

Effective screening programmes for cervical cancer in low- and middle-income developing countries

Rengaswamy Sankaranarayanan,¹ Atul Madhukar Budukh,² & Rajamanickam Rajkumar³

Abstract Cervical cancer is an important public health problem among adult women in developing countries in South and Central America, sub-Saharan Africa, and south and south-east Asia. Frequently repeated cytology screening programmes — either organized or opportunistic — have led to a large decline in cervical cancer incidence and mortality in developed countries. In contrast, cervical cancer remains largely uncontrolled in high-risk developing countries because of ineffective or no screening. This article briefly reviews the experience from existing screening and research initiatives in developing countries.

Substantial costs are involved in providing the infrastructure, manpower, consumables, follow-up and surveillance for both organized and opportunistic screening programmes for cervical cancer. Owing to their limited health care resources, developing countries cannot afford the models of frequently repeated screening of women over a wide age range that are used in developed countries. Many low-income developing countries, including most in sub-Saharan Africa, have neither the resources nor the capacity for their health services to organize and sustain any kind of screening programme. Middle-income developing countries, which currently provide inefficient screening, should reorganize their programmes in the light of experiences from other countries and lessons from their past failures. Middle-income countries intending to organize a new screening programme should start first in a limited geographical area, before considering any expansion. It is also more realistic and effective to target the screening on high-risk women once or twice in their lifetime using a highly sensitive test, with an emphasis on high coverage (>80%) of the targeted population.

Efforts to organize an effective screening programme in these developing countries will have to find adequate financial resources, develop the infrastructure, train the needed manpower, and elaborate surveillance mechanisms for screening, investigating, treating, and following up the targeted women. The findings from the large body of research on various screening approaches carried out in developing countries and from the available managerial guidelines should be taken into account when reorganizing existing programmes and when considering new screening initiatives.

Keywords Cervix neoplasms/diagnosis/prevention and control; Cervix uteri/cytology; Vaginal smears/utilization; Mass screening/organization and administration; Developing countries; Central America; South America; Africa South of the Sahara; South Africa; India; South-East Asia (*source: MeSH*).

Mots clés Tumeur col utérus/diagnostic/prévention et contrôle; Col utérin/cytologie; Frottis vaginal/utilisation; Dépistage systématique/organisation et administration; Pays en développement; Amérique centrale; Amérique du Sud; Afrique subsaharienne; Afrique du Sud; Inde; Asie Sud-Est (*source: INSERM*).

Palabras clave Neoplasmas del cuello uterino/diagnóstico/prevenición y control; Cuello uterino/citología; Frotis vaginal/utilización; Tamizaje masivo/organización y administración; Países en desarrollo; América Central; América del Sur; África del Sur del Sahara; Sudáfrica; India; Asia Sudoriental (*fuelle: BIREME*).

Bulletin of the World Health Organization, 2001, **79**: 954–962.

Voir page 960 le résumé en français. En la página 961 figura un resumen en español.

Introduction

Cervical cancer is an important public health problem for adult women in developing countries in South

and Central America, sub-Saharan Africa, and south and south-east Asia, where it is the most or second most common cancer among women. The vast majority of cervical cancer cases are caused by infection with certain subtypes of human papilloma virus (HPV), a sexually transmitted virus that infects cells and may result in precancerous lesions and invasive cancer (1). Developing countries accounted for 370 000 out of a total of 466 000 cases of cervical cancer that were estimated to occur in the world in the year 2000 (2). Worldwide, cervical cancer claims the lives of 231 000 women annually, over 80% of whom live in developing countries. A conservative

¹ Scientist, International Agency for Research on Cancer, 150 cours Albert Thomas, 69372 Lyon Cedex 08, France (email: sankar@iarc.fr). Correspondence should be addressed to this author.

² Programme Manager, Cervical Cancer Prevention Programme, Tata Memorial Centre Rural Cancer Project, Nargis Dutt Memorial Cancer Hospital, Barshi, Solapur District, Maharashtra, India.

³ Medical Officer, Christian Fellowship Community Health Centre, Ambillikai, Dindigul District, Tamil Nadu, India.

Ref. No. 01-1311

estimate of the global prevalence (based on the number of patients still alive 5 years after the diagnosis) suggests that each year there are 1.4 million cases of clinically recognized cervical cancer. It is also likely that 3–7 million women worldwide may have high grade dysplasia.

Some of the developing countries that have data on cancer incidence and/or mortality have registered either a stable or slowly declining trend in cervical cancer incidence, most likely due to socio-demographic changes rather than to early detection/prevention efforts (3). On the other hand, some regions in sub-Saharan Africa have registered an increased incidence in recent years (4). Despite the declining trends in incidence observed in some regions, the total burden of cervical cancer is rising in high-risk developing countries, mostly due to increasing populations.

In developed countries, initiation and sustenance of cervical cytology programmes involving the screening of sexually active women annually, or once in every 2–5 years, have resulted in a large decline in cervical cancer incidence and mortality (Fig. 1 and Fig. 2) over the last 40–50 years (5–8). The aim of these programmes is to detect precancerous lesions and treat them before they progress to invasive cancer. In contrast, the risks of disease and death from such lesions have remained largely uncontrolled in high-risk developing countries, mostly because of the lack of screening programmes or because of their ineffectiveness. This paper reviews existing experiences, achievements, constraints, and lessons learned in community-based, cervical cancer intervention programmes in developing countries. The sensitivity and specificity values that we report for various screening tests correspond to the detection of high-grade lesions (cervical intraepithelial neoplasia II and III) and invasive cancer.

Cervical cytology screening programmes worldwide

To date, cervical cancer prevention efforts worldwide have focused on screening sexually active women using cytology smears and treating precancerous lesions. It has been widely believed that invasive cervical cancer develops from dysplastic precursor lesions, progressing steadily from mild to moderate to severe dysplasia, then to carcinoma in situ, and finally to cancer. It now appears that the direct precursor of cervical cancer is high-grade dysplasia, which in about a third of instances may progress to cervical cancer over a period of 10–15 years, while most low-grade dysplasias regress spontaneously (9, 10).

Even though the impact of cytology screening has never been proved through randomized trials, it has been shown to be effective in reducing the incidence and mortality from cervical cancer in developed countries (5–8). The incidence of cervical cancer can be reduced by as much as 80% if the quality, coverage, and follow-up of screening are

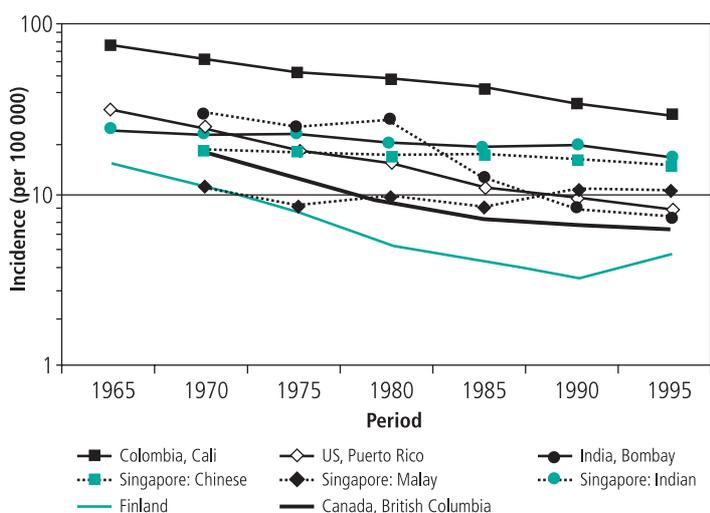
high. In most developed countries, women are advised to have their first smear test soon after becoming sexually active and subsequently once every 1–5 years. Many national guidelines are currently moving towards less frequent smear tests (once every 3–5 years) because it is recognized that cervical lesions develop slowly over several years. Women with low-grade lesions are generally advised to return for routine follow-up smears. Women with high-grade precursor lesions are further evaluated via colposcopy, biopsy, and subsequent treatment of confirmed lesions. Organized programmes with systematic call, recall, follow-up and surveillance systems that have shown the greatest effect (e.g. in Finland and Iceland), even though they use fewer resources than unorganized programmes (e.g. in the USA).

Cervical cytology is considered to be a very specific test for high-grade precancerous lesions or cancer but, even if the quality of collection and spreading of cells, fixation, and staining of smears, and reporting by well-trained technicians and cytopathologists are good, its sensitivity is only moderate. The results of meta-analyses suggest that cytological screening has a very wide range of sensitivity to detect lesions (11, 12); for example, cytology is estimated to have a mean sensitivity of 58% and a mean specificity of 69% (11). Also, estimates of sensitivity of conventional cytology (for high-grade lesions) vary greatly in individual studies, by as much as 30–87% (mean, 47%) (12). Both sampling and detection (reading) errors probably contribute to the low-to-moderate sensitivity of cytology. Assuming that cytology is only moderately sensitive, it seems likely that the observed decline in the risk of cervical cancer in developed countries may have arisen from the high screening frequency. Cervical neoplasia is a disease that progresses slowly, and many low-grade precancerous lesions regress spontaneously or do not progress further. High-grade lesions that are missed in a given screening round would probably be detected during the subsequent rounds in a frequently repeated cytological screening programme. A critical review of conventional cervical cytology in developed countries, where it was shown to be effective in cervical cancer control, provides valuable leads for public health policy decisions in low-resource environments. Current procedures, involving screening women once every 1–5 years, have considerable cost and resource implications. The limited health care budgets in most developing countries preclude initiating and sustaining such programmes, even in a limited geographic setting.

Cervical cancer screening programmes in developing countries

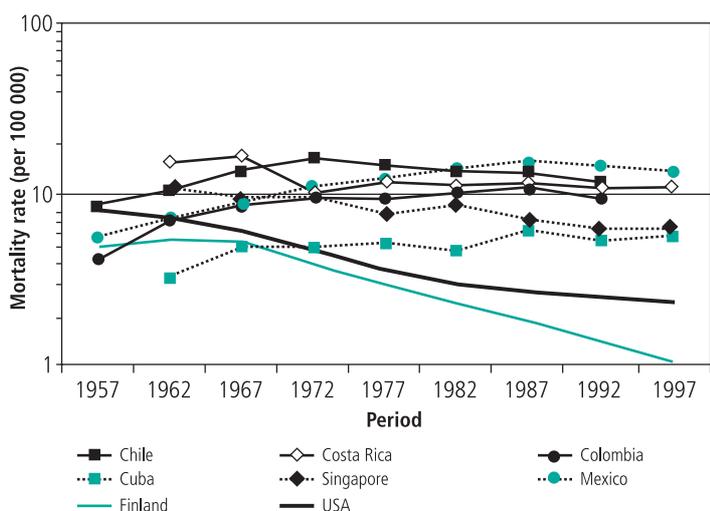
Cytology-based screening programmes for cervical cancer have been introduced in some developing countries, particularly in South and Central America,

Fig. 1. Age-standardized incidences for cervical cancer in selected developed and developing countries



WHO 01.201

Fig. 2. Age-standardized mortality rates for cervical cancer in selected developed and developing countries



WHO 01.202

over the last 30 years, but generally have achieved very limited success. In contrast, a comparison of the performance of conventional cytology and its potential alternatives in detecting cervical cancer and its precursors is ongoing in Asia, Africa, and Latin America. Both these approaches are briefly reviewed below since they provide potentially useful information for directing public health policy on introducing new and effective programmes in low-resource settings and for reorganizing existing programmes.

South and Central America

Since the 1970s there have been efforts to organize cervical cytology screening programmes nationally or regionally in selected Latin American countries.

Chile. In Chile the cervical cancer screening programme has been in operation since the early 1970s.

Cervical cancer mortality rates did not change much in the period from 1970 to 1985 after the introduction of the programme (Fig. 2). A recent evaluation of the programme indicated that more than 80% of the married women in Chile have been screened at least once. The programme was reorganized in the early 1990s, and mortality from cervical cancer has subsequently begun to decline.

Colombia. In Colombia, the Colombian National League against Cancer (a part of the public health system) and private organizations such as PROFAMILIA have been offering cytology screening since the 1970s (13). Subsequently, the cervical cancer mortality rate in the country has, however, remained stable (Fig. 2). Nevertheless, there has been a steady and substantial decline in the incidence of cervical cancer in the city of Cali (Fig. 1), possibly as a result of the ongoing screening activities carried out there since 1967, including educational and early detection campaigns. In 1990, a 5-year nationwide cervical cancer control programme was initiated to provide cytology smears to more than 60% of women aged 25–69 years over a 3-year period and to provide follow-up to over 90% of the women screened. The programme trained over 4000 nurses, 40 gynaecologists, and 36 pathologists. Cytology services were centralized and extensive community information and education campaigns were launched. Midway through the project, the centralized national health care system was reorganized and several services were decentralized to encourage the creation of efficient networks of services and surveillance. However, 5 years after the initiation of the programme, cervical cancer mortality data suggested that the situation had remained unchanged.

Costa Rica. In Costa Rica nationwide cytology services have been available to women aged ≥ 15 years since 1970. Information/education campaigns have been used to encourage sexually active women to have annual cytology smears. Invariably in all pelvic examinations a Pap smear is also obtained (14). Annually, around 250 000 smears have been performed and reported. Coverage has varied considerably according to region, with coverage of rural areas being inadequate in each given round of screening. Despite this, it seems that more than 85% of eligible women have been screened at least once. Though cervical cancer incidence remained virtually unchanged from 1983 to 1991, a significant decline has been observed more recently (i.e. a 3.6% decrease in annual incidence in 1993–97 compared with that in 1988–92) (Fig. 1). However, the cervical cancer mortality rates have remained unchanged over the last 25 years (Fig. 2) (15, 16). In an ongoing cohort study of more than 9000 women in Guanacaste Province, the cross-sectional sensitivity of HPV testing was found to be higher than that of conventional cytology (88% versus 78%) but the specificity was lower (89% versus 94%) (17).

Cuba. In Cuba a cervical cytology screening programme, offering smears every two years to women aged ≥ 20 years, was implemented through

the primary health care services in 1968 (18). Pap smears are taken by a nurse in the family doctor's office and are processed in one of the 36 regional cytology laboratories. It has been suggested that more than 80% of Cuban women aged 20–60 years have been screened at least once. However, no reduction in cervical cancer incidence and mortality (Fig. 2) has been observed since the introduction of the programme.

Mexico. A national cervical cancer screening programme was initiated in Mexico in 1974 (19, 20) and now operates in the Federal District and all 31 states of the country. Cytology smears are offered annually to women aged 25–65 years and the programme is integrated with the existing health care services. Mexico reportedly had 463 cyto-technologists, 251 reading centres, 70 dysplasia clinics, and 540 gynaecological oncology units in 1996. However, the infrastructure and resources were sufficient to carry out only 3.5 million smears annually for a target population of 16.5 million women (data for 1996); annual screening was nevertheless the “norm” for the programme. Realistically, this infrastructure is sufficient to screen the targeted women only once every 5 years. The Ministry of Health (MOH) has a total of 120 cervical cancer screening centres (CCSCs) where 230 cyto-technologists are employed. These screening centres are intended to carry out cytology screening of 6.5 million women who are not covered by social security. The Mexican Institute for Social Security (IMSS) is responsible for screening women covered by social security. In 1992, the MOH's screening centres carried out 1.02 million smears and the IMSS 1.3 million smears. There is a wide variation in the coverage of women on the national level. Studies indicate that less than 30% of the women in rural areas have been screened so far. There is no systematic effort to coordinate the programme through a central organization for call, recall, and follow-up of screened women.

An evaluation of the cervical cytology tests provided within the Mexican programme indicated that the validity and reproducibility varied greatly within and between the screening carried out by the MOH and the IMSS (21). Among the CCSCs the sensitivity to detect high-grade lesions varied from 46% to 90% and that of the specificity from 48% to 96%. The false-negative rate varied from 10% to 54%, with an average false-negative rate of 35%. Review of a random sample of 6011 negative smears indicated that 64.0% of the smears were of insufficient quality. There has been no decline in mortality from cervical cancer in Mexico since the initiation of the screening programme (Fig. 2) (22).

Brazil, Peru, and Puerto Rico. There are no organized cervical cancer screening programmes in Brazil. A high-risk of the disease (incidence >40 per 100 000 women) is reported from the north-east region. Low-level sporadic screening with opportu-

nistic cytology smears is carried out in different regions.

Peru has also recorded a high incidence of cervical cancer; there are no organized screening programmes in the country. A large demonstration project of cervical cancer screening with visual inspection with acetic acid (VIA) is currently ongoing in San Martin region of Peru.

An early detection programme for cervical cancer was established in Puerto Rico in the 1960s. This covered the metropolitan areas until 1962, and was later expanded to all health regions of the island. Cytology smears are offered to women aged ≥ 15 years and about 150 000 smears are processed annually. The incidence and mortality from cervical cancer have declined steadily over the last three decades (Fig. 1 and Fig. 2). The average, annual age-standardized incidence dropped from 38 per 100 000 women during 1950–54 to 19.9 per 100 000 women in 1990, and the mortality rate dropped from 19.1 per 100 000 women to 5.2 per 100 000 women in the same period.

Sub-Saharan Africa

There are no organized or opportunistic screening programmes for cervical cancer in any of the high-risk sub-Saharan African countries. While data from Uganda indicate that, at least in some areas of the country, substantial increases in the incidence of cervical cancer may have occurred (4), there is no evidence of an increase in incidence over time in Zimbabwe (23). Studies in Zimbabwe and South Africa have assessed the performance characteristics of potentially alternative screening tests such as visual inspection with acetic acid (VIA) and HPV testing. A cross-sectional screening study in Zimbabwe reported that the sensitivity and specificity to detect high-grade dysplasias and cancer was 77% and 64%, respectively, for VIA compared to 43% and 91% for cytology (24). The sensitivity and specificity of HPV testing using Hybrid Capture II assay (Digene Corporation, Gaithersburg, USA) were 81% and 62%, respectively (25); the sensitivity and specificity of HPV testing was, respectively, 91% and 41% for HIV-infected women and 62% and 75%, respectively, for HIV-negative women (26). It is also reported that the sensitivity and specificity of VIA and HPV testing, when used sequentially, was 64% and 82%, respectively (27).

South Africa. The South African Institute of Medical Research organized the infrastructure for mass screening of the female population of Soweto (Project Screen Soweto) so that 90 000 cytology smears could be tested annually (28). However, the lack of a planned population education and motivation programme resulted in poor participation of the target population in the programme. In a cross-sectional study that addressed the comparative performance of cytology, VIA, cervicography, and HPV testing in South Africa, the sensitivity was found to be 78%, 67%, 53%, and 73%, respectively;

the specificity was 94%, 83%, 89%, and 86%, respectively (29). In another study in South Africa, HPV testing using self-collected vaginal samples was found to be more sensitive than cytology (66% versus 61%), but less specific (83% versus 88%) (30). In an earlier study in South Africa, the sensitivity of VIA was found to be 65% (31). A recent study of the cost-effectiveness of several cervical cancer screening strategies, based on the South African experience, indicated that strategies using VIA or HPV DNA testing may offer attractive alternatives to cytology-based screening programmes in low-resource settings (32). When all the strategies were analysed on the basis of a single lifetime screening at age 35 years compared with no screening, it was found that HPV testing, followed by treatment of screen-positive women at a second visit, cost US\$ 39 per year of life saved (27% reduction in cancer incidence); VIA, coupled with immediate treatment of screen-positive women at the first visit, was the next most cost-effective (26% reduction in cancer incidence) and was cost saving; cytology, followed by treatment of screen-positive women at a second visit, was the least effective (19% reduction in cancer incidence) at a cost of US\$ 81 per year of life saved (32).

Currently, cytology smears are provided on demand in antenatal, postnatal, gynaecology, and family planning clinics in South Africa. Work to develop a cervical screening policy for South Africa, based on the models of natural history, has been ongoing for some time. It is proposed to initiate screening at the age of 30 years with three smears being carried out in a woman's lifetime. However, there has been debate about both whether this policy should be implemented and how. A pilot project to set up screening services using the health systems development approach is currently being undertaken by three provincial departments of health (Western Cape, Northern Cape, and Gauteng) in cooperation with nongovernmental organizations. This approach seeks to set up programme components such as reaching the target population, providing a competent screening service, relaying the results, and organizing referral, investigation, treatment and follow-up of screening-positive women. It is expected that these tested methods will be applied in the provinces and then nationally.

A three-arm, prospective randomized intervention trial in South Africa is currently addressing the comparative safety, acceptability and efficacy of screening women with VIA and HPV DNA testing and immediately treating screen-positive women with cryotherapy performed by nurses in a primary health care setting. Outcome measures include reduction of high-grade cervical cancer precursors in treated versus untreated women, followed over a 12-month period.

Other countries. Cross-sectional/randomized screening intervention studies are currently ongoing in several African countries — Burkina Faso, Congo (Brazzaville), Ghana, Guinea (Conakry), Kenya, Mali, Niger, and Nigeria — to address the accuracy of various screening approaches such as cytology, HPV

testing, VIA, and visual inspection with Lugol's iodine (VILI) as well as the detection rates associated with them.

South Asia

India. India accounts for one-fifth of the world burden of cervical cancer. There are no organized or high-level opportunistic screening programmes for cervical cancer in any of the provincial states. Data from population-based cancer registries in different regions indicate a slow, but steady, decline in the incidence of cervical cancer (Fig. 1). However, the rates are still too high, particularly in the rural areas, and the absolute number of cases is on the increase due to population growth. Efforts to improve awareness of the population have resulted in early detection of and improved survival from cervical cancer in a backward rural region in western India (33, 34). Also in two subdistricts of western India where the literacy among women is less than 20% there have been attempts to evaluate the role of improved awareness in the early detection and control of cervical cancer (35). Person-to-person and group health education on cervical cancer were provided to 97 000 women in Madha Tehsil, Solapur district, Maharashtra State, in western India; 79 000 women in Karmala Tehsil served as the control population. This programme was initiated in 1995 and the preliminary results for 1995–99 indicate that, compared with the control area, in the intervention subdistrict a substantially higher proportion of women presented with cervical cancer in earlier stages with significantly reduced case fatality (Table 1).

Visual inspection-based approaches to cervical cancer screening have been extensively investigated in India. The performance characteristics of unaided visual inspection (without acetic acid), also known as “downstaging”, has been addressed in several studies (36). This approach suffers from low sensitivity and specificity to detect cervical neoplasia, particularly the precursor lesions, and is no longer recommended as a screening approach. Currently there are several ongoing, cross-sectional studies being carried out on other screening approaches such as VIA, VIA with magnification (VIAM), and VILI, as well as HPV testing as alternative screening approaches. Results from two reported studies indicate that the sensitivity of VIA to detect high-grade lesions was similar or higher than that of conventional cytology but that its specificity was lower (37, 38).

There are three large, ongoing cluster-randomized intervention trials in India — in Dindigul district (Tamil Nadu), in Mumbai, and in Osmanabad district (Maharashtra) — to evaluate the effectiveness of VIA, in reducing cervical cancer incidence and mortality. The intervention programme in Osmanabad district aims to address the comparative efficacy and cost-effectiveness of three different primary screening approaches in reducing the incidence and mortality: VIA, conventional cervical cytology, and HPV testing. The results of these studies are likely to

provide valuable leads to the development of public health policies to control cervical cancer in developing countries. A recently held national workshop on control of cervical cancer in India reviewed the various methodologies for the early detection of cervical neoplasia and considered both good quality conventional cytology and VIA as suitable tests for early clinical diagnosis (39). In view of the inadequately developed cytology services, VIA was recommended as the immediate option for the introduction of cervical cancer control initiatives as part of the district cancer control programmes in 54 districts in India.

South-east Asia

In Singapore, a high level of opportunistic screening for cervical cancer has been operating over the last few years, but has had only minimal impact on the overall incidence and mortality from cervical cancer (3). However, a substantial decline in cervical cancer incidence and mortality has been observed among the Singapore Indian community, with stable trends among the Chinese and Malay communities. Efforts are currently underway to provide an organized screening programme by restructuring the existing opportunistic programme. A test-and-treat approach following VIA is currently being evaluated in Thailand. A cytology-based demonstration programme on screening is currently being implemented by the MOH in Nakornpanam Province in north-east Thailand. The comparative performance of VIA and VILI in detecting cervical neoplasia is being addressed in Vientiane, Lao People's Democratic Republic. Ongoing studies in rural China are addressing the accuracy of cytology and non-cytology-based screening approaches.

Summary

Although cytological screening is being carried out in some developing countries/regions, there are no organized programmes and the testing is often of poor quality and performed inadequately and inefficiently among the population. As a result, there has been a very limited impact on the incidence of cervical cancer, despite the large numbers of cytological smears taken in some countries such as Cuba and Mexico. The findings from completed and ongoing research on various approaches to screening (in terms of accuracy and effectiveness) and to treatment (in terms of long-term safety) — such as cryotherapy and loop electrosurgical excision procedures, carried out in field conditions, and test-and-treat approaches — should be taken into account when considering new programmes and when reorganizing existing programmes.

Effective screening programmes in developing countries

Efforts to organize effective cervical cancer screening programmes in developing countries will have to

Table 1. Outcome of information/education on the control of cervical cancer, Solapur District, Maharashtra, India, 1995–99

	Intervention area (Madha Tehsil)	Control area (Karmala Tehsil)
Total number of women	96 908	76 084
No. of women–years	352 628	380 805
No. of incident cervical cancers	80	64
Stage I and II cancers (%)	65.1	32.8
Age-standardized incidence (per 100 000) ^a	26.3	18.7
No. of deaths from cervical cancer	17	30
Age-standardized mortality rate (per 100 000) ^b	5.6	8.6

^a Incidence rate ratio: 1.41 (95% CI: 1.00–1.98).

^b Mortality rate ratio: 0.65 (95% CI: 0.36–1.18).

find adequate financial resources, develop the infrastructure, train the needed manpower, and elaborate surveillance mechanisms for screening, investigating, treating, and follow-up of the targeted women. Quite often, considerable discussion is focused on which screening test to use — cytology or alternatives to cytology, such as VIA or HPV testing — or which combinations/sequence of screening tests should be used for screening in developing countries. Choosing a suitable screening test is only one aspect of a screening programme. A more fundamental and challenging issue is the organization of the programme in its totality. Whichever screening test is to be used, the challenges in organizing a screening programme are more or less the same. However, screening tests (e.g. cytology, HPV testing) that require additional recalls and revisits for diagnostic evaluation and treatment may pose added logistic difficulties and these may emerge as another barrier for participation in low-resource settings.

The choice of screening test in countries/regions that plan to initiate new programmes should be based on the comparative performance characteristics of cytology and its potential alternatives such as VIA, their relative costs, technical requirements, the level of development of laboratory infrastructure, and the feasibility in a given country/region. Since programmes cannot afford the luxury of frequently repeated testing of women, a highly sensitive test should be provided. If cytology is chosen, considerable attention should be given to obtaining good quality smears, staining, and reporting so that a moderately high sensitivity to detect lesions is ensured. If a potential alternative to cytology, such as VIA, is chosen for screening, considerable attention should be given to the proper monitoring and evaluation of the programme inputs and outcomes before further expansion, since VIA is still an experimental option for cervical cancer screening and it remains to be demonstrated whether VIA-based

screening programmes are associated with a reduction in cervical cancer incidence and mortality. In developing countries, existing ineffective cytology-based programmes should be urgently reorganized and monitored.

Quantitative studies have shown that after two or more negative cytology smears, even screening once every 10 years yields a 64% reduction in the incidence of invasive cervical cancer, assuming 100% compliance (6, 40). Further studies based on this model indicate that once-in-a-lifetime screening may yield around 25–30% reduction in the incidence of cervical cancer (41, 42).

To have an impact on cervical cancer incidence and mortality, efforts must be focused on the following: increasing the awareness of women about cervical cancer and preventive health-seeking behaviour; screening all women aged 35–50 years at least once, before expanding the services and providing repeated screening (e.g. once in every 10 years); providing a screening test with high sensitivity (since women have less frequent opportunities for repeated screening); treating women with high-grade dysplasia and cancer; and monitoring programme inputs and evaluating the outcomes.

Conclusion

Programmes for organized screening of cervical cancer (e.g. in England and Finland) or for opportunistic/spontaneous screening (e.g. in the USA and Canada) involve substantial costs to provide for the associated infrastructure, manpower, consumables, follow-up, and surveillance. In our view, many low-income developing countries, particularly most of those in sub-Saharan Africa, currently have neither the financial and manpower resources nor the capacity in their health services to organize and sustain a screening programme of any sort. Low-income developing countries should consider

planned investments in order to improve the capacity of their health services to diagnose and treat cervical cancer precursors and early invasive cancers, before considering even limited screening programmes. VIA may be considered as a suitable early detection test in the context of early clinical diagnosis in low-income countries, particularly in those regions without extensive cytology laboratory facilities.

Those middle-income developing countries with inefficient cytology screening programmes should focus their attention on reorganizing the programme in the light of lessons from their past failures and experiences from elsewhere. Many of these programmes work with the unrealistic notion of offering frequently repeated screening tests (e.g. every year) targeted at women of wide age ranges (e.g. 20–65 years). It would be more realistic and effective to screen high-risk women (e.g. those aged 35–49 years or 30–50 years) only once or twice with a good quality and highly sensitive test, with an emphasis on wide coverage (>80%) of the targeted women. It should also be ensured that women with identified abnormalities attend for diagnosis, management and follow-up. Additional investments should also be made to improve the manpower resources and infrastructure that would sustain the programmes in these countries. Adequate information systems should also be incorporated within the programme for monitoring inputs and outcomes. Middle-income countries without any programmes for cervical cancer screening, but planning to implement such a programme, should consider organizing and sustaining it in a limited geographical region before expanding to cover a wider area. Managerial guidelines are now available to help in planning and implementing appropriate programmes in low-resource settings (13, 43). ■

Conflicts of interest: none declared.

Résumé

Programmes efficaces de dépistage du cancer du col dans les pays en développement à revenu faible ou moyen

Le cancer du col constitue un important problème de santé publique chez les femmes adultes des pays en développement d'Amérique du Sud, d'Amérique centrale, d'Afrique subsaharienne, d'Asie du Sud et d'Asie du Sud-Est. Dans les pays développés, des programmes répétés de dépistage cytologique, soit organisés soit ponctuels, ont conduit à une baisse importante de l'incidence du cancer du col et de la mortalité qui lui est associée. En revanche, le cancer du col reste une affection le plus souvent non maîtrisée dans les pays en développement à haut risque en raison de l'absence ou de l'inefficacité du dépistage. Le présent article passe brièvement en revue les initiatives actuelles en matière de dépistage et de recherche dans ces pays.

Le coût de l'infrastructure, du personnel, des produits renouvelables, du suivi et de la surveillance est élevé, qu'il s'agisse de programmes de dépistage organisés ou ponctuels. Les ressources qu'ils peuvent consacrer aux soins de santé étant limitées, les pays en développement ne peuvent adopter les programmes en usage dans les pays développés, qui comportent des dépistages fréquemment répétés sur une tranche d'âge plus étendue. Les services de santé de nombreux pays en développement à faible revenu, dont la plupart en Afrique subsaharienne, n'ont ni les ressources ni la capacité d'organiser et de poursuivre des programmes de dépistage quels qu'ils soient. Les pays en développement à revenu moyen, dans lesquels

le dépistage est actuellement inefficace, devront réorganiser leurs programmes à la lumière de l'expérience des autres pays et des leçons de leurs échecs passés. Ceux de ces pays qui envisagent d'organiser un nouveau programme de dépistage devront commencer par une région géographique limitée avant de songer à une quelconque extension. Il est également plus réaliste et plus efficace d'axer le dépistage sur les femmes à haut risque, qui seront soumise une fois ou deux dans leur vie à un test très sensible, en cherchant à obtenir une couverture élevée (>80 %) de la population visée.

Pour organiser un programme de dépistage efficace dans ces pays, il faudra trouver des ressources financières suffisantes, développer les infrastructures, former le personnel nécessaire et élaborer des mécanismes de surveillance pour dépister, examiner, traiter et suivre les femmes appartenant au groupe cible. On tiendra compte des résultats des nombreuses recherches portant sur les diverses approches du dépistage dans les pays en développement ainsi que des directives de gestion existantes lorsqu'on réorganisera des programmes en cours ou que l'on envisagera de nouvelles initiatives en matière de dépistage.

Resumen

Programas eficaces de cribado del cáncer cervicouterino en los países en desarrollo de ingresos bajos y medios

El cáncer cervicouterino representa un importante problema de salud pública entre las mujeres adultas de los países en desarrollo de América del Sur y Centroamérica, el África subsahariana y Asia meridional y sudoriental. Los programas de cribado citológico frecuente, organizados o puntuales, han logrado reducir considerablemente la incidencia de cáncer cervicouterino y la mortalidad asociada en los países desarrollados. En cambio, este tipo de cáncer sigue sin controlarse apenas en los países en desarrollo de alto riesgo, donde las medidas de cribado son ineficaces o inexistentes. El artículo analiza brevemente la experiencia de las iniciativas de cribado e investigación llevadas a cabo actualmente en países en desarrollo.

La infraestructura, los recursos humanos, el material fungible, el seguimiento y la vigilancia que requieren los programas de cribado del cáncer cervicouterino —tanto los organizados como los puntuales— entrañan grandes costos. Debido a lo limitado de sus recursos de atención sanitaria, los países en desarrollo no pueden permitirse el cribado frecuente que durante un amplio intervalo de edades aplican los países desarrollados. Muchos países en desarrollo de bajos ingresos, en particular la mayoría de los países del África subsahariana, no poseen ni los recursos ni la capacidad necesarios para que sus servicios de salud organicen

de forma sostenida programa alguno de cribado. Los países en desarrollo de ingresos medios, que aplican hoy medidas de cribado ineficientes, deberían reorganizar sus programas a la luz de las experiencias de otros países y de las lecciones extraídas de sus pasados fracasos. Los países de ingresos medios que decidan organizar un nuevo programa de cribado deberían ensayarlo primero en un área geográfica limitada, antes de estudiar su eventual ampliación. Es más realista y eficaz intentar cribar a las mujeres de alto riesgo una o dos veces a lo largo de su vida mediante una prueba de alta sensibilidad, procurando sobre todo asegurar una amplia cobertura (> 80%) de la población destinataria.

Como parte de las actividades desplegadas para organizar un programa de cribado eficaz en esos países en desarrollo, habrá que hallar recursos financieros suficientes, desarrollar la infraestructura oportuna, capacitar al personal necesario e idear mecanismos de vigilancia para el cribado, investigación, tratamiento y seguimiento de las mujeres destinatarias. A la hora de reorganizar los programas existentes y de planear nuevas iniciativas de cribado, deberán tenerse en cuenta los resultados de las numerosas investigaciones realizadas sobre los diversos enfoques de cribado aplicados en los países en desarrollo, así como las directrices de gestión disponibles.

References

1. **Walboomers JMM et al.** Human papillomavirus is a necessary cause of invasive cervical cancer worldwide. *Journal of Pathology*, 1999, **51**: 268–275.
2. **Ferlay J et al.** Globocan 2000. *Cancer incidence, mortality and prevalence worldwide, version 1.0*. Lyon, International Agency for Research on Cancer, 2001 (IARC Cancer Base No. 5).
3. **Coleman M et al.** *Time trends in cancer incidence and mortality*. Lyon, International Agency for Research on Cancer, 1995 (IARC Scientific Publications No. 121).
4. **Wabinga H et al.** Trends in cancer incidence in Kyadondo County, Uganda, 1960–1997. *British Journal of Cancer*, 2000, **82**: 585–1592.
5. **Hakama M et al.** Evaluation of screening programmes for gynaecological cancer. *British Journal of Cancer*, 1985, **52**: 669–673.
6. Control of cancer of the uterine cervix. A WHO meeting. *Bulletin of the World Health Organization*, 1986, **64**: 607–618.
7. **Hakama M et al.** *Screening for cancer of the uterine cervix*. Lyon, International Agency for Research on Cancer, 1986 (IARC Scientific Publications No. 76).
8. **Miller AB et al.** Report on a workshop UICC project on evaluation of screening for cancer. *International Journal of Cancer*, 1990, **46**: 761–769.
9. **Nasiell K et al.** Behaviour of mild dysplasia during long-term follow-up. *Obstetrics and Gynaecology*, 1986, **67**: 665–669.
10. **Holowaty P et al.** Natural history of dysplasia of the uterine cervix. *Journal of the National Cancer Institute*, 1999, **91**: 252–268.
11. **Fahey MT et al.** Meta-analysis of Pap test accuracy. *American Journal of Epidemiology*, 1995, **141**: 680–689.
12. **Nanda K et al.** Accuracy of the Papanicolaou test in screening for and follow-up of cervical cytologic abnormalities: a systematic review. *Annals of Internal Medicine*, 2000, **132**: 810–819.

13. **Herdman C et al.** *Planning appropriate cervical cancer prevention programs.* Seattle, WA, Program for Appropriate Technology in Health, 2000.
14. **Irwin IR et al.** Screening practices for cervical and breast cancer in Costa Rica. *Bulletin of the Pan American Health Organization*, 1991, **25**: 16–26.
15. **Herrero R et al.** Determinants of geographical variations of cervical cancer in Costa Rica. *Bulletin of the Pan American Health Organization*, 1993, **27**: 15–25.
16. **Sierra R et al.** *Cancer in Costa Rica.* Lyon, International Agency for Research on Cancer, 1988 (IARC Technical Report No. 1).
17. **Schiffman et al.** HPV DNA testing in cervical cancer screening: results from women in high-risk province of Costa Rica. *Journal of the American Medical Association*, 2000, **283**: 87–93.
18. **Fernandez Garrotte L.** Evaluation of the Cervical Cancer Control Program in Cuba. *Bulletin of the Pan American Health Organization*, 1996, **30**, 387–391.
19. **Lazcano-Ponce EC et al.** Evaluation model of the Mexican national program for early cervical cancer detection and proposals for a new approach. *Cancer Causes Control*, 1998, **9**: 241–251.
20. **Lazcano-Ponce EC et al.** Cervical cancer screening in developing countries: Why is it ineffective? The case of Mexico. *Archives of Medical Research*, 1999, **30**: 240–250.
21. **Lazcano-Ponce EC et al.** Validity and reproducibility of cytologic diagnosis in a sample of cervical cancer screening centers in Mexico. *Acta Cytologica*, 1997, **41**: 277–284.
22. **Lazcano-Ponce EC et al.** Mortality from cervical carcinoma in Mexico: impact of screening, 1980–1990. *Acta Cytologica*, 1996, **40**: 506–512.
23. **Chokunonga E et al.** Cancer incidence in the African population of Harare, Zimbabwe: second results from the cancer registry 1993–1995. *International Journal of Cancer*, 2000, **85**: 54–59.
24. University of Zimbabwe/JHPIEGO Cervical cancer prevention project. Visual inspection with acetic acid for cervical cancer screening: test qualities in a primary-care setting. *Lancet*, 1999, **353**: 869–873.
25. **Womack SD et al.** Evaluation of human papillomavirus assay in cervical screening in Zimbabwe. *British Journal of Obstetrics and Gynaecology*, 2000, **107**: 33–38.
26. **Womack SD et al.** HPV-based cervical cancer screening in a population at high risk for HIV infection. *International Journal of Cancer*, 2000, **85**: 206–210.
27. **Blumenthal PD et al.** Adjunctive testing for cervical cancer in low-resource settings with visual inspection, HPV, and the Pap smear. *International Journal of Gynecology and Obstetrics*, 2001, **72**: 47–53.
28. **Leiman G.** “Project Screen Soweto” — a planned cervical screening programme in a high-risk population. *South African Medical Journal*, 1987, **2**: 61–68.
29. **Denny et al.** Evaluation of alternative methods of cervical cancer screening for resource-poor settings. *Cancer*, 2000, **89**: 826–833.
30. **Wright TC et al.** HPV DNA testing of self-collected vaginal samples compared with cytologic screening to detect cervical cancer. *Journal of the American Medical Association*, 2000, **283**: 81–86.
31. **Megevand E et al.** Acetic acid visualization of the cervix: an alternative to cytologic screening. *Obstetrics and Gynecology*, 1996, **88**: 383–386.
32. **Goldie SJ et al.** Policy analysis of cervical cancer screening strategies in low-resource settings. Clinical benefits and cost effectiveness. *Journal of the American Medical Association*, 2001, **285**: 3107–3115.
33. **Jayant K et al.** Improved stage at diagnosis of cervical cancer with increased cancer awareness in a rural Indian population. *International Journal of Cancer*, 1995, **63**: 161–163.
34. **Jayant K et al.** Survival from cancer in Barshi registry, rural India. In: Sankaranarayanan R, Black RJ, Parkin DM, eds. *Cancer survival in developing countries.* Lyon, International Agency for Research on Cancer, 1988: 69–77 (IARC Scientific Publications No. 145).
35. **Parkin DM, Sankaranarayanan R.** Prevention of cervical cancer in developing countries. *Thai Journal of Obstetrics and Gynaecology*, 1999, **115**: 3–20.
36. **Sankaranarayanan R et al.** Visual inspection as a screening test for cervical cancer control in developing countries. In: Franco E, Monsonogo J, eds. *New developments in cervical cancer screening and prevention.* Oxford, Blackwell Science, 1997: 411–421.
37. **Sankaranarayanan R et al.** Performance of visual inspection after acetic acid application (VIA) in the detection of cervical cancer precursors. *Cancer*, 1998, **83**: 2150–2156.
38. **Sankaranarayanan R et al.** Visual inspection with acetic acid in the early detection of cervical cancer and precursors. *International Journal of Cancer*, 1999, **80**: 161–163.
39. *National workshop on control of cervical cancer-alternative strategies.* New Delhi, Institute of Cytology and Preventive Oncology, Indian Council of Medical Research, 2001.
40. **Hakama M et al., eds.** *Screening for cancer of the uterine cervix.* Lyon, International Agency for Research on Cancer, 1986 (IARC Scientific Publications No. 76).
41. **Prabhakar AK.** Cervical cancer in India strategy for control. *Indian Journal of Cancer*, 1992, **104**: 29–32.
42. **Murthy NS et al.** Estimation of reduction in life-time risk of cervical cancer through one life-time screening. *Neoplasma*, 1993, **40**: 255–258.
43. **Miller AB.** *Cervical cancer screening programmes — Managerial guidelines.* Geneva, World Health Organization, 1992.