

Chapter 2

Cervical Cancer Epidemiology

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Abstract Cervical cancer is a worldwide public health problem. In 2012, cervical cancer was the fourth most common disease in women and the seventh around the world, representing approximately 9 of every 10 deaths in less developed regions (87%). In Mexico, its relevance is also considerable; it is the neoplasia with the second highest incidence rates and the second leading cause of death among women of all ages. The most affected age groups are from 50–59 and 30–49 years old. Persistent infection with human papilloma virus (HPV) is a necessary factor for its development. There are certain risk factors that have been associated with cervical cancer, such as tobacco consumption, sexually transmitted diseases (STDs), oral contraceptive use and age at onset of sexual activity. In federal states such as Morelos or Chiapas, this disease has a greater impact on mortality partly because of social differences among the population. Although the strengthening of detection procedures, treatment and timely diagnosis have contributed to an important decrease in the mortality attributed to this cause in our country, there is still a need to keep improving the areas of prevention and promotion.

Keywords Neoplasia • Cervix • Mexico • Epidemiology • Detection • Prevention

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2.1 Impact of Cervical Cancer (CC)

2.1.1 In the World

In spite of being preventable, cervical cancer (CxCa) is the fourth most common type of cancer among women and the seventh among the general population. In 2012, 528,000 new cases were reported, accounting for an age-adjusted incidence rate of 14.0 per 100,000 women (Fig. 2.1). High-risk regions (with estimated age-standardized incidence rates of >30 per 100,000 women) include eastern Africa (42.7), Melanesia (33.3) and southern and middle Africa (31.5 and 30.6,

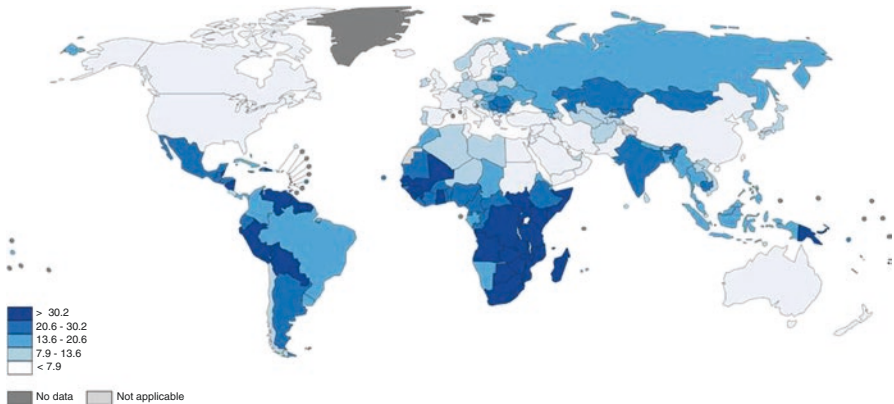


Fig. 2.1 Worldwide estimated incidence of cervical cancer in 2012* (Source: GLOBOCAN, 2012. Map production: IARC. World Health Organization http://globocan.iarc.fr/Pages/fact_sheets_cancer.aspx). *Estimated age-standardized rates per 100,000 women

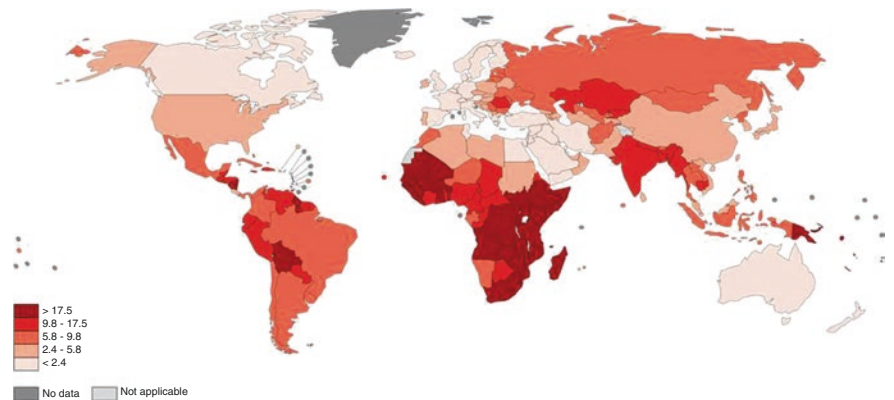


Fig. 2.2 Worldwide estimated mortality of cervical cancer in 2012*. GLOBOCAN, 2012. Map production: IARC. World Health Organization http://globocan.iarc.fr/Pages/fact_sheets_cancer.aspx. *Estimated age-standardized rates per 100,000 women

respectively). The lowest rates were present in Australia/New Zealand (5.5) and western Africa (4.4). In 2012, approximately 266,000 deaths were estimated around the world, which represents 7.5% of all female deaths attributed to cancer and an age-standardized mortality rate of 6.8 per 100,000 women (Fig. 2.2) [1].

Of the World Health Organization (WHO) regions, Africa and southeastern Asia have the highest mortality around the world (21.5 and 11.3 deaths per 100,000, respectively). Notably, approximately 9 of 10 deaths due to this malignant tumor occur in less developed regions [1]. A large majority of the global burden (approximately 85%) occurs in the less developed regions, where it accounts for 12% of almost all cancer cases in women. This disease affects primarily young women of low socio-economic status during their reproductive age, which also impacts their families. Thus, this type of cancer demonstrates the lack of equality in health status that exists [2].

2.1.2 Latin America and the Caribbean

According to GLOBOCAN, in 2012 in Latin America and the Caribbean, cervical cancer had an age-standardized rate of incidence of 21.2 per 100,000 women and a mortality rate of 8.7 per 100,000 women, which represents approximately 69,000 new cases and approximately 29,000 deaths. It is the second most common malignant tumor only after breast cancer, which is responsible for more new cases (27% and 12.2%, respectively) and deaths (14.9% and 9.9%, respectively) in these regions.

The countries with the highest estimated mortality rates are Guyana, Nicaragua, Paraguay, Surinam, Belize and Haiti, and those with the highest age-standardized incidence rates are Guyana, Surinam, French Guiana, Nicaragua and Paraguay (Table. 2.1). The estimated 1-year prevalence rate for this disease in the adult population is of 54,508 cases, but it is expected that the prevalence rates are four times higher (227,273 cases) (Fig. 2.3) [3].

Regarding the mortality rates in the year 2012, 28,565 deaths were reported in this region, with an age-standardized rate of 8.7 per 100,000 women. This rate corresponds to 10.7% of all deaths around the globe [3].

Currently, in the Americas, it is estimated that deaths due to CxCa are responsible for a great amount of years of potential life lost. As reported by the Pan-American Health Organization (PAHO), 74,855 women of 13 different countries of Latin America died because of cervical cancer between 1996 and 2001, of which 50,032 were from 25 to 64 years old. This finding indicates that more than 1.56 million years of potential life were lost because of the premature death of these women. When the morbidity burden is calculated in disability-adjusted life-years (which is equivalent to losing 1 year of healthy life), the WHO estimations suggest that in Latin America, this disease is responsible for 471,000 disability-adjusted life-years, which implies a much higher burden in comparison to any other type of cancer in women [4].

Table 2.1 Incidence and mortality rates of malignant cervical neoplasia in the Americas in 2012

País	New Cases	Deaths	Incidence rate ^a	Mortality rate ^a
Argentina	4956	2127	8.2	8.4
Bahamas	44	15	20.6	7.0
Barbados	44	15	25.4	7.2
Belice	43	17	32.7	14.9
Brasil	18,503	8414	16.3	7.3
Chile	1441	734	12.8	6.0
Colombia	4661	1986	18.7	8.0
Costa Rica	297	116	11.4	4.4
Cuba	1287	569	17.1	6.7
Ecuador	2094	1026	29.0	14.0
El Salvador	823	388	24.8	11.9
Guatemala	1393	672	22.3	12.2
Guayana Francesa	35	12	36.6	13.1
Guyana	161	71	46.9	21.9
Haití	1048	575	24.9	14.6
Jamaica	392	185	26.3	11.9
México	13,960	4769	23.3	8.1
Nicaragua	934	424	36.2	18.3
Panamá	351	134	18.7	7.1
Paraguay	1022	439	34.2	15.7
Perú	4636	1715	32.7	12.0
Puerto Rico	259	84	11.4	2.8
República Dominicana	1507	600	30.7	12.3
Surinam	107	44	38.0	15.7
Trinidad y Tobago	209	105	24.5	12.0
Uruguay	402	175	19.0	7.1
Venezuela	4973	1789	32.8	12.3

Source: GLOBOCAN 2012 (IARC). Consulted: 29/01/2016

^aIncidence and Mortality Rates were age-standardized for 100,000 women

In agreement with the PAHO data, in the Americas, 83,000 women were diagnosed with cervical cancer in 2012, and 36,000 of them died because of this disease. If this tendency continues, the number of deaths will increase by 45% by 2030. The death rates for Latin America and the Caribbean continue to be three times higher than in North America, which serves as a testimony for the considerable inequalities in health status that exist [5].

Regarding the number of deaths due to this cause, among all the other neoplasias, ten countries stand out in the Latin America and Caribbean region, with proportions higher than 11%. These same countries can be sub-classified into two groups, the first sub-group, where $\geq 18\%$ of the total deaths are due to malignant neoplasias (Guyana, 21.3%; Paraguay, 18.7%; Haiti, 18.3%; and Suriname, 17.7%), and the

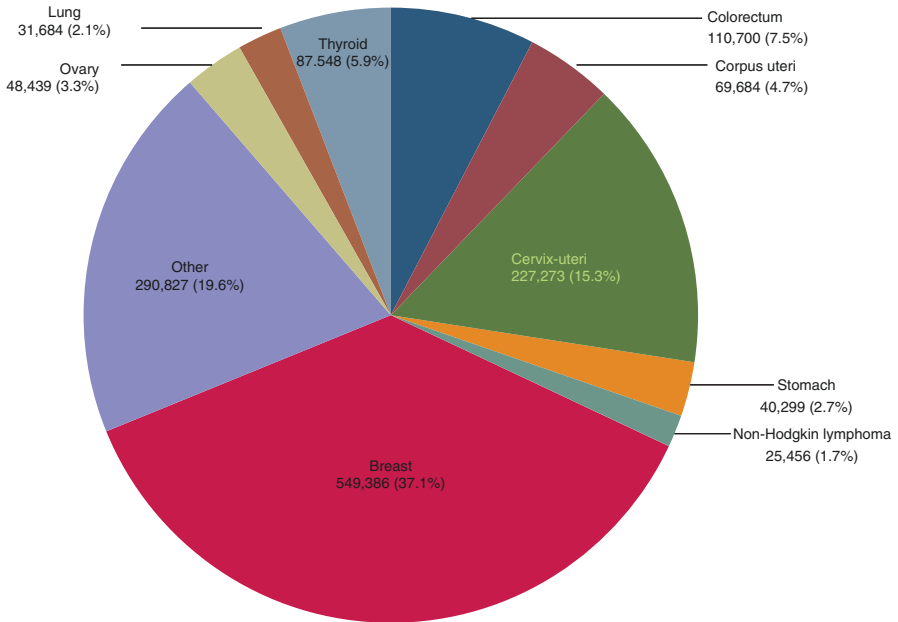


Fig. 2.3 Five-year estimated prevalence of cancer cases in women of Latin America and the Caribbean in 2012. Total population: 1,481,296 women (Source: GLOBOCAN 2012 (IARC). Consulted: 17/11/2015). Población total: 1,481,296 mujeres. Fuente: GLOBOCAN 2012 (IARC). Consultado el 17 de noviembre de 2015

second sub-group, where the ratio is slightly lower (Venezuela, Dominican Republic, Trinidad and Tobago, Jamaica, Mexico and El Salvador) (Table 2.2) [3].

2.1.3 In Mexico

Both the incidence and mortality of this malignant neoplasia are associated with demographic transition because there is a direct relationship between population aging and the appearance of new cases. However, lifestyle and the response capacity of the health departments limit the regional picture of this situation.

In México, cervical cancer is considered a public health problem, and this cancer is the second most common cause of malignant tumors in women ≥ 25 years old. Cervical cancer made up 9% (529,800) of all new cancer cases and 8% (275,100) of the total of female deaths due to cancer in 2008. Unfortunately, this type of cancer predominantly affects women in their reproductive years who find themselves in a vulnerable economic and social state, which implies a considerable impact both economically and socially and is currently the second cause of death by neoplasias in women in their reproductive years (40–59 years old) as well as in older women (55–59 years old) [6].

Table 2.2 Ratio of malignant neoplasia-caused deaths due to cervical cancer in women of the Americas in 2012

Country	Total deaths by malignant tumors ^a	Death by cervical cancer	Share of total (%)
Argentina	31,260	2127	6.8
Barbados	244	15	6.1
Brasil	103,606	8414	8.1
Canadá	35,230	503	1.4
Chile	12,063	734	6.1
Colombia	19,052	1986	10.4
Costa Rica	2005	116	5.8
Cuba	10,351	569	5.5
El Salvador	3379	388	11.5
Estados Unidos	293,353	6605	2.3
Guyana	333	71	21.3
Haití	3146	575	18.3
Jamaica	1442	185	12.8
México	40,053	4769	11.9
Panamá	1353	134	9.9
Paraguay	2345	439	18.7
República Dominicana	4044	600	14.8
Surinam	248	44	17.7
Trinidad y Tobago	811	105	12.9
Uruguay	3756	175	4.7
Venezuela	11,280	1789	15.9

Source: GLOBOCAN, 2012

^aAll cancer types excluding non-melanoma skin cancer

2.1.3.1 Morbidity

The General Direction of Epidemiology of Mexico gathers information regarding the incidence rates and number of new cases in their annual reports. These data show that 3063 new cases were reported in Mexico in 2014 (incidence rate of 6.1 cases for every 100,000 women older than 10 years), whereas in 1992, the number of cases reported was 4378; this represents a decrease of 30% in the total number of cases presented in Mexico in the last 22 years. Considering the different age groups, the highest incidence rate is present in women older than 45 years, specifically in those between 60–64 years of age (incidence rate of 15.5), followed by those between 45 and 49 years of age (incidence rate of 12.6), and last, but close to the former, the group of women between 50 and 59 years old (incidence rate of 12.4; in all three cases, the rates are calculated for every 100,000 women more than 10 years of age).

The CxCa case distribution was heterogeneous across the different federal states of the republic in 2014 (Fig. 2.4), with the highest incidence rates were reported in the states of Colima, Campeche and Aguascalientes (43.4, 18.6 and 15.6 per 100,000

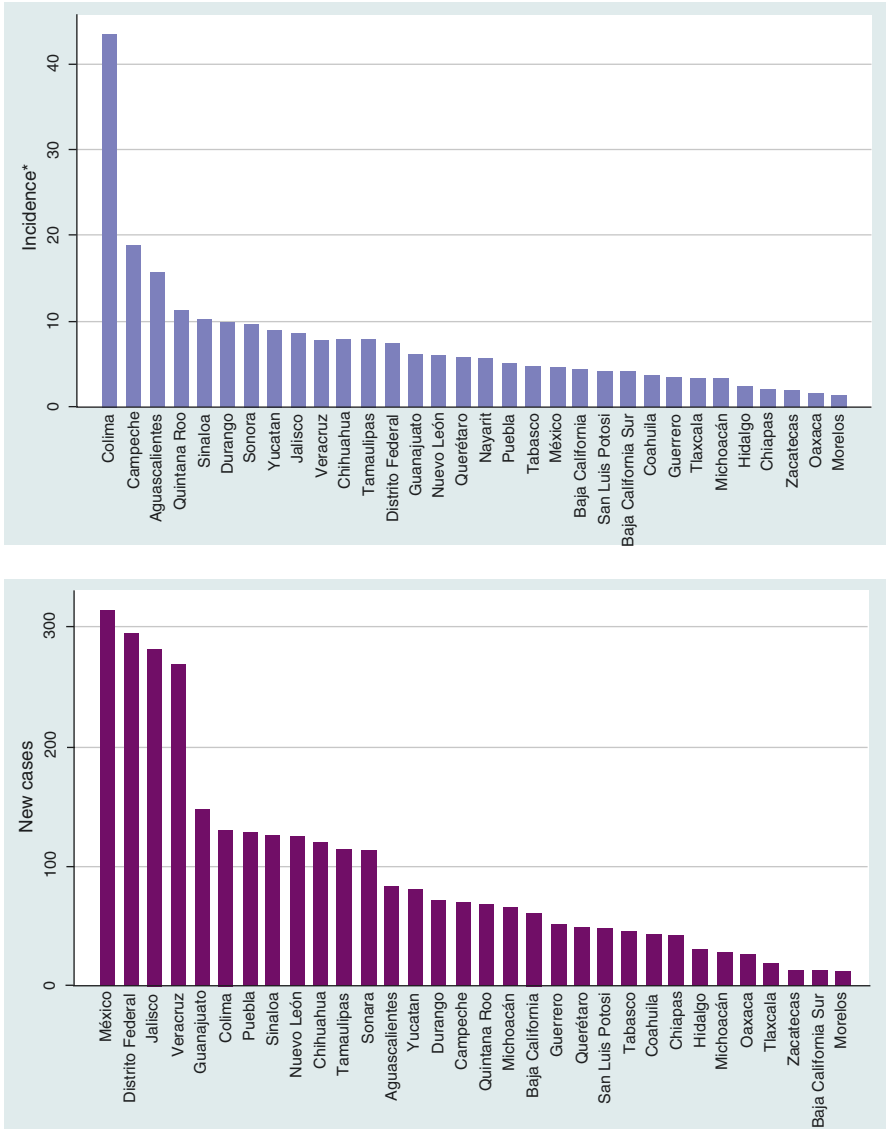


Fig. 2.4 Number of new cervical cancer cases and incidence rates* by federal state. *Rates were calculated per 100,000 women more than 10 years of age (Source: SUIVE/DGE/Secretariat of Health/United States of Mexico)

women more than 10 years of age, respectively), and the lowest incidence rates were reported in the states of Zacatecas, Oaxaca and Morelos (1.8, 1.5, and 1.3 for every 100,000 women more than 10 years of age, respectively).

Of the total cervical cancer cases registered in 2014, the majority were reported by the Mexican Social Security Institute (IMSS), followed by the Secretariat of

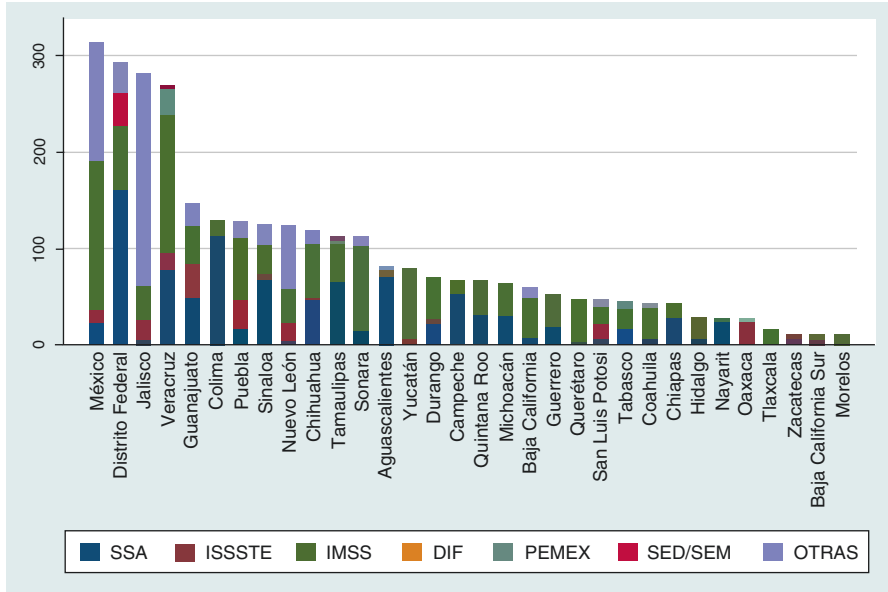


Fig. 2.5 New cases per federal state and notifying institution in Mexico in 2014. IMSS: also includes PROSPERA, and SED/SEM includes information from the Secretariat of National Defense and the Secretariat of the Navy (SEDENA and SEMAR, respectively, according to their original names in Spanish) (Source: SUIVE/DGE/Secretariat of Health/United States of Mexico)

Health and other institutions. In federal states where the Secretariat of Health is not the main reporting institution, such as Jalisco, Nuevo León, Yucatán and Baja California, its role is replaced by the IMSS or the Insurance and Social Security Institute for State Workers (ISSSTE) (Fig. 2.5).

2.1.3.2 Mortality

Cervical cancer is the second cause of death due to cancer among women since 2006, and among the countries of the Organization for Economic Cooperation and Development (OECD), Mexico is the country with the highest mortality rate because of cervical cancer.

A total of 3784 female deaths were registered in Mexico in 2013, with a raw rate of 7.0 deaths per 100,000 women. Specifically, in the group of women 25 years and older, 3776 deaths were recorded, with a raw rate of 11.3 deaths per 100,000 women and an average age of death of 59 years old [5]. A total of 67,277 deaths were registered between 1998–2013, and the most affected age groups were from 50 to 69 years old, followed by the group of 30–49 years of age, while the least affected group was that of the youngest women (between 10 and 29 years old) (Fig. 2.6).

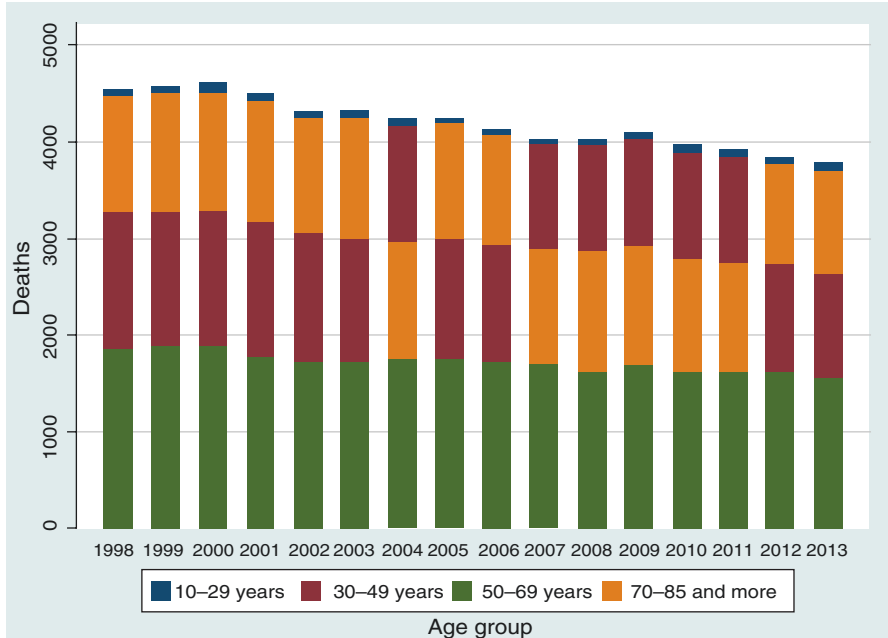


Fig. 2.6 Mortality due to cervical cancer by age group in Mexico in 1998–2013 (Source: General Directorate of Information of the Secretariat of Health of Mexico. INEGI to elaborate the leading causes of death with the Mexican list)

Between 2000 and 2013, the raw mortality rates fell from 18.9 to 11.3 deaths per 100,000 women above 25 years old, which represents a decrease of 40.2% in 13 years. If the federal states are considered during the last year (Fig. 2.7), there are different impact levels of this neoplasia; note the mortality rates between 12.7 and 18.6 deaths per 100,000 women ≥ 25 years old in the states of Morelos, Chiapas, Veracruz and Sonora (18.6, 17.2, 16.4 and 15.9, respectively) and the states with 8.1 or less deaths per 100,000 women ≥ 25 years old, which are Aguascalientes, Baja California Sur and Mexico City [7].

2.2 Risk Factors

Studies indicate that persistent infection with human papilloma virus (HPV) is a necessary requirement for the development of cervical cancer [8, 9]. It is transmitted by sexual contact, affecting 8 of every 10 persons (men and women) at some point of their life. Only one woman of every 10 that acquire this infection will develop cancer [10]. Certain factors that were formerly believed to be associated with an increased risk of developing cervical cancer are now known to be risk factors for HPV infection. Some of these risk factors are as follows [11–17]:

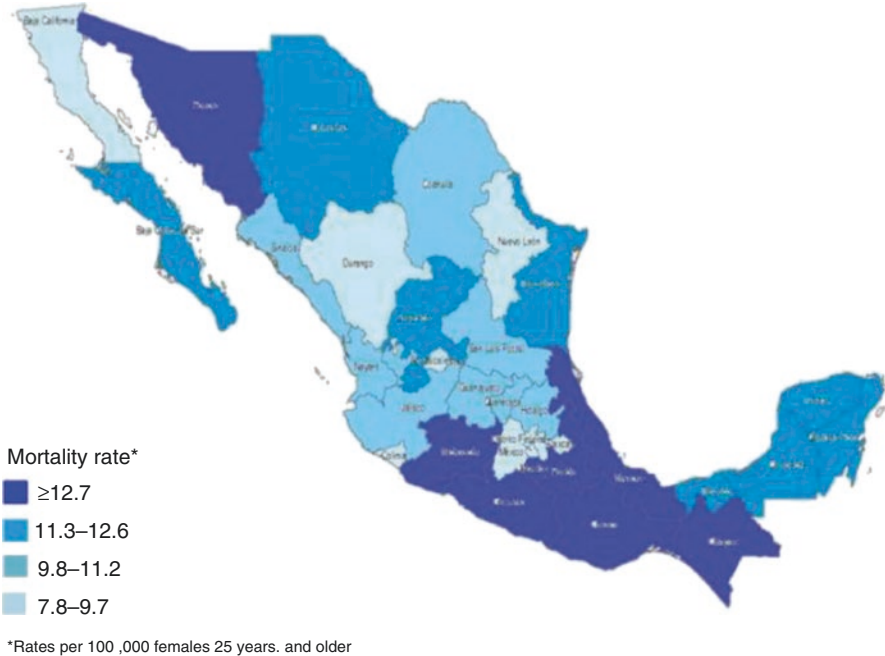


Fig. 2.7 Cervical cancer mortality rate in Mexico in 2013

- Tobacco consumption
- STDs (herpes and chlamydia)
- Use of oral hormones
- Nutritional deficiencies
- Age of onset of sexual activity and absence of protection during adolescence
- High-risk sexual behavior throughout lifetime (multiple sexual partners)

This neoplasia is 100% preventable with measures such as vaccinating against HPV, using condoms, and avoiding tobacco consumption, as well as early detection and treatment of pre-cancerous lesions.

In Mexico, the HPV type prevalence distribution is not known; recent studies have reported the prevalence and genotype distribution of HPV in Mexico in women with cervical cancer, with low- and high-grade squamous intra-epithelial lesions and with normal cytology. Of 8706 samples of tissues from Mexican females, which were stratified according to diagnosis (499, cervical cancer; 364, high-grade lesions; 1425, low-grade lesions; and 6418, normal cytology); the most frequent genotypes were as follows [18]:

- HPV 16 (63.1%), HPV 18 (8.6%) HPV 58 and HPV 31 (5%) for CxCa
- HPV 16 (28.3%), HPV 58 (12.6%), HPV 18 (7.4%) and HPV 33 (6.5%) for high-grade lesions

- HPV 16 (13.1%), HPV 33 (7.4%), HPV 18 (4.2%), HPV 18 (4.2%) and HPV 58 (2.6%) for low-grade lesions
- HPV 16 (3.4%), HPV 33 (2.1%), HPV 18 and HPV 58 (1.2% for normal cytology)

Additionally, a study conducted in heterosexual couples reported that the prevalence of HPV infection is 13.7% for women. The most frequently detected high-risk types were HPVs 59, 16, 31, 52 and 58, and the low-risk types detected were HPV 62, 71, 81 and 54 among women [19].

2.3 Evolution of the Cervical Cancer Program in Mexico

In the last decade, the reduction in mortality may be attributed to a low incidence caused by the combination of prevention activities implemented in health services together with diagnosis opportunity, treatment delivery and improvements in health care service quality and access [20, 21].

In Mexico, actions have been taken to address public health matters in the last 10 years, which has increased the current understanding of this neoplasia. One such example is Mexico's National Institute of Cancerology, a public assistance institution created on November 25th, 1946, that specializes in providing treatment for different types of cancer, together with the public health measures designed, including national campaigns against cancer. In 1974, the first National Cervical Cancer Early Detection Program was created, and it used the Pap test or cytology as the means of detection because it had been established for decades, it was the reference test for cervical cancer screening around the world, and it had reduced the mortality of this disease in developed countries with plenty of resources [22].

In 1996, the health care system of Mexico had only enough resources and infrastructure to carry out about three million Pap tests per year for a population of more than 16 million women between 25 and 65 years old. In that same year, the official Mexican standards dictated that Pap test were recommended on a yearly basis for women with an active sexual lifestyle, without delimiting an age limit, and women with a colposcopy diagnosis of HPV and even presenting slight dysplasia were attended at the colposcopy clinic with cryosurgery, electro-surgery or laser in accordance with the technical protocol of the country. At that same time, the National Cervical Cancer Early Detection Program did not consider epidemiological surveillance an important factor, which could have guaranteed the follow-up and treatment of the anomalies detected in women in which a Pap test had been carried out [23].

In 1997, steps were taken to improve the early detection and surveillance of patients, namely, the National Committee for the Prevention and Control of Cervical and Breast Cancer was created. Then, in 1998, the Secretariat of Health created the General Direction of the Prevention and Control of Cervical Cancer [24]. Additionally, since 2004, the Popular Insurance Program began including cervical

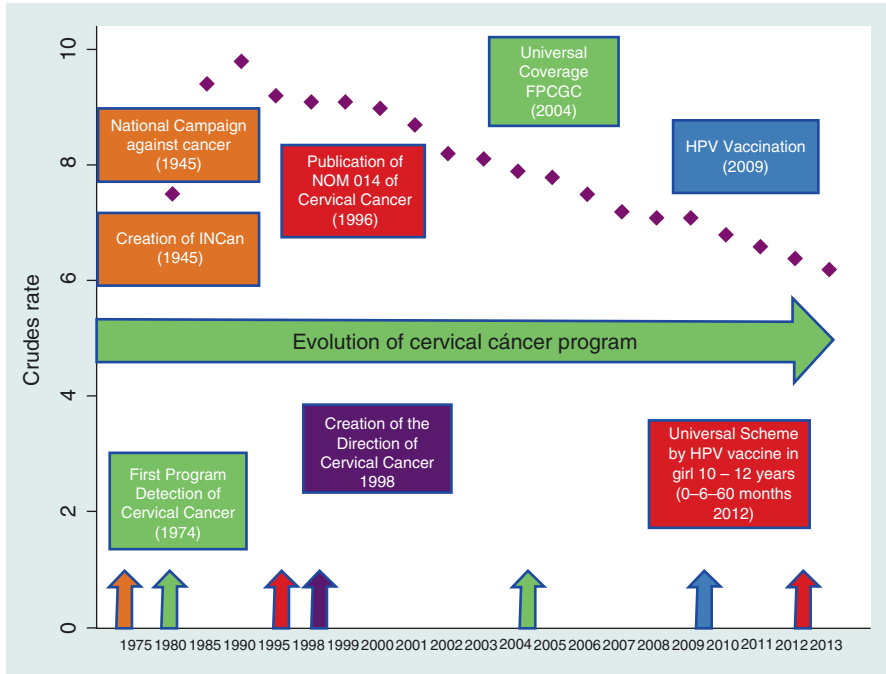


Fig. 2.8 History of the actions implemented in the country to counteract CxCa (Source: Adapted from the Secretary of Health, National Center for Gender Equality and Reproductive Health)

cancer with support from the Fund for the Protection of Catastrophic Expenses, which means that any woman, no matter her economic situation or her geographical location, could be attended free of charge in the accredited hospitals of the Popular Insurance Program [25]. The recent implementations in the health care system, such as programmed vaccination in an extended dose scheme, with two doses at 0–2 months or 0–6 months and a third dose after 60 months in girls between 9 and 11 years old (Fig. 2.8), are worth mentioning [26].

Finally, there is evidence that socioeconomic improvement and the implementation of early detection programs have significantly influenced the slowing and reduction of the mortality rates due to cervical cancer. In Mexico, this reduction is a priority, and according to the results of the ENSANUT 2012, 44.3% of women between 25 and 65 years of age had a Pap test performed in the year prior to this survey, while 37.1 and 29.4% had their tests performed 1 year before the ENSANUT 2006 and ENSA 2000 surveys. In addition, in 2012, women were also administered tests for the detection of HPV (10% of women between 35 and 50 years old) (Fig. 2.9) [27].

However, despite the benefit of preventative care, there is still a tendency to allocate a strong majority of healthcare expenditures for curative measures while neglecting preventative efforts. Healthy eating habits, an increase in physical activity, controlled alcohol consumption, and the promotion of safe sex and vaccination for

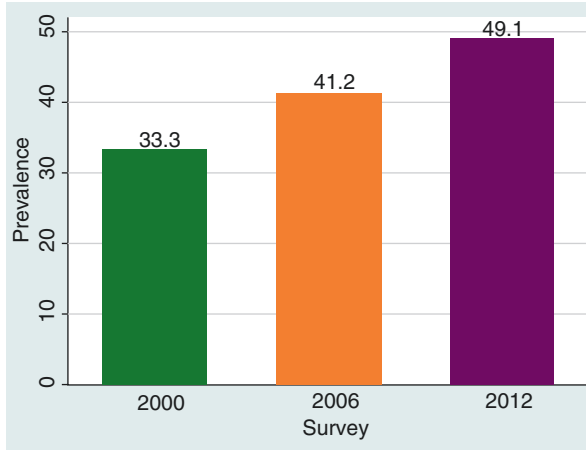


Fig. 2.9 Prevalence of the use of the Pap test during the last 12 months in women between 25 and 64 years old. Mexico ENSA, ENSANUT 2006 and 2012 (Source: ENSANUT 2012)

the prevention of the main serotypes of HPV associated with this type of cancer can reduce its incidence [10].

2.4 The Role of the Health Care System in Mexico to Prevent Mortality and Morbidity Due to Cervical Cancer: Conclusions

In spite of the difficulties, the health care system has managed to partially reduce the mortality rate due to cervical cancer through a cervical cancer prevention program, although not at the same pace at which it has been reduced in more developed countries. Thus, it is necessary to perform constant monitoring of the mortality rates due to cervical cancer with the purpose of evaluating the advances made by these programs and determining the need for interventions. It is also necessary to implement cancer archives based on the population to be able to evaluate the real impact of the implemented interventions in the future and simultaneously design and carry out interventions that allow us to develop prevention-focused policies that are more cost-effective for the healthcare system [21].

It is also necessary to continue the improvement process. Integral programs that include education, HPV vaccination, screening, treatment and palliative care, together with a monitoring and evaluation component for the prevention and control of cervical cancer, are key elements to reduce the impact of this disease.

Cervical cancer is the result of a persistent infection by certain types of HPV and develops over the course of many years, offering various windows of opportunity for its prevention, including vaccination, screening and treatment of pre-cancerous lesions.

Given the above-mentioned information, health promotion and education should have the main objective of providing women, their families and the population with the information that allows them to understand that cervical cancer is preventable; therefore, it is necessary for women to receive the screening services that the health service offers. Furthermore, women should be encouraged to receive appropriate treatment when required and provided with better access to diagnostic services and adequate and timely treatment.

References

1. Ferlay J, Soerjomataram I, Ervik M, Dikshit R, Eser S, Mathers C, Rebelo M, Parkin DM, Forman D, Bray F. GLOBOCAN 2012 v1.0, cancer incidence and mortality worldwide: IARC CancerBase No. 11 [Internet]. Lyon: International Agency for Research on Cancer; 2013. Available from: <http://globocan.iarc.fr>, accessed on 11/12/2015.
2. Almonte M, Murillo R, Sánchez GI, Jerónimo J, Salmerón J, Ferreccio C, Lazcano-Ponce E, Herrero R. New paradigms and challenges in cervical cancer prevention and control in Latin America. *Salud Publica Mex* 2010;52:544–59.
3. International Agency for Research on Cancer. Incidence and mortality rates of cervical cancer in the Americas 2012. GLOBOCAN 2012. Consulted: 11/17/2015.
4. Lewis MJ. Análisis de la situación de cáncer cervicouterino en América Latina y el Caribe. Washington, D.C. Organización Panamericana de la Salud / Organización Mundial de la Salud (OPS/OMS); 2004. p. 40.
5. Organización Panamericana de la Salud & Organización Mundial de la Salud. Nota informativa. Consulted: 01/26/2016; available at: http://www.paho.org/hq/index.php?option=com_topics&view=article&id=348&Itemid=40936&lang=es.
6. Torres-Poveda KJ, Cruz-Valdez A, Madrid-Marina V. Epidemiología del Cáncer Cérvico Uterino. *Gaceta Mexicana de Oncología*. 2014;13(4):4–17.
7. Secretaría de Salud. Centro Nacional de Equidad de Género y Salud Reproductiva. Información estadística. Available at: http://cnegsr.salud.gob.mx/contenidos/Programas_de_Accion/CancerdeLaMujer/InfEstad.html. Consulted on: 11/13/2015.
8. Bosch FX, Lörincz A, Muñoz N, Meijer CJ, Shah KV. The causal relation between human papillomavirus and cervical cancer. *J Clin Pathol*. 2002;55:244–65.
9. Muñoz N, Bosch FX, de Sanjose S, et al. Epidemiologic classification of human papillomavirus types associated with cervical cancer. *N Engl J Med*. 2003;348:518–27.
10. Secretaría de Salud. Programa de Acción Específico. Prevención y control del cáncer de la mujer 2013-2018. 98 pages. Disponible en: <http://www.spps.gob.mx/programas-accion2013-2018.html>.
11. Collins SI, Mazloomzadeh S, Winter H, et al. Proximity of first intercourse to menarche and the risk of human papillomavirus infection: a longitudinal study. *Int J Cancer*. 2005;114:498–500.
12. Ho GY, Bierman R, Beardsley L, Chang CJ, Burk RD. Natural history of cervicovaginal papillomavirus infection in young women. *N Engl J Med*. 1998;338:423–8.
13. Herrero R, Castle PE, Schiffman M, et al. Epidemiologic profile of type-specific human papillomavirus infection and cervical neoplasia in Guanacaste, Costa Rica. *J Infect Dis*. 2005;191:1796–807.
14. Hernández-Giron C, Smith JS, Lörincz A, Lazcano E, Hernandez-Avila M, Salmerón J. High-risk human papillomavirus detection and related risk factors among pregnant and nonpregnant women in Mexico. *Sex Transm Dis*. 2005;32:613–8.
15. Smith JS, Green J, Berrington de González A, et al. Cervical cancer and use of hormonal contraceptives: a systematic review. *Lancet*. 2003;361:1159–67.

16. Plummer M, Herrero R, Franceschi S, et al. Smoking and cervical cancer: pooled analysis of the IARC multi-centric case-control study. *Cancer Causes Control*. 2003;14:805-14.
17. International Collaboration of Epidemiological Studies of Cervical Cancer. Carcinoma of the cervix and tobacco smoking: Collaborative reanalysis of individual data on 13,541 women with carcinoma of the cervix and 23,017 women without carcinoma of the cervix from 23 epidemiological studies. *Int J Cancer*. 2006;118:1481-95. doi:10.1002/ijc.21493.
18. Peralta R et al. Prevalence of human papillomavirus in the cervical epithelium of Mexican women: meta-analysis. *Infect Agent Cancer*. 2012;7:34.
19. Parada R, Morales R, Giuliano AR, et al. Prevalence, concordance and determinants of human papillomavirus infection among heterosexual partners in a rural region of central Mexico. *BMC Infect Dis*. 2010;10:223.
20. Lazcano-Ponce E, Palacio-Mejía LS, Allen-Leigh B, Yunes-Díaz E, Alonso P, Schiavon R. Decreasing cervical cancer mortality in México: effect of Papanicolaou coverage, birth rate, and the importance of diagnostic validity of cytology. *Cancer Epidemiol Biomark Prev*. 2008;17:2808-17.
21. Torres-Sánchez LE, Rojas-Martínez R, Escamilla-Núñez C, de la Vara-Salazar E, Lazcano-Ponce E. Cancer mortality trends in Mexico, 1980-2011. *Salud Publica Mex* 2014;56: 473-91.
22. Organización Mundial de la Salud & Organización Panamericana de la Salud. El cáncer cérvicouterino en las Américas 2014. Available at: <http://190.34.154.93/rncp/sites/all/files/OPS-Nota-Informativa-Cancer-Cervicouterino-2014.pdf>.
23. Lazcano-Ponce E, Sue Moss s, Alonso P, Salmerón J y Hernández M. Cáncer Cérvicouterino, diagnóstico, prevención y control. Programa de detección oportuna de cáncer de cuello uterino en países en vías de desarrollo. El caso de México. Chapter 14. Mexico, D.F: Editorial Médica Panamericana; 2000. 254 pp.
24. Instituto nacional de las mujeres INMUJERES. El enfoque de género en la producción de las estadísticas sobre salud en México. Guía para el uso y una referencia para la producción de información. Available at: http://cedoc.inmujeres.gob.mx/documentos_download/100665.pdf.
25. Aracena-Genao B, González-Robledo M, González-Robledo L, Palacio-Mejía L, Nigenda-López G. El fondo de protección contra gastos catastróficos: tendencia, evolución y operación. *Salud Publica Mex*. 2011;53:s407-15.
26. Lazcano-Ponce E, Aranda Flores C, Aguado-Pérez A, Cruz-Valdez y Bojalil R. Vacunas para proteger de la infección por virus de papiloma humano. *Gaceta Mexicana de Oncología*. 2014;13(Suppl 4):39-47.
27. Gutiérrez JP, Rivera-Dommarco J, Shamah-Levy T, Villalpando-Hernández S, Franco A, Cuevas-Nasu L, Romero-Martínez M, Hernández-Ávila M. Encuesta Nacional de Salud y Nutrición 2012. Resultados Nacionales. Cuernavaca. México: Instituto Nacional de Salud Pública (MX); 2012.