer or terminal diagnosis. As a result, a cervical cancer diagnosis often is discussed quickly and superficially, if at all. Training in client communication can enable health

Palliative Care:

- ▶ affirms life and regards dying as a normal process;
- ▶ neither hastens nor postpones death;
- ▶ provides relief from pain and other distressing symptoms;
- ▶ addresses the psychological and spiritual needs of patients;
- ▶ offers a support system to help patients live as actively as possible until death;
- ▶ offers a support system to help families cope with the patient's illness and their bereavement.

(World Health Organization, 1990)¹



Hospice Uganda, established in 1993 to provide palliative care for cancer patients, works to improve access of the very ill to pain-relieving medications. The organization applies a holistic approach to care, utilizing the WHO analgesic ladder to control pain. Hospice Uganda advocates for increased accessibility to these medications at the community level by training non-physician health workers to diagnose pain and dispense analgesics.

In 1992, the Costa Rican Supreme Court declared that every Costa Rican has the right to die with dignity and with no pain. This decision was prompted by the plight of a terminally ill cervical cancer patient who was unable to obtain sufficient pain control medication because of established policies of hospital-based pharmacists.

care providers to develop the skills needed to talk with patients and their families about cancer and death.

Providers also need training in managing pain, addressing other symptoms of the disease, and providing counseling support to patients and their families. As this training is put into place, programs must ensure that the drugs proven to be effective in controlling cancer pain, including morphine and codeine, are available.

An important step to increasing access to palliative care in low-resource settings is recognizing that the vast majority of women with terminal cervical cancer will be cared for at home. Therefore, it generally makes sense to establish systems and mechanisms to support the families providing the home care, rather than to expend resources on hospital-based care or special hospices, which generally are available to only a minority of those in need. Simple techniques for helping sick women to more easily eat, breathe, and change positions while lying down can be taught to relatives and caregivers. Health care workers who provide basic counseling and emotional support can vastly improve the comfort and well-being of the very ill and their family or other caregivers.

Policy Implications

To ensure that women with advanced cervical cancer have access to effective, compassionate palliative care, cervical cancer programs, in conjunction with broader cancer programs, should address the following issues:

- ▶ disseminate information about appropriate palliative care to policy makers and providers at all levels;
- ▶ train providers in the principles of palliative care, including the medical uses of opioid drugs;
- ▶ evaluate drug regulations and medical/pharmaceutical policies that may unnecessarily restrict access to appropriate drugs, including opioids;
- ▶ train providers in interpersonal communication and counseling skills to help them discuss cancer and death with patients and their families;
- ▶ assess and implement strategies to offer support for families providing palliative care in the home, including teaching family members to administer necessary drugs and to use simple techniques to improve the ill person's comfort and well-being.

Reference

1. World Health Organization (WHO). *Cancer pain relief and palliative care: report of a WHO expert committee*. Technical Report Series 804. Geneva: WHO (1990).

Program Monitoring and Evaluation

Monitoring and evaluation of a cervical cancer prevention program's operations and impact are essential to determining whether the program is meeting its objectives effectively and efficiently. Results of program monitoring and evaluation can be used to help ensure appropriate delivery of services and to improve program operations. Positive evaluation results also can be used to mobilize continued financial and political support for the program.

Because some aspects of evaluation can be time-consuming and costly, it is important that cervical cancer prevention programs establish monitoring and evaluation strategies that are feasible given the program's technical and financial resources. Whenever possible, these strategies, along with mechanisms for quickly relaying evaluation data between program sites, should be in place at the start of program activities.

Selected Evaluation Indicators

PROCESS INDICATORS:

Screening:

- ▶ percentage of women aged 35 to 50* screened in past five years;
- ▶ percentage of women aged 35 to 50 screened for the first time in the past five years[†];
- ▶ percentage of designated health workers who perform or refer women for screening;
- ▶ percentage of health facilities offering cervical cancer screening services[†];
- ▶ percentage of all screening test results that are positive for high-grade lesions or cancer[†];
- ▶ percentage of inadequate/inconclusive screening tests;
- ▶ percentage of false-positive screening tests;
- ▶ percentage of women aged 35 to 50 who know basic screening messages;
- ▶ percentage of women aged 35 to 50 with positive attitudes toward screening services[†].

Diagnosis and Treatment:

- ▶ percentage of women with positive screening results diagnosed within three months;
- ▶ percentage of women diagnosed with high-grade dysplasia treated within three months[†];
- ▶ percentage of treated women followed up within one year;
- ▶ percentage of pre-invasive lesions treated with outpatient methods.

IMPACT INDICATORS:

- ▶ incidence of invasive cervical cancer;
- ▶ mortality rate from cervical cancer.

*A reasonable age group for a new program with limited resources.

[†]Suggested minimum indicators for new programs.

Feasible Approaches in Low-Resource Settings

Ideally, evaluation of a cervical cancer prevention program should address both ongoing activities (for instance, how well the program's screening and treatment services are functioning and whether women with untreatable disease are receiving palliative care) and long-term impact (for instance, whether the program has helped reduce cervical cancer incidence rates cost effectively). Because evaluation of program activities (process indicators) generally is faster, easier, and less costly than evaluating long-term impact, it should be the primary evaluation strategy for new programs and for those with limited resources.

Effective evaluation of a cervical cancer prevention program involves (1) identifying measurable evaluation indicators (both process and impact); (2) developing an appropriate evaluation strategy (for instance, comparing performance against set targets for a given time period); (3) gathering information about selected indicators; and (4) analyzing the information and reporting findings. Both quantitative and qualitative methods of data collection can be used.

A number of indicators can be used to measure a cervical cancer prevention program's activities and impact (see list at left). For each indicator, program evaluators must decide what constitutes success. Often this will depend upon the maturity and scope of the program as well as on the program's resources for implementing activities. For example, a newly formed program may consider itself successful if it can screen 30 percent of women aged 35 to 50 in its first year of operation, while a more established program may define success as reaching at least 90 percent of these women.

To ensure maximum impact, evaluation results should be reported to appropriate program personnel along with recommendations



Monitoring and evaluation of a cervical cancer prevention program's operations and impact are essential to determining whether the program is meeting its objectives effectively and efficiently.

for corrective action, if needed. For example, if an evaluation finds that few women referred for diagnostic follow-up are actually receiving services, action should be taken to determine why that is the case. Mechanisms then should be developed to address the problem, such as providing transportation to a clinic where diagnosis is provided, or developing new, functional links with diagnostic providers. When discussing possible solutions to problems identified during an evaluation, involving individuals who provide or receive services and/or gathering more in-depth information about the problem can be helpful.

Efficient Information Systems Are Essential

Establishing well-functioning information systems is essential to successful program monitoring and evaluation. Client records should allow programs to track individual women over time, including a client's screening results, diagnostic referrals, and treatment outcomes (See *Issue in Brief #6* on Follow-up Strategies, page 27). Ideally, information from client records should be linked into regional or national databases to allow easy aggregation of data on key evaluation indicators. Where available, a national cancer registry can be used to monitor changes in cervical cancer incidence rates. Where no such registry is available, one can be initiated by first collecting data from a limited area and then gradually expanding the reporting area. It is not necessary for the registry to cover the entire population to generate adequate data for monitoring disease patterns, however.

Information systems can help program planners and health care providers to

- ▶ identify those most in need of services (for example, women who have never been screened; women who are due for periodic screening; women with abnormal screening results who need follow-up);
- ▶ contact women with screening results;
- ▶ monitor the coverage or response rate of the recruitment program;
- ▶ record cytologic abnormalities detected on screening;
- ▶ ensure that women receive adequate follow-up care;
- ▶ collect and assess data on laboratory and diagnostic quality;
- ▶ permit comparison of data on program outcomes at the regional and/or national level.

Policy Implications

Evaluation is a necessary component of cervical cancer prevention programs. When establishing a program it is important to:

- ▶ have a monitoring and evaluation plan in place from the start to ensure that the program's objectives and supporting activities are clearly thought out;
- ▶ choose realistic and measurable indicators that correlate to program goals and objectives, making it easier to measure program progress and identify areas needing improvement;
- ▶ establish appropriate information systems to support monitoring and evaluation activities;
- ▶ act quickly on evaluation findings so that program strengths can be maximized and areas needing improvement can be corrected early.

Women's Needs Related to Cervical Cancer Prevention

Women at risk of cervical cancer need complete and accurate information so they can understand prevention options and utilize screening services. Cervical cancer prevention programs must address the cultural, emotional, and practical barriers that influence whether or not women will utilize screening services. Women may be reluctant to undergo screening due to embarrassment, fear of the screening procedure, or fear of cancer. Women frequently mistrust health care providers and have various family pressures that prevent them from seeking health care, especially gynecological care. Therefore, women require information that will address their concerns in a respectful and culturally appropriate manner.^{1,2,3}

Lack of Awareness Is a Major Barrier

In many countries, women's lack of awareness of cervical cancer and its prevention is a major barrier to seeking screening services. One Nigerian study of women aged 20 to 65 found that only 15 percent had heard of the disease.³ Another smaller study in Kenya found that, when asked to identify the biggest cancer threat in their community, almost 60 percent of providers but only 10 percent of clients identified cervical cancer. When asked what could be done to prevent cervical cancer, 80 percent of clients said they did not know; only two percent mentioned Pap smears.² In a Mexican study, women cited an array of barriers to seeking screening services, including a lack of knowledge about cervical cancer or Pap smears, the perception that cancer is an inevitably fatal disease, problems in client-provider relationships, opposition by male sexual partners, and rejection of the pelvic exam.¹

To ensure that programs address women's needs and concerns, women who are at risk of cervical cancer should be involved in developing program interventions and key informational messages. Participatory qualitative research methods such as focus group discussions, in-depth interviews, or community mapping with women of various ages and their partners can provide valuable insights into their needs and concerns. Program managers seeking ongoing input may consider establishing an advisory team comprised of women at risk as well as other key community members.

Involving women in program design can help ensure that women in the program's target population receive persuasive information from their preferred sources and at their preferred delivery sites. The availability of services that meet their needs and address their concerns increases women's willingness to seek screening, as well as to return for necessary follow-up care.

The best approaches for increasing awareness of cervical cancer prevention options among at-risk women will vary from place to place. General principles relating to women's needs are outlined below.

Developing Messages That Effectively Inform Women

One of the most significant barriers experienced by women seeking cervical cancer screening is their lack of access to information about the disease. An important consideration for programs is reaching women at highest risk for treatable, high-grade lesions—typically, women aged 35 to 50—with messages that encourage them to seek cervical cancer prevention services. Key information messages will explain:

- Cervical cancer develops slowly.
- Screening can detect treatable, precancerous lesions before they progress to cancer.
- Women age 35 and older are more likely to develop cervical cancer than younger women.



- ▶ Women in their thirties and forties should be screened at least once.
- ▶ The screening procedure is relatively simple and quick.
- ▶ Screening generally is not painful.
- ▶ The small number of women who need treatment after screening generally receive a simple outpatient procedure to remove the lesion.

Women may prefer to learn about cervical cancer in various ways

Through certain channels:

- ▶ radio messages
- ▶ newspaper advertisements or articles
- ▶ posters or pamphlets
- ▶ plays
- ▶ community health meetings
- ▶ direct personal contact

From specific community members:

- ▶ doctors
- ▶ nurses or nurse practitioners
- ▶ midwives
- ▶ public health workers
- ▶ community leaders
- ▶ community health promoters
- ▶ members and leaders of women's groups
- ▶ traditional healers and traditional birth attendants
- ▶ their peers

In a specific location:

- ▶ health centers
- ▶ hospitals
- ▶ churches
- ▶ family planning or maternal and child health centers
- ▶ their own or their partner's workplace or employment center
- ▶ public meetings
- ▶ schools (through their school-age children)
- ▶ local women's groups or clubs

The specific wording and presentation of motivational messages should be created by and pretested with members of the intended audience to ensure that the messages are appropriate and easily understood.

The best format for delivering the messages also will vary among communities. In some communities, radio announcements made by senior public health officials may be most effective in increasing awareness. In other communities, inviting nurses to speak at women's group meetings may be more appropriate.

Women require information that not only describes the basic facts about cervical cancer prevention, but also explains the concepts of preventive health care. Information that communicates the relative ease and economy with which women can be screened combined with the benefits of screening and early intervention will likely lead to improved health-seeking behavior. Linking screening to other life events or needs, such as becoming a grandmother or the desire for contraceptive sterilization, may increase the acceptability of screening. Ensuring that cervical cancer prevention is understood in the context of women's broader health needs and priorities also is essential.

Communication Skills

Cervical cancer, like many other illnesses, is a taboo subject in some communities. As a result, women frequently are unprepared to discuss cervical cancer prevention with their health care providers, partners, or close family members. Counseling by health care providers can inform women and help them develop the skills necessary to discuss cervical cancer with those closest to them. Counseling can be particularly helpful to women who receive treatment for precancerous lesions and who must abstain from intercourse for several weeks afterward. A woman in this situation can benefit greatly from discussing with a health care provider why she must not have intercourse so that she can explain this to her partner. Involving partners in the discussion also can be important.

Access to Services

Women are most likely to seek services from providers who are sensitive and responsive to their specific needs. Services should be culturally

appropriate and available in languages spoken by the women most at risk. Women who are employed or who are otherwise working during the day may require services that are available at locations and times that are convenient to them, such as during the evenings and on weekends. Costs should not place services out of reach of the women who need them. In addition, confidentiality and privacy of those seeking services must be safeguarded.

Women at risk of cervical cancer often report concerns about how they will be treated by a health care provider. These concerns may be so great that they prevent women from seeking screening or other health services. Health care providers who are skilled at establishing a respectful rapport with women help ensure that they get the information they need and feel comfortable returning for required follow-up visits. Counseling that addresses women's concerns and questions is a critical component of cervical cancer prevention services.

Women may prefer to receive cervical cancer prevention services that are integrated into other services they consider important. For example, providing cervical cancer prevention services at a primary health center where older women already receive health services may be more convenient and increase a woman's willingness to seek screening and follow-up services, if needed.

Policy Implications

In developing effective mechanisms to meet women's need for cervical cancer prevention information and services, program planners should consider the following issues:

- ▶ involve women at risk in the design, implementation, and evaluation of cervical cancer prevention programs;
- ▶ ensure that outreach efforts reach the majority of women aged 35 to 50 (including difficult-to-reach populations such as poor, urban women; women in remote areas; indigenous women; and low-literate women);
- ▶ develop key culturally acceptable messages in collaboration with the community the program is designed to reach;
- ▶ help women develop communication skills that strengthen their ability to discuss cervical cancer prevention with friends and/or family members;
- ▶ train health care providers so that they are skilled in communicating effectively and respectfully with women seeking services;
- ▶ ensure that cervical cancer prevention services are accessible to women by minimizing costs and offering services at convenient times and places;
- ▶ integrate cervical cancer prevention services with other services considered important to women.

Since the goal of many cervical cancer screening programs is to screen women only once every five to ten years, a "campaign" strategy may be effective. A well-designed campaign that periodically reaches all women in the target population may effectively and efficiently educate women about the importance of screening and where they can go to receive services.



References

1. Lazcano-Ponce EC, Castro R, Allen B, et al. Barriers to early detection of cervical-uterine cancer in Mexico. *Journal of Women's Health* 8(3):399–408 (April 1999).
2. PATH (Program for Appropriate Technology in Health). Assessing health need/community demand for cervical cancer control: results from a study in Kenya. *Reproductive Health Reports* No. 1 (December 1996).
3. Ajayi IO, Adewolfe IF. Knowledge and attitude of general outpatient attendants in Nigeria to cervical cancer. *Central African Journal of Medicine* 44(2):41–43 (February 1998).

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#10

Advocating for Cervical Cancer Screening and Treatment

Advocacy is any organized activity directed at changing policies, positions, or programs. It can take many shapes. For example, local advocacy may take place within an existing organization to bring about internal policy change. National level advocacy can focus on persuading Ministry of Health officials to support new or strengthened country-wide initiatives.

Individuals and organizations advocating for new or improved cervical cancer prevention initiatives must be prepared to build a solid case underscoring the need for and feasibility of implementing effective screening and treatment protocols. Advocates for cervical cancer prevention include anyone who participates in an organized effort to increase public and/or policy support for prevention initiatives. This may include medical providers, health educators, community leaders, women's groups, and others.

Advocacy can take many shapes. It may take place within an existing organization as a means of bringing about internal policy or procedure changes. For example, a health center's cervical cancer prevention program may have policies in place that encourage younger women to receive cytological screening. In this case, advocates could develop a strategy focused on persuading decision makers to change the target age for screening to women in their thirties and forties who are at highest risk of precancerous cervical disease.

Advocacy also can be effective on a larger scale. For example, a community-based advocacy campaign may persuade local health officials to provide cervical cancer screening services at district hospitals. A larger-scale campaign could focus on persuading Ministry of Health officials to support a new national cervical cancer prevention initiative or strengthen existing efforts.

Regardless of whether advocates are working toward policy change at the local or national levels, they must present their case to influential groups or individuals in a powerful and compelling way. Most cervical cancer prevention programs must be endorsed by key decision makers, such as Ministry of Health officials, to be successfully implemented. Even when non-governmental organizations take the lead in providing screenings, the infrastructure necessary to implement cervical cancer prevention programs, such as cytology laboratories, often functions through the government. Government-supported health centers, clinics, and hospitals operating at the national and sub-national levels need official endorsement to ensure their success.

High-level endorsement of cervical cancer prevention programs may be demonstrated in a variety of ways. The government may agree, for example, to increase funding for prevention efforts, or it may appoint a committee to develop national guidelines on cervical cancer prevention. Other support may be embodied by an influential government official offering verbal support or agreeing to participate on an advisory board.



Building a Case for Cervical Cancer Prevention

Decision makers have limited time, competing health priorities, and finite resources with which to address a spectrum of demands. Because cervical cancer is associated with sexual activity, some decision makers may lack the political will to support or draw attention to a health subject that may be considered controversial. Adequate research and planning are essential to successfully advocating for new or strengthened cervical cancer prevention programs and policies. A core working group of advocates can use the following guidelines when mobilizing to improve cervical cancer prevention.

Obtain information.

Advocates seeking to improve cervical cancer prevention first must understand the level of need for services and the feasibility of implementing services within the target area. This information will help to substantiate and guide their efforts. Key information would include current data on the disease and its precursors among defined populations, the availability and utilization of prevention and treatment services, and policies currently in place that affect access to and use of services. Individuals and organizations advocating for a new cervical cancer initiative where none is in place must compile the information to persuade decision makers that a real need exists. The information then not only serves as an advocacy tool, but also can be used to shape program strategies once support has been secured.

Develop advocacy goals and objectives.

Identification of advocacy goals and objectives should be based upon key information findings described above. Advocates should analyze the information using pre-established criteria to help them identify and rank needs within a target area. The primary need identified through this process usually will emerge as the goal of the advocacy effort. Channels of access to key decision makers may also be identified at this point. Objectives that are specific, measurable, achievable, realistic, and time-bound then should be developed to help achieve the advocacy effort's long-term goal.

Examples of advocacy goals include:

- ▶ increasing government funds allocated for cervical cancer prevention programs;
- ▶ establishing national guidelines for cervical cancer screening and treatment;
- ▶ revising specific health policies, such as the age of the target screening population.

Examples of advocacy objectives include:

- ▶ meeting with three Ministry of Health officials in the first six months of the project;
- ▶ distributing 25 information packets to key community leaders in the first three months of the project;
- ▶ convening technical meetings on cervical cancer at three district hospitals in the first three months of the project.

Establish a broad coalition.

Establishing a broad coalition that includes a range of organizations and individuals demonstrates wide support of cervical cancer prevention to policy makers. Women from the target population should be involved in the coalition to ensure that their needs and concerns are represented. Coalition members should work collaboratively to develop a plan of action, undertake activities to increase public awareness, and respond to opposition.

Mobilize the public.

To be most effective, advocacy campaigns must capture the attention and support of key decision makers, opinion leaders, the public, and the media. These groups influence one another directly and indirectly; advocates therefore need to provide information tailored to the specific needs of each group. For example, informal community meetings utilizing low-literate educational materials may be suitable for increasing public awareness in some communities, while meetings with health officials will require more formal and technical presentation of epidemiological and cost data.

Evaluate advocacy efforts.

There are many ways to evaluate advocacy efforts, and even the most basic process data can be valuable in guiding advocacy activities. Process evaluation can provide information about the number of activities that took place (for example, the number of informational pamphlets that were distributed to policy makers or the number of public meetings that were held). Impact evaluation can illustrate progress made toward reaching long-term goals, such as the percentage increase in funding of cervical cancer prevention in a given time period.

Evaluation results can provide information valuable to streamlining advocacy efforts and motivating advocates. Results also can be used to identify the most and least effective components of an advocacy effort.



Policy Implications

As part of an effort to advocate for increased cervical cancer prevention services, program planners should consider the following:

- ▶ obtain information from the target area to accurately determine the need for services and the feasibility of providing them;
- ▶ recognize that even in cases where there is demonstrable need, a lack of infrastructure, political will, or funding may make the development of new or improved interventions infeasible;
- ▶ develop a broad coalition that includes all key leaders, demonstrating that the subject is one of significant concern;
- ▶ be prepared for opposition from those who hold different views or represent competing interests by planning strategically and developing persuasive public health messages;
- ▶ tailor persuasive advocacy messages so that they appeal to different target audiences, bearing in mind that messages developed for national-level health officials may not appeal to community health care providers;
- ▶ build a long-term advocacy strategy into program activities to ensure ongoing support for cervical cancer prevention.

Launching an Effective Cervical Cancer Prevention Program

Program planners need to consider the *minimum level of services* required to reduce cervical cancer morbidity and mortality when deciding whether and how to launch a cervical cancer prevention program. The technical and financial resources available to a program, as well as the health care infrastructure already in place, are key determinants of whether a minimum set of cervical cancer prevention services can be established. Systematic consideration of these factors will help decision makers assess the feasibility and appropriateness of initiating new services or expanding existing services.

Assessment of Existing Program Environment and Capabilities

Before launching any new health program, it is important to verify the need for services and to assess the program environment and existing capabilities.

Cervical cancer incidence data from national or local records, if available, can help decision makers **verify the need** for cervical cancer screening and treatment services, particularly in comparison to other health priorities. In general, an age-standardized incidence level greater than 30 to 40 per 100,000 women indicates a strong need for these services. A high prevalence of sexually transmitted infections (STIs) (for instance, a syphilis, gonorrhea, human papillomavirus, or chlamydia incidence greater than eight percent) also indicates need. Where national or local cancer or STI incidence data are not available, discussions with health care providers can help decision makers get a sense of the magnitude of the problem.

Decision makers also should **assess the local environment and service-delivery capabilities** that might affect initiation of cervical cancer services. In some cases, strong community support and complementary existing services will provide a solid foundation for initiating services. In others, provider biases and a weak infrastructure may make provision of even basic cervical cancer services infeasible. The assessment can be performed using a combination of existing data on clinic services and facilities, small-scale provider surveys, and focus group discussions with women, providers, and key community members. It should assess the following elements:

1. Political, provider, and community support for initiating services.

Important points to assess include whether policy makers, service providers, and community leaders understand and agree with a public health approach to cervical cancer prevention (e.g., where resources are scarce, using targeted and infrequent screening combined with



outpatient treatment of precancerous lesions). In addition, it is important to assess whether policy makers, service providers, and community leaders support preventive care, particularly for older women; whether they see cervical cancer as a priority compared to other health needs; and whether they are willing to allocate financial resources to cervical cancer prevention efforts.

2. Existing service delivery capabilities and system infrastructure.

This includes the number and location of clinic and hospital facilities, their ability to take on new responsibilities for screening and treatment, and the level of staff expertise and training. In addition, availability of necessary equipment and supplies, availability, capacity, and reliability of cytology laboratory services, and availability and functioning of referral networks should be assessed.

3. Awareness of cervical cancer among women aged 35 to 50.

Key points to assess include women's perceptions and misperceptions of cervical cancer as a health problem, awareness and acceptability of prevention options, preferred information sources, preferred service delivery sites, and linkages to community groups.

The information gained during such an assessment will be helpful in deciding whether to proceed with initiating services. In addition, the information will guide the design of services and will provide a baseline measurement by which to monitor and evaluate progress toward achieving program goals.

Using Assessment Results to Guide Program Development

Information from an assessment of the local environment and capacities can provide useful guidance to program managers in formulating strategies for providing cervical cancer information, screening, and treatment services. The information can help determine the types of advocacy that may be necessary to gain public and/or governmental support for program efforts. In many cases the assessment also will uncover challenges to offering services that can be addressed through program activities. Likewise, findings may reveal unexpected assets within a community that may enhance program delivery.

Some examples of common assessment findings and the types of actions that can be taken to address those findings are:

- | | |
|-------------------------|--|
| Finding: | Providers favor frequent screening of women starting at age 18. |
| Possible action: | Provide information about the health and cost rationale for focusing on screening women in their middle years. |
| Finding: | Women fear that they will receive "bad news" from screening. |
| Possible action: | Develop and pretest reassuring messages that emphasize that screening helps women avoid serious disease. |

- Finding:** A prominent, respected woman in the community once received successful early treatment of severe precancerous lesions.
- Possible action:** Enlist this woman's support in speaking publicly about the importance of screening.

Minimum Level of Services Required

To be effective, a cervical cancer prevention program must consist of a package of education, screening, and treatment services that reach the majority of at-risk women. Implementing any one of these elements without the others will not result in a substantial positive impact. For example, screening services must be supported both by educational efforts to motivate women to seek screening services, and by treatment services to ensure that disease identified through screening is appropriately managed.

At a minimum, programs must be able to reach women at highest risk of cervical lesions (those aged 35 to 50 are a reasonable starting point) with effective educational messages, screen those women at least once, and provide appropriate treatment or palliative care to those who need it (see Figure 4). Experience suggests that a management information system also must be in place at the onset of program activities for maximum program efficiency and impact. The specific financial and technical inputs needed to achieve this program initiation threshold (such as the number of health care providers and cytologists) will depend on the size of the population to be served and the existing health infrastructure.

Key Steps in Program Planning

When deciding whether to initiate cervical cancer prevention services, decision makers must compare information on existing capabilities/ infrastructure with the estimated inputs needed to achieve the minimum service-delivery goals for a given population (see Figure 4). Programs can then define the additional technical and financial resources needed to initiate program activities and determine whether these resources are available. Programs that are unable to meet a minimum service level should delay initiation of services until the level can be achieved.

1. The first step in making this comparison is to define the target audience for program activities. As mentioned previously, a reasonable target group for a new program is women aged 35 to 50. Furthermore, most new programs will initially want to limit the geographic scope of their activities, starting in a well-defined area and then gradually expanding to other regions as technical capabilities and financial resources allow. Information from the assessment can help program planners decide where to target services by identifying areas with the greatest need and readiness.
2. Once the size and composition of the target population has been established, programs can quantify the number and types of personnel, equipment, and facilities that will be needed to meet information, screening, and treatment needs. To accomplish this, program planners



Figure 4. Program Initiation Threshold: Minimum Program Goals and Necessary Inputs to Achieve Them*

Information, Education, and Communication (IEC)

Goal: Increase awareness of cervical cancer and preventive health-seeking behavior among women aged 35 to 50.[†]

Necessary Inputs:

- ▶ Guidance from women representative of the target population to shape IEC messages that will most effectively (1) increase awareness of cervical cancer and available prevention services among women aged 35 to 50, and (2) motivate women to seek screening services and treatment, when needed.
- ▶ Providers trained to counsel women about the screening process and provide respectful, confidential services.

Screening

Goal: Screen all women aged 35 to 50 at least once.

Necessary Inputs for Cytologic Screening:

- ▶ Trained Pap smear providers (including non-physicians).
- ▶ Pap smear supplies.
- ▶ Pelvic exam equipment (including tables, specula, and a light source).
- ▶ Reliable cytology laboratory, including trained cytologists.
- ▶ Proven mechanism for timely communication of Pap smear results to provider/client.
- ▶ Effective referral system for diagnosis and treatment.

Necessary Inputs for Visual Inspection with Acetic Acid (VIA):

- ▶ Providers trained in VIA (including non-physicians).
- ▶ VIA supplies.
- ▶ Pelvic exam equipment (including tables, specula, and a light source).
- ▶ Effective referral system for diagnosis and treatment.

Diagnosis and Treatment

Goal: Treat women with high-grade dysplasia, refer those with invasive disease to hospitals where possible, and provide palliative care for women with advanced cancer.

Necessary Inputs:

- ▶ Providers (including non-physicians, when appropriate) trained in cervical visualization and treatment of high-grade dysplasia/carcinoma *in situ*.
- ▶ Colposcopes or other appropriate means of visualizing the cervix.
- ▶ Treatment equipment (cryotherapy or loop excision) for high-grade dysplasia.
- ▶ Centrally available surgical treatment for early invasive cancer.
- ▶ Palliative care for advanced cancer (pain control and counseling).

Monitoring and Evaluation

Goal: Collect data on information and service delivery to facilitate ongoing monitoring and evaluation of program activities and outputs.

Necessary Inputs:

- ▶ Local information system for tracking number and identities of women screened, cytology results, and follow-up actions and results.
- ▶ Clinical registry of Pap smear results.
- ▶ Qualitative client assessment of the adequacy of information and services.

*The level of input needed (for instance, the number of trained Pap smear providers) will depend on the size of the population being served and available resources and health care infrastructure.

[†]Ages 35 to 50 is a reasonable target group for a new program with limited resources. As the program matures, the age group can be expanded first to older women (up to age 60) then to younger women (from age 30) to fit the local epidemiological profile.

should consult with service providers (such as reproductive health care providers and cytology laboratory personnel) to determine what would be required to meet the program's service-delivery goals. For instance, cytology laboratory staff will be able to estimate the resources (staff, equipment, and supplies) required to process a given number of Pap smears and compare these estimates to existing service capacity.

3. After quantifying what is needed to achieve a basic level of services, program planners need to estimate the costs of providing these services (See Cost Considerations on page 47). Costs will vary by location according to the local costs of supplies, availability of equipment and facilities, and current skills and efficiency of program personnel. If many of the inputs needed to achieve the basic level of services already exist in the service areas, the costs of adding cervical cancer prevention services may be minimal. On the other hand, if considerable equipment, facilities, and training programs are needed, start-up costs could be quite high. If costs appear to be a major barrier, it is important to estimate how much a health care system currently may be spending on treating cervical cancer cases (for example, surgical, hospitalization, and radiotherapy costs) before deciding against a program. Limited health resources are better spent on efforts to prevent cancer from occurring than on treatment of advanced cases, which is costly and rarely successful.

Programs that have additional financial resources or are operating in the context of a relatively well-developed infrastructure can consider expanding beyond the basic goals listed in Figure 4. If this is the case, program managers should determine feasible approaches to expanding the program's scope given available resources, including:

- increasing the percentage of women in the high-risk age group that attends screening services;
- expanding the targeted age group first to older women (up to age 60) and then to younger women (from age 30);
- decreasing the interval between screenings of high-risk women;
- expanding the availability of treatment services to reduce the distance that referred women must travel for care.



Cost Considerations

The cost implications of cervical cancer control must be taken into account when planning for a new or expanded cancer screening program. Programs generally are interested in a range of cost information, including:

- ▶ The yearly incremental costs of providing cervical cancer services as part of integrated women's health services.
- ▶ The cost-effectiveness of offering effective cervical cancer interventions (for example, the cost per life saved, cost per case detected).
- ▶ The relative cost-effectiveness of cervical cancer interventions compared with other important health interventions.

Addressing the first issue requires calculating the expected expenditures of a given cancer control strategy, including necessary capital expenditures (annualized or depreciated) and regular incremental expenditures (staff, supplies, and other ongoing needs beyond what already is available) for both screening and treatment interventions. An accurate cost analysis also requires an understanding of dysplasia prevalence, the average dysplasia-cancer progression rate, and the effectiveness of proposed screening and treatment interventions. Some expected expenditures may decrease over time with economies of scale, others may increase; these types of changes need to be considered. The example from South Africa on page 49 illustrates the considerations and results of this type of analysis.

To address the second issue, a cost-effectiveness analysis can be carried out in which the expected expenditures described above are compared with the potential benefits of a new intervention. This analysis produces a cost-effectiveness ratio of costs to health benefits (i.e., cost per cases detected, lives saved, or other benefit). The example from Chile on page 50 demonstrates how cost-effectiveness ratios can be useful in highlighting differences between two proposed program approaches. Where cost-effectiveness analyses have been carried out for other health interventions, the costs of cervical cancer control strategies can be compared to other health interventions.

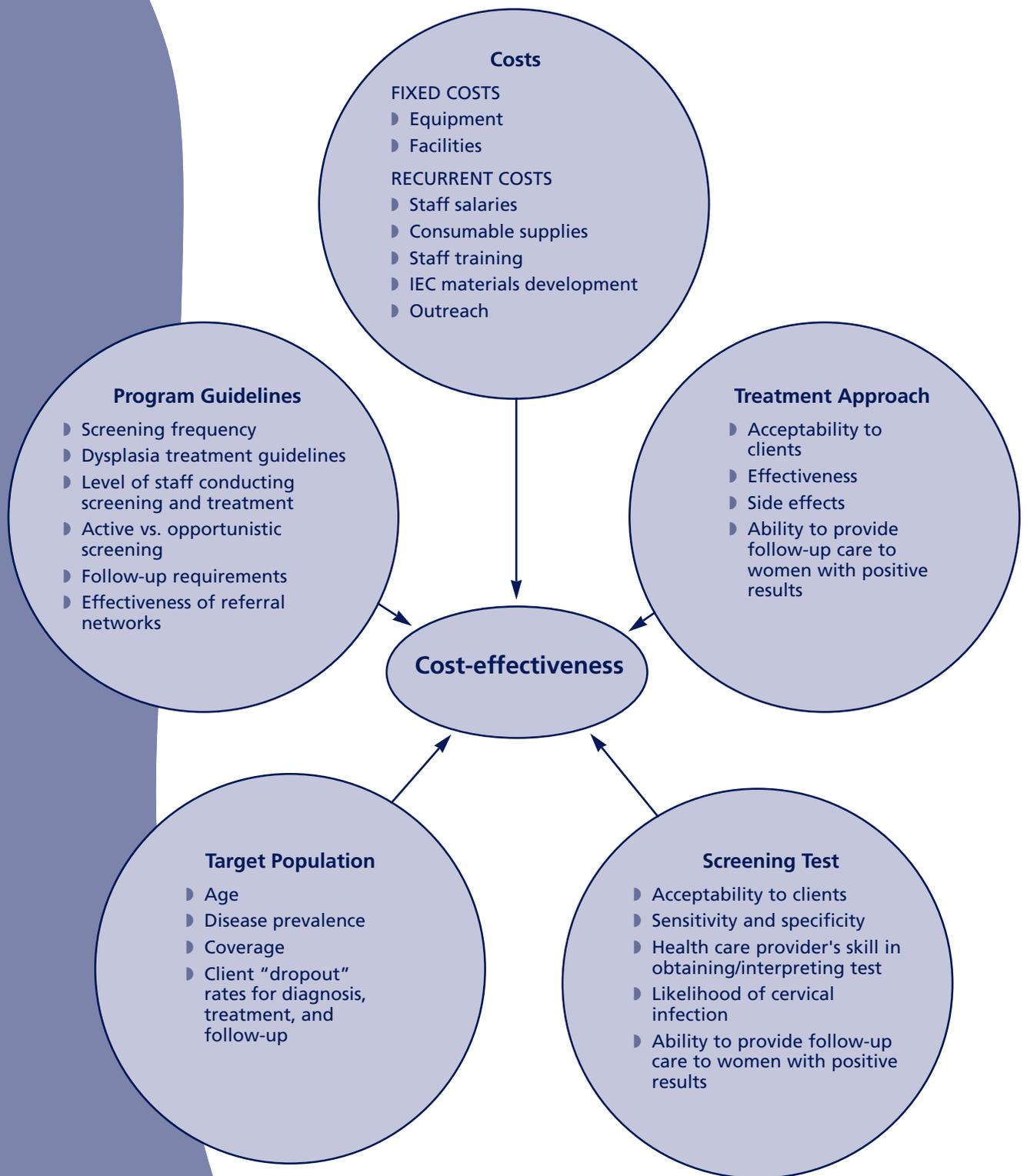
Completing cost-effectiveness analyses for cervical cancer control requires accurate data on the expected capital and incremental expenditures for a new intervention and agreement on a range of assumptions related to the proposed control strategy. The assumptions include prevalence of cervical dysplasia and invasive cancer, the dysplasia-cancer progression rate, sensitivity of the screening approach, and effectiveness of the dysplasia treatment approach (see Figure 5). Furthermore, programs must have (or acquire) the technical capability to gather necessary data and carry out the calculations involved in cost analyses.

Once a cost analysis is completed, the next challenge is to interpret the results. It is key to understand that parameter selection can have a significant effect on the results of an analysis. For example, in general:

- ▶ Assuming a higher baseline incidence of cervical cancer will increase cost-effectiveness.



Figure 5. Components That Influence Cost-effectiveness of a Cervical Cancer Intervention



Note: Figure is intended to be illustrative, not comprehensive.

- ▮ Assuming a lower screening sensitivity will lower cost-effectiveness.
- ▮ Assuming a higher program coverage will increase cost-effectiveness.
- ▮ Assuming an adequate existing health infrastructure will increase cost-effectiveness.

Most importantly, program managers must recognize that cost-effectiveness results are an aid to decision making, not the key component. A variety of medical, ethical, cultural, and practical considerations also are important to making an appropriate decision regarding allocation of health resources.

While a thorough explanation of cost analyses is beyond the scope of this document, this section provides examples of how various cost analyses have helped programs to make decisions about different strategies. The section also provides guidance on the cost implications of specific screening and treatment strategies.

Examples of Cost Analyses of Cervical Cancer Programs

South Africa: cost analysis highlights value of screening¹

As part of a comprehensive evaluation of factors affecting cervical cancer screening in South Africa, an analysis of total costs of program implementation was completed. While the estimated program costs are higher than in many other African countries (for example the estimated total cost of a single screening in Zimbabwe is US\$3.50, in Kenya US\$3.00), this cost analysis is a useful example of how total costs information can be used. The analysis quantified the costs of:

- ▮ Screening (obtaining/reading Pap smears)—US\$22 per screening by a specialist, \$11 per screening by public sector.
- ▮ Dysplasia treatment (colposcopy and laser or cryotherapy)—US\$89 per treatment.
- ▮ Treatment for invasive cancer (biopsy, hysterectomy, radiotherapy)—US\$3,573 per case.

The analysis then compared the total costs of two program approaches: (1) one that did not attempt to screen women, but instead focused on treating women with symptomatic, invasive cancer; and (2) a second that screened women and then treated both precancer and cancer. According to the analysis, the first approach of treating only invasive cancer would cost over 80 percent more than a screening program using public-sector providers. When specialists were used to perform screening, the cost saving was only 12 percent. (The analysis assumed a 2 percent CIN prevalence and a 50 percent CIN progression rate, which are reasonable assumptions given the limited data available on cervical dysplasia in South Africa.) Even when the prevalence was assumed to be 1.5 percent *or* the progression rate was assumed to be 25 percent, a screening program using public-sector facilities still was less expensive than a program based on treatment only. Lowering both assumptions made a public-sector screening program the more expensive option.



Cost-effectiveness of two screening strategies in Chile²

The cost-effectiveness analysis illustrated below compares two strategies for cervical cancer screening in Chile. The comparison illustrates the relative effectiveness of less frequent screening of most at-risk women compared with more frequent screening of fewer than half of at-risk women. This type of analysis can be useful to program managers in deciding what program strategies to implement.

Table 4. Comparison of Two Screening Strategies

	Program 1	Program 2
Age	30-55 years	30-50 years
Frequency of screening	3 years	10 years
Coverage	30%	90%
Reduction in mortality	15%	44%
Cost per case detected	US\$2,522	US\$556

Source: Eddy, 1986.²

Cost-effectiveness of non-cytologic screening approach in South Africa³

A cost-effectiveness analysis of different strategies for screening, diagnosis, and treatment of cervical dysplasia in South Africa was carried out in early 2000. The analysis suggested that a single lifetime screening with a competitively priced human papillomavirus (HPV) test, or possibly visual inspection (VIA), is likely to be clinically and cost-effective in reducing cervical cancer deaths.

The analysis was carried out from a societal and public health perspective and estimated the cancer incidence, life expectancy, lifetime costs, and incremental cost-effectiveness ratios associated with the use of three screening tests, VIA, Pap tests, and HPV-DNA tests (the Digene Hybrid Capture II test). It was assumed that a positive screen triggered colposcopy/biopsy and cryotherapy, or immediate cryotherapy. The analysis used natural history, clinical, epidemiological, and test performance data from ongoing studies in South Africa, published literature, and other sources.

The model suggested that a single lifetime screen between ages 35 and 50 would reduce the incidence of cervical cancer in South Africa by 25 to 30 percent. More frequent screening reduced incidence further. The most cost-effective strategy was use of a single lifetime HPV test followed by cryotherapy for HPV-positive women (assuming that the HPV test was more than 75 percent sensitive for detecting dysplasia and that it cost US\$6 or less). Other assumptions addressed client dropout rates and HIV prevalence in the community. If the cost of the HPV test exceeded US\$6, or the sensitivity of HPV testing was less than 60 percent, VIA followed by cryotherapy was the more cost-effective approach.

Comparing the cost-effectiveness of cervical cancer screening to other health interventions

To be useful, any health cost analysis must consider other health needs. In most developing countries, there are many serious health needs that

“compete” for available resources. Where cervical cancer is a serious problem, other women’s health problems probably exist, for example maternal morbidity and mortality; reproductive tract infections, including human immunodeficiency virus (HIV); and tuberculosis. Serious children’s health problems may include neonatal morbidity and mortality, diarrheal disease, various other infectious diseases, and nutritional deficiencies.

Data from the early 1990s suggest that cervical cancer is among the top five causes of death among developing world women aged 45 to 59 (along with tuberculosis and cardiovascular diseases). Even for women aged 30 to 44, it is among the top ten causes of death (with tuberculosis, obstetric, cardiovascular, cirrhosis, and HIV deaths rated higher). The World Bank has identified cervical cancer as a moderately cost-effective intervention compared with other health interventions, and a very cost-effective intervention compared with other cancer control efforts. The Bank estimated that screening women at five-year intervals would cost about US\$100 per disability-adjusted life year (DALY[†]) gained (assuming that an appropriate referral system for necessary treatment exists). This amount is a fraction of the estimated costs of cervical and breast cancer treatment. Compared with some other interventions, however, cervical cancer screening is relatively expensive.

Table 5 illustrates how the costs of cervical cancer screening compare with costs of other health interventions.^{4,5}

Table 5. Comparing Costs of Cervical Cancer Screening to Costs of Other Health Interventions

Intervention	Cost per DALY (US\$)
Lung cancer prevention (smoking cessation programs)	20
Polio vaccination	20 in a high-mortality environment 40 in a low-mortality environment
Sexually transmitted disease management	1–55
Cervical cancer screening	100
Integrated antenatal/delivery care for maternal mortality	30–250
Malaria treatment	200–500
Malaria control (through mosquito control)	5–250 depending on mosquito type
Cervical cancer treatment/palliative care	2,600

Sources: Jamison 1993,⁴ Murray 1994.⁵

Cost Implications of Selected Screening and Treatment Strategies

Screening

Screening costs vary according to the cost and accuracy of the method selected, the populations screened, screening frequency, client dropout rates at each phase of screening and treatment, and recruitment strategies adopted.

[†]DALYs are a measure of life years gained that combine the number of years of healthy life lost due to both premature morbidity and mortality, using a set of age and disability estimated weights.



high-risk groups and therefore increase screening efficiency. Passive or opportunistic recruitment does not require any additional expense and may be appropriate in settings where high-risk women already are being seen for other services.

Dysplasia Treatment

Dysplasia treatment costs vary according to the cost and accuracy of the method selected, the service delivery strategy, the type of provider, the grade of dysplasia treated, and the rate of side effects and complications.

- ▶ **Treatment methods:** Outpatient methods like cryotherapy and loop electrosurgical excision procedure (LEEP) are less expensive, similarly effective, and have fewer complications than methods such as cone biopsy and hysterectomy. All, however, require colposcopy or an alternative method to visualize the cervix. Colposcopes generally cost at least US\$3,000.
 - ▷ **Cryotherapy:** Initial costs for cryotherapy range from US\$1,000 to US\$3,000, while recurrent costs (for refrigerant and other consumable supplies) are generally low. Non-physician providers can be trained in the method, which reduces salary costs, and electricity is not required, which reduces overhead. This approach, however, can be less effective in treating large, precancerous lesions than some other methods.
 - ▷ **LEEP:** Initial costs for LEEP range from US\$4,000 to US\$6,000. Recurrent costs are moderately high and include loops (US\$15 to US\$60 per loop), local anesthesia, electrodes, and smoke evacuator. The method is somewhat more effective (90 to 95 percent) in treating all CIN grades, which may partially offset its relatively higher initial costs compared to cryotherapy. At the same time, side effects and complications, particularly bleeding, are more of a concern with LEEP.
 - ▷ **Cone biopsy and hysterectomy:** Both of these methods are inpatient procedures and require sophisticated training and equipment. General anesthesia also is required, which can be very costly. Further, serious side effects and complications such as bleeding, cervical stenosis, spontaneous miscarriage, and infection are associated with these approaches. In developing countries, clients may be charged US\$75 or more for cone biopsies and US\$1,500 for hysterectomies.
- ▶ **Service delivery strategies:** Options include central, district, or mobile delivery of treatment services. The most cost-effective approach will depend on staff availability, distance and ease of travel, and availability of equipment and supplies. Centrally-based services shift the cost of travel to the client, but follow-up rates may be lower, which could undercut the value of screening.
- ▶ **Provider:** Currently, physicians generally provide CIN treatment. Nurses are being trained to provide cryotherapy in some studies, however, which has the potential to reduce costs and increase the availability of services.



- ▶ Grade of dysplasia treated: Because more than half of low-grade dysplasias regress without treatment, maximum cost-effectiveness may be achieved by treating only moderate and severe (or only severe) dysplasias.

Cancer Treatment

Treating cancer is generally very expensive and often not successful. Hysterectomy and radiotherapy, if available, are recommended for early-stage cancer. Depending on availability, these services can cost hundreds or thousands of dollars to the patient. For late-stage cancer cases, palliative care (including counseling and pain control) is recommended. Palliative care includes the cost of medication, counselors, and, in some cases, hospitalization. In many countries, the limited cancer funds are used to buy chemotherapeutic drugs and radiotherapy equipment, rather than to support improved detection and treatment of preinvasive conditions.

Policy Implications

New or expanded cervical cancer prevention interventions must address the following in order to maximize cost-effectiveness:

- ▶ Focus program efforts on women most at risk of precancerous lesions (generally those aged 35 to 50).
- ▶ Ensure that the screening strategy selected is as inexpensive and accurate as possible, and that it is based upon recognized screening frequency recommendations (every three, five, or ten years, or even just once in a woman's lifetime where resources are very limited).
- ▶ Work to maximize screening coverage before increasing the frequency of screening.
- ▶ Select a treatment strategy that is as inexpensive, safe, and effective as possible and is based upon recommended treatment protocols.
- ▶ Implement cost analyses as an aid to decision-making whenever possible.
- ▶ Train non-physicians to conduct effective screening and treatment services whenever possible.
- ▶ Develop effective information and outreach systems to maximize the proportion of women who receive necessary follow-up care.

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Country Profiles

Following are profiles of five cervical cancer prevention programs, interventions, and studies undertaken in a variety of countries. These profiles represent a range of approaches; some are relatively well funded and are national or regional in scope, while others are local, clinic-based efforts. Several summaries also illustrate the role of research and advocacy in developing effective programs.

In addition to project descriptions, all profiles provide information on the challenges faced by providers and program managers in implementation, as well as the implications of these efforts for other programs. Some of the common themes that emerge from these profiles include the importance of:

- ▶ establishing strong management and long-term commitment at all levels of the health care system, as well as supportive health policies;
- ▶ working strategically to increase policy makers' awareness of and support for effective cervical cancer prevention policies and programs;
- ▶ educating at-risk women about cervical cancer and involving potential clients and the community in program planning to ensure that client concerns and cultural constraints are addressed;
- ▶ coordinating/integrating cervical cancer prevention efforts with other services and/or programs;
- ▶ providing initial and refresher training for key personnel, including non-physicians, cytologists, and others; and
- ▶ developing adequate information systems and quality-control protocols to facilitate program monitoring and evaluation.

Contact information for the managers of each program or project is provided at the end of each profile so that readers may directly request additional information about these various efforts.



COLOMBIA: Activities to Prevent Cervical Cancer During Health Care Reform

Health care reform in Colombia has brought about marked improvements in some aspects of women's health. Yet, cervical cancer remains a serious health problem throughout the country, despite efforts to make screening more accessible. National health care reform has introduced an additional layer of complexity to the provision of adequate cervical cancer prevention services.

A 1999 study found that cervical cancer was the leading cause of cancer deaths among Colombian women. An estimated 32 out of 100,000 women develop cervical cancer. Further, data suggest that the mortality rate from cervical cancer has not decreased since the early 1960s, and even may have increased slightly.

Program Description

The Colombian public health system, private organizations such as PRO-FAMILIA, and the Colombian National League Against Cancer have been offering Pap smear screening since the mid-1970s. Yet, as described above, these efforts did not seem to have an impact on cervical cancer morbidity and mortality. In 1990, a five-year, nationwide cervical cancer control program was initiated with the goal of reducing the incidence of invasive cervical cancer by 25 percent. The three main program objectives were to:

- ▶ provide Pap smears to 60 to 90 percent of women aged 25 to 69 within a three-year period, with special emphasis on reaching women of low socioeconomic status;
- ▶ provide follow-up care to 90 percent of all women obtaining Pap smears through the program;
- ▶ establish reference centers for diagnosis and treatment of women with precancerous lesions.

The program was integrated into existing health services and resulted in the training of more than 4,000 nurses, 39 gynecologists, and 36 pathologists. The program also purchased supplies and equipment, and implemented extensive community information, education, and communication (IEC) strategies aimed at educating communities about cervical cancer. These strategies included workshops involving local health services and influential women in the community. The program also worked to centralize cytology services and standardize protocols.

During the middle stage of the project, the new government recognized the shortcomings of the centralized national health care system and approved legislation to create the New Colombian Social Security System. This system, which is financed through employee contributions and government subsidy, gives local health authorities the responsibility for improving their infrastructure for providing cervical cancer prevention services. In addition, the legislation provided financial mechanisms to support these activities.



The decentralization of health care was intended to strengthen cervical cancer prevention efforts at the local level and encourage creation of efficient network services and surveillance systems. The deterioration of political and social conditions in Colombia, however, has presented considerable challenges to providing high-quality prevention services. The most recent data indicate that, five years after the beginning of this program, cervical cancer incidence and mortality rates remained unchanged.

Program Challenges

- ▶ It was difficult to clarify roles and responsibilities during the transition to decentralized health care. During the legal transition period in 1993, confusion arose regarding which new health divisions were responsible for providing education and screening services, resulting in an initial decrease of coverage. The development of more effective government financial mechanisms appears to be resolving this challenge.
- ▶ Programs experienced pressure to balance quality of care with the need to recuperate costs. Implementation of health care reform highlighted the tension between provision of cost-effective services and broad access to quality services.
- ▶ The lack of an effective information system made it difficult to evaluate the impact of the program on screening coverage, and, ultimately, on mortality and morbidity.
- ▶ Facilities lacked an adequate number of trained cytologists. Although women's knowledge of Pap screening is high, poor municipalities lacked trained cytologists to provide services.

Implications for Other Programs

- ▶ Decentralization or other types of governmental changes can pose serious challenges to maintaining high quality and continuity of health care. Roles, responsibilities, and decision-making authority between new or reorganized health structures must be clearly established and effectively communicated to ensure that services are not interrupted or diminished.
- ▶ It is crucial to develop an effective information system that allows regular evaluation of program activities and achievements. This evaluation can help to identify program successes and areas in need of improvement.
- ▶ Bottlenecks to program implementation should be identified at the start. In the Colombian program, the shortage of cytotechnicians was a key barrier to meeting program goals. In addition, the growing demand from women asking for Pap smears put pressure on the system to train more cytologists. In most countries, developing systems to ensure the growing availability of cytotechnicians is essential.

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COSTA RICA: Sustaining Participation Rates in a High-Incidence Region

Guanacaste is a rural province in northwest Costa Rica. The estimated total population of Guanacaste is 240,000 inhabitants, which accounts for approximately eight percent of the total Costa Rican population. General mortality in the region in 1990 was fairly low—about 3.7 per 1,000 inhabitants. Infant mortality was moderate at 14.6 per 1,000 live births, and life expectancy was 73.6 years.

Despite the existence of a national cervical cancer screening and treatment program, however, Guanacaste reported consistently high rates of invasive cervical cancer. During the five-year period from 1988 to 1992, incidence rates of invasive cervical cancer ranged from 24 to 45 per 100,000 women. This is higher than average in Costa Rica and at least four times higher than comparable rates in the United States. The main difference between high- and low-incidence areas in Costa Rica may be related more to varying prevalence of risk factors than to the intensity of screening.

Program Description

In an attempt to better understand why cervical cancer incidence in Guanacaste has remained high despite availability of screening and treatment, the Costa Rican Foundation for Education in Medical Sciences—a part of the Bureau of Social Security of Costa Rica (CCSS)—is implementing a nine-year study that will be completed in late 2001. The purpose of the study is to better understand the role of HPV infection and its cofactors in the etiology of high-grade cervical neoplasia, and also to evaluate new cervical cancer screening technologies. The study is being carried out in collaboration with (and with funding from) the U.S. National Cancer Institute.

The study began in 1992 with the enrollment of over 10,000 women. All sexually active women (identified through a questionnaire) had a pelvic exam, visual inspection of the cervix, and a conventional Pap smear. In addition, three new cervical cancer screening technologies were used: (1) liquid-based monolayer cytology using ThinPrep®; (2) detection of HPV DNA with the Hybrid Capture I HPV test; and (3) cervicography. Women with abnormalities were referred for colposcopy where all visible lesions were biopsied and treated according to local protocols.

Since the enrollment phase, women have been followed at different intervals. Women with low-grade cervical lesions are examined every six months. Women with less severe abnormalities in any of the screening tests, those who reported five or more sexual partners, those with a positive HPV test, and a subset of the remaining women are re-screened annually. From women not included in these activities, the program randomly selected nearly 60 percent for a new screening visit at the fifth or sixth anniversary of enrollment. At any time in the study, women with high-grade dysplasia in any of the screening tests were referred to the CCSS for proper treatment and removed from the study.



Participation rates have been above 93 percent for all components of the study including interviews, exams, and biological sample collection. Follow-up participation rates have remained over 90 percent, due in large part to the available study resources. These resources have allowed personal visits to women who need follow-up care as well as an “open house” policy allowing participants to obtain convenient appointment dates (and travel expenses to the appointment, if necessary). Also, study personnel have been specially trained to provide sensitive, high-quality care, and they have acquired great expertise in the procedures involved. These services will continue until all women have completed seven years of follow-up.

Efforts are under way to use the results of this study to develop national screening policy recommendations, as well as recommendations for management of precancerous conditions. Results of the enrollment phase of the study have provided useful input for the reorganization of the national screening program. Findings from a detailed cost-benefit analysis currently under way will guide the development of program recommendations.

Program Challenges

- ▶ The cost of maintaining the number of full-time staff necessary to achieve high follow-up rates is high.
- ▶ It has been difficult to ensure use of standard protocols for colposcopic examination and associated histological follow-up.

Implications for Other Programs

- ▶ It is possible to achieve high participation in cervical cancer screening programs and necessary follow-up through personal attention to patients, flexible clinic schedules, and allocation of resources for follow-up.
- ▶ Results from well-designed research efforts can be strategically used to inform the development of national policies.

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CUBA: Using Research to Guide Screening Recommendations

Cuba is the largest island in the West Indies and has more than 11 million inhabitants, with about 2 million living in the capital city of Havana. While the country's fertile soil, abundant sugar, and tobacco production has long contributed to Cuba's position as the wealthiest Caribbean country, Cuba has experienced significant political and economic hardship during recent decades, and particularly during the last decade.

Cervical cancer is a moderate problem in Cuba, with an estimated age-standardized incidence rate of 9 cases per 100,000 women in 1996. Age-specific incidence rates are 5 per 100,000 women aged 20 to 24, 20 per 100,000 women aged 25 to 29, 43 per 100,000 women aged 40 to 44, and 50 per 100,000 women aged 45 to 49. Cervical cancer is the fourth most common type of cancer among women, and the tenth most common cause of cancer deaths among the general population.

Since 1968, Cuba's national health guidelines recommended screening women every two years starting at age 20. In 1986, the Cuban National Cancer Control Program (the technical adviser to the Ministry of Public Health) recognized that, while a diagnosis of dysplasia was not uncommon among women younger than 30 years, most of these cases regressed and treatment was not required. Women older than 35 were at a much higher risk of developing cervical cancer. Based on this information, the Cuban National Cancer Control Program recommended that when programs are only able to screen a woman once in her lifetime, they should screen her at age 35 or older. While this recommendation reached health care providers and the public, the Ministry of Public Health did not formally adopt the recommendations. Data from national cervical cancer prevention evaluations in 1993 and 1996 indicated that high-risk women still were not being adequately reached by screening programs. In fact, fewer than 40 percent of women aged 40 and older were being screened.

In 1997, the Cuban National Cancer Control Program moved to convince the Ministry of Public Health to officially change its screening recommendations. The Cuban National Cancer Control Program compiled current research and presented a strong case to policy makers and clinicians regarding the most recent findings related to screening age and frequency. The organization successfully persuaded policy makers and clinicians to support increasing the recommended age of screening to 25 years and to decrease screening frequency to every three years. Recognizing that providing high-quality tests is essential from both an economic and a service-provision standpoint, the Cuban National Cancer Control Program also gained support for providing ongoing clinical and laboratory training. The new recommendations include periodic evaluation of all aspects of service provision and modification of screening and treatment recommendations accordingly.

Results from national cervical cancer prevention efforts have been impressive. In 1982, 21 percent of all cancers discovered were Stage I,



compared to 40 percent in 1996. Stage IV disease decreased from 15 percent in 1982 to three percent in 1996. Seventy percent of discovered cases today are Stage 0 and I.

Program Challenges

- ▶ Long-held beliefs about who is most at risk of cervical cancer and how frequently screening should take place were difficult to overcome. The Cuban National Cancer Control Program made sound recommendations based upon solid research, which helped overcome these barriers.
- ▶ Cuba suffered economic hardship in the 1990s that interfered with the prevention effort's ability to process cytology samples in a timely manner.
- ▶ Cultural barriers to women obtaining pelvic exams had to be overcome. To ensure adequate screening coverage at the decreased screening frequency rate, the program implemented extensive outreach and community mobilization efforts.

Implications for Other Programs

- ▶ Research results are essential to the development of sound cervical cancer prevention policies and guidelines. Research can help guide the establishment of new policies or the modification of existing policies, resulting in significant improvements in a program's effectiveness.
- ▶ An ongoing commitment to screening quality and coverage is key to implementing effective cervical cancer prevention efforts. Programs should ensure that they are providing adequate coverage of women in the target population prior to reducing screening intervals.

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SOUTH AFRICA: One Organization's Efforts to Create Policy Change

Cervical cancer is the most common cancer among African women in South Africa, comprising 30 percent of all cancers. The disease is the fourth most common cancer among white South African women.

Approximately 76 out of 100,000 women aged 35 to 64 are estimated to have cervical cancer, and one in 41 women will develop cervical cancer in her lifetime. Some 5,000 new cases are reported annually, nearly 90 percent of which occur among women over 35 years of age; 1,500 deaths from cervical cancer are reported annually.

To date, South Africa has not had a great deal of success in implementing effective cervical cancer prevention efforts. Since the 1970s, various policies have been developed in attempts to address cervical cancer, but they generally have been ineffective. In 1993, researchers from the Women's Health Project (WHP) at the University of Witwatersrand in Johannesburg recognized this and reviewed the cost-effectiveness of various screening assumptions, including screening interval. A summary of their findings was presented in a policy paper titled *Toward a National Screening Policy for Cancer of the Cervix in South Africa*, which concluded that a policy aimed at screening either 100 percent or 60 percent of all women over age 20 every five years would be *at least as cost-effective* as the then-current policy of treating women without an organized screening program. The paper concluded that the use of specialists to perform Pap smears is neither practical nor cost-effective, and that South African guidelines should recommend screening all women once in the ensuing five years.

Working for Policy Change

WHP presented their findings at a meeting of key stakeholders to build consensus on the development of effective cervical cancer prevention guidelines. At this meeting, research findings and women's perspectives were assessed in relation to available resources, and a consensus was established supporting a "three smears in a lifetime" proposal. The legitimacy of this policy proposal was strengthened by the support of a broader range of stakeholders. The policy recommendation was then presented at the 1994 Women's Health Conference, where it became one of 13 recommendations to be approved, published, and highlighted through press briefings and distribution of information, education, and communication materials. WHP also lobbied the Parliamentary Select Committee on Health as well as the national Director General for Health, who supported this policy.

The WHP had demonstrated its commitment to meeting the individual needs of women through its longstanding work with women in a variety of health projects. WHP involved women throughout the process of researching and planning cervical cancer prevention recommendations and lobbied for national policy change. In 1997, WHP was appointed to the National Cancer Control Advisory Committee. Shortly thereafter, the



full proposal for a National Cancer Control Strategy was presented to the Department of Health and, after two years of internal debate, the cervical cancer prevention recommendations were adopted.

From Policy to Implementation

WHP is now engaged in various activities to promote implementation of the new cervical cancer prevention policy. In conjunction with one province in South Africa, the group is evaluating pilot efforts to implement policies, and will advise on how to extend cervical screening services. In conjunction with other non-governmental organizations, and in partnership with health services, WHP is extending existing primary health care services to include cervical screening. WHP also is working with the National Department of Health to set in place the requirements (including uniform cytology reporting) for a national cervical cancer screening program.

Program Challenges

- ▶ Policy change requires financial commitment. Required budgetary allocations must accompany the introduction of new policies.
- ▶ Many complex factors (e.g., political, interpersonal, economic) can interfere with the ability to bring about policy change.

Implications for Other Programs

- ▶ Familiarity with and responsiveness to women's needs related to cervical cancer prevention is key to informing effective policy development. Knowing about women's unique concerns as they relate to cervical cancer provides legitimacy and context to policy recommendations.
- ▶ Realistic proposals must take economic considerations into account, but they should not be the sole determinant of policy development.
- ▶ Collaborating with other respected organizations can strengthen an advocacy effort by combining talents and resources, and it also can help raise visibility and credibility of efforts to influence policies.

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Based in part on Klugman, B. "Responding to Demands, Initiating Policy: The Story of the South African Women's Health Project." In Turshen, M. (ed.) *Women's Health, Africa*. World Press Inc., USA (forthcoming).

VIET NAM: Establishing a Pap Smear Screening Program in Viet Nam

Cervical cancer is the leading cause of cancer-related deaths among women in the Socialist Republic of Viet Nam. Until recently, Viet Nam was one of many developing countries in which Pap smear screening programs were virtually nonexistent. Because of the widespread belief that cytology screening programs would be too expensive to undertake on a wide scale in developing countries, Vietnamese and international health authorities were doubtful that sustainable Pap smear screening programs could be implemented in Viet Nam. This summary describes efforts to establish such a program in Viet Nam.

Program Description

The Viet/American Cervical Cancer Prevention Project, initiated in 1993 by physicians in Viet Nam and the United States, supports the development of a comprehensive, cost-effective cervical cancer prevention program in Viet Nam. The organization completed a cost-effectiveness analysis in 1999 that estimated that building a nationwide Pap screening program in Viet Nam (based on five-year intervals between screenings) would average less than US\$150,000 (1999 constant-value) annually during the ten years assumed necessary to develop the program. This figure includes costs for salaries, disposable supplies, equipment, clinic space, laboratory space, and overhead related to Pap smear screening and preventive treatment. It does not include costs of training by international consultants for community mobilization, cytology, or treatment. The estimate also excludes costs associated with the treatment and care of women with invasive cervical cancer. (Women in Viet Nam with invasive cervical cancer currently are treated with surgery and radiation therapy.)

Annual program maintenance costs were estimated to average less than US\$0.092 per woman in the target screening population (women 30 to 55 years of age), an amount that appears affordable for the 1999 average per-capita income of US\$300. At this level of investment, the Viet/American Cervical Cancer Prevention Project estimated that cervical cancer incidence and mortality in Viet Nam would be reduced by 37 percent with participation by 60 percent of women in the target screening population, and by 58 percent with participation of 100 percent of women in the target screening population.

In 1999, under the auspices of the Ho Chi Minh City Department of Health Services, the Ho Chi Minh City Cancer Center, the Ho Chi Minh City Department of Maternal and Child Health Services, and the Binh Thanh District Community Health Center, population-based Pap smear screening was instituted in Ho Chi Minh City at an initial screening rate of 150 women per day. Women with Pap smear diagnoses of atypical glandular cells of uncertain significance, high-grade squamous intraepithelial lesions, or carcinoma are referred for colposcopy. Women with biopsy-confirmed high-grade cervical dysplasia are treated with loop



electrosurgical excision procedure. Women with invasive disease are referred out of the program for appropriate staging, treatment, and follow-up care. Smaller-scale programs also have been established in Hanoi, Hue, and Danang, and will be scaled up as quickly as resources permit. As Viet Nam's nationwide cervical cancer prevention program expands, the primary staffing needs will be for cytotechnologists to analyze Pap smears, and for Pap smear collectors who will work closely with a variety of community-outreach organizations. Whether those staffing requirements are attainable is not yet clear.

The Viet/American Cervical Cancer Prevention Project's goals now are to build capacity for high-quality cytology screening services in Viet Nam, and to analyze whether Viet Nam's program experiences apply to other settings.

Program Challenges

Some of the challenges to developing a successful screening program in Viet Nam include:

- ▶ developing effective community-outreach methods to maximize the level of participation among women in the target screening population;
- ▶ implementing and maintaining effective quality control and quality assurance programs, particularly in the centralized cytology laboratories;
- ▶ improving curative treatment services for women who are discovered to have invasive cervical cancer;
- ▶ maintaining excellent working relationships among diverse groups and institutions in order to ensure the success of cervical cancer prevention efforts in Viet Nam.

Implications for Other Programs

- ▶ The study results suggest that Pap smear screening programs can be developed in some settings, with a relatively low level of investment, assuming external assistance is available for training and technical assistance.
 - ▶ Results of a well-designed cost-effectiveness analysis can provide persuasive evidence that can help gain support for cervical cancer prevention activities.
 - ▶ Training of non-physician providers to provide cytologic screening services is a cost-effective strategy.

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Glossary of Terms

Acetic acid A three to five percent 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.

Adenocarcinoma A malignant neoplasm primarily arising from the glandular epithelium of the cervix. Adenocarcinoma accounts for approximately five percent of cervical cancer cases worldwide.

Automated Pap screening Computerized reading of Pap smears to identify smears with abnormal appearing features, which should then be examined by cytologists.

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

Carcinoma *in situ* (CIS) Localized cellular changes in the stratified squamous epithelium but not extending through the basement membrane into the underlying stroma. CIS is generally recognized as the precursor of invasive squamous cell cancer.

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 is categorized as CIN I, moderate cervical dysplasia as CIN II, and severe cervical dysplasia and CIS as CIN III.

Cervical crypt Openings on the surface of new cervical squamous epithelium. The outermost crypt or gland openings around the os define the outer border of the transformation zone.

Cervical stenosis A narrowing of the cervical canal.

Cervicography Technique for photographing the cervix to identify dysplasia or cancer. Photographs are then sent to a central site for evaluation.

Colposcopy Examination of the vagina and cervix using an instrument (colposcope) that magnifies vaginal and cervical tissue.

Cryotherapy Outpatient treatment that uses extremely low temperatures (lower than -60°C) to freeze and destroy abnormal tissue.

Cytology or exfoliative cytology Terms used to describe evaluation of cells (obtained by a Pap smear) for abnormalities associated with CIN and cervical cancer



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

Disability-adjusted life year (DALY) A measure of life years gained that estimates the number of years of healthy life lost due to both premature morbidity and mortality, using a set of age and disability estimated weights.

Downstaging Visual inspection without use of acetic acid or magnification to identify early cancer.

Dysplasia of the uterine cervix Epithelial abnormality of the cervical squamous epithelium. Other terms used to describe this disease process are cervical intraepithelial neoplasia (CIN) or squamous intraepithelial lesion (SIL).

Ectocervix The external portion of the uterine cervix and os.

Electrocautery (electrocoagulation) The process of using an electrically heated metal probe to destroy abnormal tissue.

Endocervix The mucous membrane of the cervical canal.

High-grade squamous intraepithelial lesion (HSIL) A term used in the Bethesda Disease Classification system to describe moderate to severe cervical cellular abnormalities that have a higher likelihood of progressing to cancer than LSIL. More than one-third of the depth of the cervical epithelium contains dysplastic cells in a woman with HSIL.

Human papillomavirus (HPV) A sexually transmitted agent that infects the cells of the cervix and can slowly cause cellular changes that result in cervical cancer.

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 (600 kHz).

Low-grade squamous intraepithelial lesion (LSIL) A term used in the Bethesda Disease Classification system to describe mild cervical abnormalities that are present only in the surface layer of cells. One-third or less of the epithelium contains dysplastic cells in a woman with LSIL, and LSIL is likely to regress to normal.

Lugol's solution An iodine solution that can be used instead of acetic acid when performing visual screening. The solution stains normal cervical cells brown, leaving the abnormal cells with a yellow or unstained appearance.

Microinvasion Presence of cancer in the stromal tissue immediately adjacent to the epithelium, usually to a depth of no more than a few millimeters; the earliest stage of malignant neoplastic invasion.

Os The opening or entrance to the endocervical canal.

Pap smear A test in which a smear of vaginal or cervical secretion is examined for exfoliated cells to detect abnormal cells.

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

Self-collection The process in which a woman obtains her own specimen for testing (e.g., a vaginal swab, vulvar swab, or urine sample) rather than a health care provider doing so.

Sensitivity A test characteristic that describes the proportion of people with a given condition who are correctly classified as test positive. The sensitivity of a test indicates the degree to which the test accurately identifies the condition.

Specificity A test characteristic that describes the proportion of people without a given condition who are correctly classified as test negative. The specificity of a test indicates the degree to which the test reacts only to a specific condition.

Speculoscopy Visual inspection of the cervix using a chemiluminescent light source and magnification.

Squamocolumnar junction The point at which columnar cells meet ectocervical squamous cells on the cervix. This junction marks the furthest extent of the transformation zone towards or, in the case of postmenopausal women, into the cervical canal.

Squamous cell A thin, flat cell found in the tissue that forms the surface of the skin, the lining of the upper passages of the respiratory and digestive tracts, and the vagina and outer cervix.

Transformation zone (T-zone) The area of the ectocervix demarcated by the outermost cervical crypt openings. The T-zone extends to the squamocolumnar junction, which is usually near the entrance to the endocervical canal. Cervical cancer usually originates in the T-zone.

Visual inspection with acetic acid (VIA) Speculum examination of the cervix with a three to five percent diluted acetic acid wash (without magnification) to screen for cervical dysplasia. VIA is sometimes referred to as direct visual inspection or unaided visual inspection.

Visual inspection with acetic acid and magnification (VIAM) Speculum examination of the cervix using acetic acid and a portable, low-power magnification device (as opposed to a colposcope) to facilitate dysplasia screening (and/or possibly to guide biopsy and outpatient treatment of pre-invasive lesions).



Annotated Bibliography

General

- Abwao S, Greene P, Sanghvi H, et al. (eds.). *Prevention and Control of Cervical Cancer in the East and Southern Africa Region*. Summary of proceedings of regional meeting held in Nairobi, Kenya, 29 March to 1 April, 1998. [Available online at http://www.rho.org/meeting_report_Kenya.pdf].

The document provides summaries of the technical papers, the subsequent discussion sessions, and the country profiles. Action plans developed by the 15 country teams that participated, an overview of available funding and technical resources, and the consensus recommendations from the 3-day meeting are included.

- Bishop A, Wells E, Sherris J, et al. Cervical cancer: evolving prevention strategies for developing countries. *Reproductive Health Matters* (6):60–71 (November 1995).

This article makes a strong case for rational, public health approaches to the prevention and treatment of cervical cancer, focusing on practical strategies that can be used in developing countries. The authors note that scarce resources, limited infrastructure, and competing health priorities have prevented most developing-country health systems from implementing successful programs. Three approaches to cervical cancer screening are suggested for programs with limited resources: (1) screening women aged 30–35 or older; (2) screening women relatively infrequently; and (3) considering alternate approaches to conventional screening techniques. For women identified as needing treatment, the authors discuss outpatient approaches, such as cryotherapy and loop electrosurgical excision procedure (LEEP), that can effectively treat most pre-cancerous lesions and reduce the number of clinic visits. The authors recommend coordinating efforts to achieve broader screening and treatment coverage, and they note that introducing alternate approaches requires policy changes, for which community input is essential.

- Fahey MT, Irwig L, Macaskill P. Meta-analysis of Pap test accuracy. *American Journal of Epidemiology* 141:680–689 (April 1995).

This meta-analysis examined 62 studies published by August 1992 that compared Papanicolaou (Pap) test results with histology. Data from 59 of the studies were used to assess the accuracy of the Pap test. Estimates of Pap smear sensitivity ranged from 11 percent to 99 percent and estimates of specificity ranged from 14 percent to 97 percent. The authors found that a specificity in the 90–95 percent range on a Pap test corresponds to a sensitivity in the 20–35 percent range. While many studies had methodological weaknesses, the authors concluded that an increase in sensitivity almost always corresponded to a decrease in specificity or vice versa and that the Pap cannot achieve concurrently high sensitivity and specificity. They recommended that future studies follow methodological standards for diagnostic test evaluation more closely.

- Fahs MC, Plichta SB, Mandelblatt JS. Cost-effective policies for cervical cancer screening: an international review. *Pharmacoeconomics* 3: 211–230 (March 1996).

This international review of the cervical cancer literature focuses on studies that address the cost-effectiveness of cervical cancer screening. The authors conclude that centrally organized screening programs implemented by the public sector are the most cost-effective type of program. Many programs are not effective (and have limited impact) due to over-screening of younger, affluent, lower-risk women, and under-screening of older, less affluent, and minority women. The authors also conclude that it is more cost-effective to begin screening women between the ages of 25 and 35. The appropriate cost-effective age to end screening is less clear. The authors found that the interval of screening with the best balance between cost and life



years saved was between 3 and 5 years. However, when repeat screening is not feasible, even one test per lifetime can significantly reduce mortality of a population. Efforts to reach unscreened women are particularly important as this population is typically at higher risk of developing cervical cancer. The authors noted three factors that can heavily impact the cost-effectiveness of a screening program: proportion of women screened by the program, quality of the Pap smear, and the cost of the Pap smear.

- ▶ Hernandez-Avila M, Lazcano-Ponce EC, de Ruiz PA, et al. Evaluation of the cervical cancer screening programme in Mexico: a population-based case-control study. *International Journal of Epidemiology* 27:1–7 (June 1998).

This case-control study evaluated the preventative effect of the cervical cancer screening program in Mexico City between September 1990 and December 1992. The authors selected 233 cases of cancer *in situ* and 397 cases of invasive cancer from women attending the gynecological clinics at six hospitals in Mexico City for histological confirmation following cytological diagnosis of cervical neoplasm. The 1,003 controls were an age-stratified random sample of residents of the Mexico City metropolitan area. When interviewed about their Pap smear history, cases were asked about the 12-month period before their diagnosis and controls were asked about the 12-month period before their interview. The authors found that cervical cancer screening had a protective effect in relation to invasive cervical cancer. Women who had a history of a Pap smear, who did not seek screening due to gynecological symptoms, and who had received their Pap results had a 2.63 times lower risk of developing invasive cervical cancer (OR = 0.38; 95 percent CI: 0.28–0.52). No protective effect was found for *in situ* cancer.

- ▶ Jones SB. Cancer in the developing world: a call to action. *British Medical Journal* 319:505–508 (August 1999).

This article synthesizes several themes from a 1999 WHO conference on “Cancer Strategies for the New Millennium.” The author uses charts to characterize global cancer incidence by country, cancer type, incidence, and mortality rates. He notes that developing countries experience a disproportionate disease impact. For cancers with a known cause, such as cervical cancer, he recommends pursuing affordable approaches to prevention combined with development of new technologies appropriate to low-resource settings. The author also notes that clinical trials are underway for two prophylactic HPV vaccines and a therapeutic vaccine that stimulates cell immunity to viral proteins E6 and E7. Development of vaccines and low-technology approaches to detection offer the best promise for controlling cervical cancer in the developing world.

- ▶ Parkin DM, Pisani P, Ferlay J. Estimates of the worldwide incidence of 25 major cancers in 1990. *International Journal of Cancer* 80:827–841 (March 1999).

This comprehensive review of the worldwide burden of cancer estimates the annual incidence rates (crude and age-standardized) and numbers of new cases of 25 different cancers in 23 areas of the world as of 1990. In 1990, more than 371,000 new cases of cervical cancer were identified among women worldwide. Nearly 290,000 of these cases are estimated to have occurred in developing countries. The highest age-standardized incidence of cervical cancer in 1990 was reported in southern Africa, Central America, and Melanesia, where the rates were over 40 per 100,000 women. Rates of more than 30 per 100,000 were reported in eastern Africa, the Caribbean, and tropical South America.

- ▶ Parkin DM, Sankaranarayanan R. Prevention of cervical cancer in developing countries. *Thai Journal of Obstetrics and Gynaecology*. 11(Suppl 1):3–20 (August 1999).

This article provides a review of methods available for preventing cervical cancer in developing countries. It describes the acceptance of the human papillomavirus (HPV) as the most important etiological agent and the difficulty involved in primary prevention of HPV. It describes the methods and difficulties involved with screening/early detection of cervical cancer through health education strategies and

downstaging (which the authors conclude is not a cost-effective procedure). It also describes screening for pre-invasive disease through Pap smears, its effectiveness and difficulties in the organization of screening programs in developing countries, and visual inspection using acetic acid, which the authors report to be as sensitive as Pap tests, though generally less specific. Finally, the authors review testing for human papillomavirus, the value of which they conclude will have to await the development of tests that can be applied rapidly and relatively cheaply.

- ▶ PATH (Program for Appropriate Technology in Health). Preventing cervical cancer in low-resource settings. *Outlook* 18(1):1–8 (September 2000). (<http://www.path.org/outlook/>)

This issue of *Outlook* provides updated information that describes the problem of cervical cancer in developing countries, the basic principles of cervical cancer control, screening and treatment options, and more.

- ▶ Pisani P, Parkin DM, Bray F, et al. Estimates of the worldwide mortality from 25 cancers in 1990. *International Journal of Cancer* 83:18–29 (September 1999).

This article presents worldwide estimates of annual mortality from all cancers and for 25 specific cancer sites from 1990. Crude and age-standardized mortality rates and numbers of deaths were computed for 23 geographical areas. The study estimated the global number of deaths from cervical cancer in 1990 at 190,000. Eighty percent of these deaths occurred in developing countries, where cervical cancer remains the largest cause of cancer death among women (followed closely by breast and stomach cancers). Some 40 percent of the estimated 148,500 cervical cancer deaths in developing countries occur in south central Asia, a region that includes India, Pakistan, Bangladesh, Afghanistan, and Iran, among others.

- ▶ Ponten J, Adami HO, Bergstrom R, et al. Strategies for global control of cervical cancer. *International Journal of Cancer* 60:1–26 (January 1995).

This extensive review summarizes data from around the world on cervical cancer. Topics addressed include the tumor biology and natural history of cervical cancer, etiology of the disease (including impact of HPV), strategies for reducing mortality without screening (including focusing on treatment of early-stage disease), and cytological screening. The authors conclude that the natural history and disease patterns of cervical cancer are similar throughout the world. They argue that HPV testing as a strategy for cervical cancer control remains experimental, and that providing treatment for early-stage disease, where feasible, can help reduce mortality. They discuss the challenges of ensuring maximum coverage with cytological screening without wasting resources on frequent testing of women at lower risk.

- ▶ Rogo KO, Omany J, Onyango JN, et al. Carcinoma of the cervix in the African setting. *International Journal of Gynecology and Obstetrics* 33:249–255 (November 1990).

Data on 1,210 patients treated in Kenya between 1974 and 1979 formed the basis for this study. The authors compared Kenyan data to statistics for cervical cancer incidence in developed countries and found Kenyan patients to be both younger (mean age 42 versus 54 years) and more likely to present with late-stage disease (55 percent Stage 3 compared to 25 percent). A high loss to follow-up and limited treatment resources contributed to poor survival outcomes. The authors cited some possible additional contributors to high mortality, including tumor bulk, nutrition, and individual immunity. They concluded that further study of the differences in findings is needed and noted that cytologic screening is less likely to succeed in developing-country settings.

- ▶ Sherris JD. Cervical cancer prevention: a strategic opportunity to improve women's reproductive health. *International Family Planning Perspectives* 25 (Suppl):556–557 (1999).

This article summarizes the issues associated with preventing cervical cancer in developing countries and the steps needed to strengthen prevention efforts. The article also reports the initial findings of the Cervical Cancer Consultative Group, which, in 1997, identified a list of ten questions felt to be of highest



priority in guiding strategy development for preventing cervical cancer in low-resource settings. The author concludes by stating that activities focused on answering these questions will contribute to preventing some of the 200,000 deaths from cervical cancer that occur each year in developing countries.

Epidemiology and natural history of cervical cancer

- ▶ Bosch FX, Manos MM, Muñoz N, et al. Prevalence of human papillomavirus in cervical cancer: a worldwide perspective. *Journal of the National Cancer Institute* 87(11):796–802 (June 1995).

This study confirmed an extensive, global association between human papillomavirus (HPV) infection and cervical cancer. The study had two objectives: to determine whether the association between cervical cancer and HPV was consistent worldwide, and to investigate geographic variation in the distribution of over 20 types of cancer-associated HPV. Investigators collected more than 1,000 specimens from cervical cancer patients in 22 countries with high recorded cervical cancer incidence. HPV DNA was detected in 93 percent of the tumors. Although HPV types differed somewhat by geographic region, HPV 16 was present in 50 percent of all specimens. The second most predominant type, HPV 18, was present in 14 percent of all specimens.

- ▶ Brinton LA. Epidemiology of cervical cancer—an overview. In: *The Epidemiology of Cervical Cancer and Human Papillomavirus*. Muñoz N et al., eds. Lyon: International Agency for Research on Cancer. Scientific Publication No. 119:3–23 (1992).

Numerous studies of cervical cancer epidemiology are reviewed in this 1992 publication that examines factors other than HPV associated with cervical cancer. In tables summarizing findings from multiple studies, the author demonstrates the strong association between cervical cancer risk and number of sexual partners and age at first intercourse (which may be markers for HPV risk). She then examines epidemiologic evidence for contributory or interactive roles of other suspected risk factors, such as the relationship between HPV and other sexually transmitted diseases. She reviews study findings for more speculative risk factors also, particularly cigarette smoking and use of oral contraceptives. She concludes by noting that disease risk may be affected by changes in recent times including the tendency for women to initiate sexual intercourse at earlier ages, increased exposure by younger women to cigarette smoking and oral contraceptives, and changes in the sexual behavior of their male partners.

- ▶ Ho GY, Burk RD, Klein S, et al. Persistent genital human papillomavirus infection as a risk factor for persistent cervical dysplasia. *Journal of the National Cancer Institute* 87(18):1365–1371 (September 1995).

This study analyzed the factors that determine cervical intraepithelial neoplasia (CIN) persistence or regression and found that persistent CIN is linked to chronic HPV infection, particularly HPV infection with a high viral load. The study enrolled 100 U.S. women diagnosed with CIN II. About one-third of the women experienced regression; the remaining 70 were evaluated at 3-month intervals for 15 months. Women who had chronic HPV infection had a fourfold higher risk for persistent CIN than those without HPV. The authors noted that repeated testing for HPV infection may help clinicians to differentiate between women who are likely to experience spontaneous regression and women whose lesions will persist or progress.

- ▶ Holowaty P, Miller AB, Rohan T, et al. Natural history of dysplasia of the uterine cervix. *Journal of the National Cancer Institute* 91(3):252–258 (February 1999).

This article reviews a historical cohort of women in Toronto, Canada, whose Pap smear histories were recorded at a major cytopathology laboratory. These authors studied progression and regression of cervical dysplasia in this cohort during the period 1962 to 1980. The cohort size and time period covered by the analysis distinguishes this study from others, which tend to be much smaller and of shorter duration (the article includes a useful summary table illustrating the results of previous studies). The

results of the study confirm those of smaller studies: the risk of mild dysplasia progressing to cervical cancer *in situ* (CIS) is small—about 1 percent per year. The study results support the recommendation of following patients with mild dysplasia with periodic cytology rather than immediate referral to colposcopy. The study also found that the risk of moderate dysplasia progressing to CIS is intermediate between the risks associated with mild and severe dysplasia—16 percent in 2 years.

- ▶ Lancaster EJ, Banach L, Lekalakala T, et al. Carcinoma of the uterine cervix: results of Ka-Ngwane screening programme and comparison between the results obtained from urban and other unscreened rural communities. *East African Medical Journal* 76(2):101–104 (February 1999).

This study revived data from 10,000 consecutive Pap smears from women attending Ob/Gyn clinics in Ka-Ngwane, Pretoria (urban area), and Transkei (rural area) in South Africa. The study found positive Pap smears (mild dysplasia through cancer) in 3 percent of patients in Ka-Ngwane, 5 percent in Greater Pretoria, and more than 6 percent in Transkei. Of the positive cases, cervical cancer accounted for 12 percent of cases in Ka-Ngwane, 5 percent in Pretoria, and 26 percent in Transkei. The majority of positive cases were younger than 41 years (the article did not indicate the age distribution of all 10,000 patients). The authors concluded that there is a high incidence of dysplasia and cervical cancer in previously unscreened populations in South Africa, and that there is an urgent need to develop education and screening programs in the region. The authors also noted that a significant proportion of cervical cancer cases occurred in women below 40 years of age.

- ▶ Nasiell K, Roger V, Nasiell M. Behavior of mild cervical dysplasia during long-term follow-up. *Obstetrics and Gynecology* 67(5):665–669 (May 1986).

This Swedish study evaluated follow-up data from 555 women diagnosed with mild cervical dysplasia between 1962 and 1983. Of these mild dysplasias, 62 percent regressed, 22 percent persisted, and 16 percent progressed. Patients with regression were followed for an average of 39 months; patients with persistent dysplasia were followed for an average of 52 months. Where mild dysplasia progressed to more severe disease, the average time to progression was 48 months. Two cases of invasive cancer occurred in women lost to follow-up for several years during the study. The invasive cancers were diagnosed at 79 and 125 months after initial diagnosis of mild dysplasia. This study is often cited as evidence that a significant proportion of mild dysplasia does not progress to more severe disease. At the same time, the study results highlight the importance of regular follow-up of women diagnosed with mild dysplasia, given the potential of progression in more than a sixth of cases.

- ▶ Robles S, White F, Peruga A. Trends in cervical cancer mortality in the Americas. *Bulletin of PAHO* 30(4):290–301 (December 1996).

This article provides an assessment of cervical cancer mortality trends in the Americas using data from the Pan American Health Organization. While cervical cancer in Canada and the United States has declined steadily over the past 30 years (to about 1.4 and 1.7 deaths per 100,000 women, respectively, in 1990), most Latin American and Caribbean countries with available data have experienced constant or increasing levels of cervical cancer mortality (generally in the range of 5 to 6 deaths per 100,000 women). The authors suggest that, while not all changes in cervical cancer mortality can be directly attributed to screening, a correlation clearly can be drawn. They suggest that screening services in Latin America have been linked to family planning and prenatal care services, and have not appropriately targeted older women with the highest risk of cervical cancer.

- ▶ Schiffman MH. New epidemiology of human papillomavirus infection and cervical neoplasia. *Journal of the National Cancer Institute* 87(18):1345–1347 (September 1995).

This article discusses the link between persistent detection of HPV DNA (especially high levels of DNA) and persistent diagnosis of CIN. A companion study by Ho, et al., in the same journal issue tracked HPV



and CIN transience versus persistence, and Schiffman notes that the findings of Ho, et al. have implications for the development of screening strategies that include HPV DNA testing. The author notes several findings and factors that complicate epidemiologic analysis: (1) HPV-negative CIN does exist, although it occurs in 10 percent or fewer cases; (2) up to 10 percent of women may develop CIN2 or CIN3 lesions initially instead of progressing from lower- to higher-grade lesions; (3) diagnostic uncertainty and the lack of a reference standard complicate interpretations of data; (4) the cervix may contain discrete lesions with separate natural histories (for example, CIN1 lesions may progress to CIN3 over time or simply emerge adjacent to CIN3 lesions).

Role of HPV tests and possible HPV vaccines in cervical cancer control

- ▶ Cuzick J. Human papillomavirus testing for primary cervical cancer screening [editorial]. *JAMA* 283(1):108–109 (January 2000).

This editorial reviewed two articles appearing in the January 5, 2000, *JAMA* issue, Schiffman, et al., and Wright, et al. The editorial noted that the two articles made important contributions to assessing use of HPV for primary screening for cervical cancer. The Schiffman article focused on performance of HPV DNA testing according to different thresholds of test positivity (a test using a 1 pg/ml cutoff for HPV positivity performed best) and according to patient age (specificity was highest for test results among older women). The Wright study evaluated results of HPV DNA testing in an unscreened population using self-collected and clinician-collected samples. While the self-collected samples resulted in lower sensitivity than the clinician-collected samples, sensitivity was higher than Pap smear testing in that setting. Specificity remained a problem, however. The author concluded that HPV DNA testing has significant potential for making cervical cancer screening available in settings where traditional approaches may not be feasible. Further study is necessary to clarify optimal approaches that will ultimately lead to reduced morbidity and mortality.

- ▶ Galloway DA. Is vaccination against human papillomavirus a possibility? *Lancet* 351:22–24 (1998).

HPV potentially is amenable to vaccination because it is not prone to mutation and has just eight genes. Animal models suggest that both prophylactic and therapeutic vaccination is feasible. To make a substantial impact on the prevalence of cervical cancer, a prophylactic vaccine must be multivalent and must generate high titers of neutralizing antibodies at the mucosal surface. Goals for a therapeutic vaccine include eliminating residual cancer, the regression of existing disease, and/or preventing the progression of low-grade disease. The scientific basis for a therapeutic vaccine is weakened by two unresolved questions: which antigen should be targeted, and what type of immune response mediates regression. Despite these and other challenges, the author concludes that the prospects for HPV vaccination are strong.

- ▶ Hernandez-Avila M, Lazcano-Ponce EC, Berumen-Campos J, et al. Human papilloma virus 16–18 infection and cervical cancer in Mexico: a case-control study. *Archives of Medical Research* 28(2):265–271 (1997).

The goal of this case-control study was to evaluate the association between HPV types 16 and 18 and cervical cancer in women living in Mexico City. One hundred forty-eight cases and 204 controls were tested for HPV types 16 and 18 using polymerase chain reaction (PCR) technique. HPV 16 was detected in 48.3 percent of 60 *in situ* cases, 48.8 percent of 88 invasive cases, and 13.2 percent in controls. HPV 18 was detected only in 6.7 percent of invasive cases. The odds ratio for HPV 16 infection in *in situ* cases was 5.17 and the odds ratio for invasive cases was 3.84. The results showed that all women with a strong positive PCR reaction had the greatest risk; the odds ratio was 38 compared to 23 and 11 of intermediate and weak PCR reactions respectively. The finding provided further evidence for the association between HPV types 16 and 18 infection and cervical cancer. The authors considered that the Pap test is still the single most effective measure in cervical cancer control.

- ▶ Hillemanns P, Kimmig R, Huttemann U, et al. Screening for cervical neoplasia by self-assessment for human papillomavirus DNA [research letter]. *Lancet* 354:1970 (December 1999).

This study evaluated the sensitivity of HPV tests on self-collected specimens and compared it with the detection rate of specimens obtained from the cervix by gynecologists. A total of 247 patients attending a German colposcopy clinic self-introduced a cytobrush into the vagina for specimen collection and were examined by gynecologists who took Pap smears and an additional cytobrush specimen. Ninety-four percent of patients reported preferring the self-sampling to sampling by a physician. HPV positive results were found by 53 percent of the patients' samples compared to 42 percent by physician-collected specimens. Both test methods had a sensitivity of 93 percent for high-grade dysplasia and invasive cervical cancer. The authors concluded that self-sampling is a reliable method of testing for HPV and may be useful in settings in which cytology is not readily available, especially if these study findings can be reproduced in larger studies.

- ▶ Lowy DR, Schiller JT. Papillomaviruses: prophylactic vaccine prospects. *Biochimica et Biophysica Acta* 1423: M1–M8 (1998).

This article concentrates on one type of potential prophylactic HPV vaccine: virus-like particles. The molecular structure and immunogenicity of viral capsids make virus-like particles a strong candidate vaccine. Studies in dogs, rabbits, and cows confirm that these particles protect against challenge with papillomavirus, probably by inducing neutralizing antibodies. However, it is not yet certain whether systemic immunization with virus-like particles will confer protection against genital mucosal HPV infections in humans. This may require a different vaccine protocol. Alternatively, non-structural proteins might be added to increase their effectiveness as vaccines; these chimeric virus-like particles might be able to eliminate early cervical lesions that escaped neutralization.

- ▶ Manos MM, Kinney WK, Hurley LB, et al. Identifying women with cervical neoplasia: using human papillomavirus DNA testing for equivocal Papanicolaou results. *Journal of the American Medical Association* 281(17):1605–1610 (May 1999).

This study, conducted in California, USA compared a newer screening method with a more traditional method to determine whether women with atypical squamous cells of undetermined significance (ASCUS) could be better served by the newer screening method. A total of 995 women with ASCUS Pap test results participated in the study. Under the new method, HPV DNA testing was conducted on 995 ASCUS specimens, and those cases found to be HPV positive were referred directly to colposcopy. The authors found that the sensitivity of this method for detecting high-grade squamous intraepithelial lesions (HSILs) was equivalent to or greater than the traditional method of taking repeat Pap smears. In addition, because this screening method uses the same specimen for both cytology and HPV testing, it reduces the number of colposcopic examinations and follow-up visits (as well as patient anxiety and loss to follow-up). The authors believed the savings achieved by fewer visits and procedures would offset the cost of implementing the HPV DNA testing.

- ▶ Schiffman M, Herrero R, Hildesheim A, et al. HPV DNA testing in cervical cancer screening: results from women in a high-risk province of Costa Rica. *JAMA* 283(1):87–93 (January 2000).

This study evaluated use of an HPV screening test to detect high-grade cervical lesions and cancer among more than 9,000 sexually active women age 18 and older in Guanacaste province, Costa Rica. In addition to HPV testing, women underwent conventional Pap smears and visual screening using cervicography. Samples also were prepared for ThinPrep cytologic analysis. The study found that HPV screening (using the Digene Hybrid Capture II test with a detection threshold of 1.0 pg/mL for 13 oncogenic HPV types) resulted in detection of 88.4 percent of high-grade cervical lesions and cancers, with a specificity of 89 percent. When results were calculated by age tertile (18 to 30, 31 to 40, and 41 and older), specificity was highest (94



percent) for older women. The percentage of lesions/cancers detected was lower (75 percent) for the original Hybrid Capture test (which has a detection threshold of 10 pg/mL for 11 oncogenic types). Overall, HPV DNA testing using the Hybrid Capture II test was more sensitive than conventional Pap testing (88.4 vs. 77.7 percent) for detection of high-grade lesions and cancers, but less specific (89 vs. 94 percent). The authors concluded that, while more data are needed on various factors that can impact the results of HPV, the method clearly has “come of age” technically and should be increasingly useful in cervical factors screening efforts.

- Walboomers JM, Jacobs MV, Manos MM, et al. Human papillomavirus is a necessary cause of invasive cervical cancer worldwide. *Journal of Pathology* 189(1):12–19 (September 1999).

In this study, researchers reexamined data from an earlier study (Bosch et al., 1995) that had confirmed a global association between HPV infection and cervical cancer by detecting HPV DNA in 93 percent of over 1,000 cervical cancer specimens collected worldwide. The reexamination of data found many HPV-positive samples that had been false-negative in the previous study due to integration events affecting L1 sequences, a possibility that had been suggested by Bosch, et al. By reanalyzing samples and excluding inadequate specimens, the current study found the worldwide HPV prevalence in cervical carcinoma to be 99.7 percent. This represents the highest percentage reported to date. The authors argue that the extreme rarity of HPV-negative cervical cancer reinforces the rationale for HPV testing in addition to, or perhaps even instead of, conventional screening methods.

- Womack SD, Chirenje ZM, Gaffikin L, et al. HPV-based cervical cancer screening in a population at high risk for HIV infection. *International Journal of Cancer* 85(2):206–210 (January 2000).

This study, involving 466 Zimbabwean women, evaluated the potential for using HPV testing to screen HIV-infected women for cervical dysplasia. Pap smears and samples for HIV and HPV testing (using Digene’s HC II test) were obtained from all women. The study found that over half of the women tested were HIV-positive. HIV positivity was associated with a twofold increase in HPV prevalence and a threefold increase in HGSIL prevalence. The sensitivity and specificity of HPV DNA testing for HGSIL were 91 percent (95% CI – 78–97%) and 41 percent (95% CI – 35–48%) for HIV-positive women; 62 (95% CI – 32–86%) and 75 percent (95% CI – 68–80%) for HIV-negative women. The negative predictive value for the test for each group was over 95 percent. The authors conclude that HPV DNA testing is not an ideal test for HGSIL in HIV-positive women because of its relatively low specificity. At the same time, they noted that since HIV-positive women infected with HPV are at high risk of cervical disease, they should be provided with regular follow-up care. The authors also note that the ultimate usefulness of HPV DNA testing as a screening test for cervical cancer must be decided based on local health priorities, policies, and capabilities.

- Wright TC Jr, Denny L, Kuhn L, et al. HPV DNA testing of self-collected vaginal samples compared with cytologic screening to detect cervical cancer. *JAMA* 283(1):81–86 (January 2000).

This study evaluated use of HPV screening tests (using self-collected and clinician-obtained samples) to detect high-grade cervical lesions and cancer among more than 1,400 previously unscreened black South African women aged 35 to 65. In addition to HPV testing, women underwent conventional Pap smears, STD testing, visual inspection of the cervix with acetic acid wash (magnified and unmagnified), and cervicography. The sensitivity of HPV DNA testing (see Schiffman, 2000 for more information about the Digene Hybrid Capture II test) of self-collected vaginal samples was 66.1 percent for detection of high-grade lesions and cancer; the false-positive rate was 17.1 percent. The sensitivity of HPV DNA testing of clinician-collected samples was 83.9 percent; the false-positive rate was 15.5 percent. In comparison, the sensitivity of conventional Pap smear (with low-grade SIL and higher cytologic abnormality classified as positive) was 60.7 percent, with a false-positive rate of 3.2 percent. In summary, HPV DNA testing using self-collected vaginal samples was less specific, but as sensitive as conventional Pap testing for detecting high-grade cervical disease in women age 35 or older (it is important to note that selfcollection occurred at

a clinic after specific instructions on how to obtain the sample). The authors concluded that HPV-DNA testing using self-collected vaginal samples holds promise for simplifying cervical cancer screening in many settings, although low specificity remains a problem. They discussed the need to assess two-stage screening protocols (for example HPV testing followed by a Pap smear or visual inspection) to improve specificity.

Primary prevention of cervical cancer

- ▶ Koutsky LA, Kiviat NB. Genital human papillomavirus. In: *Sexually Transmitted Diseases* 3rd ed. Holmes KK, et al., eds. New York: McGraw-Hill (1999).

This chapter provides a detailed overview of the issues related to genital human papillomavirus, including the definition, prevalence and incidence, geographic distribution, transmission, risk factors, clinical manifestations, management, and prevention.

- ▶ Shepherd J, Weston R, Peersman G, et al. Interventions for encouraging sexual lifestyles and behaviours intended to prevent cervical cancer (Cochrane Review). In: *The Cochrane Library*, Issue 3, 1999. Oxford: Update Software.

This meta-analysis reviews the effectiveness of health education in promoting sexual risk reduction among women in order to reduce transmission of human papillomavirus (HPV). The review included ten studies of education programs, all of which had the primary aim of preventing HIV and other STDs rather than cervical cancer. The review found that educational interventions targeting socially and economically disadvantaged women in which information provision is complemented by sexual negotiation skill development can encourage at least short-term sexual risk reduction behavior. This has the potential to reduce the transmission of HPV and, as a result, the incidence of cervical cancer.

- ▶ Wen LM, Estcourt CS, Simpson JM, et al. Risk factors for the acquisition of genital warts: are condoms protective? *Sexually Transmitted Infections* 75(5):312–316 (1999).

This study, conducted at Australia's largest STD clinic, included 977 patients with genital warts and 977 controls matched by sex and date of clinic attendance. The study goals were to determine risk factors for acquiring genital warts and to determine whether condoms offer protection against infection. Independent risk factors for genital warts were found to be younger age, greater number of lifetime sexual partners (primarily true for men) and smoking (men only). The authors noted that, although previous studies have failed to show a protective effect of condom use, this study found that consistent condom use significantly reduced the risk for both sexes of acquiring genital warts.

- ▶ World Health Organization (WHO). *Primary Prevention of Cervical Cancer*. CAN/85.1. Geneva: WHO (October 3–November 2, 1985).

A WHO consulting group met in 1985 to consider possible approaches for primary prevention of cervical cancer. Given that cervical cancer is strongly linked to early onset of sexual activity and multiple sexual partners, the WHO group recommended sex education and studies in sexual behavior, while acknowledging that behavior is difficult to change. They recommended that development of vaccines for HPV be made a high priority, together with further study of the possible contribution of smoking to cervical cancer. They noted that there is no evidence to suggest a protective effect from hygiene, male circumcision, or nutrition, and that data are inconclusive on the role of oral or injectable contraceptives. They recommended that use of barrier methods, particularly condoms, should be encouraged.



Screening: assessment of alternative approaches

- ▶ Coppleson, M. An electronic approach to the detection of precancer and cancer of the uterine cervix: a preliminary evaluation of Polarprobe. *International Journal of Gynecological Cancer* 4:79–83 (1994).

This article describes preliminary results of an electronic device for detection of cervical cancer and its precursors, known as the Polarprobe. The Polarprobe is a computerized diagnostic instrument consisting of a pen-sized probe that is inserted into the vagina and moved across the cervix. The probe is attached to a portable computer that processes electrical and optical properties of cervical tissue and compares the information with data from normal or abnormal tissue. The study established recognition algorithms from analysis of results of 106 volunteers and then tested 77 additional volunteers. When comparing Polarprobe diagnosis with concurrently obtained histologiccolposcopic diagnosis, concordance between the two was 85 percent for low-grade intraepithelial abnormalities, 90 percent for high-grade abnormalities, and 99 percent for cancer.

- ▶ Lazcano-Ponce EC, Moss S, Alonso de Ruiz P, et al. Cervical cancer screening in developing countries: why is it ineffective? The case of Mexico. *Archives of Medical Research* 30:240–250 (May–June 1999).

This evaluation of the Mexican national cervical screening program seeks to explain why the program (established in 1974) has failed to decrease cervical cancer mortality in Mexico. The authors found that the low effectiveness of screening is due primarily to issues surrounding Pap smear quality and coverage. Pap quality is low: 64 percent of a random sample of specimens lacked endocervical cells, and false-negative indices from reading centers ranged between 10 and 54 percent. Women tend to seek screening only after they are symptomatic, rather than as a preventive measure. Pap smear coverage is particularly low in rural areas (30 percent compared to 64 percent of women age 15–49 in Mexico City). Qualitative research highlighted additional difficulties, including a preference for female providers and a perception that public services are impersonal and lack necessary privacy. In rural areas, the perception of cancer and death were synonymous and women were reluctant to risk disapproval from their sexual partners by seeking testing. The authors offer a proposal to reorganize Mexico's screening program through five main strategies: (1) increased coverage; (2) improved quality control of how cervical smears are taken; (3) better interpretation of Pap tests; (4) guaranteed treatment for those whose tests show abnormalities; and (5) improved follow-up.

- ▶ Megevand E, Van Wyk W, Knight B, et al. Acetic acid visualization of the cervix: an alternative to cytologic screening. *Obstetrics & Gynecology* 88(3):383–386 (September 1996).

This prospective study of 2,426 women in a squatter area in Cape Town, South Africa, investigated the value of visual inspection of the cervix using acetic acid as an alternative to cytologic screening. All women with a positive visual inspection screening or a positive cytology were referred for colposcopy and biopsy. Histology was obtained on all women with positive results on either test. The authors reported that 76 women had positive visual inspection results; of these, subsequent smears revealed squamous intraepithelial lesions (SIL) in 61, and no evidence of SIL in 15. The remaining 2,350 women had negative visual inspection results. Of these, 254 had positive cervical smears; only 11 of these had high-grade SIL on histology-confirmed cytology, however. Visual screening detected 20 of the 31 women (64 percent) who had high-grade SIL on both cytology and histology. The authors concluded that in situations where cytology-based screening for pre-cancerous lesions is not available, visual inspection with acetic acid warrants consideration as an alternative screening method.

- ▶ Murthy NS, Agarwal SS, Prabhakar AK, et al. Estimation of reduction in life-time risk of cervical cancer through one life-time screening. *Neoplasia* 40(4):255–258 (1993).

Given the recommendation by the World Health Organization (WHO) in 1986 that countries with limited resources should aim to screen every woman once in her lifetime, this study attempted to determine at what age that screening could contribute to the greatest overall reduction in mortality from cervical

cancer. The study, using data from three cities in India, compared rates of cervical cancer incidence in unscreened women with incidence in women screened once in their lifetime at different ages (between ages 20 and 64). The authors found that screening at age 45 would be most effective, factoring in the number of cervical cancer cases prevented and the number of productive years of life saved.

- ▶ Ottaviano M, La Torre P. Examination of the cervix with the naked eye using acetic acid test. *American Journal of Obstetrics & Gynecology* 143:139–142 (1982).

This study of 2,400 patients between the ages of 18 and 65 in Florence, Italy, evaluated the use of visual inspection and colposcopy before and after the application of acetic acid, and compared the results of the two techniques. Before the application of acetic acid, they found that no clinical diagnosis, except overt carcinoma, was possible either with visual inspection or with the colposcope. In the comparison between “naked-eye” visual inspection with acetic acid (VIA) and colposcopy with acetic acid, VIA identified 307 of 312 women (98.4 percent) colposcopically assessed as having an atypical transformation zone. VIA also identified 1,568 of 1,584 (98.9 percent) of cases where colposcopy identified the cervix as normal. The authors concluded that the detection of precancerous cervical lesions should not depend on the possession of a colposcope.

- ▶ Pengsaa P, Vatanasapt V, Sriamporn S, et al. A self-administered device for cervical cancer screening in northeast Thailand. *Acta Cytologica* 41(3):749–754 (May–June 1997).

The goals of this study were to compare results of screening through a self-scraping device against a routine scraping method, and to evaluate the acceptance of this new device among a group of rural women from Northeast Thailand. A total of 552 women participated in the study. The women were trained to use the self-scraping device, and were reexamined by a gynecologist using the routine scraping method one week later. In both cases, the specimens were stained as Pap smears. The self-scraping method detected 13 abnormal Pap readings, 11 of which were confirmed by physician examination. No false negative readings were found, but the self-scraping method was not as accurate as physician examination for detection of inflammation. Responses to questionnaires about the device showed general acceptance among the women. The authors concluded that, in areas where trained medical personnel are not available to carry out regular tests, the self-scraping method can be a useful screening tool.

- ▶ Richart R. Screening: the next century. *Cancer* 76:1919–1927 (November 1995).

This article provides a comprehensive overview of existing and potential screening methods for application in both developing and developed countries. In addition to Pap smears, technologies reviewed for developing countries include unaided visual inspection with and without acetic acid (downstaging), aided visual inspection, and cervicography. Automated Pap machines and HPV DNA tests also are reviewed in the context of both high- and low-resource settings. The author addresses the effectiveness of various screening options as well as the likelihood that they will be available and cost-effective in high- and low-resource settings.

- ▶ Sankaranarayanan R, Wesley R, Somanathan T, et al. Visual inspection of the uterine cervix after the application of acetic acid in the detection of cervical carcinoma and its precursors. *Cancer* 83(10):2150–6 (November 1998).

The goal of this study in Kerala, India was to compare visual inspection of the cervix after the application of acetic acid (VIA) with cytology as methods for detecting cervical cancer and its precursors. Subjects with positive VIA or Pap smear findings as well as subjects with an abnormal-looking cervix (defined by criteria such as bleeding on touch, suspected growth or ulcer, or other cervical abnormality) were invited for diagnostic evaluation by colposcopy and biopsy if appropriate. Of the 3,000 women in the study, 298 (9.9 percent) were positive on VIA, 307 (10.2 percent) had atypia or dysplasia on Pap smears, and 182 (6.1 percent) were positive on both VIA and cytology. An additional 215 women (7.2 percent) were referred for colposcopy because they were identified as having an abnormal cervix on speculum exam,



although they were negative on VIA and Pap. Of the 51 true positive cases, VIA detected 46 (90.1 percent) and cytology 44 (86.2 percent). The approximate specificities were 92.2 percent for VIA and 91.3 percent for cytology. The authors conclude that if VIA continues to show satisfactory results, this technique is likely to be useful in developing countries where it is not feasible to introduce cytology screening and in developed countries as an adjunct to improve sensitivity of cervical cytology.

- ▶ Sankaranarayanan R, Shyamalakumary B, Wesley R, et al. Visual inspection with acetic acid in the early detection of cervical cancer and precursors [letter to the editor]. *International Journal of Cancer* 80(1):161–163 (January 1999).

This letter to the editor reports on the authors' ongoing study comparing the performance of visual inspection with acetic acid (VIA) to cervical cytology in detecting cervical lesions in Kerala, India. Study subjects were 1,351 women age 22 to 70 years (mean age 39). VIA (used by nurses) detected 95.8 percent of dysplasias and cancers; cytology detected 62 percent (VIA detected more mild and moderate dysplasias than cytology). The approximate specificity of VIA was 68 percent and that of cytology was 89.5 percent. The author notes that the effectiveness of VIA in detecting pre-cancerous lesions in this setting, as well as the immediacy of VIA results, make it a potentially attractive case-finding tool in developing-country settings.

- ▶ Spitzer M. Cervical screening adjuncts: recent advances. *American Journal of Obstetrics and Gynecology* 179(2):544–556 (August 1998).

This article reviews six technologies that have been proposed as ways to improve the effectiveness of cervical cancer screening: automated cytologic screening, fluid-based technology (e.g., ThinPrep), HPV testing, cervicography, speculscopy, and the Polarprobe. The author notes that use of automated cytologic screening may prove to be an effective approach to primary screening, although wide-scale testing in various settings needs to be implemented. He states that there is insufficient evidence to conclude that fluid-based technologies for producing monolayer slides are superior to standard Pap screening approaches. HPV testing may hold promise for use in multiple test screening protocols, and as a primary screening tool for women older than 35. The author concludes that cervicography and speculscopy are unlikely to be useful in large-scale screening efforts. The Polarprobe is an “in development” technology that measures voltage decay and the scattering of light through cervical tissue, and preliminary results are promising (see Coppleson, 1994).

- ▶ University of Zimbabwe/JHPIEGO Cervical Cancer Project. Visual inspection with acetic acid for cervical-cancer screening: test qualities in a primary-care setting. *Lancet* 353(9156): 869–873 (March 1999).

The study involved screening by trained nurse-midwives of almost 11,000 women attending 15 primary care clinics in Zimbabwe and found that, in identifying HGSIL and above, visual inspection with acetic acid (VIA) had a sensitivity of 76.6 percent and a specificity of 64.1 percent. The comparable results for Pap smears were 44.3 percent sensitivity and 90.6 percent specificity. As the accompanying *Lancet* commentary noted, the study provides valuable data on the feasibility and effectiveness of alternative screening approaches in developing-country primary health care settings, and confirmed the relative sensitivity of VIA in comparison to Pap smears in some settings. The commentary also addressed the potential for other new approaches, including HPV screening, and noted the relatively low specificity of VIA in comparison to Pap smears and the potential for overtreatment. The article authors also commented on the ongoing need to carefully assess the implications for programs and patients of a high false positive rate.

- ▶ Wesley R, Sankaranarayanan R, Mathew B, et al. Evaluation of visual inspection as a screening test for cervical cancer. *British Journal of Cancer* 75(3):436–440 (March 1997).

The goal of this study was to evaluate the performance of visual inspection by trained paramedical workers in detecting precursor cervical lesions and cancer in resource-poor settings. In Kerala, India, 2843 married women participated in the study and were subjected to visual inspection of the cervix and a

cytology examination. Results showed that 1279 (45 percent) and 179 (6.3 percent) of women were found to have a positive visual inspection using the low- and high-threshold criteria. With a low threshold, sensitivity and specificity values for detecting moderate dysplasia and above were 65.8 percent and 55.3 percent respectively; the values for detecting severe dysplasia and above were 71.9 percent and 55.3 percent respectively and 92.3 percent and 55.2 percent respectively for invasive cancer. With a high threshold, the sensitivity values decreased significantly and the specificity increased to about 94 percent. The authors concluded that the use of unaided visual inspection does not appear very promising as a pre-selection procedure for cytology or as a low technology measure for cervical cancer control, and that the procedure is unlikely to be cost-effective.

Treatment: evaluation of simple approaches

- Andersen ES, Husth M. Cryosurgery for cervical intraepithelial neoplasia: 10-year follow-up. *Gynecologic Oncology* 45:240–242 (1992).

The goal of this study was to evaluate the long-term results of cryotherapy treatment of CIN. Some 261 patients in Denmark were evaluated over a 5–10 year period following cryotherapy. The authors reported an overall cure rate after 5 years of 83.5 percent. Consistent with findings elsewhere, the cure rates of patients with CIN III were significantly lower than those with CIN I and CIN II. Patients with endocervical involvement had lower cure-rate as well. The authors concluded that this long-term study had demonstrated the effectiveness of cryotherapy, but cautioned that it also confirmed the need for other treatment methods for patients with endocervical involvement, and for careful follow-up, given the risk of treatment failure.

- Bishop A, Sherris J, Tsu V. *Cervical Dysplasia Treatment in Developing Countries: A Situation Analysis*. Seattle, WA: PATH (July 1995).

This extensive review summarizes issues related to cervical dysplasia treatment in developing countries, including appropriate treatment strategies and technologies, a survey of current CIN treatment practices in developing countries, treatment costs analyses, and guidelines for establishing a treatment plan of action.

- Burger RA, Monk BJ, Van Nostrand KM, et al. Single-visit program for cervical cancer prevention in a high-risk population. *Obstetrics and Gynecology* 86(4): Part 1, 491–498 (October 1995).

The three goals of this study were to screen and treat—in a single visit—women at increased risk for cervical cancer, to determine the feasibility of this single-visit approach, and to evaluate its acceptability to study participants. Some 126 women in southern California, USA, were recruited for the study through Spanish-language media; all had at least one risk factor for cervical cancer, and most reported some barrier, usually cost, to obtaining health care. The single-visit program included a Pap smear; immediate cytologic evaluation; and, for those with cytology results consistent with low- or high-grade SIL, a loop electrosurgical excision or biopsy. Patients who underwent excision or biopsy were asked to return in two weeks for evaluation. The study found the “See and Treat” approach to be feasible and well accepted. Overtreatment (i.e., no histologic abnormality identified in the excised specimen) occurred in an estimated 5 percent of patients, a figure the authors deemed acceptable, given the tradeoff of convenient, effective, inexpensive care that does not rely on follow-up visits.

- Flannelly G, Langan H, Jandial L, et al. A study of treatment failures following large loop excision of the transformation zone for the treatment of cervical intraepithelial neoplasia. *British Journal of Obstetrics and Gynecology* 104(6):718–722 (June 1997).

The goals of this study were to examine the long term efficacy of large loop excision of the transformation zone (LLETZ) in the treatment of CIN and to evaluate the relative diagnostic merits of colposcopy and cytology in the follow up of these women. The study examined cytology, colposcopy, and histology records of the first 1,000 women treated with LLETZ in the Colposcopy Clinic, Aberdeen Royal



Infirmery, Scotland, from 1989 to 1991. A total of 2,812 woman years of follow-up were obtained. The recurrent rate of CIN was 27/1,000 woman years and the cumulative recurrent rate at four years was 10.1 per 100 women. Of the women with abnormal colposcopy and proven CIN, 47 percent had a concurrent smear that did not show dyskaryosis. The authors concluded that LLETZ is effective in treatment for CIN, and colposcopy was useful in the follow-up of these woman and expedited the treatment of persistent disease. They recommend that any follow-up protocol should include a colposcopic assessment and cytological follow-up for at least four years following treatment.

- ▶ Hulman G, Pickles CJ, Gie CA, et al. Frequency of cervical intraepithelial neoplasia following large loop excision of the transformation zone. *Journal of Clinical Pathology* 51:375–377 (May 1998).

This retrospective study of 669 women in the United Kingdom assessed the risk of persistent/recurrent CIN following treatment by large loop excision of the transformation zone (LLETZ). With LLETZ biopsies, physicians must preserve as much healthy tissue as possible while ensuring that the CIN has been completely removed. Since doctors may be unable to determine the full extent of CIN presence in the endocervical canal, LLETZ biopsies may be incomplete or equivocal. This study found that the persistence/recurrence of CIN was significantly lower in cases where complete excision had occurred. The study also found that persistence/recurrence increased by grade of CIN (for example, from 6.7 percent of patients with CIN I to 21.7 percent of patients with CIN III). The authors conclude that physicians should carefully follow up on patients with either high-grade CIN or incomplete or equivocal excision.

- ▶ Megevand E, Van Wyk W, Knight B, et al. Can cervical cancer be prevented by a see, screen, and treat program? A pilot study. *American Journal of Obstetrics and Gynecology* 174(3):923–928 (March 1996).

The goal of this prospective study was to determine the feasibility of providing cervical cancer diagnosis and treatment on site through a mobile clinic at the time of screening, or with minimal delay. A total of 5,054 women attended a mobile clinic in Cape Town, South Africa, where they received a free Pap smear and information about cervical cancer and its prevention. In phase 1 of the study, women diagnosed with high-grade squamous intraepithelial lesion were referred to a nearby clinic for colposcopy and treatment. In phase 2, colposcopy and treatment were given on site. Thirty-four percent of 86 women with high-grade lesions in phase 1 attended the colposcopy clinic and received proper treatment (default rate, 66 percent). In contrast, 97 percent of 33 women with high-grade lesions in phase 2 attended the clinic and received proper treatment (default rate, 3 percent). The authors emphasized that education is an essential component in any successful screening program. They concluded that most women will undergo colposcopy and treatment when screening results are obtained quickly and when a colposcopy facility is located at the screening site.

- ▶ Mitchell MF, Tortolero-Luna G, Cook E, et al. A randomized clinical trial of cryotherapy, laser vaporization, and loop electrosurgical excision for treatment of squamous intraepithelial lesions of the cervix. *Obstetrics & Gynecology* 92(5):737–744 (November 1998).

The goal of this randomized clinical trial was to compare the complications and cure rates of three methods of treating squamous intraepithelial lesions (SIL) of the cervix. The analysis compared data from 390 women randomly assigned to treatment with cryotherapy, laser vaporization, or loop electrosurgical excision after grouping by SIL grade, endocervical gland involvement, and lesion size. Patients were followed for a period of 6–37 months with a mean of 16 months. The authors found no statistically significant differences in the complication rates, the persistence of disease within six months of treatment, or the recurrence of disease at least six months after treatment among the three groups. They did find that the risk of persistent disease was 18 times higher (risk ratio [RR], 18.9; 95 percent confidence interval [CI], 3.2, 110.6) among women with lesions more than two-thirds the size of the surface area of the cervix. They also found that recurrent disease was higher among women who were 30 years and older (RR, 2.1; 95 percent CI, 1.2, 4.3), women positive for HPV types 16 or 18 (RR, 2.1; 95 percent CI, 1.1, 4.0), and women with a prior

history of treatment for CIN (RR, 2.1; 95 percent CI, 1.1, 3.9). The authors concluded that these three treatment methods had comparable rates of success and complications for the period of follow-up in this study.

Cervical cancer and HIV

- Fruchter RG, Maiman M, Arrastia CD, et al. Is HIV infection a risk factor for advanced cervical cancer? *Journal of Acquired Immune Deficiency Syndromes and Human Retrovirology* 18(3):241–245 (July 1998).

The goal of this study was to compare HIV-infected and HIV-negative women with invasive cervical cancer with respect to predictors of advanced disease. The study compared 28 HIV-infected and 132 HIV-negative cervical cancer patients with regard to stage of disease, demographic and behavioral variables, and risk factors for advanced disease. Results from a retrospective analysis of the data showed that HIV-infected women had a fivefold greater rate of cervical intraepithelial neoplasia or unevaluated abnormal smears than did the HIV-negative women. A univariate analysis indicated that HIV infection was associated with a threefold increase in advanced-stage cervical cancer. However, a multiple logistic regression analysis showed that the major predictors of advanced cervical cancer in HIV-infected and HIV-negative women were similar and that only lack of cytologic screening and prolonged duration of symptoms were significant predictors of advanced disease. The authors stated that it is likely that a large proportion of HIV-infected women with cervical cancer acquire HIV infection after the initiation of the neoplastic process, rather than as a result of immunodeficiency, demonstrating an association of the common behavioral risk factors of the two diseases, rather than a causal effect of HIV immunodeficiency.

- La Ruche G. Human papillomavirus and human immunodeficiency virus infections: relation with cervical dysplasia-neoplasia in African women. *International Journal of Cancer* 76:480–486 (1998).

The goal of this study was to assess the factors associated with squamous intraepithelial lesions (SILs) and invasive cervical cancer, with special attention to human immunodeficiency virus (HIV) and human papillomavirus (HPV). Women were recruited from three outpatient gynecology clinics of Abidjan, Côte d'Ivoire, and screened for cervical abnormalities. The women were placed into three case-control groups: 151 women with low-grade SILs and 151 controls, 60 women with high-grade SILs and 240 controls, and 13 women with invasive cancer and 65 controls. Results from multivariate analyses showed that factors associated with low-grade SILs were HPV positivity, HIV-1 seropositivity, and parity greater than 3. Factors associated with high-grade SILs were HPV positivity, chewing tobacco, HIV-1 seropositivity, and illiteracy. The only factor associated with invasive cancer was HPV positivity. The results show that, in HIV-infected women, SILs occurred at an early stage of HIV disease. Women infected with both HIV and HPV were at a much higher risk of SILs than women infected with either of the two viruses separately. Based on the study findings, the authors suggest that cervical screening could be directed preferentially to women with low-educational levels or women of high parity.

- Leroy V, Ladner J, De Clercq A, et al. Cervical dysplasia and HIV type 1 infection in African pregnant women: a cross sectional study, Kigali, Rwanda. *Sexually Transmitted Infections* 75:103–106 (April 1999).

The goal of this study was to determine the prevalence of cervical squamous intraepithelial lesions (SILs) and their association with HIV-1 infection and immunodeficiency among pregnant women in Kigali, Rwanda. A total of 103 HIV-positive and 107 HIV-negative women participated in the study. The participants were recruited at the maternity ward of the Centre Hospitalier de Kigali. At inclusion, the women were screened for sexually transmitted diseases (STDs) including syphilis, gonorrhea, chlamydia, and trichomoniasis. CD4 cell counts were measured and Pap smears were performed. The study results showed that the prevalence of SILs was significantly higher in HIV-infected women than in HIV-negative women: 24.3 percent versus 6.5 percent, respectively. Furthermore, SIL-positive women tended to have more STDs than SIL-negative women (37.5 percent and 24.7 percent, respectively), but this did not reach a statistical difference. The authors conclude that the prevalence of SILs was high in this population of pregnant



women with high STD/HIV prevalence. They note that this cross-sectional study cannot establish a causal relation between HIV infection and SILs. Other factors such as age, age at first intercourse, parity, STDs, and number of sexual partners may be confounding factors in the analysis of this association.

- ▶ Palefsky JM, Minkoff H, Kalish LA, et al. Cervicovaginal human papillomavirus infection in human immunodeficiency virus-1 (HIV)-positive and high-risk HIV-negative women. *Journal of the National Cancer Institute* 91(3):226–236 (February 1999).

The goal of this study was to determine the prevalence of and risk factors for cervicovaginal HPV infection in HIV-positive women. A total of 1,778 HIV-positive and 500 HIV-negative women were recruited from a pool of women enrolled in the Women's Interagency HIV Study. The study results confirmed earlier observations that HPV infection is significantly more common among HIV-positive women than in high-risk HIV-negative women. Compared with HIV-negative women, HIV-positive women with CD4 cell count of less than 200/mm³ were at the highest risk of HPV infection, regardless of HIV RNA load, followed by women with a CD4 cell count greater than 200/mm³ and an HIV RNA load greater than 20,000 copies/mL, and women with CD4 count greater than 200/mm³ and an HIV RNA load less than 20,000 copies/mL. Other risk factors among HIV-positive women included racial/ethnic background (African American versus Caucasian, OR=1.64), current smoking (yes versus no, OR=1.55), and younger age (age <30 years versus ≥40 years, OR=1.75). The study results suggest that detection of HPV in HIV positive women more likely reflects either reactivation or persistence of pre-existing HPV types rather than recent HPV acquisition.

Client perceptions

- ▶ Ajayi IO, Adewolfe IF. Knowledge and attitude of general outpatient attendants in Nigeria to cervical cancer. *Central African Journal of Medicine* 44(2):41–43 (February 1998).

This cross-sectional study of women between the ages of 20 and 65 investigated Nigerian women's knowledge about cervical cancer, their source of information, and their general attitude about cancer. A total of 254 women were randomly selected from patients and accompanying persons attending a general outpatient clinic at a tertiary hospital in Ibadan, Nigeria, to complete a structured questionnaire. The authors found that 90 percent of these women had heard of cancer (most commonly, breast cancer [64.5 percent]). Only 15 percent had heard of cancer of the cervix. Media and peers were the major sources of information on cancer. Over half of the respondents had no knowledge of the description of cervical cancer, clinical presentation, or causes. The authors conclude that knowledge of cervical cancer is poor, and that there is a need to educate women about cervical cancer and its early warning signs in Nigeria.

- ▶ Jameson A, Sligo F, Comrie M. Barriers to Pacific women's use of cervical screening services. *Australian and New Zealand Journal of Public Health*, 23(1):89–92 (April 1999).

This study explored perceived barriers to cervical screening information services from the perspective of Pacific Island women living in New Zealand. Face-to-face, in-depth interviews based on a snowballing technique were used to assess attitudes among 20 Pacific women. Women identified numerous barriers, including a perception that Pacific women were being defined as socially problematic, a belief in the sacred nature of human sexuality, anxiety about a lack of confidentiality within community groups, and the perceived relationship between cervical smears and sexual activity. Study participants also voiced a strong preference for formal and interpersonal rather than informal sources of information. Formal sources included doctors, nurses, clinics, hospitals, and women's health centers. Talking with female rather than male professionals was strongly preferred. Women also agreed that the preferable role of a Pacific Island health professional would be in disseminating information, rather than taking Pap smears. They recommended that multi-racial images of women be used in advertising, illustrating that Pap smears are necessary for all women.

- ▶ Lauver DR, Kruse K, Baggot A. Women's uncertainties, coping, and moods regarding abnormal Papanicolaou results. *Journal of Women's Health & Gender-based Medicine* 8(8):1103–1112 (October 1999).

The goal of this study was to understand the process of coping with the news of abnormal cervical cancer screening results. The specific aims were to (1) compare women's uncertainty about the implications of abnormal Pap tests and their psychological distress over time; and (2) describe relationships among uncertainty, perceived coping ability, coping strategies that were used and helpful, and psychological distress. Between January 1995 and March 1996, 75 women from multiple health clinics participated in the study after receiving abnormal Pap test results. Forty women completed follow-up questionnaires before their colposcopy, and 35 of these women also completed questionnaires after their colposcopy follow-up. The study results showed that women's uncertainty about abnormal Pap test results decreased over time. Negative mood scores, reflecting psychological distress, did not change over time. Uncertainty about Pap tests, ambiguity about cancer, and perceived inability to deal with Pap test results were positively related. The coping strategy of catharsis (that is, expression of emotions) was associated with greater psychological distress (high negative mood scores) after learning of the news, but acceptance was associated with less psychological distress. The authors conclude that clinical interventions can address uncertainty and promote coping strategies such as relaxation, acceptance, and diversion to reduce psychological distress among women with abnormal cervical smear results.

- ▶ Lazcano-Ponce EC, Castro R, Allen B, et al. Barriers to early detection of cervical-uterine cancer in Mexico. *Journal of Women's Health* 8(3):399–408 (April 1999).

This qualitative study of barriers to early detection of cervical cancer included four focus groups—two in the urban setting of Mexico City and two in rural communities in the state of Oaxaca. In each setting, one focus group included women with at least one previous Pap test, and one focus group included women who had never had the test. The authors found that barriers to the Pap test included lack of knowledge about cervical cancer etiology, lack of knowing of the Pap test, the perception that cancer is an inevitably fatal disease, problems in client-provider relationships, giving priority to unmet needs related to extreme poverty, opposition by male sexual partners, rejection of the pelvic examination, long waits for sample collection and results, and perceived high costs for care. Based on these findings, the authors recommend that more information be given to women in an effort to create “a culture of prevention” that incorporates use of the early detection program for cervical-uterine cancer. They recommend that the campaign include information about age at which testing should begin and end, time lapse between tests, instructions for preparing for the sample, a description of the procedure for taking the sample, instructions about when and where to return for the results, and basic etiology of cervical cancer. They also suggest that multiple communication strategies be used to promote the use of the Pap test, including promotion during contacts between health personnel and women; distribution of information by radio, posters, and pamphlets; promotion through community groups; and incorporating promotion of cervical cancer prevention into existing health programs.

- ▶ Lazcano-Ponce EC, Najera-Aguilar P, Buiatti E, et al. The cervical cancer screening program in Mexico: problems with access and coverage. *Cancer Causes Control* 8(5):698–704 (September 1997).

The goal of this cross-sectional study was to determine the main factors for predicting participation in Cervical Cytology Screening Programs in populations with high mortality due to cervical cancer. A total of 4,208 women aged between 15 and 49 years from Oaxaca state (rural area) and Mexico City (urban area) were randomly selected through a national household-sample frame. The authors found that knowledge of what the Pap smear test is used for strongly predisposes use of screening programs in Oaxaca state and Mexico City. Other predicting factors included high socioeconomic level, high education level, and access to social security. The authors confirmed low coverage of the screening programs as an important problem in Mexico.



- ▶ Marcus AC, Crane LA. A review of cervical cancer screening intervention research: implications for public health programs and future research. *Preventative Medicine* 27:13–31 (1998).

This article provides an overview of the published literature regarding intervention strategies for promoting cervical cancer screening and reducing loss to follow-up among women with abnormal smears. The authors found that mass-media campaigns have had varying effects. These campaigns may work best when multiple media are used, when they promote specific screening programs that eliminate or reduce barriers for women, or when they are used in combination with other strategies. The authors also note many positive examples of using outreach staff to promote cervical cancer screening. Mobile exam rooms also have been successful. Personalized letters to patient populations have been found to be effective; however, mass/bulk mailings have not yielded impressive results. Several effective strategies were identified to reduce loss to follow-up, including multiple follow-up contacts, educational mail-outs, audiovisual programs, on-site educational presentations, transportation incentives, and economic vouchers.

- ▶ Masood, S. A plea for a worldwide volunteer cervical cancer education and awareness program. A proposal from the International Academy of Cytology Committee on Cancer Detection for Medically Underserved Women. *Journal of Clinical Cytology and Cytopathology* 43(4):539–543 (July–August 1999).

This editorial provides a brief review of the problem of cervical cancer and discusses the reasons why women still die from cervical cancer. The author suggests that lack of effective screening programs, especially for medically underserved women, and the continued dilemmas surrounding the practice of the Pap screening test are the two main reasons for the medical community's failure to eradicate cervical cancer. The author recommends that effective screening programs must integrate education and accessibility to health-care services for all women regardless of age, race, ethnic background, and socioeconomic status. It is essential to reach women, educate them, and to develop effective screening tests and responsive health care facilities. Integration of educational programs, Pap testing, and other diagnostic methods such as colposcopy in a mobile clinic is one innovative way of convincing women to utilize cancer prevention programs.

- ▶ PATH (Program for Appropriate Technology in Health). Assessing Health Need/Community Demand for Cervical Cancer Control: Results From a Study in Kenya. *Reproductive Health Reports* No. 1 (December 1996).

This report summarizes the purposes of an assessment tool to assess the health need/community demand for cervical cancer services and results generated by use of the tool in two Kenyan sites. It also includes a complete reproduction of the tool, including questionnaires used in interviewing health care providers and prospective cervical cancer service clients about cervical and cancer and other related health services.

Key resource documents

- ▶ Miller AB. *Cervical Cancer Screening Programmes: Managerial Guidelines*. Geneva: World Health Organization (1992).

These guidelines outline management issues that must be considered when setting up a cytology screening program. After reviewing the natural history of cervical cancer, the guidelines detail strategies for: deciding whether to initiate cervical cancer screening; health service sectors through which screening can be offered; issues related to age of initiation and frequency of screening; health education needs; monitoring and evaluation needs; and other areas. The guidelines then provide specific strategies for providing cervical screening in primary health care settings and outline issues surrounding information systems for cervical screening, including the goals, characteristics, and data requirements of information systems. Lastly, the guidelines describe an approach to reducing cervical cancer mortality in countries where cytological screening cannot be provided. This approach, called downstaging, focuses on detecting early cancer when it is still treatable.

- ▶ PAHO (Pan American Health Organization). Cancer of the uterine cervix. *Bulletin of the Pan American Health Organization* 30(4) (December 1996). (Available in English and Spanish.)

This special issue of the *PAHO Bulletin* includes 11 reviews and research articles on cervical cancer in the Latin American and Caribbean region. The articles include information on the epidemiology of cervical cancer in the region, the effectiveness of Pap testing in several countries, and women's knowledge and concerns about Pap testing in Chile and Mexico. Short communications on specific program activities and reports from the field also are included, as well as a list of recommended readings.

- ▶ PAHO (Organización Panamericana de la Salud). *Manual de normas y procedimientos para el control del cancer de cuello uterino*. Organización Panamericana de la Salud, Serie PALTEX Para Ejecutores de Programas de Salud, No. 6, Washington, DC (1990).

This Spanish-language PAHO publication reviews key managerial and technical aspects regarding cervical cancer control, with an emphasis on norms and procedures appropriate for the Latin American/Caribbean setting. The document includes sections that describe basic considerations for cervical cancer control, guidelines for cytological screening, diagnostic and treatment procedures, management of an effective program, and program monitoring and evaluation. The publication also includes several useful appendices which illustrate specific equipment and supply needs, evaluation indicators for cervical cancer control programs, and clinic and cytology registry forms.

- ▶ World Health Organization (WHO). *Cytological screening in the control of cervical cancer: technical guidelines*. Geneva: WHO (1988).

These guidelines were designed to be used in conjunction with the WHO managerial guidelines abstracted previously (Miller 1992). After a general introduction to the problem of cervical cancer and the role of cervical cytology in cervical cancer control, the guidelines provided detailed information on collection of cervical smears; cytology laboratory processes; diagnostic, treatment, and follow-up procedures; monitoring and evaluation issues; and personnel, equipment, and supply needs. One section of the guidelines also outlines common faults of screening programs and suggested solutions.

- ▶ World Health Organization (WHO). *Cancer pain relief and palliative care: report of a WHO expert committee*. Technical Report Series 804. Geneva: WHO (1990).

This report summarizes the findings of a meeting of the *WHO Expert Committee on Cancer Pain Relief and Active Supportive Care*. The report reviews the principles of palliative care, including obstacles to implementing effective palliative care. It defines the type of pain associated with cancer, as well as other symptoms associated with advanced cancer, and describes the drugs used to treat cancer pain. The report emphasizes that palliative care must encompass the psychosocial and spiritual needs of cancer patients, and discusses ethical issues that providers may need to consider when working with terminally ill people. Lastly, the report lists key program issues that must be considered before implementing palliative care (including education and training needs), and includes recommendations to WHO and WHO member-states on key strategies for making palliative care accessible to those who need it.

- ▶ World Health Organization (WHO). *Cancer Pain Relief 2nd ed. (with a guide to opioid availability)*. Geneva: WHO (1996).

This document updates the 1990 WHO report summarized above. In particular, opioid availability is addressed, including strategies for overcoming barriers to obtaining a regular supply of opioids.



