1. General topic: Cervical cancer as a public health issue in Mexico and other developing countries

Kirvis Janneth Torres-Poveda\textsuperscript{1,2}, Gabriela Angélica Martínez-Nava\textsuperscript{1} and Vicente Madrid-Marina\textsuperscript{1}

\textsuperscript{1}Dirección de Infecciones Crónicas y Cáncer. Centro de Investigación sobre Enfermedades Infecciosas (CISEI), Instituto Nacional de Salud Pública, Cuernavaca, Morelos, Mexico. (Chronic Infectious Diseases and Cancer Division. Center for Infectious Diseases Research National Institute of Public Health, Mexico); \textsuperscript{2}Dirección de Desarrollo Científico Consejo Nacional de Ciencia y Tecnología (CONACYT). Mexico City, Mexico. (Scientific Development Division. National Council of Science and Technology of Mexico)

Abstract. In this chapter we will discuss cervical cancer (CC) incidence and mortality trends in Mexico and other developing countries, the rationale for cervical screening, the problems and challenges facing CC screening programs especially in Latin America and lastly, public health perspectives in terms of the prevention and control of this disease. CC disproportionately affects poorer countries, and within countries, poorer communities due to their lack of effective prevention programs. The CC mortality rates are seven times greater in Latin America and the Caribbean than in North America and the CC ranks as the 4th most frequent cancer in women in America, and the 2nd most frequent among women between 15 and 44 years of age. The highest disease burden is borne by Caribbean and Central American women. Since CC is the neoplasm with the highest...
demonstrated potential for secondary prevention, it is an entirely preventable and curable disease: It implies low cost and low risk when methods are available for screening asymptomatic women, along with appropriate diagnosis, treatment and follow-up. Despite advances in health systems in the Region of the Americas, poor communities, will likely to develop technically avoidable diseases such as CC, while conditions of inequality persist in access to health and all its determinants.

Introduction

Cervical cancer (CC) is a worldwide disease that constitutes a significant public health problem especially in developing countries, not only due to its high incidence but also because the most affected population comprises women who belong to marginalized socio-economic classes including indigenous groups; these people are the most vulnerable given their limited access to health services and gynecological care. There are several reasons that explain this and they might appear confusing when addressed. They include the very complexity of the disease’s natural history linked to sexual activity and multiple risk factors (genetic, environmental, social, economic and cultural), as well as availability issues concerning specific care services for women in all stages of life, and the cultural barriers that hinder health care and sanitation coverage in this population.

Even though it is the cancer with the greatest demonstrated potential for secondary prevention, today CC remains a significant cause of mortality among women globally. CC ranks third in incidence rates in women worldwide, with an estimated 530,000 new cases in 2008 (overall mortality rate of 15 per 100,000 women) [1]. More than 85% of the global burden of this disease occurs in developing countries, where represents 13% of all female cancers [2]. The regions with the highest incidence and mortality rates for CC respectively, in descending order are the East (34.5/100,000 and 25.3/100, 000) and West (33.7/100 000 and 24.0/100, 000) from Africa, South Africa (26.8/100,000 and 14.8/100,000), South and Central Asia (24.5/100,000 and 14.0/100,000), South America (24.1/100,000 and 10.8/100,000) and Melanesia (23.7/100,000 and 16.6/100,000). The age-standardized rates of incidence and mortality by CC are lower in Australia/New Zealand (5.0/100,000 and 1.4/100,000), North America (5.7/100,000 and 1.7/100,000) and Eastern Europe (6.9/100,000 and 2.0/100,000) (Figure 1 and 2) [2].

The overall incidence rate for CC is 52% (8 per 100,000 women) and in 2008 was the cause of 275,000 deaths, of which about 88% occurred in developing countries: 53,000 in Africa, 31,400 in Latin America and the Caribbean and 159,800 in Asia [2]. The incidence and mortality age-
**Figure 1.** CC incidence rates (per 100,000 woman-years) by country, estimated for 2012. The 5 categories of incidence rate increase as the intensity of blue color gradient increases. Available in http://globocan.iarc.fr/. Accessed: May 29, 2014.

**Figure 2.** Mortality rate (per 100,000 woman-years) for CC, by country, estimated for 2012. The 5 categories of mortality rate increase as the intensity of red color gradient increases. Available in http://globocan.iarc.fr/. Accessed: May 29, 2014.
standardized rates were 18 and 10 per 100,000 women, respectively, in developing countries; in contrast, in developed countries were 9 and 3 per 100,000 women, respectively [2]. In developing countries, 1.9% of women developed CC and 1.1% died from the disease before having 75 years of age. In most developed countries, the incidence and mortality from CC is 0.9% and 0.3%, respectively, being two to three times less than in developing countries [2]. India is the country with the highest number of cases (134,000) and deaths (73,000 deaths), representing a quarter of the global burden of CC. The correlation of incidence and mortality age-standardized rates for CC demonstrate similar geographic distribution (Pearson's correlation (q) =0.95). However, the variation is larger for mortality (range 3 to 514) rather than to the impact (range 3 to 344), which is attributed to a lower survival rate in countries with the highest incidence (Pearson correlation's (q) = 20.49) [2].

CC incidence and mortality rates in the last thirty years decreased in most developed countries, probably as a result of screening and treatment programs. On the contrary, these rates increased or remained invariable in most developing countries, where cases are not diagnosed or not treated in a timely manner. Hence the majority turns out to be mortal, causing enormous pain and suffering to women and exerting adverse effects on the well-being of the family and the community of the affected person [2].

1. CC incidence and mortality trends in Mexico and other developing countries in the region of the Americas

Latin America and the Caribbean have some of the highest age-standardized incidence rates (29.2 per 100,000) and mortality (13.6 per 100,000) by CC in the world, only surpassed by those in Africa (except for the region of Northern Africa) and Melanesia (Figure 3) [2]. Approximately, 15% of CC new cases occur in Latin America, with a five-year prevalence of 207,031 cases [3]. The highest incidence rates of CC in the region of the Americas are observed in Bolivia (47.7/100,000) and Guyana (46.9/100,000) (Figure 4) [4]. Although population screening with Pap was introduced in Latin America in the early 60's, the reduction of incidence and mortality in developed countries has not been replicated in the region. The CC mortality rates were unchanged between 1975 and 1990 in the Americas except Canada and the United States of America [3], possibly with some limitations as underreporting. The huge disparity in terms of CC morbidity and mortality between high- and low-income populations can also be seen in America. Over the last 40 years, declines in CC incidence have resulted in significantly low rates (less than 10 cases per 100,000 females in Canada, the United States and other established market economies). However, in
most countries of Latin America and the Caribbean, the annual CC incidence rates remain high, generally above 20 cases per 100,000 females. Higher mortality rates for CC in the United States mortality occur in Latinas than in other ethnic groups. Latina women have twice the possibility to die by CC than non-Hispanic women [5].

In terms of CC mortality rates in the region of Latin America and the Caribbean, Puerto Rico is the only country that has maintained a rate below four deaths per 100,000 women since the 1970s. Countries that already had

Figure 3. Incidence and age-standardized mortality rate per 100,000, by geographic regions worldwide. Women of all ages are included. Taken from: International Agency for Research on Cancer. GLOBOCAN 2012: 1. Available in http://globocan.iarc.fr/. Accessed: May 29, 2014.
mortality rates below 10 deaths per 100,000 women in the same years, such as Cuba, Argentina, Brazil and Uruguay, have achieved a greater reduction in CC mortality risk, whereas Chile, Costa Rica, Mexico and Colombia show moderate significant reductions but still have mortality rates above five deaths per 100,000 women [6,7].

In addition, CC is the main cause of disability-adjusted life years (DALYs), one DALY being equal to one year of healthy life lost, among the women of Latin America and the Caribbean. In 1995, 6,065 women aged between 35 and 64 years died from CC in 16 countries, resulting in the loss of 183,487 years of potential life, assuming a life expectancy at birth of 75.8 years [8]. According to records from Globocan 2012 and assuming that the estimated CC incidence rates remained constant in Latin America and the Caribbean, a 20% increase of CC cases in this region is estimated by the year

![Figure 4](http://globocan.iarc.fr/).

**Figure 4.** Incidence and age-standardized mortality rate per 100,000, in 20 countries with rates highest in the Americas. Women of all ages are included. Taken from: International Agency for Research on Cancer. GLOBOCAN 2012: 1. Available in http://globocan.iarc.fr/. Accessed: May 29, 2014.
2020 [4]. If prevention programs in this region do not improve, new CC cases will rise from 68,818 in 2012 to 82,785 cases in all ages in 2020, just based on the growth and aging of the population [4,7].

In the case of Mexico, during the period 1976-2006, there were 102,544 deaths from CC. In the decade of the 80s, the national program for prevention and control of CC faced enormous challenges. National trends indicate an increase in CC mortality rate at all ages, <15% of the eligible female population had ever had a Pap smear, and coverage was very low in underdeveloped and poor areas. There was also a lack of epidemiological control and quality control measures for taking and diagnosis of cervical cytology samples. Early in the decade of the 90s, an assessment of the quality of cervical cytology in Mexico reported that >60% lacked endocervical, mucus cells and/or cell metaplasia. In addition, some centers reported cervical cytology screening >50% false negative results [9]. For the period 1989-2004, the mortality rate was reduced by 2.94, equivalent to about three fewer deaths per 100,000 women. Factors associated with decreased mortality rates by CC were an increase in Pap coverage and a lower birth rate. Thus, for each unit increase in the Pap coverage, mortality by CC decreased 0.069 and for each unit decrease in the birth rate, death rate by CC decreased 0.054 [9].

Mortality rates reported for 2000 and 2006 were 19.2 and 14.6 per hundred thousand women aged 25 years and over, respectively, representing a decrease of 24.2% in the period. For 2000, a Mexican woman who lived in a rural area had three times more possibilities of dying by CC than a woman living in an urban area; likewise, women who lived in central and southern Mexico had a relative risk of 1.04 and 1.47 respectively of dying by CC compared to those living in the North. However, for 2006 no differences were observed in the risk of dying from CC in relation to area of residence (rural vs. town) [9].

In 2007 was reported an incidence rate of 40.5 per 100,000 inhabitants and a mortality rate of 14.3 per 100,000 inhabitants, being the states with strong indigenous presence, which have the highest mortality rates by CC in Mexico [1]. According to the study "The burden of disease of women in Mexico, 2005," the DALYs in both sexes by non communicable diseases, category where CC is located, were 5,278,491 DALYs (49%) [10]. The states with the highest death rates in 2008 were CC Colima (Relative risk, RR: 1.92, 95% CI:1.29-2 .85), Veracruz (RR: 1.91, 95% CI :1.55-2 .35) and Yucatan (RR: 1.90, 95% CI :1.44-2 .49) [11].

The latest CC mortality data are reported by the National Institute of Statistics and Geography in 2012. In 2011, CC was the second malignancy for which killed women in Mexico (10.4%) and when analyzed by age
group, rose from 10 deaths per 100,000 women aged 40 to 49 years, to 30 deaths per 100,000 women aged 65 to 74 years, until to reach 55 deaths per 100,000 in older women 80 years and older [12]. Mexico has a population of 46.06 million women who are 15 years of age and older and are at risk of developing CC. Current estimates indicate that every year 13,960 women are diagnosed with CC and 4,769 die from this disease. [13].

According to records from Globocan 2012 and assuming that the estimated CC incidence rates remained constant in Mexico, a 28% increase of CC cases in this region is estimated by the year 2020 [4]. If prevention programs in this region do not improve, new CC cases will rise from 13,960 in 2012 to 17,940 cases in all ages in 2020, just based on the growth and aging of the population [4].

The geographical distribution of this neoplasm mortality rates displays the opposite behavior of that of breast cancer: The highest mortality rates appear in southern and southeastern states, reflecting the social and economic disparities associated to it (Figure 5) [14].

![Image showing geographical distribution of cervical cancer mortality rates in Mexico by region, 2008.](http://www.sinais.salud.gob.mx/descargas/xls/m_016.xls)

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Even though in Mexico less than 13 percent of the potentially preventable cases are averted, the CC mortality rate has maintained a downward trend over the past 15 years, with a rate of 13.5 deaths per 100,000 women in 2000, a rate of 9.1 per 100,000 women in 2008, and a rate of 8.0 per 100,000 women in 2012 which represents a 32.7% decrease from 2000 to 2008, and a 40.7% decrease from 2000 to 2012. Still, the phenomenon has not been uniform across the country, as has happened globally; a higher mortality is concentrated in states with a lower human development index [15, 16].

At present, there are still marked differences in mortality from CC between states associated with social inequality. The gradual decrease in the mortality rate in Mexico, which began in the early nineties, has been faster in the past six years, as a result of the confluence of several factors: increased coverage and capacity colposcopy services and cancer centers, likewise, infrastructure, equipment and training of human resources were improved. Other important aspects that have increased the coverage of detection and timely treatment of injuries precursor and CC are the improvement in quality of life of the population, increased awareness of women about the importance of prevention, and increased political and financial support [10].

Supporting this, the national health and nutrition survey 2012 of Mexico (ENSANUT2012) reports an increase in the number of women that attended medical service to have a Pap smear. Of the women 20-65 years old surveyed, 44.3% had a Pap smear the year later of the survey, while in 2000 and 2006 was the 29.4% and 37.1%, respectively. Also, 10.3% of the 35-50 year old women in the survey had a HPV detection test, information not available for the previous surveys due to lack of test implantation in the screening program in such years [17]. However, although they have been advances in the program, are not considered sufficient for a highly preventable disease.

2. Rationale for cervical screening

To prevent CC or its precursor lesions during adolescence, young people should be informed of the various risks threatening their health, with special emphasis on detailed information on sexually transmitted diseases and contraceptive methods. An effective prevention of CC requires strict adherence to the secondary prevention protocol that includes: 1) screening, 2) diagnosis, 3) treatment and 4) monitoring of both high-grade squamous intraepithelial lesions (HG-SIL) with potential to progress to cancer as well as micro-invasive carcinoma [18].
The validated technique for population-based CC screening is the cervical cytology known as Papanicolaou test, Pap smear o Pap test. Its effectiveness and efficiency have been widely supported in the countries where it has been applied in a planned, systematic and continuous manner. An HPV DNA detection test can be complementary to cytology screening, but it has not yet been validated as a screening technique in most countries and its use is currently under study. Its features make it applicable in developing countries with high prevalence of CC [19].

Since cervical cytology is not a diagnostic technique, for the prevention of CC it should be implemented along with a colposcopy to improve its sensitivity. When used together, their negative predictive value is close to 100% for cervical neoplasia, so their joint implementation should be recommended. In the diagnosis of an abnormal cytology, the colposcopic study aims to: 1) confirm the lesion, 2) rule out invasion, 3) establish the lesion degree, 4) determine the lesion characteristics (topography, extent, gland involvement), 5) diagnose multi-centric tumors, and 6) select the therapeutic behavior and the type of treatment, if needed [19]. Considerable work has been done to optimize cytological screening, including quality assurance, bench marking, and the introduction of liquid-based cytology. Nevertheless, the characterization of morphological changes in cervical cells remains subjective with a marked inter-observer and intra-observer variability in terms of the colposcopic diagnosis.

Viral detection has been proposed and partially evaluated as a complementary diagnostic technique in four instances: 1) as a method of triage of equivocal cytological diagnoses, classified as abnormalities of uncertain significance (ASCUS / AGUS); 2) as an alternative quality control system of cytodiagnostic programs; 3) as a general screening technique for selected populations, particularly middle and advanced age people, and 4) as a primary screening technique in populations that are scarcely protected by cytological screening programs [20].

A molecular HPV DNA detection test avoids the limitations of cytological testing, since its quantitative result is based on a predetermined cut-off and its results can be well reproduced. There is enough evidence to recommend HPV testing as a screening procedure complementary to the cervical cytology test in countries like Mexico, in women with abnormalities (cellular atypia) and as an epidemiological surveillance system in patients under treatment for CC precursor lesions [21].

In population-based programs with broad coverage, the HPV test conducted by a health professional can be used as an adjunct to Pap smear for the detection of cases among asymptomatic women older than 35 years of age without a diagnostic reference. This test can also be used for the
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surveillance of women diagnosed with atypical squamous cells of undetermined significance and for the follow-up of treated cases, because it improves the monitoring of recurrent lesions after treatment [21]. The HPV test used as an adjunct to cervical cytology with negative results can be used less often than every five years because previous studies showed that a woman with a normal Pap test and a negative HPV test virtually does not develop CC for periods of up to 10 years [21].

Some studies suggest that viral detection is 10 to 15% more sensitive than conventional cervical cytology in the case of HG-SIL in cytological samples with an initial cytological diagnosis of ASCUS, with minor specificities in age groups under 30 years [20]. Under some circumstances, the vaginal sampling for viral detection can be performed by the woman herself. This fact could be decisive for women in conditions health precariousness. In Mexico, vaginal self-sampling at home has been recommended for sexually active women older than 25 years of age [21].

As an adjunct to Pap testing, routine screening with HPV has turned out to be a more sensitive indicator to identify prevalent high-grade cervical intraepithelial neoplasia (CIN) lesions than the conventional Pap test or a liquid cytology [22,23]. A combination of HPV and Papanicolaou testing has almost a 100% sensitivity and negative predictive value. The specificity of the combined tests was slightly lower than that of the Pap test. A double negative HPV and cytology test gives women a better prognosis in terms of the risk of developing cervical neoplasia, compared to three consecutive Pap smears, and can provide a safe screening at three-year intervals in the case of low-risk women. It is likely that HPV Testing may become the most common screening strategy in population-based programs for the timely detection of cancer. Continuous research will improve the sensitivity and the cost-effectiveness of these HPV-detection methods [23].

The main advantages of HPV testing include the following: 1) less dependence on the quality of the collected sample; 2) objective and quantitative interpretation of the results; 3) easy transference to the clinical laboratory for an automated process; 4) high performance with respect to person-time units, and 5) high interlaboratory reproducibility. The current limitations of the system have to do mainly with costs and with the need to modify standards. HPV analysis has great potential in terms of primary screening. However, population-based studies are needed to evaluate its usefulness and to demonstrate that its use reduces the rate of invasive cancers, as has been shown in the case of cytological tests. One advantage of HPV testing is that it allows self-sampling, thus facilitating the screening of women who do not belong to the screening program [20].
High sensitivity and specificity are required for the detection of HG-SIL. Given the natural history of HPV, it is indicated for the screening of women older than 35-40 years of age. Among young women, detecting the presence of high-risk HPV (HR-HPV) would be useful to select the high-risk-for-cancer group. There are ongoing cost-effectiveness studies are underway to assess if HR-HPV-negative women can be monitored in a longer term, taking into account not only the cost of cytological and HPV testing but also the safety interval conferred by a negative screening [18].

In addition to high sensitivity, the ideal screening test should have high positive predictive value and should be able to select only women with significant disease (SIL or high-grade cancer) or with potential for progression. However, both the cytological and the HR-HPV test detect too many women with positive or inconclusive results, but without significant lesions or the kind that will spontaneously return. This result in an overburden in terms of motivates a high overload care for diagnosis or treatment for the health systems. When considering an HPV test as a screening method it should be taken into account that most HPV infections diagnosed do not progress to cancer, so we might be taking an unnecessary risk by implementing a costly intervention and increasing the negative psychological impact on patients.

From the standpoint of public health, the Pap smear and the HPV test have a synergistic effect which allows an increase of the interval between screening exams. The protective effect of a joint Pap and HPV testing negative result is at least five years long, compared with the two years associated to a negative cervical cytology. Clinical studies have shown that HPV testing can be used to follow-up on abnormal Pap results, to monitor women that have been treated for CIN III and CC, and for the primary screening of cervical neoplasia.

HPV testing is more sensitive and has more negative predictive value for identifying women with CIN III than the Pap test. However, its specificity is lower than that of conventional Pap smears. Therefore, there is a restriction for the use of HPV testing as a screening method in population-based programs for the early detection of cancer: age. The programs that use both tests should focus on women over 35 years of age with a persistent HPV infection (at least two positive HPV DNA results in a one year period), which according to the International Agency for Research on Cancer has carcinogenic properties. Programs based on vaginal self-sampling at home should send HPV-positive women for a colposcopy as a complementary diagnostic and therapeutic strategy [21].

Whereas the risk of significant cervical lesion (HR-SIL or CC) in the first years after the first exposure to HPV is low, it is advisable to start
screening three years after first vaginal intercourse or at age 25. The recurrence interval of cervical cytology depends on the quality of previous cytology, age and level of risk. In women younger than 30 years, an annual Pap is recommended. Three consecutive negative Pap smears can be considered satisfactory and the test can then be repeated every three years. Women with risky sexual behavior, with changes in personal circumstances and/or partner, immunosuppressed women are advised to follow annual checks. Similarly, if no metaplastic or endocervical cells are observed in the Pap smear or there are other limiting factors, its annual repetition should be considered [18].

Mexico has issued an official Mexican standard (NOM-014-SSA2-1994) on the control and treatment of CC, which defines the guidelines to be followed, both with respect to the national screening program (NSP-CC) and to the treatment of identified cases [24]. The NSP-CC instituted in the late 1970s has gained relevance and coverage since 1998. Each year there are on average 7.2 million cervical cytology screenings performed free; of these 1.2% turns out to be positive, and this allows an 80% coverage to be reached every three years among the female population aged 25 to 64 years [25].

Despite the achievements in terms of coverage, NSP-CC entails operational problems, including the low sensitivity of Pap smears, which results in nearly 40% of cases, most often in early stages, not being recognized. It also requires prepared staff and specialized equipment to ensure a good sampling and its interpretation depends on the ability of the laboratorian [26]. In Mexico, the Social security absorbs the cost of treatment the CC since 1943 and since 2004 the “Seguro Popular de Salud”, covers treatment of the women without social security, either by universal catalog of essential health services “CAUSES”, in the case of dysplasia, or the fund protection against catastrophic expenses “FPGC” to more advanced stages [27].

Mexico has focused its interest to identify interventions that strengthens prevention and the NSP-CC in a context of constraint financial. In 2007 was published a generalized cost-effectiveness analysis (GCEA) of 10 possible scenarios of interventions that included Papanicolaou screening, HPV vaccine, hybrid capture screening (HC) using a Markov model from the public sector perspective as payer. Scenarios considering 80% coverage show an average cost-effectiveness ratio (ACER) per DALY averted of $16,678 pesos for Pap of women between ages 25 and 64, $17,277 pesos for HC of women between ages 30 and 64, and $84,008 pesos for vaccination of 12-year-old girls. Annual financing of $621 million pesos, $741 million pesos and $2,255 million pesos, respectively, was necessary for these scenarios. After this analysis suggested a selective, combined introduction of
Pap-HC screening that considers the comparative advantages of application in different populations and geographical areas is suggested. Additionally, was suggested to introduce the vaccine once a threshold price of $181 pesos per dose – when the vaccine becomes equal in terms of cost-effectiveness to HC – has been achieved [28].

3. Problems and challenges facing CC screening programs especially in Latin America

An effective CC prevention and control must address several issues: coverage and quality screening services and early detection; availability of fast, reliable and affordable diagnosis, treatment and subsequent care; and support infrastructure such as counseling and information systems to improve the quality of care and enhance the effective management of patients and programs.

Some of the obstacles to an effective prevention and control of CC in Latin America include the following:

a) Religious, socio-cultural and gender perspectives of women: Some studies have reported that in some regions, women are reluctant to undergo CC screening because they perceive it as a synonym for death. Furthermore, some women can be discouraged by the presence of male healthcare providers. In Mexico, a study reported that knowledge about the benefits of screening tests, socio-economic status and level of education were the main factors to predict the use of screening services. Specifically, women with university education were four times more likely of having attended the Program for Early Detection of Cancer (DOC), and women who had a health insurance program were twice as likely. The coverage of Pap smear among women living in good housing conditions was four times higher than among those living in poor physical conditions [29,30]. Social norms and a strong distrust of allopathic medicine contribute to the alienation of women from institutional health-care [31]. Even though the costs of screening are affordable, the socio-cultural context has not been conducive to the widespread use of screening and diagnostic tests [26].

A 2008 study reported the results of the implementation of an educational program called Porque me quiero, me cuido (Because I love myself, I take care of myself) in rural and indigenous populations in the central valleys of Oaxaca, one of Mexico’s poorest states. This program was aimed at promoting the use of screening services and CC prevention by changing the behavior of the individuals and the community. For this
purpose, interactive workshops focused on the development of skills and knowledge among women of 15 to 64 years of age. These workshops were supplemented with community campaigns and workshops for men to elicit their support. The Pap tests performed in the 10 populations where the intervention was carried out and in the six populations with similar characteristics used as control were quantified. The changes in behavior, knowledge and attitudes were also evaluated by means of a questionnaire. There were significantly more Pap tests performed in the populations where the program was carried out than in the control ones. It found Positive changes in the level of knowledge that women had on the causes of CC and the measures to prevent it were found [26].

b) Quality of care in public institutions: Some studies have documented problems in terms of timing: the delivery of results is often delayed, and women lose interest in the program and often do not return. Additionally, the physical conditions in which the Pap smear is taken in most health institutions belonging to the public sector (usually in crowded places and without privacy) do not contribute to create a positive experience, especially when services in the private sector are perceived as broader and with more privacy [32,33]. After a confirmatory result of a cervical lesion is issued and communicated to the patient, the practice of not automatically scheduling the diagnosis and treatment results in a lack of appropriate and timely monitoring of the affected women. In Peru, even though treatment modalities were programmed additional, factors related to geographic access and cost barriers still pose considerable obstacles. Furthermore, the manner in which health workers communicate with the women involved, lacking friendliness and warmth, represents an additional barrier with respect to the quality of care.

c) Quality of the cytological screening methods: The frequency of false negative cytology results remains one of the limitations of the screening programs. Approximately one third of the not diagnosed cases are attributable to interpretation, and the remaining two thirds are attributable either to inadequate smear sampling and preparation or inadequate follow-up of identified cases. Alternatives coming from different stages of worldwide evaluations include the following: i) preparation of cell suspensions in a liquid medium and obtainment of single-cell plates free of residue and cellular clots production of clean sheets and clumps of cellular waste (liquid based cytology), ii) computerized reading of smears with field selection of suspicious images for professional review, iii) association of cytology and HPV DNA testing, iv) cervicography, magnified pictures of the
cervix that are submitted to specialized readers for interpretation magnified, v) polar probe based on a transmitterreceiver of optical and electrical waves capable of differentiating normal from neoplastic tissue. Problems with respect to the sampling, collection, preparation and interpretation of the Pap smears have been found in numerous evaluations of such programs in the Region of the Americas. In Venezuela, a review of the diagnoses of 341 women from the CC Control Program in the state of Aragua between 1995 and 1996, found that in 22% (75/341) a CIN III was diagnosed by cytology, whereas the histological examination confirmed the same lesion in 31% (105/341) [34].

A Mexican study from 1996 on the quality of cytological samples, reported that 64% of a random sample of Pap smears lacked endocervical cells, mucus, and squamous metaplasia, whose presence points to the fact that the sample was taken from the transformation zone. The false negative results rates oscillated between 10% and 54% in 16 interpretation centers. Thirty-seven out of 1,039 Pap smears classified as negative by cytotechnicians were identified as invasive cancer by an expert [32].

In response to the interpretation problems of the Pap smears, PAHO launched an external quality control system in 1998 with the aim of improving the effectiveness of cytology laboratories in selected countries of Latin America. This Pan American Cytology Network (Red Panamericana de Citología – RedPAC) consists of 45 laboratories in seven Latin American countries (Chile, Mexico, Peru, Costa Rica, Ecuador, Venezuela and Bolivia), with a reference center in Santiago de Chile. Through RedPAC, great efforts have been made to improve the technical and administrative quality of cytology laboratories, including the evaluation of laboratory operations, a proficiency testing program that compares the cytological interpretations of technicians with those of a panel experts, on-going education activities to strengthen the technical skills and the management of laboratories, and technical assistance to implement internal methods of quality control. A performance analysis of RedPAC revealed improvements in some laboratories regarding their diagnostic concordance with the external panel of experts in three series of skill tests; however, this was not the case in all of them [8].

d) Coverage of the CC Prevention and Control: Based on a sub-regional workshop held in Cuba in October 2001, only Cuba and Puerto Rico reported coverage rates between 60% and 80%. All other participating countries indicated that their coverage was less than 60% [8]. The analysis of the age-specific coverage of this program has shown that
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younger women seek screening disproportionately and more often. In most Latin American countries, efforts to detect CC are linked to family planning and prenatal care; therefore, targeted women are mostly young, usually between 20 and 30 years of age, when their risk of invasive CC is much lower than that of older women [8].

In 2001, WHO conducted a survey to assess the national capacities to prevent and control of chronic diseases. Only 19 (54.2%) of the countries included from the Americas reported having a cancer control plan aimed at CC. About 46% (16/35) of the participating countries reported having surveillance or information systems on CC. Around 24 countries (68.5%) reported having guidelines or standards for CC prevention and treatment, and about 77% (27/35) reported having equipment and means for CC surveillance at primary health care units [8].

The scarce number of CC surveillance or information systems precludes a reliable monitoring of the program and an accurate assessment of their impact. Similarly, the lack of national plans against CC limits the efforts in terms of lobbying, information spreading and resource mobilization. Even though there are plans in many Latin American countries, they are not often evidence-based nor are they appropriate in terms of local resources and capacity, particularly with regard to primary health-care [8].

Between June and October 2001, four workshops on CC prevention were held in some sub-regions of the Americas: the English-speaking Caribbean, Central America, the Southern Cone and the Andean sub-region. It was found that some issues related to CC programs were common to all sub-regions, whereas other were unique or posed major challenges to some countries. For example, small-sized Caribbean countries have a limited ability to get and retain skilled personnel and thus maintain skill levels regarding cytology. Similarly, warranting a quality CC prevention service in the highlands of Bolivia, including diagnosis and treatment, poses significant challenges due to its high altitude and difficult of access [8].

Some of the problems and challenges for an effective CC prevention and control in the Region of the Americas include the following:

a) Not recognizing CC as a preventable health problem: Within the political structures of many countries in the region, there is no genuine support for effective CC prevention. This is related to the unawareness of its preventable nature or to the impression that the disease does not cause immediate death or acute epidemics that require prompt containment.

b) Insufficient financial resources: In all sub-regional discussions the lack of financial resources as a factor limiting the effectiveness of programs was mentioned. It is also recognized that substantial investments are
needed regarding secondary prevention, not only in terms of screening, but also to provide essential diagnostic, therapeutic and palliative services. Even if current funding of programs against CC may be inappropriate, an important and early requirement with respect to the estimation of needs is to count on a careful evaluation of the program’s efficiency and effectiveness. This guarantees that any request for additional resources be based on a rational analysis. Such is the case of the CC prevention and control program in Mexico, where the allocation of resources comes directly from Congress, where decisions are made and emergencies addressed such as the budget cutback when resources were needed to meet the H1N1 pandemic influenza [35].

c) Inadequate human resources: One of the limitations of the cancer prevention and control programs is the lack of human resources, quantity and quality-wise, mainly cytopathologists and cytotechnologists. In some countries like El Salvador, although human resources are enough, they are poorly distributed which results in insufficient attention to the rural areas and inadequate internal quality control [8].

d) Falling population coverage, especially in younger women: There is persistent evidence of falling coverage, especially in women in the 25-29 age groups. Reasons for this are not know, but may include general features of this age group reflected in low rates of other community-based activities. Improving access for women of all cultures is important, as well as the quality of written information. Recently, several programs have launched advertisements with eye-catching slogans, backed up by radio and television articles to try to reach this group of women.

e) Suboptimal organization and management of the programs: The lack of rules of procedure and guidelines for CC prevention and control of hinders the institutionalization of programs and does not allow standardization. For example, only a few countries in the English-speaking Caribbean have established anti-CC programs and rules of procedure. In many countries, even though CC screening is carried out, the public and private components of an efficient cancer prevention program are neither fully integrated nor well-coordinated. This is the case of Guatemala, Honduras and the Dominican Republic. Many countries lack adequate information systems that enable the effective management of CC prevention programs. This situation prevents patients from receiving effective follow-up and management, carrying out a steady coverage assessment, and determining the effectiveness of a program through continuous evaluation [8].
4. Public health perspectives on CC prevention and control in Latin America

In light of the significant public health burden in terms of CC in Latin America and the Caribbean, PAHO has drafted a Regional Strategy for CC Prevention and Control. The strategy calls for increased action to strengthen programs through an integrated package of services: health information and education; screening and pre-cancer treatment; invasive CC treatment and palliative care; and evidence-based policy decisions on whether and how to introduce HPV vaccines. It comprises a seven-point plan of action: carrying out a situation analysis; intensifying information, education and counseling; scaling up screening and linking it to pre-cancer treatment; strengthening information systems and cancer registries; improving access to and quality of cancer treatment and palliative care; generating evidence to facilitate decision-making regarding the introduction of the HPV vaccine, and advocating for equitable access and affordable HPV vaccines. This proposed strategy, approved by PAHO Directing Council on October 1st, 2008 has the possibility of stimulating and accelerating the introduction of new screening technology and HPV vaccines into programs throughout Latin America and the Caribbean [36].

Screening probably remains the only viable option for adult women with little chance of receiving prophylactic vaccines on time in the region. Future generations could live in a totally different scenario where adolescent vaccination will be common and CC prevalence will decrease. However, the availability of new and superior technology will not suffice. Even if vaccination were implemented, an additional two decades will be required to observe its impact on HPV-related disease and cancer.

Research activities on screening methods in Latin America has been carried out through programs such as the Guanacaste Project in Costa Rica [37]; the TATI project (Spanish acronym for “screening and immediate treatment”) in San Martin, Peru [38]; the evaluation of vaginal self-sampling in Chile [39]; HPV testing as primary screening at the Mexican Institute for Social Security (IMSS) in Morelos, Mexico [40]; self-sampling and HPV testing among insured women in Mexico [41]; comparison of HPV testing and cytology strategies among IMSS population between 2005–2009 in Mexico [41], and the evaluation of visual inspection with acetic acid (VIA), visual inspection with Lugol’s iodine (VILI), cervical cytology and HPV testing in Brazil and Argentina through the Latin American Screening Study (LAMS) [42].
These studies recommend that each country establishes a properly staffed and funded group dedicated to CC control, responsible for developing and monitoring all of the program’s activities, including strict evaluation of the compliance of all health providers. Screening and treatment should be provided free of charge to all women. The different areas of the country should be categorized according to their level of development and infrastructure to define the specific interventions to be implemented in each area. Additionally, in places where no other methods are available or the existing options have poor quality and limited coverage, the implementation of visual inspection by primary care nurses or physicians is recommended, with cryotherapy of positives after proper referral of possible invasive cancers. The emphasis should be on complete coverage of women older than 25–30 years of age [41].

The primary screening with HPV testing, with its high sensitivity and negative predictive value, should become the standard of care, including algorithms using cytology or VIA as secondary evaluations according to the local infrastructure and resources [41]. Vaccines and improved screening methods only work for women who receive them. In this sense, the cost and coverage issues become essential. The proper monitoring of women at risk (whether high-risk HPV carriers or patients with advanced NIC) requires adequacy and efficiency of logistics infrastructure, as well as trained medical personnel and health education. All these have been difficult issues to tackle in many regions of Latin America. In addition, urban areas tend to concentrate the above mentioned preventive efforts while rural areas suffer from lack of access to health services.

Progress in preventing CC entails several aspects: a) promoting social awareness of the problems caused by CC and of the new advances in understanding of its etiology, b) empowering women and their male partners with updated health education, c) incorporating new technology into screening strategies, which will make the number of visits less demanding and more efficient in terms of the protection provided at each visit, and finally d) supporting the current efforts to develop and test vaccines that will very useful in terms of the acceptance of vaccination strategies, both for the health professionals and the general population. After mass vaccination is introduced, HPV testing will also become the preferred screening method. However, the collaboration of governments, women’s groups, academicians, industries, donors and international organizations is essential for the success of efforts to control CC in Latin America.

In conclusion, CC persists as a significant public health problem in Latin America and the Caribbean. Each year, about 77,000 new cases are diagnosed and 30,000 women die prematurely from this disease. It is a fact
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that CC is the neoplasm with the greatest demonstrated potential for secondary prevention; the disease is entirely preventable and curable, at low cost and low risk when there are methods for screening asymptomatic women, along with appropriate diagnosis, treatment and follow-up options.

In spite of the existence of secondary prevention through screening and early detection, which has proven to be effective when combined with appropriate and timely treatment, it requires high-level management and organization, including appropriate financial and human resources, to warrant and keep the quality and effectiveness of the programs. The most important challenge that developing countries in Latin America and the Caribbean is the inability to maintain the infrastructure, organization and essential quality in all service delivery points across the entire spectrum of cancer care.

Most countries in the Region of the Americas already have some elements to conform a CC prevention program. However, the fragmentation and lack of coordination have prevented such elements to be integrated into cohesive and effective strategies. For optimal effectiveness, screening programs must be better integrated with treatment and monitoring ones. Moreover, to ensure that women throughout the region have access to CC screening and treatment, it is imperative to demand political commitment and financial support. The educational and outreach programs to generate awareness about CC as a preventable disease should be directed both to women and to the community at large.

Continuous assessment is necessary, either through surveillance or investigation, to provide the necessary public health scientific evidence on which to base policies and programs. The cumulative result of these efforts will result in the establishment and use of cost-effective prevention programs designed to meet the needs of women throughout the region. The final product could be fewer deaths due to CC in the Region of the Americas.

References


