HPV Prevention and Control Board

Prevention and control of HPV and HPV related cancers in Colombia: Lessons learnt and the way forward.

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BACKGROUND DOCUMENT

Alex Vorsters
HPV Prevention and Control Board

Executive Secretariat, Vaccine & Infectious Disease Institute, University of Antwerp, Campus Drie Eiken, Universiteitsplein 1, 2610 Antwerpen, Belgium, +32 (0)3 265 26 64; alex.vorsters@uantwerpen.be

Content

Introduction

Objectives of the meeting:

1. Give an overview of the health care systems in Colombia.
2. Provide a summary of the epidemiology, burden of disease and surveillance related to HPV and HPV related cancers in Colombia.
3. Discuss successes, topical issues and challenges related to HPV vaccination and screening particular to Colombia.
4. Review country examples from Latin America to learn from their successes and challenges.
5. Gain insight in the various stakeholder perspectives.
6. Propose recommendations for the way forward.

Target audience:

The HPV Prevention & Control Board brings together the immunization, screening, clinical, health economics and academic key experts, as well as patient/advocacy groups and government officials in countries/regions so that they could present their data and discuss programs, strategies, successes and problems. Board members will use their experience to give advice on how challenges might be addressed. Lessons learnt will be collected and disseminated via the web site www.hpvboard.org, a meeting report and possibly via a publication in a peer reviewed journal.

Purpose of the background document

This background document provides an overview of articles related to the meeting and a concise bibliography of speakers. The main purpose of the document is to frame the topics of the country meeting on '**Prevention and control of HPV and HPV related cancers in Colombia: Lessons learnt and the way forward**', 15 November – 16 November 2018, Bogota.

The document should not be considered as an an exhaustive report of scientific articles related to the themes of the meeting.

Inclusion of references in this document does not indicate that the Executive Secretariat agrees with the content or correctness of the content. The first objective of this list is to give an overview of what has been published on this topic.

References applicable to different sessions are duplicated in all relevant sessions, abstract of the reference is only added the first time the reference is mentioned.

Part 1: Presentation related references by session

List obtained via speakers and via a PubMed search. The items retrieved via PubMed were added in Endnote (version X7.7.1). The background document contains a selected list of publications based on a manual selection in Endnote.

The board is indebted to Jade Pattyn for her assistance in the PubMed search.

Session 2 The Health Care Systems in Colombia

References session 2 via PubMed search:

Colombia AND health care system (title/abstract) in the last 10 years: 40 items retrieved.

The list contains a manual selection of **11** publications relevant to session 2.

Alvarez, L. S., et al. (2011). **"The Colombian health insurance system and its effect on access to health care."** Int J Health Serv **41**(2): 355-370.

> In 1993, the Colombian government sought to reform its health care system under the guidance of international financial institutions (the World Bank and International Monetary Fund). These institutions maintain that individual private health insurance systems are more appropriate than previously established national public health structures for overcoming inequities in health care in developing countries. The reforms carried out following international financial institution guidelines are known as "neoliberal reforms." This qualitative study explores consumer health choices and associated factors, based on interviews with citizens living in Medellin, Colombia, in 2005-2006. The results show that most study participants belonging to low-income and middle-income strata, even with medical expense subsidies, faced significant barriers to accessing health care. Only upper-income participants reported a selection of different options without barriers, such as complementary and alternative medicines, along with private Western biomedicine. This study is unique in that the informal health system is linked to overall neo-liberal policy change.

Augustovski, F., et al. (2012). "**Status Update of the Reimbursement Review Environment in the Public Sector across Four Latin American Countries**." Value Health Reg Issues **1**(2): 223-227.

> In Latin America, social security and public sectors represent the largest financiers and providers of health care. Many countries in the region have compulsory packages of basic health care benefits. As part of an effort to improve quality of care and access, several health technology assessment agencies, both governmental and academia, among a number of Latin American countries have been formally established in the past few years. Several Latin American countries have recently developed and published methodological guidelines in economic evaluation, indicating that there is a growing interest in evaluating health-related products, drugs, and technologies used by the population. Presentations on the health care system and the role of health technology assessment, pharmacoeconomics, and risk sharing policies, from the public sector perspective, in the Latin American countries Argentina, Brazil, Colombia, and Mexico were made at the 3rd Latin American ISPOR Conference held in Mexico City in 2011 and are discussed in this article. In conclusion, there is a clear need for Latin American countries to evaluate the value of new technologies that are being incorporated into their health care system. In addition, health technology assessment guidelines are important for their local needs in terms of regulation along with common country unions. In the future, the Latin American region needs to increase drug access along with implementing cost-containment measures to improve quality and health outcomes.

Maria del Pilar, C. P., et al. (2012). "**Neoliberal-oriented health care system answer to global competition or a threat to health equality for people with chronic illness**." ANS Adv Nurs Sci **35**(2): 166-181.

The aim of this article is to explore how a neoliberal-oriented health care system affects the experience of people living with chronic illness. We report findings from a critical hermeneutic phenomenological research study that explored how the social, economic, and political structures impinge on the lives of people with chronic illness. Research findings of this study show how the people with chronic illness in Colombia live through the effects and pressures of globalization and corporate agendas. Results also showed how the marked social inequities caused by the unequal distribution of power, services, and goods leads to health inequities and social exclusion of research participants.

Atehortua, S., et al. (2013). "**[Quality assessment of economic evaluations in health care in Colombia: a systematic review]**." Biomedica **33**(4): 615-630.

INTRODUCTION: Economic evaluation is a tool that can provide useful information to decision-makers in health. The methodological quality of Colombian studies has not been assessed in a systematic way. OBJECTIVE: To assess the methodological quality of economic evaluations in health care in Colombia. MATERIALS AND METHODS: Systematic review of economic studies that assessed both costs and effectiveness of at least two technologies related to a decision problem in Colombia. Search was performed in international and Colombian databases and was completed with manual searches and contact with authors. Data was synthesized in tables that included relevant information about the studies. Methodological quality was evaluated using a predefined instrument. Searches were performed between January and February. RESULTS: 48 studies were included in the review. Perspective of the study, incremental analyzes and description of alternatives were usually well specified. However, more than half of the articles did not state clearly the time horizon or discount rate and most studies did not address equity and implementation issues. Management of uncertainty was also problematic. CONCLUSIONS: Economic evaluation in health care in Colombia has grown considerably in recent years. However, methods vary considerably between studies and therefore their usefulness for decisionmaking in health is limited. It is necessary to standardize methods in order to generate evidence of higher quality to support decisions within the Colombian health care system.

Flood, C. and A. Gross (2014). "**Litigating the right to health: what can we learn from a comparative law and health care systems approach**." Health Hum Rights 16(2): E62-72.

This article presents research demonstrating that the right to health plays different roles in different types of health systems. In high-income countries with tax-funded health systems, we usually encounter a lack of an enforceable right to heath. In contrast, rights play a more significant role in social health insurance/managed competition systems (which are present in a mixture of high-income and middle-income countries). There is concern, for example in Colombia, that a high volume of rights litigation can challenge the very sustainability of a public health care system and distort resources away from those most in need. Finally, in middle-income countries with big gaps between a poor public health system and a rich private one, we are more likely to find an express constitutional right to health care (or one is inferred from, for example, the right to life). In some of these countries, constitutional rights were included as part of the transition to democracy and an attempt to address huge inequities within society. Here

the scale of health inequities suggests that courts need to be bolder in their interpretation of health care rights. We conclude that in adjudicating health rights, courts should scrutinize decision-making through the lens of health equity and equality to better achieve the inherent values of health human rights.

Mosquera, P. A., et al. (2014). "**Challenges of implementing a primary health care strategy in a context of a market-oriented health care system: the experience of Bogota, Colombia**." Int J Health Plann Manage 29(4): e347-367.

BACKGROUND: Although Colombia has a health system based on market and neoliberal principles, in 2004, the government of the capital-Bogota-took the decision to formulate a health policy that included the implementation of a comprehensive primary health care (PHC) strategy. This study aims to identify the enablers and barriers to the PHC implementation in Bogota. METHODS: The study used a qualitative multiple case study methodology. Seven Bogota's localities were included. Eighteen semi-structured interviews with key informants (decision-makers at each locality and members of the District Health Secretariat) and fourteen FGDs (one focus group with staff members and one with community members) were carried out. Data were analysed using a thematic analysis approach. RESULTS: The main enablers found across the district and local levels showed a similar pattern, all were related to the good will and commitment of actors at different levels. Barriers included the approach of the national policies and a health system based on neoliberal principles, the lack of a stable funding source, the confusing and rigid guidelines, the high turnover of human resources, the lack of competencies among health workers regarding family focus and community orientation, and the limited involvement of institutions outside the health sector in generating intersectoral responses and promoting community participation. CONCLUSION: Significant efforts are required to overcome the market approach of the national health system. Interventions must be designed to include well-trained and motivated human resources, as well as to establish available and stable financial resources for the PHC strategy.

Patino Suaza, A. E. and M. Sandin Vasquez (2014). **"[Dialogue and respect: the basis for constructing an intercultural health system for indigenous communities in Puerto Narino, Amazonas, Colombia]**." Salud Colect 10(3): 379-396.

This paper presents the ideas on health and disease as well as proposals regarding the health care system voiced by indigenous communities belonging to the Tikunas, Cocama and Yagua ethnicities of the Puerto Narino municipality in the department of Amazonas, Colombia. The study was conducted between 2010 and 2013. The tools used to obtain the data were participant observation, interviews and discussion groups. The study evidenced a profound lack of information and understanding on the part of state health agencies. As a principal demand, indigenous communities ask to be heard when decisions affecting their health or their way of understanding health are made. These results should be taken into account in the development of future health programs and provide a basis for the construction of an adequate intercultural health system for the town of Port Narino.

De Vos, P. and P. Van der Stuyft (2015). "**Sociopolitical determinants of international health policy**." Int J Health Serv 45(2): 363-377.

For decades, two opposing logics have dominated the health policy debate: a comprehensive health care approach, with the 1978 Alma Ata Declaration as its cornerstone, and a private competition logic, emphasizing the role of the private sector. We present this debate and its influence on international health policies in the context of changing global economic and sociopolitical power relations in the second half of the last century. The neoliberal approach is illustrated with Chile's health sector reform in the 1980s and the Colombian reform since 1993. The comprehensive "public logic" is shown through the social insurance models in Costa Rica and in Brazil and through the national public health systems in Cuba since 1959 and in Nicaragua during the 1980s. These experiences emphasize that health care systems do not naturally gravitate toward greater fairness and efficiency, but require deliberate policy decisions.

Machado-Alba, J. E., et al. (2015). "**Results of the Inclusion of New Medications in the Obligatory Health System Plan in Colombia, 2012-2013.**" Value Health Reg Issues 8: 28-35.

BACKGROUND: The Colombian health care system has had a plan with limited benefits, but since 2012, 57 drugs have been added to this plan. OBJECTIVES: The objective of this article was to describe the trends of utilization and costs of medications covered by the Agreement 029/2011 and compare them with those that were contained in the benefits plan. METHODS: This descriptive study involved a group of 3.8 million people affiliated with the Colombian health care system, in 110 cities from July 2011 until June 2013. The variables were new medications that were included, comparing them with homologous medications that were already in the plan, age, sex, dispensed quantities, and monthly billing. The study established the defined daily dosage per thousand inhabitants per day, cost per thousand inhabitants per day, cost per capita, and the rate of adoption or replacement medicines. RESULTS: The growth in the consumption of new medications was 830.0%. The defined daily dosage per thousand inhabitants per day grew from 4.3 to 42.9, with an increase of 905.5%. Medications with the highest growth were losartan/hydrochlorothiazide (15,723%), esomeprazole (4193%), atorvastatin (1402%), and sertraline (298%). There was an increase of US $16.40 in the cost per thousand inhabitants per day, which is equivalent to an increase of 61.7% and represents a rise of US $0.49 in cost per capita per month. CONCLUSIONS: The consumption behavior of new medications and the economic implications for Colombia can be demonstrated. In particular, the growth in the consumption of medications for chronic diseases can be seen, which would represent an increase of US $22.6 million per month to the entire population of the country.

Sanz, C. (2017). "**Out-of-Sync Cancer Care: Health Insurance Companies, Biomedical Practices, and Clinical Time in Colombia**." Med Anthropol 36(3): 187-201.

I discuss the physical wearing out of low-income cancer patients in the aftermath of the neoliberal restructuring of the Colombian health care system in 1993. The settings for this struggle are the hospitals and the health insurance companies; the actors are bodies with cancer, the physicians who diagnose people with cancer, and the relatives who care for them. I show how most low-income patients, instead of accessing complete anticancer treatments in a timely fashion, have to negotiate and confront health insurance companies and profit-making. This results in a wait, where the time needs of the bureaucracy of the health care system and

the time needs of patients' bodies are discordant, at a cost to patients.

Valencia, O., et al. (2018). "**Incidence and Prevalence of Cancer in Colombia: The Methodology Used Matters.**" J Glob Oncol(4): 1-7.

PURPOSE: Incidence and prevalence are important factors in policy making and planning in health care systems. The aim of this study was to compare two different estimates of the incidence and prevalence of cancer in Colombia-real-world data from the health care system and estimates from cancer registries. MATERIALS AND METHODS: Data from all providers were aggregated by the High-Cost Diseases Office (Cuenta de Alto Costo [CAC]). The real-world, age-standardized observed incidence (OI) and observed prevalence (OP) rates were calculated using the number of patients with a diagnosis of cancer who were cared for in the national health system between 2014 and 2015. The registry estimated incidence (EI) and estimated prevalence (EP) were extracted from GLOBOCAN population fact sheets for 2012, which use data from four Colombian city-based registries and extrapolate survival using the average for Asian countries, together with registries from Uganda and Zimbabwe. RESULTS: A total of 130,441 patients were analyzed. The OI of cancer in Colombia was 69.2 and the OP was 479 (per 100,000 people) in early 2015, whereas the EI was 175.2 and the 5-year EP was 501.2 (per 100,000 people), showing a higher estimate from GLOBOCAN data for 2012 than was observed in early 2015 by the CAC. Some differences were higher in specific cancers. CONCLUSION: Because of differences in methodology, the EI and the EP are not comparable to the OI and the OP. Policymakers need robust and current information to prioritize disease prevention and control programs. In Colombia, the OI and the OP-calculated by the CAC with data from the whole country-offer an opportunity for a more precise real-world estimation of patients with cancer in Colombia.

Session 3 Epidemiology of HPV and cervical cancer screening in Colombia

References session 3 via PubMed search:

A PubMed search was performed with the following selection criteria:

1. Colombia AND HPV AND epidemiology; Colombia AND HPV AND burden of disease; Colombia AND HPV AND surveillance; Colombia AND HPV AND cervical screening in the last 10 years: 68 items retrieved

The list contains a manual selection of 29 publications relevant to session 3.

De la Hoz-Restrepo, F., et al. (2009). "[**Evaluating the burden of disease caused by human papillomavirus. Bogota**]." Rev Salud Publica (Bogota) **11**(3): 454-467

OBJECTIVE: A study was carried out in Bogota aimed at estimating the burden of disease associated with human papillomavirus infection (HPV) and the potentially avoidable percentage due to using new vaccines. METHODS: A literature review was combined with analysing surveillance system data and disease cost evaluation. RESULTS: After adjusting for underreporting and misclassification, it was estimated that 322 deaths from cervical cancer occur annually in Bogota (corresponding to 676 new cases). This would cause the loss of 15 years of life for each 1,000 women per year (most occurring amongst women aged 40 to 69). In addition to cervical cancer, there would be around 6,084 cases of high-grade and 22,984 low-grade cervical lesions yearly. The disease's yearly cost would amount to around 7 million dollars. Important weaknesses were found in the clinical management of women suffering from cervical lesions. CONCLUSION: Strengthening cervical cancer prevention programmes in Bogota would lead to saving a significant number of deaths, cases of cancer and the costs associated with HPV infection. Introducing an anti-HPV vaccine may be considered, but only as part of a more widespread preventative strategy and provided that more affordable prices have been found.

Murillo, R., et al. (2009). "**HPV prevalence in Colombian women with cervical cancer: implications for vaccination in a developing country**." Infect Dis Obstet Gynecol **2009**: 653598.

Human Papillomavirus (HPV) vaccines have been considered potentially cost-effective for the reduction of cervical cancer burden in developing countries; their effectiveness in a public health setting continues to be researched. We conducted an HPV prevalence survey among Colombian women with invasive cancer. Paraffin-embedded biopsies were obtained from one high-risk and one low-middle-risk regions. GP5+/GP6+ L1 primers, RLB assays, and E7 type specific PCR were used for HPV-DNA detection. 217 cases were analyzed with 97.7% HPV detection rate. HPV-16/18 prevalence was 63.1%; HPV-18 had lower occurrence in the high-risk population (13.8% versus 9.6%) allowing for the participation of less common HPV types; HPV-45 was present mainly in women under 50 and age-specific HPV type prevalence revealed significant differences. Multiple high-risk infections appeared in 16.6% of cases and represent a chance of replacement. Age-specific HPV prevalence and multiple high-risk infections might influence vaccine impact. Both factors highlight the role of HPVs other than 16/18, which should be considered in cost-effectiveness analyses for potential vaccine impact.

Soto-De Leon, S. C., et al. (2009). "**Prevalence of infection with high-risk human papillomavirus in women in Colombia**." Clin Microbiol Infect **15**(1): 100-102.

The prevalence of human papillomavirus (HPV) infections in 2109 females inhabiting five cities of Colombia was determined. Of the 49.2% with an HPV infection, 59.8% were infected with more than one viral type. Species 7 (of the the genus Alphapapillomavirus) was associated with multiple infections. Analysis of the socio-demographic data revealed a statistically significant protective effect associated with the status of civil union (civil recognition of cohabitation without marriage), and indigenous ethnicity proved to be a risk factor for HPV infection. This is the first study comparing HPV infection among women from geographical regions of Colombia with different socio-cultural structures.

Camargo, M., et al. (2011). "**Frequency of human papillomavirus infection, coinfection, and association with different risk factors in Colombia**." Ann Epidemiol **21**(3): 204-213.

PURPOSE: The aims of this study were to provide new insights into infection patterns of six high-risk human papillomaviruses (HR-HPV-16, -18, -31, -33, -45, and -58) and two low-risk HPV types (LR-HPV-6 and -11), their association with risk factors and coinfection. METHODS: Cervical samples of 2110 women were tested for the presence of HPV-DNA by polymerase chain reaction. Statistical analyses were performed to determine viral-type frequencies in single and multiple infections and association between infection and different risk factors. RESULTS: HPV-16 was the most prevalent type among the studied population, followed by HPV-31. This last viral type showed a variable distribution between the different cities evaluated. The results showed distinct type-specific distributions among regions and a high association between absence of pregnancies, cities as Girardot and Leticia, the indigenous ethnicity, and coinfection. CONCLUSIONS: The results showed a variable distribution of HPV types according to the geographical region analyzed. In addition, data suggest that some sociodemographic-factors such as ethnicity, number of pregnancies, lifetime number of sexual partners, and geographic region were significantly associated, and our results showed little differences between single and multiple infections by HPV with regard to risk factors. Furthermore, these results provide relevant information that will allow assessing in further studies the impact that vaccination programs on these populations and the selective pressure would have on the distribution of HPV types.

Castillo, A., et al. (2011). "**Human papillomavirus in upper digestive tract tumors from three countries**." World J Gastroenterol **17**(48): 5295-5304.

AIM: To clarify human papillomavirus (HPV) involvement in carcinogenesis of the upper digestive tract of virological and pathological analyses. METHODS: The present study examined the presence of HPV in squamous cell carcinomas of the oral cavity (n = 71), and esophagus (n = 166) collected from Japan, Pakistan and Colombia, with different HPV exposure risk and genetic backgrounds. The viral load and physical status of HPV16 and HPV16-E6 variants were examined. Comparison of p53 and p16(INK4a) expression in HPV-positive and HPV-negative cases was also made. RESULTS: HPV16 was found in 39 (55%) oral carcinomas (OCs) and 24 (14%) esophageal carcinomas (ECs). This site-specific difference in HPV detection between OCs and ECs was statistically significant ($P < 0.001$). There was a significant difference in the geographical distribution of HPV16-E6 variants. Multiple infections of different HPV types were found in 13 ECs, but multiple infections were not found in OCs. This difference was statistically significant ($P = 0.001$). The geometric means (95% confidence interval) of HPV16 viral load in OCs and ECs were 0.06 (0.02-0.18) and 0.12 (0.05-0.27) copies per cell, respectively. The expression of p16(INK4a) proteins was increased by the presence of HPV in ECs (53% and 33% in HPV-positive and -

negative ECs, respectively; P = 0.036), and the high-risk type of the HPV genome was not detected in surrounding normal esophageal mucosa of HPV-positive ECs. CONCLUSION: Based on our results, we cannot deny the possibility of HPV16 involvement in the carcinogenesis of the esophagus.

Soto-De Leon, S., et al. (2011). "**Distribution patterns of infection with multiple types of human papillomaviruses and their association with risk factors**." PLoS One **6**(2): e14705.

BACKGROUND: Infection with multiple types of human papillomavirus (HPV) is one of the main risk factors associated with the development of cervical lesions. In this study, cervical samples collected from 1,810 women with diverse sociocultural backgrounds, who attended to their cervical screening program in different geographical regions of Colombia, were examined for the presence of cervical lesions and HPV by Papanicolau testing and DNA PCR detection, respectively. PRINCIPAL FINDINGS: The negative binomial distribution model used in this study showed differences between the observed and expected values within some risk factor categories analyzed. Particularly in the case of single infection and coinfection with more than 4 HPV types, observed frequencies were smaller than expected, while the number of women infected with 2 to 4 viral types were higher than expected. Data analysis according to a negative binomial regression showed an increase in the risk of acquiring more HPV types in women who were of indigenous ethnicity (+37.8%), while this risk decreased in women who had given birth more than 4 times (-31.1%), or were of mestizo (-24.6%) or black (-40.9%) ethnicity. CONCLUSIONS: According to a theoretical probability distribution, the observed number of women having either a single infection or more than 4 viral types was smaller than expected, while for those infected with 2-4 HPV types it was larger than expected. Taking into account that this study showed a higher HPV coinfection rate in the indigenous ethnicity, the role of underlying factors should be assessed in detail in future studies.

Bedoya, A. M., et al. (2012). "**Age-specific seroprevalence of human papillomavirus 16, 18, 31, and 58 in women of a rural town of Colombia.**" Int J Gynecol Cancer **22**(2): 303-310.

OBJECTIVE: The study's objective was to estimate human papillomavirus (HPV) genotype-specific seroprevalence to determine population HPV exposure and inform vaccine policy. METHODS: This study is a cross-sectional prevalence survey of 878 women of Pueblorrico, a rural town of Colombia. A standardized questionnaire was used to obtain information on demographic characteristics, sexual and reproductive history, and smoking habits. Seropositivity to HPV-16, -18, -31, and -58 was determined by virus-like particles in an enzyme-linked immunosorbent assay. RESULTS: Overall seropositivity to any HPV genotype was 27.9%. The combined seroprevalence of women 15 to 19 and 20 to 24 years old was 35.4% (95% confidence interval [CI], 25.9-46.2) and 36.0% (95% CI, 27.7-45.3), respectively. Seroprevalence for HPV-16 was 17% (95% CI, 14.6-19.6); for HPV-18, 9.8% (95% CI, 8.0-11.9); for HPV-31, 11.4% (95% CI, 9.5-13.7); and for HPV 58, 12.5% (95% CI, 10.5-14.9). Higher HPV seropositivity was associated with the lifetime number of occasional sexual partners (odds ratio, 3.05; 95% CI, 1.26-7.37) and having more than 2 regular sexual partners (odds ratio, 3.00; 95% CI, 1.21-7.45) in women younger than 44 and older than 45 years old, respectively. Use of oral contraceptives and tobacco/cigarettes was significantly associated with reduced HPV seropositivity in women older than 45 but not in women younger than 44 years old. CONCLUSIONS: Human papillomavirus seropositivity is associated with measures of sexual behavior, particularly a greater lifetime number of sexual partners. Hormonal and tobacco/cigarette use may be factors influencing the HPV seropositivity in women older than 45 years old.

Munoz, N. and L. E. Bravo (2012). "**Epidemiology of cervical cancer in Colombia**." Colomb Med (Cali) **43**(4): 298-304.

Worldwide, cervical cancer is the third most common cancer in women, and the first or second most common in developing countries. Cervical cancer remains in Colombia the first cause of cancer mortality and the second cause of cancer incidence among women, despite the existence of screening programs during the last 3 decades. Bucaramanga, Manizales and Cali reported rates around 20 per 100,000and Pasto 27 per 100,000. The Cali cancer registry has reported a progressive decrease in the age standardized incidence and mortality rates of cervical cancer over the past 40 years. Reasons for the decline in incidence and mortality of cervical cancer are multiple and probably include: improvement in socio-economic conditions, decrease in parity rates and some effect of screening programs. Human papilloma Virus is the main cause of cervical cancer, HPV natural history studies have now revealed that HPVs are the commonest of the sexually transmitted infections in most populations. Most HPV exposures result in spontaneous clearance without clinical manifestations and only a small fraction of the infected persons, known as chronic or persistent carriers, will retain the virus and progress to precancerous and cancer. HPV 16 and 18 account for 70% of cervical cancer and the 8 most common types. (HPV 16, 18, 45, 33, 31, 52, 58 and 35) account for about 90% of cervical cancer. Case-control studies also allowed the identification of the following cofactors that acting together with HPV increase the risk of progression from HPV persistent infection to cervical cancer: tobacco, high parity, long term use of oral contraceptives and past infections with herpes simplex type 2 and Chlamydia trachomatis. The demonstration that infection with certain types of human papillomavirus (HPV) is not only the main cause but also a necessary cause of cervical cancer has led to great advances in the prevention of this disease on two fronts: (i) Primary prevention by the use of prophylactic HPV vaccines; and (ii) secondary prevention by increasing the accuracy of cervical cancer screening.

Ruiz, A. M., et al. (2012). "**Proximity of first sexual intercourse to menarche and risk of high-grade cervical disease**." J Infect Dis **206**(12): 1887-1896.

BACKGROUND: We assessed if risk of developing cervical intraepithelial neoplasia grade 2/3 (CIN2/3) or adenocarcinoma in situ (AIS) is associated with a short interval between menarche and first sexual intercourse (FSI). METHODS: A total of 1009 Colombian and 1012 Finnish females, aged 16-23, who were enrolled in the phase 3 trials of a quadrivalent human papillomavirus (HPV) 6/11/16/18 vaccine had nonmissing data for age of menarche and FSI. The impact of menarche interval on the odds of developing CIN2-3/AIS was evaluated in placebo recipients who were DNA negative to HPV 6/11/16/18/31/33/35/39/45/51/52/56/58/59 and seronegative to HPV 6/11/16/18 at day 1, and had a normal Pap result at day 1 and month 7, thus approximating sexually naive adolescents (n = 504). RESULTS: The mean age of menarche and FSI was 12.4 and 16.0 years, respectively. Among the women approximating sexually naive adolescents, 18 developed CIN2-3/AIS. Compared with women who postponed FSI beyond 3 years of menarche, those with FSI within 3 years of menarche had a greater risk of cytologic abnormalities (odds ratio [OR], 1.65; 95% confidence interval [CI], 1.02-2.68; P = .04) and CIN2-3/AIS (OR, 3.56; 95% CI, 1.02-12.47; P = .05). CONCLUSIONS: A short interval between menarche and FSI was a risk factor for cytologic abnormalities and high-grade cervical disease. These data emphasize the importance of primary prevention through education and vaccination. CLINICAL TRIALS REGISTRATION: NCT00092521 and NCT00092534.

Wiesner, C., et al. (2012). "**Social representations of human papillomavirus in Bogota, Colombia**." Med Anthropol **31**(1): 77-92.

Identifying DNA of Human papillomavirus (HPV) has been proposed as a new screening method for cervical cancer control. Conventionally, health education for screening programs is based on scientific information without considering any community cognitive processes. We examine HPV social representations of 124 men and women from diverse educational status living in Bogota, Colombia. The social representation of HPV involves a series of figurative nuclei derived from meanings linked to scientific information. While women focused on symbols associated to contagion, men focused on its venereal character. Figurative nuclei also included long-term uncertainty, need or urgent treatment, and feelings of imminent death associated with cancer and chronic sexually transmitted infections. The social representation of HPV impeded many participants from clearly understanding written information about HPV transmission, clearance, and cancer risk; they are built into a framework of values, which must be deconstructed to allow women full participation in HPV screening programs.

Aponte-Gonzalez, J., et al. (2013). "**Cost-effectiveness analysis of the bivalent and quadrivalent human papillomavirus vaccines from a societal perspective in Colombia**." PLoS One **8**(11): e80639.

OBJECTIVE: To compare costs and effectiveness of three strategies used against cervical cancer (CC) and genital warts: (i) Screening for CC; (ii) Bivalent Human Papillomavirus (HPV) 16/18 vaccine added to screening; (iii) Quadrivalent HPV 6/11/16/18 vaccine added to screening. METHODS: A Markov model was designed in order to simulate the natural history of the disease from 12 years of age (vaccination) until death. Transition probabilities were selected or adjusted to match the HPV infection profile in Colombia. A systematic review was undertaken in order to derive efficacy values for the two vaccines as well as for the operational characteristics of the cytology test. The societal perspective was used. Effectiveness was measured in number of averted Disability Adjusted Life Years (DALYS). RESULTS: At commercial prices reported for 2010 the two vaccines were shown to be non-cost-effective alternatives when compared with the existing screening strategy. Sensitivity analyses showed that results are affected by the cost of vaccines and their efficacy values, making it difficult to determine with certainty which of the two vaccines has the best cost-effectiveness profile. To be 'cost-effective' vaccines should cost between 141 and 147 USD (Unite States Dollars) per vaccinated girl at the most. But at lower prices such as those recommended by WHO or the price of other vaccines in Colombia, HPV vaccination could be considered very cost-effective. CONCLUSIONS: HPV vaccination could be a convenient alternative for the prevention of CC in Colombia. However, the price of the vaccine should be lower for this vaccination strategy to be cost-effective. It is also important to take into consideration the willingness to pay, budgetary impact, and program implications, in order to determine the relevance of a vaccination program in this country, as well as which vaccine should be selected for use in the program.

Hernandez-Suarez, G., et al. (2013). "**Human papillomavirus genotypes in genital warts in Latin America: a cross-sectional study in Bogota, Colombia**." Int J STD AIDS **24**(7): 567-572.

Epidemiological studies on benign lesions related to human papillomavirus (HPV) infection are scarce in Latin America. We enrolled 342 consecutive patients with lesions suspected of being genital warts (GW). All patients underwent confirmatory biopsy and GP5+/GP6+/- Reverse Line Blot HPV testing on frozen tissue. In 261 (81%) cases, the diagnosis was confirmed by histopathology and HPV was detected in 90.6% of men and 87.7% of women. HPV 6 was by far the most common type in both women (62%) and men (56%), followed by HPV 11 (approximately 20%). Co-infection with these two types occurred in 7% and 12% of women and men, respectively. HPV16 ranked third in prevalence, with 16% of patients testing positive. Twenty-five percent of cases tested positive for multiple HPV genotypes. Although HPV 6 and HPV 11 were the main types detected and no differences between men and women were

observed, we found HPV 11 contributed more to GW aetiology compared with previous reports, showing a variability of HPV type distribution in GW across populations. This information is valuable baseline data in Latin America for future estimations of the burden of GW in men and women and shows the potential benefit obtainable by prophylactic vaccination against HPV types 6 and 11.

Pineros, M., et al. (2013). "**HPV knowledge and impact of genital warts on self esteem and sexual life in Colombian patients**." BMC Public Health **13**: 272.

BACKGROUND: Information on HPV knowledge in patients with genital warts is scarse as is the information on factors related to the impact on self-esteem and sex life among them. METHODS: We conducted a cross-sectional study in adult patients with a clinical diagnosis of genital warts (GW) attending a major private out-patient clinic in Bogota, Colombia. Patients underwent biopsy for pathological diagnosis, HPV-DNA testing and completed a questionnaire assessing HPV knowledge, and the consequences of GW on self-esteem and sexual life. Differences in proportions were assessed with a chi2 test. RESULTS: 106 men and 155 women had pathologic confirmation of GW. 51% of subjects had heard of HPV before consultation coming mainly from the media (82%). Less than half of the participants knew that HPV could be transmitted through non-penetrant sexual intercourse and only two thirds acknowledged HPV vaccine as a preventive measure against HPV infection. Impact on self-esteem was higher among women than men (90.3% vs 60.4%, [$p < 0.01$]). In men, factors related to a higher impact on sexual life were HPV awareness and age; in women they were higher education and anatomic location; external GW had a higher impact on sexual life in women (83% vs. 66%; [$p = 0.05$]). CONCLUSIONS: We found a low awareness of HPV and low knowledge on the vaccine as a preventive measure for associated diseases even in patients suffering from genital warts, highlighting the need for communication and education on HPV. Greater impact on self-esteem in women might reflect higher health consciousness among Latin American women.

Quintero, K., et al. (2013). "**Human papillomavirus types in cases of squamous cell carcinoma of head and neck in Colombia**." Braz J Otorhinolaryngol **79**(3): 375-381.

UNLABELLED: Estimating the type-specific prevalence of human papillomavirus (HPV) in head and neck cancer (HNSCC) is helpful in predicting the impact of HPV immunization. OBJECTIVE: To estimate the overall prevalence, and gender and age-specific prevalence of HPV in HNSCC. METHOD: This cross sectional retrospective study was carried out in four pathology laboratories of Medellin, Colombia. HPV testing was performed by GP5+/6+ PCR-based RLB and HPV 16 and 18 type-specific PCR. RESULTS: 175 primary HNSCC cases consecutively diagnosed between 1999 and 2008 with confirmed diagnosis and amplifiable DNA were included. Overall HPV prevalence was 18.9%. HPV was found in 23.9%, 17.5% and 13.3% of the oral cavity, larynx and oropharynx cases respectively. Among HPV positive cases, 82% were HPV 16 and 18% were HPV 18. No other HPV genotypes were identified. Most patients were males. Male patients were younger that their female counterparts, particularly in oral cavity cancer cases. CONCLUSION: HPV 16 and 18 genotypes were found in nearly 20% of HNSCC cases in Colombian patients. The impact of HPV vaccination for the prevention of HNSCC in this population deserves further evaluation.

Sanchez, G. I., et al. (2013). "**Human papillomavirus genotype detection in recurrent respiratory papillomatosis (RRP) in Colombia**." Head Neck **35**(2): 229-234.

BACKGROUND: Knowledge on human papillomavirus (HPV) genotype distribution in recurrent respiratory papillomatosis (RRP) is essential to assess the impact of HPV vaccine. It is provided information for Colombia. METHODS: In all, 189 RRP primary cases diagnosed between 1985 and 2009 were identified from 5 pathology laboratories of Cali and Medellin, Colombia. HPV DNA testing in 129 cases that fulfilled inclusion criteria (available paraffin blocks, amplifiable DNA, and confirmed histologic diagnosis of RRP) was performed by the SPF-10/LiPA25 assay (version 1). RESULTS: Of all cases 36.1% were juvenile (<12 years old) and a majority of adults were males (p = .09); 95% of cases were HPV positive. HPV 6, 11, and 16 contributed to 69%, 27.1%, and 7.8% of all HPV positive cases. Twelve cases (9.3%) showed multiple infections; 8 of these were HPV 6 or 11 positive. CONCLUSIONS: HPV prophylactic vaccine including HPV 6 and 11 may have a major impact against RRP.

Ruiz-Sternberg, A. M. and A. M. Pinzon-Rondon (2014). "**Risk perception and sexual behavior in HPV-vaccinated and unvaccinated young Colombian women**." Int J Gynaecol Obstet 126(3): 205-208.

OBJECTIVE: To compare sexual behaviors and risk perception between young women vaccinated for HPV and unvaccinated Colombian women. METHODS: In a cross-sectional design study, 1436 women (231 adolescents, <18 years; 1205 young women, 18-26 years) completed a self-administered questionnaire between May 2011 and March 2012 in Bogota, Colombia. Data from vaccinated and unvaccinated women were compared by descriptive statistics and multivariate models. RESULTS: Sexual risk behaviors were not associated with vaccination after adjustment for risk perception, age, educational level, and HPV knowledge. By contrast, vaccination was associated with higher routine Pap smear screening (odds ratio [OR], 2.35; 95% confidence interval [CI], 1.69-3.28), use of modern contraceptives (OR, 2.02; 95% CI, 1.26-3.22), and consistent use of condoms (OR, 1.49; 95% CI, 1.11-2.01). Vaccinated young women were more likely to have had sex (OR, 2.08; 95% CI, 1.56-2.78), but sexual debut among adolescents was not associated with vaccination. In bivariate and multivariate analyses, vaccination status was negatively associated with perceived risk of HPV infection, warts, and cervical cancer. There was no association between vaccination and perceived risk of sexually transmitted infections in any model. CONCLUSION: No association was found between changes in risk perception after HPV vaccination and sexual risk behaviors.

Camargo, M., et al. (2014). "**Human papillomavirus detection in women with and without human immunodeficiency virus infection in Colombia**." BMC Cancer **14**: 451.

BACKGROUND: HIV infection leads to a decreasing immune response, thereby facilitating the appearance of other infections, one of the most important ones being HPV. However, studies are needed for determining associations between immunodeficiency caused by HIV and/or the presence of HPV during the course of cervical lesions and their degree of malignancy. This study describes the cytological findings revealed by the Papanicolaou test, laboratory characteristics and HPV molecular profile in women with and without HIV infection. METHODS: A total of 216 HIV-positive and 1,159 HIV-negative women were invited to participate in the study; PCR was used for the molecular detection of HPV in cervical samples. Statistical analysis (such as percentages, Chi-square test and Fisher's exact test when applicable) determined human papillomavirus (HPV) infection frequency (single and multiple) and the distribution of six types of high-risk-HPV in women with and without HIV infection. Likewise, a logistic regression model was run to evaluate the relationship between HIV-HPV infection and different risk factors. RESULTS: An association was found between the frequency of HPV infection and infection involving 2 or more HPV types (also known as multiple HPV infection) in HIV-positive women (69.0% and 54.2%, respectively); such frequency was greater than that found in HIV-negative women (44.3% and

22.7%, respectively). Statistically significant differences were observed between both groups (p = 0.001) regarding HPV presence (both in infection and multiple HPV infection). HPV-16 was the most prevalent type in the population being studied (p = 0.001); other viral types had variable distribution in both groups (HIV-positive and HIV-negative). HPV detection was associated with <500 cell/mm(3) CD4-count (p = 0.004) and higher HIV-viral-load (p = 0.001). HPV-DNA detection, <200 cell/mm(3) CD4-count (p = 0.001), and higher HIV-viral-load (p = 0.001) were associated with abnormal cytological findings. CONCLUSIONS: The HIV-1 positive population in this study had high multiple HPV infection prevalence. The results for this population group also suggested a greater association between HPV-DNA presence and cytological findings. HPV detection, together with low CD4 count, could represent useful tools for identifying HIV-positive women at risk of developing cervical lesions.

Munoz, N. and L. E. Bravo (2014). "**Epidemiology of cervical cancer in Colombia**." Salud Publica Mex **56**(5): 431-439.

OBJECTIVE: To describe the incidence, mortality, time trends and prognostic factors for cervical cancer in Cali, Colombia, and to review the molecular epidemiological evidence showing that HPV is the major and necessary cause of cervical cancer and the implications of this discovery for primary and secondary prevention. MATERIALS AND METHODS: Incidence rates of cervical cancer during a 45-year period (1962-2007) were estimated based on the population-based cancer registry of Cali and the mortality statistics from the Municipal Health Secretariat of Cali. Prognostic factors were estimated based on relative survival. Review of the molecular epidemiological evidence linking HPV to cervical cancer was focused on the studies carried out in Cali and in other countries. RESULTS: Incidence rates of squamous cell carcinoma (SCC) declined from 120.4 per 100 000 in 1962-1966 to 25.7 in 2003-2007 while those of adenocarcinoma increased from 4.2 to 5.8. Mortality rates for cervical cancer declined from 18.5 in 1984-1988 to 7.0 per 100 000 in 2009-2011. Survival was lower in women over 65 years of age and in clinical stages 3-4. Review of the molecular epidemiological evidence showed that certain types of HPV are the central and necessary cause of cervical cancer. CONCLUSIONS: A decline in the incidence and mortality of SCC and an increase in the incidence of adenocarcinoma during a 45-year period was documented in Cali, Colombia.

Del Rio-Ospina, L., et al. (2016). "**The Prevalence of High-Risk HPV Types and Factors Determining Infection in Female Colombian Adolescents**." PLoS One **11**(11): e0166502.

This study reports six HR-HPV types' infection prevalence discriminated by species and multiple infection in unvaccinated Colombian female adolescents, as well as some factors modulating the risk of infection. HPV DNA for six high-risk viral types was identified in cervical samples taken from 2,134 12-19 year-old females using conventional generic and type-specific PCR. Binomial logistical regression analysis was used for modelling HR-HPV infection and multiple infection risk. The interaction between variables in a stepwise model was also included in such analysis. Viral DNA was detected in 48.97% of the females; 28.52% of them had multiple infections, HPV-16 being the most frequently occurring type (37.44%). Cytological abnormality prevalence was 15.61%. Being over 16 years-old (1.66: 1.01-2.71 95%CI), white ethnicity (4.40: 1.16-16.73 95%CI), having had 3 or more sexual partners (1.77: 1.11-2.81 95%CI) and prior sexually-transmitted infections (STI) (1.65: 1.17-2.32 95%CI) were associated with a greater risk of HPV infection. Having given birth was related to a higher risk of infection by A7 species and antecedent of abortion to less risk of coinfection. Where the females in this study came from also influenced the risk of infection by A7 species as female adolescents from the Andean region had a lower risk of infection (0.42: 0.18-0.99 95%CI). The presence of factors related to risky sexual behaviour in the study

population indicated that public health services should pay special attention to female adolescents to modify the risk of infection by high-risk HPV types and decrease their impact on this age group.

Combita, A. L., et al. (2016). "**Comparison between Urine and Cervical Samples for HPV DNA Detection and Typing in Young Women in Colombia.**" Cancer Prev Res (Phila) 9(9): 766-771.

Urine sampling for HPV DNA detection has been proposed as an effective method for monitoring the impact of HPV vaccination programs; however, conflicting results have been reported. The goal of this study was to evaluate the performance of optimized urine HPV DNA testing in women aged 19 to 25 years. Optimization process included the use of first void urine, immediate mixing of urine with DNA preservative, and the concentration of all HPV DNA, including cell-free DNA fragments. Urine and cervical samples were collected from 535 young women attending cervical screening at health centers from two Colombian cities. HPV DNA detection and genotyping was performed using an HPV type-specific multiplex genotyping assay, which combines multiplex polymerase chain reaction with bead-based Luminex technology. Concordance between HPV DNA detection in urine and cervical samples was determined using kappa statistics and McNemar tests. The accuracy of HPV DNA testing in urine samples was evaluated measuring sensitivity and specificity using as reference the results obtained from cervical samples. Statistical analysis was performed using STATA11.2 software. The findings revealed an overall HPV prevalence of 60.00% in cervical samples and 64.72% in urine samples, HPV-16 being the most frequent HPV type detected in both specimens. Moreover, our results indicate that detection of HPV DNA in first void urine provides similar results to those obtained with cervical samples and can be used to monitor HPV vaccination trials and programs as evidenced by the substantial concordance found for the detection of the four vaccine types. Cancer Prev Res; 9(9); 766-71. (c)2016 AACR.

Hernandez-Avila, M., et al. (2016). "**Evaluation of the immunogenicity of the quadrivalent HPV vaccine using 2 versus 3 doses at month 21: An epidemiological surveillance mechanism for alternate vaccination schemes**." Hum Vaccin Immunother **12**(1): 30-38.

The cost of HPV vaccines and the need for 3 doses remains a barrier for their inclusion in routine vaccination schedules for girls in low and middle income countries. In a non-inferiority study, we aimed to compare the immunogenicity of a standard 3 doses and a 2 doses schedule. We enrolled 450 participants in an open-label non-randomized clinical trial to evaluate the immunogenicity induced at different ages by the licensed HPV6/11/16/18 quadrivalent vaccine in a 2 doses schedule (0-6 months, n = 150 girls aged 9-10 y) and 3 doses schedule (0, 2, and 6 months; n = 150 girls aged 9-10 y and n=150 women aged 18 to 24 years). To assess the antibody response, blood samples were obtained at Month 7 and 21 after the first vaccination from participants in all study groups. cLIA testing was performed at Merck Research Laboratories. Antibody levels were expressed as milli-Merck units (mMU) per ml. Primary outcome was non-inferiority (95% CI, lower bound >0.5) of the geometric mean titers (GMT) ratios for HPV6, HPV11, HPV16 and HPV18 antibodies 7 and 21 months after the first dose among girls receiving 2 doses compared with young women and girls receiving 3 doses. All vaccinees were seropositive for both HPV16 and HPV18 antibodies at month 7. At month 21, 98.5 and 56.6% of women 18-24 y old were seropositive for HPV16 and 18, respectively. For girls in the three doses group, seropositivity rates were 99.3 and 86.3% for HPV16 and 18, respectively. For girls in the two doses group rates were 99.3 and 70.2% for HPV16 and 18, respectively. The two doses schedule was non-inferior compared to the 3 doses schedule in same-age girls and to the group of adult women after 21 months of the first vaccine dose. Our results are in agreement with similar trials evaluating the immune response

of a 2 doses schedule of both HPV vaccines, supporting the recent WHO recommendation as well as the Mexican policy to incorporate the 2 doses schedule for girls aged 9-11 y.

Lechuga, J., et al. (2016). "**HPV Vaccine Awareness, Barriers, Intentions, and Uptake in Latina Women**." J Immigr Minor Health **18**(1): 173-178.

Latina women are at heightened risk of cervical cancer incidence and mortality. The human papillomavirus (HPV) is the principal cause of the majority of cervical cancer cases. A vaccine that protects against HPV was licensed in 2006. Eight years post-licensure, mixed research findings exist regarding the factors that predict vaccine uptake in Latinas. We conducted a population-based phone survey with a random sample of 296 Latinas living in a Midwestern U.S. City. Intention to vaccinate was significantly associated with health care provider recommendations, worry about side effects, knowing other parents have vaccinated, perceived severity of HPV, and worry that daughter may become sexually active following vaccination. Worry that daughter may become sexually active was the only factor related to vaccine uptake. Findings suggest that training providers to discuss the low risk of severe side effects, consequences of persistent HPV, and sexuality related concerns with Latino women may encourage vaccination.

Quinonez-Calvache, E. M., et al. (2016). "**Chlamydia trachomatis Frequency in a Cohort of HPV-Infected Colombian Women.**" PLoS One **11**(1): e0147504.

BACKGROUND: Chlamydia trachomatis (C. trachomatis), an obligate intracellular bacterium, is the commonest infectious bacterial agent of sexual transmission throughout the world. It has been shown that the presence of this bacteria in the cervix represents a risk regarding HPV persistence and, thereafter, in developing cervical cancer (CC). Prevalence rates may vary from 2% to 17% in asymptomatic females, depending on the population being analysed. This study reports the identification of C. trachomatis in a cohort of 219 HPV-infected Colombian females. METHODS: C. trachomatis infection frequency was determined during each of the study's follow-up visits; it was detected by amplifying the cryptic plasmid sequence by polymerase chain reaction (PCR) using two sets of primers: KL5/KL6 and KL1/KL2. Infection was defined as a positive PCR result using either set of primers at any time during the study. Cox proportional risk models were used for evaluating the association between the appearance of infection and a group of independent variables. RESULTS: Base line C. trachomatis infection frequency was 28% (n = 61). Most females infected by C. trachomatis were infected by multiple types of HPV (77.42%), greater prevalence occurring in females infected with HPV-16 (19.18%), followed by HPV-58 (17.81%). It was observed that females having had the most sexual partners (HR = 6.44: 1.59-26.05 95%CI) or infection with multiple types of HPV (HR = 2.85: 1.22-6.63 95%CI) had the greatest risk of developing C. trachomatis. CONCLUSIONS: The study provides data regarding the epidemiology of C. trachomatis /HPV coinfection in different population groups of Colombian females and contributes towards understanding the natural history of C. trachomatis infection.

Vargas, H., et al. (2016). "**Type-Specific Identification of Genital Human Papillomavirus Infection in Women with Cytological Abnormality**." Acta Cytol **60**(3): 211-216.

OBJECTIVES: To estimate the frequency of human papillomavirus (HPV) infection and the genotype distribution of HPV among women with a Pap smear showing atypical squamous cells of undetermined significance (ASC-US) attending the Program for the Detection and Control of Cervical Cancer in Bogota,

Colombia. STUDY DESIGN: Cervical samples from 200 women with an ASC-US Pap smear were analyzed for the presence of HPV DNA and genotype distribution using a commercial molecular technique (Linear Array(R); Roche Molecular Systems, USA). RESULTS: HPV infection was found in 140 women (70%). High-risk HPV types were present in 46.4% of the samples; 16.4% showed a low-risk HPV type, and 37.1% showed both. Of the positive samples, 42.9% were infected with a single viral genotype, whereas 57.1% exhibited multiple HPV infections. The most common HPV genotypes were HPV 16, 53, and 52 with a prevalence of 26.4, 16.4, and 13.6%, respectively. CONCLUSION: The epidemiological characterization of HPV infections described in this study might guide actions for epidemiological surveillance to strengthen the program in Bogota and to develop appropriate HPV vaccination programs.

Akhavan-Tabatabaei, R., et al. (2017). "**A Markov Decision Process Model for Cervical Cancer Screening Policies in Colombia**." Med Decis Making **37**(2): 196-211.

Cervical cancer is the second most common cancer in women around the world, and the human papillomavirus (HPV) is universally known as the necessary agent for developing this disease. Through early detection of abnormal cells and HPV virus types, cervical cancer incidents can be reduced and disease progression prevented. We propose a finite-horizon Markov decision process model to determine the optimal screening policies for cervical cancer prevention. The optimal decision is given in terms of when and what type of screening test to be performed on a patient based on her current diagnosis, age, HPV contraction risk, and screening test results. The cost function considers the tradeoff between the cost of prevention and treatment procedures and the risk of taking no action while taking into account a cost assigned to loss of life quality in each state. We apply the model to data collected from a representative sample of 1141 affiliates at a health care provider located in Bogota, Colombia. To track the disease incidence more effectively and avoid higher cancer rates and future costs, the optimal policies recommend more frequent colposcopies and Pap tests for women with riskier profiles.

Hooi, D. J., et al. (2018). "**Human papillomavirus (HPV) types prevalence in cervical samples of female sex-workers on Curacao**." Prev Med Rep **11**: 120-124.

Sex-workers have an increased risk for high-risk HPV(hrHPV) cervical cancer. On Curacao, legal and illegal prostitution practice is high and the promiscuous lifestyle is common. We aimed to gain insight in HPV-genotype prevalence in cervical scrapes of female sex workers (FSW) and related risk factors in comparison with women not working in the sex industry. Cervical samples were taken from 76 FSW and 228 non-FSW (NFSW) age matched controls in the period between 2013 and 2015. HPV was detected by GP5+/6+ PCR-EIA followed by genotyping via reverse line-blot. HPV prevalence in FSWs was 25.0% and in NFSWs 29.4% (p=0.14). NFSW had more often untypable HPV-genotypes (HPV-X:5.3% vs 0.0%; p=0.042). A trend for statistical difference was observed in HPV prevalence between FSWs from Dominican Republic (42.1%) and FSWs from Colombia (19.2%; p=0.067). Young age was the only risk factor related to HPV prevalence in FSWs. (Mean age FSW 29.2y +/-7.8 and NFSW 33y +/-6.2) Smoking and drugs consumption were significantly higher among FSW. A significant higher number of women with history of any STD was reported by NFSWs. In addition, >90% of FSW had their previous Pap smear <3years ago, while >35% NFSW never had a previous Pap smear (p<0.001). IN CONCLUSION: no significant difference in HPV prevalence is observed between FSW and NFSW. HPV prevalence in FSW was associated with a lower age. During interviews, FSW seemed more aware about prevention strategies, reported less history of STD's and were more updated with cervical cancer screening, compared to NFSWs.

Lamb, R. L. B., et al. (2018). "**Evaluation of Entertainment Education Strategies to Promote Cervical Cancer Screening and Knowledge in Colombian Women**." J Cancer Educ **33**(5): 1094-1101.

Cervical cancer is considered to be a major health problem for women in developing countries, but it is also problematic for more developed countries as global migration increases and health behaviors move from the countries of origin to new places of residence. We designed and produced a testimonial video and a fotonovela (printed short story) to educate women about cervical cancer and screening. The development of the materials included formative research, production, pretesting, dissemination, and evaluation. The evaluation included 100 women that completed a pretest and a posttest at eight health clinics in Medellin. The pretest and posttest were analyzed using McNemar's test for categorical variables and paired t test for continuous variables. Women in the study had a high initial Stage of Change as defined by the Transtheoretical Model and a high baseline knowledge of HPV and cervical cancer, with the caveat of specific knowledge deficiencies especially for HPV. While not statistically significant, postintervention Transtheoretical Model status in both interventions changed towards higher stages, specifically, from Precontemplation to Contemplation and Preparation. Women who participated in the study liked the educational materials and their knowledge increased, especially for HPV. However, the perception of risk did not change.

Puerto, D., et al. (2018). "**Detection and Genotyping of HPV DNA in a Group of Unvaccinated Young Women from Colombia: Baseline Measures Prior to Future Monitoring Program**." Cancer Prev Res (Phila) 11(9): 581-592.

In 2012, Colombia launched human papillomavirus (HPV) vaccination program for girls ages 9 to 12, and in 2013, the target age was expanded to 9 to 17 years. Monitoring the changes of HPV infection prevalence among young women has been proposed as an endpoint for early assessment of HPV vaccination programs. However, the data on HPV prevalence in young ages are very limited. The purpose of this study was to determine the prevalence of HPV infection and the distribution of genotypes in a group of nonvaccinated women ages 18 to 25 years old in three Colombian cities as baseline for the monitoring of the HPV national vaccination program. A total of 1,782 sexually active women were included. Cervical smear samples were collected to perform the Pap smear and HPV DNA detection using a Linear Array HPV assay. Of the 1,782 specimens analyzed, 60.3% were positive for any HPV type; 42.2% were positive for high-risk HPV (HR-HVP) types, and 44.4% for low-risk HPV (LR-HPV) types. Multiple and single infections were identified in 37.1% and 23.2% of samples, respectively. HR-HPV types -16, -52, and -51 were the most predominant with proportions of 11.3%, 7.92%, and 7.9%, correspondingly. The prevalence for HR-HPV 16/18 was 14.4%. HR-HPV prevalence in women with abnormal cytology (75.16%) was higher than in women with normal cytology (38.6%). In conclusion, a high prevalence of HR-HPV was observed among younger women. This HPV type-specific prevalence baseline may be used to monitor postvaccination longitudinal changes and to determine its impact on HPV-related disease incidence in Colombia population. Cancer Prev Res; 11(9); 581-92. (c)2018 AACR.

Robles, C., et al. (2018). **"Impact of operational factors on HPV positivity rates in an HPV-based screening study in Colombia."** Int J Gynaecol Obstet 143(1): 44-51.

OBJECTIVE: To assess the effect of operational factors on the positivity rates of three HPV assays. METHODS: Within the cross-sectional ESTAMPA study, women aged 30-64 years were recruited at healthcare centers from Soacha, Colombia, during 2012-2015. Cervical samples were collected for cotesting with Hybrid Capture 2 (HC2; Qiagen, Gaithersburg, MD, USA), and either Aptima (Hologic, Marlborough, MA, USA) or Cobas 4800 (Roche Diagnostics, Indianapolis, IN, USA). The effect of

operational factors on assay performance was assessed using adjusted positivity rates obtained from logistic regression models. RESULTS: There were 4168 women included. For samples collected in assay-specific medium, positivity rate differences were associated with the expertise of the nurse collecting the sample (P=0.014 HC2; P=0.091 Aptima) and if sample collection occurred after an initial cytology (P=0.025 HC2; P=0.033 Aptima). If PreservCyt medium (Hologic) was used, HC2 positivity differences were observed depending on the time between sample collection and processing (P=0.026) and on the laboratory technician processing the samples (P=0.003). No differences were observed for PreservCyt samples processed with Aptima or Cobas. CONCLUSION: Nurse expertise, collection of previous cytology, processing time, and laboratory technician could influence HPV assay performance. Suitable quality assurance protocols for HPV-based screening programs are required. ClinicalTrials.gov: NCT01881659.

Session 4 Prevention and control of HPV in Colombia

References session 4 via PubMed search:

A PubMed search was performed with the following selection criteria. 28 items retrieved.

1. Colombia AND HPV AND vaccination program in the last 10 years:
2. Colombia AND "cervical cancer" AND prevention AND control AND treatment in the last 10 years:

The list contains a manual selection of 15 publications relevant to session 4.

Murillo, R. (2008). **"[Cervical cancer control in Colombia: achievements and challenges of cytology based programs].**" Biomedica 28(4): 467-470. [Article in Spanish]

Murillo, R., et al. (2009). "**HPV prevalence in Colombian women with cervical cancer: implications for vaccination in a developing country**." Infect Dis Obstet Gynecol 2009: 653598.

> Human Papillomavirus (HPV) vaccines have been considered potentially cost-effective for the reduction of cervical cancer burden in developing countries; their effectiveness in a public health setting continues to be researched. We conducted an HPV prevalence survey among Colombian women with invasive cancer. Paraffin-embedded biopsies were obtained from one high-risk and one low-middle-risk regions. GP5+/GP6+ L1 primers, RLB assays, and E7 type specific PCR were used for HPV-DNA detection. 217 cases were analyzed with 97.7% HPV detection rate. HPV-16/18 prevalence was 63.1%; HPV-18 had lower occurrence in the high-risk population (13.8% versus 9.6%) allowing for the participation of less common HPV types; HPV-45 was present mainly in women under 50 and age-specific HPV type prevalence revealed significant differences. Multiple high-risk infections appeared in 16.6% of cases and represent a chance of replacement. Age-specific HPV prevalence and multiple high-risk infections might influence vaccine impact. Both factors highlight the role of HPVs other than 16/18, which should be considered in cost-effectiveness analyses for potential vaccine impact.

Wiesner-Ceballos, C., et al. (2009). **"[Control of cervical cancer in Colombia: the perspective of the health system]**." Rev Panam Salud Publica 25(1): 1-8.

> OBJECTIVES: To characterize the health system stakeholder's perspective on the basics of the political, economic, and sanitary context, as well as the ways in which control activities are being realized in four of Colombia's health departments. METHODS: This was a qualitative study of four Colombian health departments chosen for their differing cervical cancer mortality rates and their planned disease control efforts (Boyaca, Caldas, Magdalena, and Tolima). Semistructured interviews were conducted of health care managers, insurance coordinators, and public and private health institutions at the departmental and municipals levels. Focus groups comprised of professionals from health insurance companies and health care services providers were convened. Data analysis was based on the grounded theory with open codes related to the roles of health care managers, insurance companies, and heath care services provided. The technical

reports were compared to the testimonies of interviewees. RESULTS: Thirty-eight interviews and 14 focus groups (70.9% response rate) were conducted and 12 technical reports reviewed. Cervical cancer is not perceived to be a public health priority. Interest centers on the flow of financial resources within the health system. Findings indicated unsatisfactory communication among the stakeholders and no consensus on the subject. Planning is limited to meeting the status quo. Staffing is inadequate. Cases with positive outcomes are lost to follow-up due to the fragmentation that results from affiliation with different health care systems. CONCLUSIONS: The financial situation, normative planning, and the challenges of decentralization affect the skill-building, at-risk coverage, and the control activities needed for effective screening programs. What is needed is an integrated, more efficiently organized program in which all the health system stakeholders participate.

Choconta-Piraquive, L. A., et al. (2010). "**How protective is cervical cancer screening against cervical cancer mortality in developing countries? The Colombian case."** BMC Health Serv Res 10: 270.

BACKGROUND: Cervical cancer is one of the top causes of cancer morbidity and mortality in Colombia despite the existence of a national preventive program. Screening coverage with cervical cytology does not explain the lack of success of the program in reducing incidence and mortality rates by cervical cancer. To address this problem an ecological analysis, at department level, was carried out in Colombia to assess the relationship between cervical screening characteristics and cervical cancer mortality rates. METHODS: Mortality rates by cervical cancer were estimated at the department level for the period 2000-2005. Levels of mortality rates were compared to cervical screening coverage and other characteristics of the program. A Poisson regression was used to estimate the effect of different dimensions of program performance on mortality by cervical cancer. RESULTS: Screening coverage ranged from 28.7% to 65.6% by department but increases on this variable were not related to decreases in mortality rates. A significant reduction in mortality was found in departments where a higher proportion of women looked for medical advice when abnormal findings were reported in Pap smears. Geographic areas where a higher proportion of women lack health insurance had higher rates of mortality by cervical cancer. CONCLUSIONS: These results suggest that coverage is not adequate to prevent mortality due to cervical cancer if women with abnormal results are not provided with adequate follow up and treatment. The role of different dimensions of health care such as insurance coverage, quality of care, and barriers for accessing health care needs to be evaluated and addressed in future studies.

Garces-Palacio, I. C., et al. (2010). "**Contribution of health care coverage in cervical cancer screening follow-up: findings from a cross-sectional study in Colombia.**" Int J Gynecol Cancer 20(7): 1232-1239.

OBJECTIVE: To determine the role of health care coverage (HCC) in follow-up of cervical cancer screening (seeking Papanicolaou test results and follow-up when abnormal results were found) among Colombian women. METHODS: A population-based cross-sectional study of 24,717 women, using the 2005 Colombian Demographic and Health Survey, was conducted. RESULTS: Nearly 4% of women screened did not seek their results. For approximately 17% of the women, there was no follow-up when abnormal results were found. Women in the contributory regime (private insurance) and those in the subsidized regime (public insurance) were more likely to seek Papanicolaou test results than women without HCC, even after adjusting for sociodemographic factors (adjusted odds ratio [ORa], 1.96; 95% confidence interval [CI], 1.60-

2.41 and ORa, 1.34; 95% CI, 1.14-1.58, respectively). For follow-up when abnormal results were found, there was no difference between the subsidized regime and no HCC, but women in the contributory regime were more likely to follow-up than women without HCC (ORa, 1.40; 95% CI, 1.05-1.86). CONCLUSIONS: Seeking Papanicolaou test results is relatively high among Colombian women; however, there are differences according to HCC. Follow-up when abnormal Papanicolaou test results were found was positively associated only with private insurance; follow-up is the same for women without insurance and with public insurance. Exploring strategies to promote follow-up among women and to improve cervical cancer follow-up services for those enrolled in the subsidized regime may increase follow-up rates among Colombian women.

Mousa, S. M., et al. (2010). "**Community health workers speak out about the Kin KeeperSM model**." J Cancer Educ 25(2): 236-241.

Community health workers (CHWs) informed students and researcher alike on the Kin Keeper(SM) Cancer Prevention Intervention. Students interested in medicine, guided by faculty, conducted a focus group session with 13 CHWs to find out if the intervention was effective for delivering breast and cervical cancer education. Strengths reported were (1) cultural appropriateness, (2) home visits, (3) CHW resource kits, and (4) increased awareness. The barriers were privacy perceptions and scheduling home visits. Overall, the CHWs indicated that the intervention was effective and flexible enough to accommodate the African American, Latina, and Arab groups of women.

Wiesner, C., et al. (2010). **"[Following-up females having an abnormal Pap smear in Colombia]**." Rev Salud Publica (Bogota) 12(1): 1-13.

OBJECTIVE: Evaluating the opportunity and access to diagnosis and treatment for females having had an abnormal Pap smear (high-grade epithelial lesion and cervical cancer) in Colombia from June 2005 to June 2006. MATERIALS AND METHODS: This was a retrospective appraisal using a semi-closed survey of females having had an abnormal Pap smear with high squamous intraepithelial lesions or cervical cancer living in four Colombian departments. These areas were conveniently selected according to their different mortality rates. A descriptive analysis was made and the departments differences compared. RESULTS: It was found that 27 % of females having high-grade squamous intraepithelial lesion or cervical cancer had no access to any of the diagnostic or therapeutic services. Health service administration problems and clinical and cultural ones affecting the females in the study could explain such results. DISCUSSION: Follow-up care after abnormal cytology was very poor and could explain the lack of cervical cancer screening impact in Colombia and in most Latin-American countries.

Aponte-Gonzalez, J., et al. (2013). "**Cost-effectiveness analysis of the bivalent and quadrivalent human papillomavirus vaccines from a societal perspective in Colombia**." PLoS One 8(11): e80639.

OBJECTIVE: To compare costs and effectiveness of three strategies used against cervical cancer (CC) and genital warts: (i) Screening for CC; (ii) Bivalent Human Papillomavirus (HPV) 16/18 vaccine added to screening; (iii) Quadrivalent HPV 6/11/16/18 vaccine added to screening.

METHODS: A Markov model was designed in order to simulate the natural history of the disease from 12 years of age (vaccination) until death. Transition probabilities were selected or adjusted to match the HPV infection profile in Colombia. A systematic review was undertaken in order to derive efficacy values for the two vaccines as well as for the operational characteristics of the cytology test. The societal perspective was used. Effectiveness was measured in number of averted Disability Adjusted Life Years (DALYS). RESULTS: At commercial prices reported for 2010 the two vaccines were shown to be non-cost-effective alternatives when compared with the existing screening strategy. Sensitivity analyses showed that results are affected by the cost of vaccines and their efficacy values, making it difficult to determine with certainty which of the two vaccines has the best cost-effectiveness profile. To be 'cost-effective' vaccines should cost between 141 and 147 USD (Unite States Dollars) per vaccinated girl at the most. But at lower prices such as those recommended by WHO or the price of other vaccines in Colombia, HPV vaccination could be considered very cost-effective. CONCLUSIONS: HPV vaccination could be a convenient alternative for the prevention of CC in Colombia. However, the price of the vaccine should be lower for this vaccination strategy to be cost-effective. It is also important to take into consideration the willingness to pay, budgetary impact, and program implications, in order to determine the relevance of a vaccination program in this country, as well as which vaccine should be selected for use in the program.

Munoz, M., et al. (2013). "**Human papillomavirus detection from human immunodeficiency virus-infected Colombian women's paired urine and cervical samples.**" PLoS One 8(2): e56509.

Infection, coinfection and type-specific human papillomavirus (HPV) distribution was evaluated in human immunodeficiency virus (HIV)-positive women from paired cervical and urine samples. Paired cervical and urine samples (n = 204) were taken from HIV-positive women for identifying HPV-DNA presence by using polymerase chain reaction (PCR) with three generic primer sets (GP5+/6+, MY09/11 and pU1M/2R). HPV-positive samples were typed for six high-risk HPV (HR-HPV) (HPV-16, -18, -31, -33, -45 and -58) and two low-risk (LR-HPV) (HPV-6/11) types. Agreement between paired sample results and diagnostic performance was evaluated. HPV infection prevalence was 70.6% in cervical and 63.2% in urine samples. HPV-16 was the most prevalent HPV type in both types of sample (66.7% in cervical samples and 62.0% in urine) followed by HPV-31(47.2%) in cervical samples and HPV-58 (35.7%) in urine samples. There was 55.4% coinfection (infection by more than one type of HPV) in cervical samples and 40.2% in urine samples. Abnormal Papanicolau smears were observed in 25.3% of the women, presenting significant association with HPV-DNA being identified in urine samples. There was poor agreement of cervical and urine sample results in generic and type-specific detection of HPV. Urine samples provided the best diagnosis when taking cytological findings as reference. In conclusion including urine samples could be a good strategy for ensuring adherence to screening programs aimed at reducing the impact of cervical cancer, since this sample is easy to obtain and showed good diagnostic performance.

Bermedo-Carrasco, S., et al. (2015). "**Predictors of having heard about human papillomavirus vaccination: Critical aspects for cervical cancer prevention among Colombian women**." Gac Sanit 29(2): 112-117.

OBJECTIVES: To determine whether the probability of having heard about human papillomavirus (HPV) vaccination differs by socio-demographic characteristics among Colombian women; and

whether the effect of predictors of having heard about HPV vaccination varies by educational levels and rural/urban area of residence. METHODS: Data of 53,521 women aged 13-49 years were drawn from the 2010 Colombian National Demographic and Health Survey. Women were asked about aspects of their health and their socio-demographic characteristics. A logistic regression model was used to identify factors associated with having heard about HPV vaccination. Educational level and rural/urban area of residence of the women were tested as modifier effects of predictors. RESULTS: 26.8% of the women had heard about HPV vaccination. The odds of having heard about HPV vaccination were lower among women: in low wealth quintiles, without health insurance, with subsidized health insurance, and those who had children ($p<0.001$). Although women in older age groups and with better education had higher probabilities of having heard about HPV vaccination, differences in these probabilities by age group were more evident among educated women compared to non-educated ones. Probability gaps between non-educated and highly educated women were wider in the Eastern region. Living in rural areas decreased the probability of having heard about HPV vaccination, although narrower rural/urban gaps were observed in the Atlantic and Amazon-Orinoquia regions. CONCLUSIONS: Almost three quarters of the Colombian women had not heard about HPV vaccination, with variations by socio-demographic characteristics. Women in disadvantaged groups were less likely to have heard about HPV vaccination.

Bermedo-Carrasco, S., et al. (2016). "**Spatial variations in cervical cancer prevention in Colombia: Geographical differences and associated socio-demographic factors."** Spat Spatiotemporal Epidemiol 19: 78-90.

We examined spatial variations in the frequencies of women who had not heard of human papillomavirus vaccination (NHrd-Vac) and who had not had Pap testing (NHd-Pap) among Colombian administrative divisions (departments), before and after considering differences in socio-demographic factors. Following global and local tests for clustering, Bayesian Poisson hierarchical models identified department factors associated with NHrd-Vac and NHd-Pap, as well as the extent of the spatially structured and unstructured heterogeneity. Models of spatial variations for both outcomes included the department percentage of women with subsidised health insurance. The relative risks of NHrd-Vac and NHd-Pap were highest in several departments adjacent to the Colombian border. Our finding that the risk of not having adequate access to cervical cancer (CC) prevention programmes in Colombia was location-dependent, could be used to focus resources for CC prevention programmes.

Lechuga, J., et al. (2016). "**HPV Vaccine Awareness, Barriers, Intentions, and Uptake in Latina Women**." J Immigr Minor Health 18(1): 173-178.

Latina women are at heightened risk of cervical cancer incidence and mortality. The human papillomavirus (HPV) is the principal cause of the majority of cervical cancer cases. A vaccine that protects against HPV was licensed in 2006. Eight years post-licensure, mixed research findings exist regarding the factors that predict vaccine uptake in Latinas. We conducted a population-based phone survey with a random sample of 296 Latinas living in a Midwestern U.S. City. Intention to vaccinate was significantly associated with health care provider recommendations, worry about side effects, knowing other parents have vaccinated, perceived severity of HPV, and worry that daughter may become sexually active following vaccination. Worry that daughter may become sexually active was the only factor related to vaccine uptake.

Findings suggest that training providers to discuss the low risk of severe side effects, consequences of persistent HPV, and sexuality related concerns with Latino women may encourage vaccination.

Rodriguez-Feria, P., et al. (2016). "**Knowledge, attitudes and practices of prevention for cervical cancer and breast cancer among medical students**." Rev Salud Publica (Bogota) 18(3): 354-366.

Objective To assess the knowledge, attitudes and practices of medical students for health promotion, primary prevention and early detection of breast neoplasm and uterine cervical neoplasm, as well as to make recommendations for improving the Public Health curriculum at the Universidad de los Andes. Methodology This study utilized a survey of medical knowledge, attitudes and practices applied to fifth year Colombian medical students attending the Universidad de los Andes in the first semester of 2013. Results 64/76 students answered the surveys (response rate 84.2 %): 62.5 % (40/64) and 37.5 % (24/64) response rates from students in their ninth and tenth semesters, respectively; and 64.1 % (41/64) and 35.9 % (23/64) response rates from female and male students, respectively. Knowledge: clinical breast exam (CBE), breast self-examination (BSE) and mammography were recommended by 95.3 % (61/64) of students, 96.9 % (62/64) of medical students and 90.7 % (58/64) of students, respectively. Attitude: the most effective tests to reduce mortality in women aged >/= 50 years were the Papanicolaou test according to 90.6 % (58/64) of students and mammography according to 82.8 % (53/64) of students. Practice: 55.0 % (35/64) of students had received training in the guidelines and protocols for breast neoplasm and uterine cervical neoplasm screening. Discussion To promote early detection of cervical and breast cancer, knowledge, attitudes and practices must be improved to enhance clinical practices (e.g. Papanicolaou test) and medical student training guidelines or protocols for these two cancers. Overall, with induced demand and support from research communities and institutions seeking to make these improvements, we collaborate to decrease missed opportunities in medical research and Public Health.

Caro Martinez, A., et al. (2017). "**Adoption of the HPV vaccine: a case study of three emerging countries**." J Comp Eff Res 6(3): 195-204.

BACKGROUND: The human papillomavirus (HPV) vaccine has recently attracted considerable attention in emerging countries, due to its potential to reduce the impact of HPV-related diseases. This case study sheds new light about the variety of HTA arrangements, methods and processes involved in the adoption and use of HPV vaccines in a selected sample of central, eastern and southern Europe and Latin America and the Caribbean, all of them emerging in the use of HTA. MATERIALS & METHODS: A multi-country case study was designed. Mixed methods, document review, semi-structured surveys and personal communication with experts, were used for data collection and triangulation. RESULTS: This study shows that common elements of good practice exist in the processes and methods used, with all countries arriving at the same appraisal recommendations. However, the influence of socio-politico-economic factors appears to be determinant on the final decisions and restrictions to access made. CONCLUSION: This case study intends to draw useful lessons for policymakers in emerging settings interested in the adoption of the HPV vaccine supported by evidence-informed processes, such as those offered by institutionalized HTA. Future studies are also recommended to elucidate the specific roles that social values and uncertainties play in vaccine decision-making across different societies.

Puerto, D., et al. (2018). "**Detection and Genotyping of HPV DNA in a Group of Unvaccinated Young Women from Colombia: Baseline Measures Prior to Future Monitoring Program**." Cancer Prev Res (Phila) 11(9): 581-592.

In 2012, Colombia launched human papillomavirus (HPV) vaccination program for girls ages 9 to 12, and in 2013, the target age was expanded to 9 to 17 years. Monitoring the changes of HPV infection prevalence among young women has been proposed as an endpoint for early assessment of HPV vaccination programs. However, the data on HPV prevalence in young ages are very limited. The purpose of this study was to determine the prevalence of HPV infection and the distribution of genotypes in a group of nonvaccinated women ages 18 to 25 years old in three Colombian cities as baseline for the monitoring of the HPV national vaccination program. A total of 1,782 sexually active women were included. Cervical smear samples were collected to perform the Pap smear and HPV DNA detection using a Linear Array HPV assay. Of the 1,782 specimens analyzed, 60.3% were positive for any HPV type; 42.2% were positive for high-risk HPV (HR-HVP) types, and 44.4% for low-risk HPV (LR-HPV) types. Multiple and single infections were identified in 37.1% and 23.2% of samples, respectively. HR-HPV types -16, -52, and -51 were the most predominant with proportions of 11.3%, 7.92%, and 7.9%, correspondingly. The prevalence for HR-HPV 16/18 was 14.4%. HR-HPV prevalence in women with abnormal cytology (75.16%) was higher than in women with normal cytology (38.6%). In conclusion, a high prevalence of HR-HPV was observed among younger women. This HPV type-specific prevalence baseline may be used to monitor postvaccination longitudinal changes and to determine its impact on HPV-related disease incidence in Colombia population. Cancer Prev Res; 11(9); 581-92. (c)2018 AACR.

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NA

Giana Henriquez

NA

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NA

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Yvonne Morrissey, Health Service Executive (HSE) National Immunisation Office, Ireland,Communications Manager.

As communications Manager she is responsible for managing campaigns on behalf of the National Immunisation Office this includes developing campaign materials, maintaining the immunisation websites **www.immunisation.ie**, **www.hpv.ie** and **www.hse.ie/flu**, maintaining WHO vaccine safety network accreditation for said websites and managing the twitter account @hseimm.

Monica Zuñiga Nuñez, ACEMI-Asociación Colombiana de Empresas de Medicina Integral, Nurse Epidemiologist

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Part 3: Safety of HPV vaccines. Assessments from the Global Advisory Committee on Vaccine Safety. Presenation by Patrick Zuber provided to the MOH, and other stake holders in Colombia.

Safety of HPV vaccines

Assessments from the Global Advisory Committee on Vaccine Safety

Disclosure

I have no actual or potential conflict of interest in relation to this presentation

Global Advisory Committee on Vaccine Safety (GACVS)

World Health Organization

A resource for policy makers

Advisory body to WHO

Response to vaccine safety issues of potential global importance:

- Promptly
- Efficiently
- with scientific rigor

Broad expertise

Independence

Decisions and recommendations based on best available evidence


2017, 92, 393–404 No 28

World Health Organization
Organisation mondiale de la Santé

Weekly epidemiological record
Relevé épidémiologique hebdomadaire

14 JULY 2017, 92th YEAR / 14 JUILLET 2017, 92e ANNÉE
No 28, 2017, 92, 393–404
http://www.who.int/wer

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Meeting of the Global Advisory Committee on Vaccine Safety, 7–8 June 2017

The Global Advisory Committee on Vaccine Safety (GACVS), an independent expert clinical and scientific advisory body, provides WHO with scientifically

Réunion du Comité consultatif mondial pour la sécurité des vaccins, 7-8 juin 2017

Le Comité consultatif mondial pour la sécurité des vaccins (GACVS), un organe consultatif indépendant composé d'experts cliniques et scientifiques, fournit à l'OMS des conseils

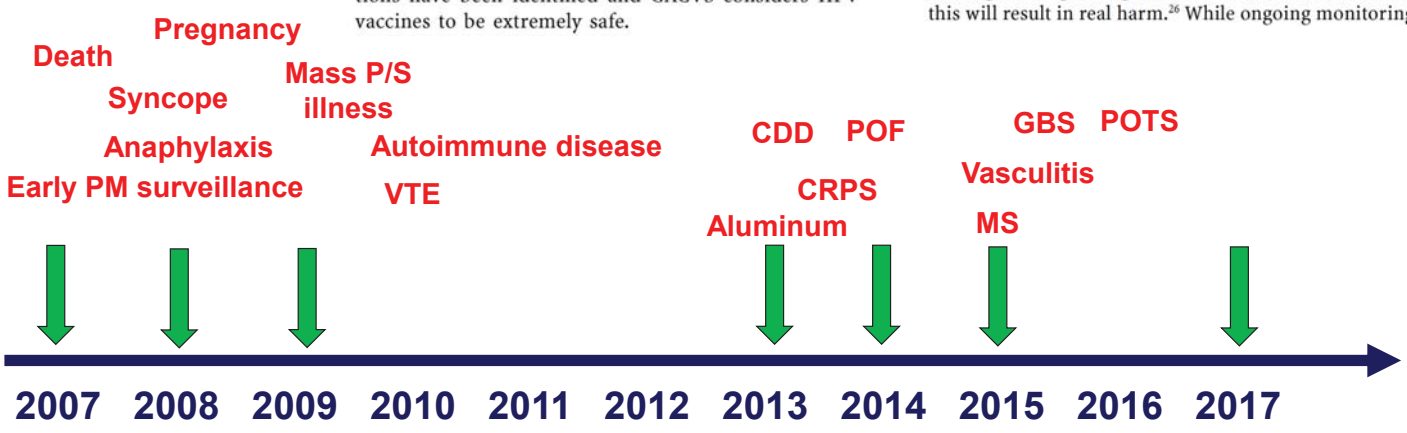
Reports and statements: http://www.who.int/vaccine_safety/committee/en/

GAVS meetings related to HPV vaccines

World Health Organization

Since licensure in 2006, over 270 million doses of HPV vaccines have been distributed. GACVS first reviewed the safety data in 2007,[12] and subsequently in 2008,[13] 2009,[14] 2013,[15] 2014[16] and 2015.[17] Early on, the Committee was presented signals related to anaphylaxis and syncope. The risk of anaphylaxis has been characterized as approximately 1.7 cases per million doses, and syncope was established as a common anxiety or stress-related reaction to the injection. No other adverse reactions have been identified and GACVS considers HPV vaccines to be extremely safe.

There are now accumulated safety studies that include several million persons[25] and which compare the risks for a wide range of health outcomes in vaccinated and unvaccinated subjects. However, despite the extensive safety data available for this vaccine, attention has continued to focus on spurious case reports and unsubstantiated allegations. The Committee continues to express concern that the ongoing unsubstantiated allegations have a demonstrable negative impact on vaccine coverage in a growing number of countries, and that this will result in real harm.[26] While ongoing monitoring



Concerns related to HPV vaccine safety publicized very early

November 2007 – Austria

- Teenage girl dies 3 weeks after vaccination
- Delays in getting autopsy report
- Next day…
  most Austrian newspapers covered this story
- The public prosecutor confirms as result of the forensic report:
  No causal connection between vaccination and death could be found

Dramatic mediatic report of vaccine risk UK 2009

For UK case, see full interactive case study at: http://vaccine-safety-training.org/c-introduction.html

UK Cervarix death Emotional statements

"Jab as deadly as cancer".

Sunday Express 4 October

"What has this jab done to our girls?"

"A giant vaccine program is a tacit agreement that sexual activity for teenage girls is all right".

Sunday Times 4 October

"The tragedy of (…) death highlights the scandal that this government went for the cheapest option".

"Why were we not told a deluxe version was available?"

Daily Mail several issues

Reported by Rebecca Coombs, BMJ 2009;339:b4124

The importance of assessing background rates for selected conditions

Human Papilloma Virus Immunization in Adolescent and Young Adults

A Cohort Study to Illustrate What Events Might be Mistaken for Adverse Reactions

Claire-Anne Siegrist, MD, Edwin M. Lewis, MPH,† Juhani Eskola, MD,‡ Stephen J. W. Evans, MSc,§ and Steven B. Black, MD‖*

(*Pediatr Infect Dis J* 2007;26: 979–984)

Conditions of particular interest for adolescents and adults

TABLE 3. Coincident Temporal Associations With Putative Placebo Injections Administered at 0–1–6 Months to All Adolescent and Young Women

Age Group	Condition	Rate per 100,000 by Temporal Association Windows		
		1 d	1 wk	6 wk
Adolescent	ER consultation/asthma	2.7	18.8	81.3
	ER consultation/allergy	1.5	10.6	45.8
	ER consultation/diabetes	0.4	2.9	12.8
	Hospitalization/inflammatory bowel disease	0.2	1.0	4.5
	Hospitalization/thyroid disease	0.1	0.9	4.0
	Hospitalization/SLE	0.1	0.5	2.0
	Hospitalization/MS or optic neuritis	0.0	0.2	1.0
Adults	ER consultation/asthma	3.0	21.2	91.5
	ER consultation/allergy	2.5	17.4	75.3
	ER consultation/diabetes	0.6	3.9	17.0
	Hospitalization/thyroid disease	2.4	16.6	71.8
	Hospitalization/inflammatory bowel disease	0.3	2.0	8.8
	Hospitalization/SLE	0.3	1.8	7.8
	Hospitalization/MS or optic neuritis	0.1	0.7	3.0

MS indicates multiple sclerosis; SLE, systemic lupus erythematosus.

Quality of evidence in epidemiologic studies

Case reports, case series:

- Clinical observations without control groups, can provide basis for hypothesis generation.
- Not an epidemiological study.

Ecologic:

- Compare secular trends over time with trends in vaccine coverage rates, exposure.
- Weakest kind of study.

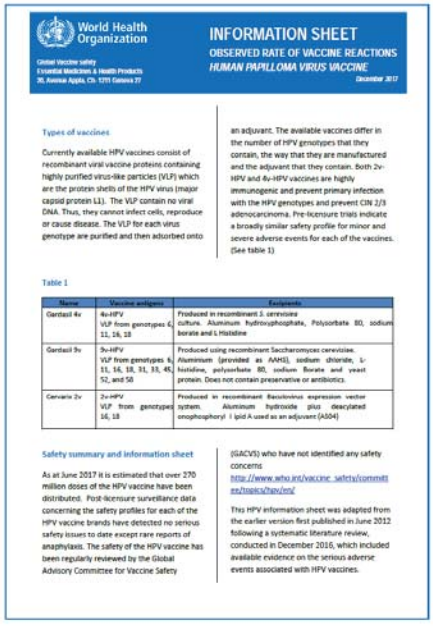
Case-Control:

- Compare exposures in cases and controls to measure odds ratio which approximates relative risk.
- Requires careful control selection and adjusting for possible biases and confounders.

Cohort:

- Compares incident rates in subjects exposed and not exposed to vaccines to measure relative risk.
- Can look for a dose-response effect.
- Randomized double-blind studies provide the highest level of certainty.

HPV vaccine safety information sheet



World Health Organization

INFORMATION SHEET
OBSERVED RATE OF VACCINE REACTIONS
HUMAN PAPILLOMA VIRUS VACCINE

Types of vaccines

Currently available HPV vaccines consist of recombinant viral vaccine proteins containing highly purified virus-like particles (VLP) which are the protein shells of the HPV virus (major capsid protein L1). The VLP contain no viral DNA. Thus, they cannot infect cells, reproduce or cause disease. The VLP for each virus genotype are purified and then adsorbed onto an adjuvant. The available vaccines differ in the number of HPV genotypes that they contain, the way that they are manufactured and the adjuvant that they contain. Both 2v-HPV and 4v-HPV vaccines are highly immunogenic and prevent primary infection with the HPV genotypes and prevent CIN 2/3 adenocarcinoma. Pre-licensure trials indicate a broadly similar safety profile for minor and severe adverse events for each of the vaccines. (See table 1)

Table 1

Name	Vaccine antigens	Excipients
Gardasil 4v	4v-HPV VLP from genotypes 6, 11, 16, 18	Produced in recombinant *S. cerevisiae* culture. Aluminium hydroxyphosphate, Polysorbate 80, sodium borate and L Histidine
Gardasil 9v	9v-HPV VLP from genotypes 6, 11, 16, 18, 31, 33, 45, 52, and 58	Produced using recombinant Saccharomyces cerevisiae. Aluminium (provided as AAHS), sodium chloride, L-histidine, polysorbate 80, sodium borate and yeast protein. Does not contain preservative or antibiotics.
Cervarix 2v	2v-HPV VLP from genotypes 16, 18	Produced in recombinant Baculovirus expression vector system. Aluminium hydroxide plus deacylated monophosphoryl lipid A used as an adjuvant (AS04)

Safety summary and information sheet

As at June 2017 it is estimated that over 270 million doses of the HPV vaccine have been distributed. Post-licensure surveillance data concerning the safety profiles for each of the HPV vaccine brands have detected no serious safety issues to date except rare reports of anaphylaxis. The safety of the HPV vaccine has been regularly reviewed by the Global Advisory Committee for Vaccine Safety (GACVS) who have not identified any safety concerns http://www.who.int/vaccine_safety/committee/topics/hpv/en/

This HPV information sheet was adapted from the earlier version first published in June 2012 following a systematic literature review, conducted in December 2016, which included available evidence on the serious adverse events associated with HPV vaccines.

Table 2
Summary of minor adverse events – local and systemic

Outcome	Description	Rate per 100 doses		
		9v-HPV	4v-HPV	2v-HPV
Local	Injection site reaction		83	----
	Pain		-----	78
	Swelling	26.9 - 40.3	25	26
	Erythema	24.9 - 34.0	-----	30
	Severe - injection site erythema and/or swelling > 2 inches in size and pain severe		5.7	-----
Systemic	Fatigue		----	33
	Pyrexia		13	3
	Urticaria		3	28
	Headache		26	30
	Myalgia		2	28
	Arthalgia		1	10
	Gastrointestinal disorders		17	13
	Rash		----	1
	Urticaria		------	0.46 100

file:///D:/data/Antigens/HPV/HPV_vaccine_rates_information_sheet_1217.pdf

HPV vaccine safety information sheet

Outcome	Data size and source	Comparison of effects*		Size of effect	Certainty of the evidence (GRADE)
		Vaccine	Control		
Serious adverse events (1 month – 9yrs follow-up)	Gardasil versus placebo: Based on data from 28,671 subjects in 7 randomised controlled trials	858.2 / 100,000	935.8 / 100,000	No Difference	⊕⊕⊕⊕ HIGH
		Absolute event rate difference: Rate per 100,000 (%, 95%CI) -77.6 (0.08%, 95%CI -0.2%, 0.3%) Relative difference: RR 0.93 (95% CI 0.17.22,1)			
	Gardasil versus control vaccine: Based on data from 3,810 subjects in 1 randomised controlled trial	733.8 / 100,000	841.2 / 100,000	No Difference	⊕⊕⊕⊕ HIGH
		Absolute event rate difference: Rate per 100,000 (%, 95%CI) -107.4 (0.11%, 95%CI -0.5%, 0.7%) Relative difference: RR 0.87 (95% CI 0.43, 1.78)			
	Cervarix versus placebo: Based on data from 14,268 subjects in 10 randomised controlled trials	1836.6 / 100,000	1876.2 / 100,000	No Difference	⊕⊕⊕⊕ HIGH
		Absolute event rate difference: Rate per 100,000 (%, 95%CI) -39.6 (0.04%, 95%CI -0.4%, 0.5%) Relative difference: RR 0.91 (95% CI 0.68, 1.22)			
	Cervarix versus control: Based on data from 30,843 subjects in 8 randomised controlled trials	11,676.8/ 100,000	11,595.7 / 100,000	No Difference	⊕⊕⊕⊕ HIGH
		Absolute event rate difference: Rate per 100,000 (%, 95%CI) 81.1 (0.1%, 95%CI -0.8%, 1.0%) Relative difference: RR 1.01 (95% CI 0.95, 1.07)			
New onset chronic disease (1 month – 9 yrs)	Cervarix versus placebo: Based on data from 9,511 subjects in 9 randomised controlled trials	1240.1 / 100,000	1306.6 / 100,000	No Difference	⊕⊕⊕⊕ HIGH
		Absolute event rate difference: Rate per 100,000 (%, 95%CI) -66.5 (0.07%, 95%CI -0.4%, 0.5%) Relative difference: RR 0.83 (95% CI 0.58, 1.20)			
	Cervarix versus control: Based on data from 30,349 subject in 7 randomised controlled trials	4680.8 / 100,000	5079.9 / 100,000	No Difference	⊕⊕⊕⊕ HIGH
		Absolute event rate difference: Rate per 100,000 (%, 95%CI) -399.1 (0.4%, 95%CI -0.9%, 0.9%) Relative difference: RR 0.93 (95% CI 0.84, 1.03)			

Outcome	Data size and source	Comparison of effects*		Size of effect	Certainty of the evidence (GRADE)
		Vaccine	Control		
Medically significant conditions (1 month – 9 yrs)	Cervarix versus placebo: Based on data from 7,623 subjects in 6 RCTs	8201.4 / 100,000	6949.6 / 100,000	No Difference	⊕⊕⊕⊕ HIGH
		Absolute event rate difference: Rate per 100,000 (%, 95%CI) 1251.8 (1.25%, 95%CI 0.04%, 2.5%) Relative difference: RR 1.15 (95% CI 0.88, 1.50)			
	Cervarix versus control: Based on data from 28,498 subjects in 4 RCTs	29,372.9 / 100,000	30,069.4 / 100,000	No Difference	⊕⊕⊕⊕ HIGH
		Absolute event rate difference: Rate per 100,000 (%, 95%CI) -696.5 (0.7%, 95%CI -0.4%, 1.8%) Relative difference: RR 0.98 (95% CI 0.92, 1.05)			
Auto-immune diseases following HPV vacci-nation	Data from 4 high quality cohort studies	No difference in rates of most autoimmune diseases between those exposed to vaccine and those unexposed. No findings equated to a safety signal.		No Difference	⊕⊕⊕2 MODERATE
Venous Thrombo-embolism	Data from 2 high quality cohort studies	No difference in the rate of thromboembolism in those exposed to vaccine and those unexposed.		No difference	⊕⊕⊕2 MODERATE
Multiple sclerosis and other demyeli-nating conditions	Data from 1 high quality cohort study	Exposed MS	Unexposed	No Difference	⊕⊕⊕2 MODERATE
		6.12 / 100,000 person years	21.54 / 100,000 person years		
		IRR 0.90 (95%CI 0.70, 1.15)			
		Other: 7.54 / 100,000 person years	16.14 / 100,000 person years		
		IRR 1.00 (95%CI 0.80, 1.26)			

*Systematic review of serious adverse events associated with HPV vaccination - http://www.who.int/vaccine_safety/HPV_vaccination_safety_report_AHTA_dec17.pdf

file:///D:/data/Antigens/HPV/HPV_vaccine_rates_information_sheet_1217.pdf

Evidence related to autoimmune diseases

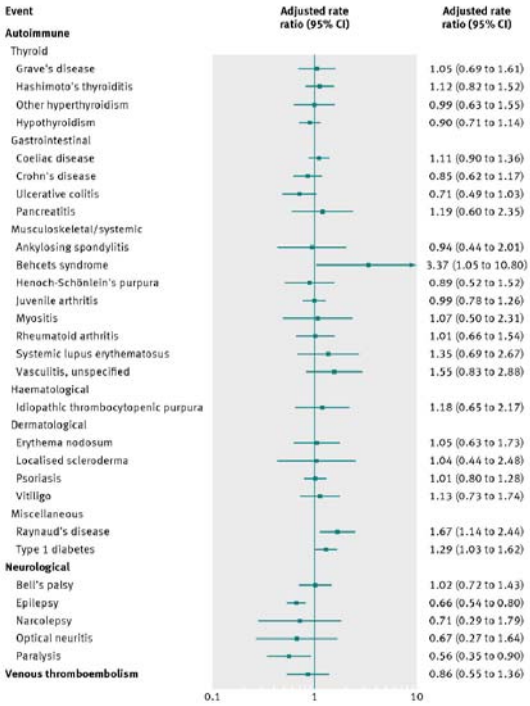
BMJ 2013;347:f5906 doi: 10.1136/bmj.f5906 (Published 9 October 2013) Page 1 of 11

RESEARCH

Autoimmune, neurological, and venous thromboembolic adverse events after immunisation of adolescent girls with quadrivalent human papillomavirus vaccine in Denmark and Sweden: cohort study

OPEN ACCESS

Lisen Arnheim-Dahlström *associate professor*[1], Björn Pasternak *postdoctoral fellow*[2], Henrik Svanström *statistician*[2], Pär Sparén *professor*[1], Anders Hviid *senior investigator*[2]



Evidence related to autoimmune diseases

Original Article | Journal of INTERNAL MEDICINE

doi: 10.1111/j.1365-2796.2011.02467.x

Surveillance of autoimmune conditions following routine use of quadrivalent human papillomavirus vaccine

C. Chao[1], N. P. Klein[2], C. M. Velicer[3], L. S. Sy[1], J. M. Slezak[1], H. Takhar[1], B. Ackerson[4], T. C. Cheetham[1,5], J. Hansen[2], K. Deosaransingh[2], M. Emery[2], K.-L. Liaw[3] & S. J. Jacobsen[1]

Table 3 *Incidence rate ratio (IRR) and 95% confidence interval (CI) of select autoimmune conditions in the vaccinated vs. nonvaccinated female populations of similar age in Kaiser Permanente Southern California*

	Main comparison				Sensitivity analysis 1 Direct comparison with electronic case identification only (not incorporating new-onset confirmation rate obtained from case review)				Sensitivity analysis 2 Case identification with original ICD-9 codes only[a] (incorporating new-onset confirmation rate obtained from case review)			
	Vaccinated	Unvaccinated			Vaccinated	Unvaccinated			Vaccinated	Unvaccinated		
Condition	No. of Observed cases[b] (Incidence[c])	No. of Estimated cases (Incidence[c])	IRR	95% CI	No. of Observed cases[b] (Incidence[c])	No. of Estimated cases (Incidence[c])	IRR	*P*-value[d]	No. of Observed cases[b] (Incidence[c])	No. of Estimated cases (Incidence[c])	IRR	95% CI
Rheumatologic/autoimmune												
Immune thrombocytopenia	6 (6.8)	33 (5.9)	1.16	(0.85–1.83)	10 (11.4)	56 (10.0)	1.14	0.70	6 (6.8)	31 (5.5)	1.24	(0.91–2.02)
Autoimmune haemolytic anaemia	–	–	–	–	–	–	–	–	–	–	–	–
Systemic lupus erythematosus	10 (11.4)	58 (10.3)	1.07	(0.69–1.60)	31 (35.3)	157 (28.0)	1.26	0.24	8 (9.1)	46 (8.2)	1.10	(0.71–1.66)
Rheumatoid arthritis	4 (4.6)	39 (7.0)	0.71	(0.39–1.45)	8 (9.1)	95 (16.9)	0.54	0.09	3 (3.4)	31 (5.5)	0.70	(0.41–1.60)
Juvenile rheumatoid arthritis	3 (3.4)	43 (7.7)	0.48	(0.26–0.91)	11 (12.5)	106 (18.9)	0.66	0.20	2 (2.3)	38 (6.8)	0.36	(0.14–0.71)
Endocrine												
Type 1 diabetes	9 (10.3)	101 (18.0)	0.57	(0.47–0.73)	12 (13.7)	139 (24.8)	0.55	0.05	8 (9.1)	95 (16.9)	0.54	(0.45–0.70)
Hashimoto's disease[b]	92 (104.8)	455 (81.1)	1.29	(1.08–1.56)	241 (274.6)	1406 (250.6)	1.10	0.19	27 (30.8)	85 (15.2)	2.02	(1.65–2.60)
Graves' disease[b]	16 (18.2)	145 (25.8)	0.72	(0.50–1.01)	44 (50.1)	348 (62.0)	0.81	0.18	6 (6.8)	51 (9.1)	0.76	(0.42–1.10)
Combined Hashimoto's and Graves' disease[b,e]	108 (123.1)	601 (107.1)	1.15	(0.97–1.36)	285 (324.7)	1754 (312.6)	1.04	0.55	33 (37.6)	137 (24.4)	1.54	(1.27–1.92)
Neurological/ophthalmic												
Multiple sclerosis	3 (3.4)	14 (2.5)	1.37	(0.74–3.20)	7 (8.0)	39 (7.0)	1.15	0.74	3 (3.4)	14 (2.5)	1.37	(0.74–3.20)
Acute disseminated encephalomyelitis	–	–	–	–	–	–	–	–	–	–	–	–
Other demyelinating diseases of central nervous system	1 (1.1)	9 (1.6)	0.71	(0.38–2.13)	2 (2.3)	23 (4.1)	0.56	0.43	1 (1.1)	9 (1.6)	0.71	(0.38–2.13)

Evidence related to neurological disorders

Original Investigation

Quadrivalent HPV Vaccination and Risk of Multiple Sclerosis and Other Demyelinating Diseases of the Central Nervous System

Nikolai Madrid Scheller, MB; Henrik Svanström, MSc; Björn Pasternak, MD, PhD; Lisen Arnheim-Dahlström, PhD; Karin Sundström, MD, PhD; Katharina Fink, MD, DrMed; Anders Hviid, DrMedSci

Table 2. Adjusted Rate Ratios of Multiple Sclerosis and Other Demyelinating Diseases in Quadrivalent HPV-Vaccinated and Quadrivalent HPV-Unvaccinated Girls and Women

	Unvaccinated			Vaccinated				
Outcome	No. of Cases	Person-Years	Crude Incidence Rate (95% CI), Events/100 000 Person-Years	No. of Cases	Person-Years	Crude Incidence Rate (95% CI), Events/100 000 Person-Years	Adjusted RR (95% CI)[a]	*P* Value
Multiple Sclerosis								
Main analysis	4208	19 532 311	21.54 (20.90-22.20)	73	1 193 703	6.12 (4.86-7.69)	0.90 (0.70-1.15)	
Analysis by age, y								
10-29	1374	10 095 340	13.61 (12.91-14.35)	62	1 166 450	5.32 (4.14-6.82)	0.77 (0.58-1.02)	.15[c]
30-44	2834	9 436 971	30.03 (28.95-31.16)	11	27 253	40.36 (22.35-72.88)	1.28 (0.71-2.33)	
Analysis by country								
Denmark	1807	7 410 041	24.39 (23.29-25.54)	57	774 158	7.36 (5.68-9.55)	1.02 (0.76-1.36)	.16[c]
Sweden	2401	12 122 270	19.81 (19.03-20.61)	16	419 545	3.81 (2.34-6.23)	0.68 (0.41-1.13)	
Analysis of different risk windows, d								
0-179	4208[b]	19 532 311[b]	21.54 (20.90-22.20)[b]	47	595 851	7.89 (5.93-10.50)	1.06 (0.78-1.43)	
180-364				14	224 952	6.22 (3.69-10.51)	1.10 (0.65-1.87)	
365-729				12	372 900	3.22 (1.83-5.67)	0.50 (0.28-0.88)	
>729				41	565 225	7.25 (5.34-9.85)	0.75 (0.54-1.03)	
Other Demyelinating Diseases								
Main analysis	3154	19 546 190	16.14 (15.58-16.71)	90	1 193 591	7.54 (6.13-9.27)	1.00 (0.80-1.26)	
Analysis by age, y								
10-29	1175	10 095 490	11.64 (10.99-12.32)	85	1 166 289	7.29 (5.89-9.01)	1.00 (0.78-1.28)	.51[c]
30-44	1979	9 450 700	20.94 (20.04-21.88)	5	27 302	18.31 (7.62-44.00)	0.75 (0.31-1.80)	
Analysis by country								
Denmark	1369	7 416 343	18.46 (17.51-19.46)	73	774 095	9.43 (7.50-11.86)	1.10 (0.84-1.44)	.14[c]
Sweden	1785	12 129 846	14.72 (14.05-15.41)	17	419 496	4.05 (2.52-6.52)	0.73 (0.44-1.20)	
Analysis of different risk windows, d								
0-179	3154[b]	19 546 190[b]	16.14 (15.58-16.71)[b]	54	595 804	9.06 (6.94-11.83)	1.13 (0.85-1.51)	
180-364				11	224 930	4.89 (2.71-8.83)	0.73 (0.40-1.33)	
365-729				25	372 857	6.71 (4.53-9.92)	0.91 (0.61-1.37)	
>729				56	565 106	9.91 (7.63-12.88)	1.01 (0.76-1.34)	

CRPS and POTS

CRPS symptoms

- Severe pain.
- Swelling and changes in the skin temperature and colour of the arms or legs.
- Headache, general fatigue, coldness of the legs, limb pain and weakness.

POTS signs and symptoms

- Abnormally large increase in heart rate when changing from a lying down to a standing up position, without any orthostatic hypotension.
- Light headedness, visual blurring, palpitations, tremulousness and weakness (especially of the legs), as well as fatigue, shortness of breath, chest pain, concentration difficulties, and headaches.

CRPS and POTS
EMA Pharmacovigilance Risk Assessment Committee

Gardasil

Available data provides some support for a **causal association between injection trauma and CRPS** but **not for a causal relation between the qHPV vaccine itself and CRPS**. It is not considered appropriate with any addition to SmPC regarding a potential risk related to the injection trauma.

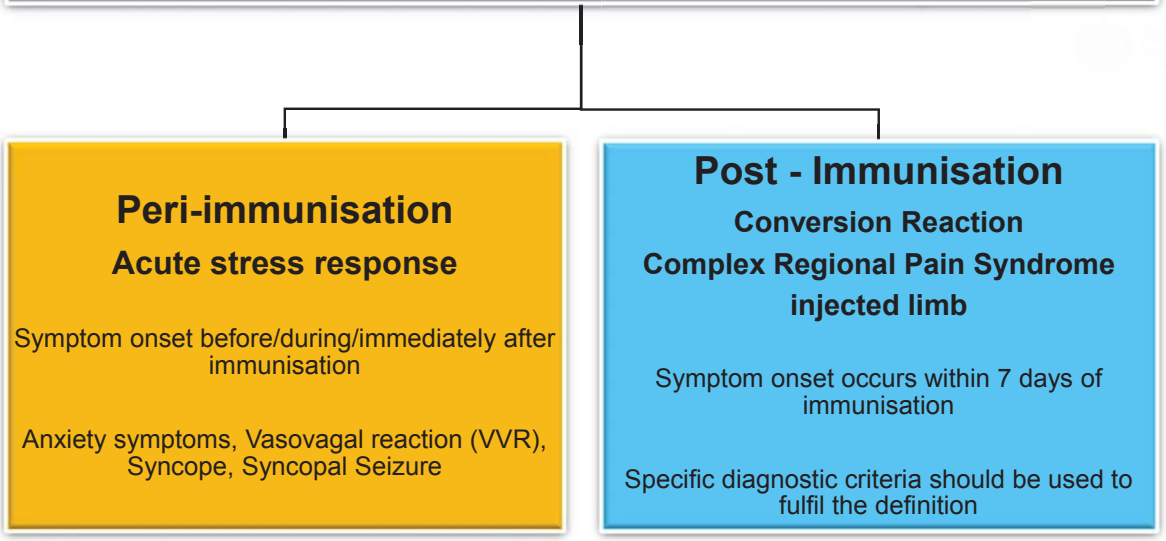
Available data does **not provide support for a causal relation between the qHPV vaccine and POTS**. No changes to the product information or other risk minimisation measures are proposed.

PRAC updated reports dated 28 October 2015

Cervarix

- In conclusion, the co-rapporteur is of the opinion that further monitoring of CRPS and POTS in PSUR, including an extensive review of the literature and a follow-up of reported cases of CRPS and POTS, should be performed.
- Since POTS and CRPS remain a public concern in a number of countries, the SAG supports such an enhanced surveillance despite its opinion that **there is no evidence of a signal**.

Immunisation Stress Related Response



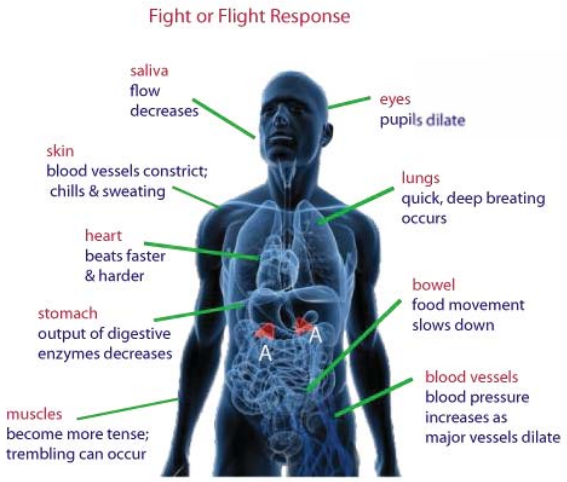
- These conditions most commonly occur independently of immunisation and may follow other stress events.
- These conditions have been reported post-immunisation.
- In these cases, the immunisation may be best understood as a stress event contributing to their presentation
- Such events are best understood within a multifactorial etiology from a biopsychosocial perspective.

Periimmunisation

Acute stress response

Symptom onset before/during/immediately after immunisation

"Anxiety symptoms", vasovagal reaction (VVR), syncope, syncopal seizure



Post - Immunisation

Conversion Reaction

Complex Regional Pain Syndrome-injected limb

Symptom onset occurs within 7 days of immunisation.

Specific diagnostic criteria should be used to fulfil the definition

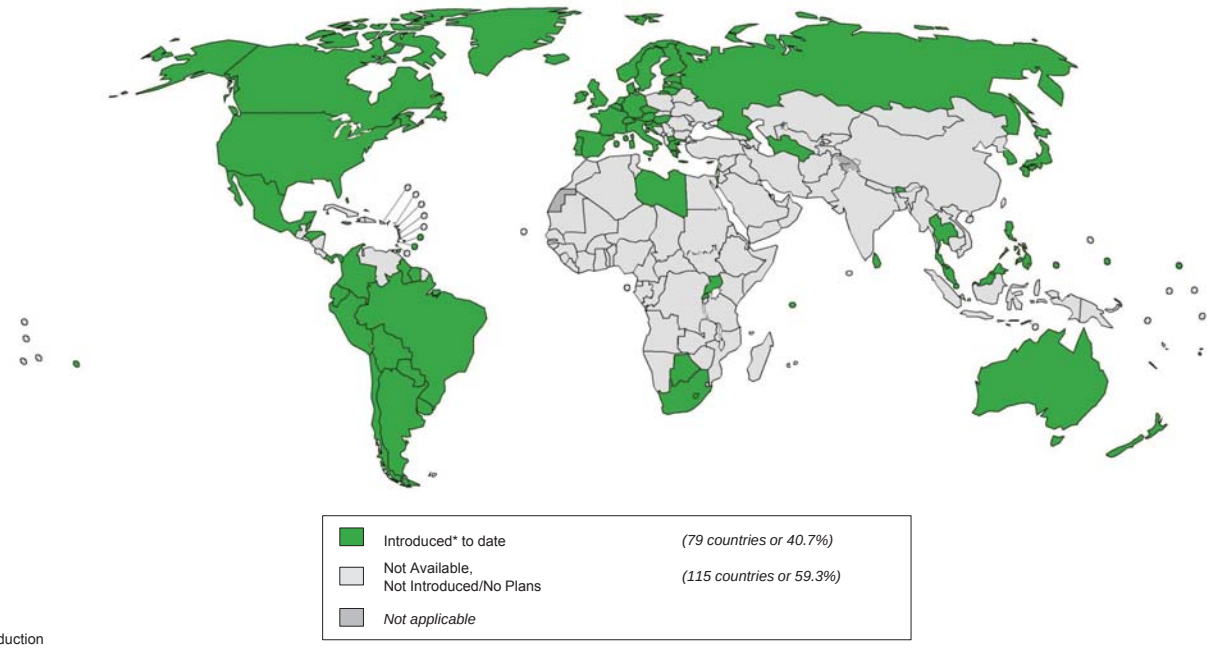
Conversion reaction

Included in the ICD-10's (World Health Organization 2016) grouping for dissociative disorders and are characterized by disruptions in sensation and control of bodily movements with no identifiable organic pathology.

Conversion symptoms can include **weakness** or **paralysis**, **abnormal movements or limb posturing, gait irregularities, speech difficulties, and non-epileptic seizures (NES)** with no apparent physiological basis.

- Appear to be more common in females.
- Not typically diagnosed in infants.
- In children, conversion reactions may more typically manifest with a single symptoms rather than multiple (Mink 2013).

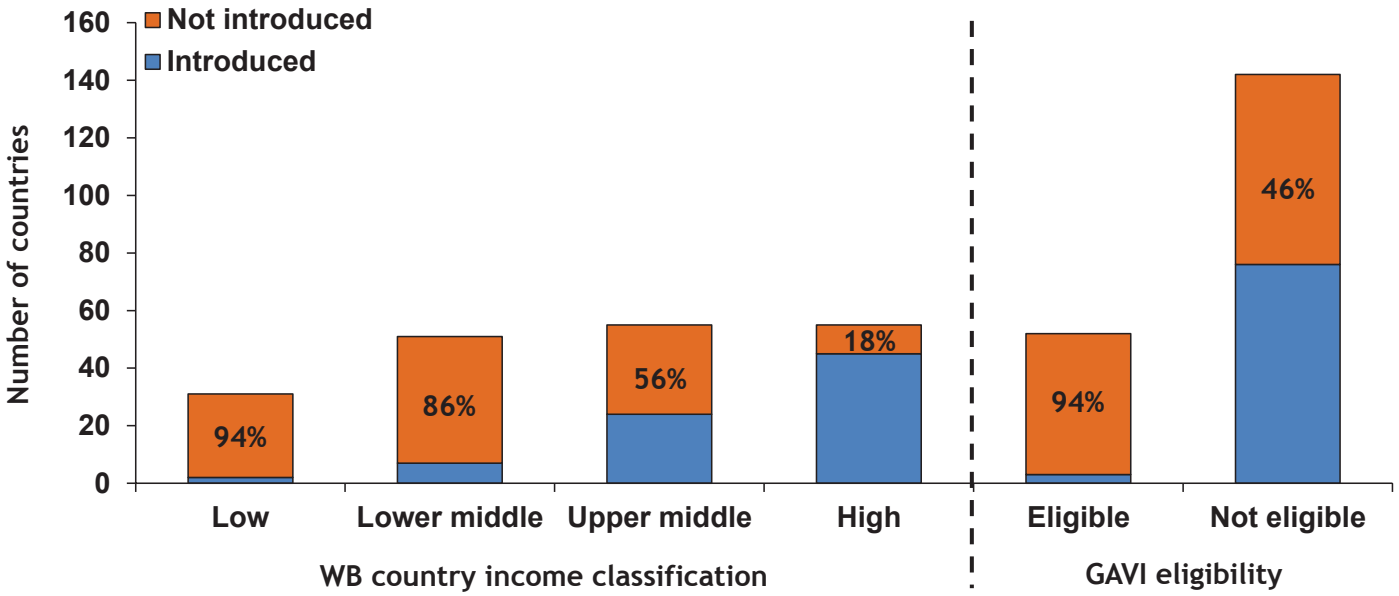
Countries with HPV vaccine in the national immunization programme



* Includes partial introduction

Data source: WHO/IVB Database, as of 26 January 2018
Map production Immunization Vaccines and Biologicals (IVB),
World Health Organization

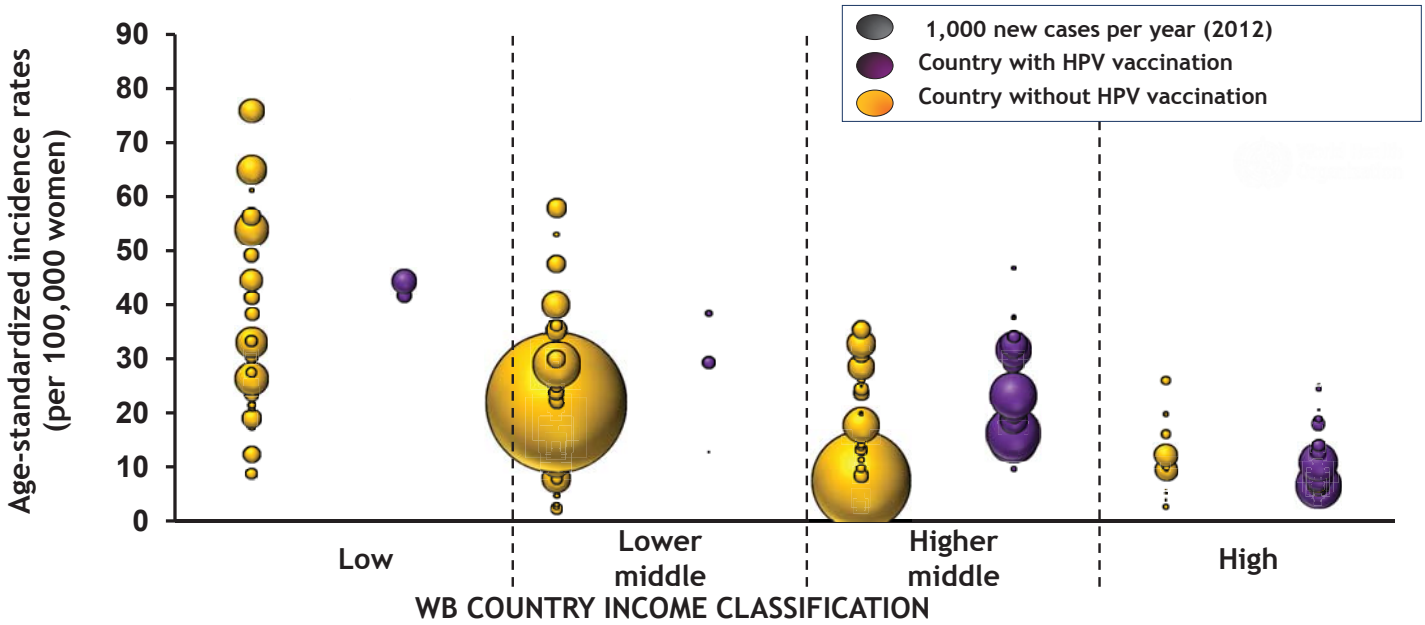
National HPV vaccine introduction by WB income classification or GAVI eligibility, as of January 2018



Sources: WHO/IVB Database, as of 22 January 2018, based on country reports; World Bank, List of economies, July 2017; GAVI, Countries eligible to apply for new vaccines support in 2017.

World Health Organization

Cervical cancer incidence by income group and national HPV vaccine introduction



Sources: IARC, GLOBOCAN 2012 (estimated annual number of cervical cancer cases); World Bank, List of economies, July 2016; WHO/IVB Database, national as of HPV vaccine introductions as of 27 June 2016, based on country reports.

HPV vaccines are very effective – Herd effect

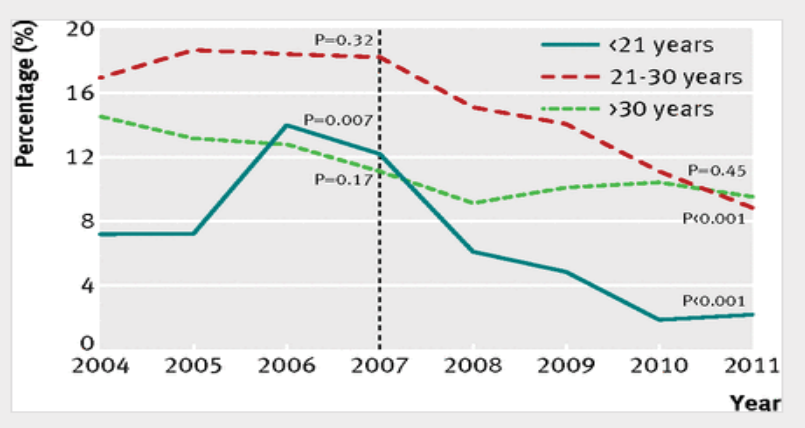
See also

Sando et *al, Acta Derm Venereol* 2014

Tabrizi and Brotherton et al, *Lancet Infect Dis* 2014

Drolet et al, *Lancet Infect Dis* 2015

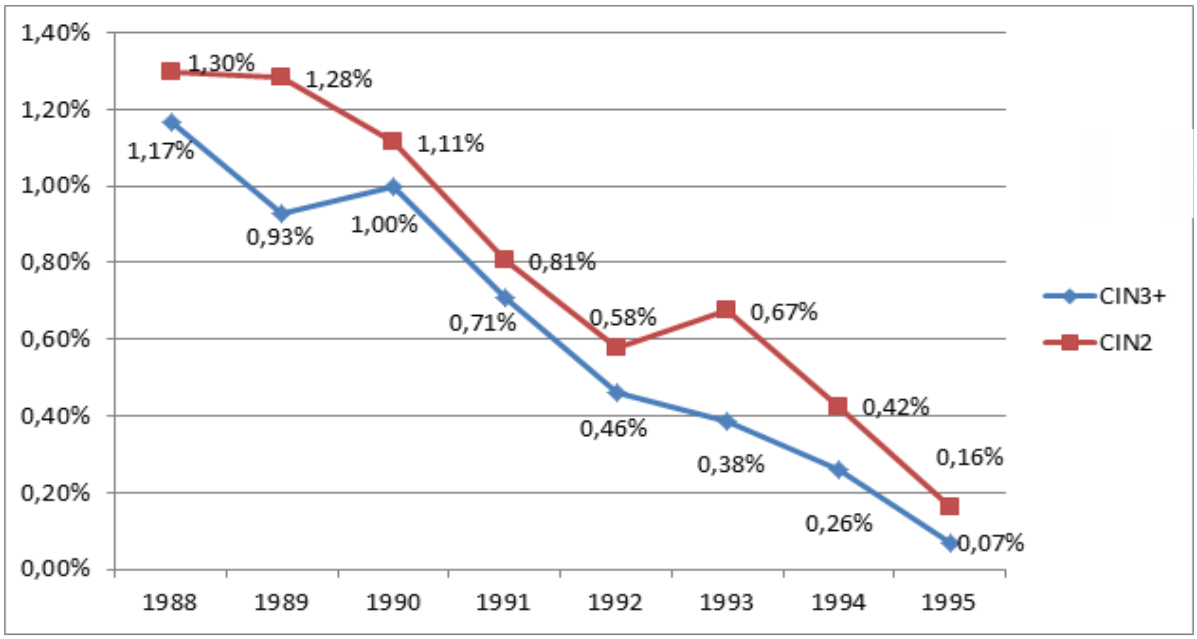
Proportion of Australian born heterosexual men diagnosed as having genital warts at first visit



Males <21 years : 81.8% decline post vaccine introduction
Males 21-30 yrs : 51.1% decline post vaccine introduction

Ali et al., BMJ 2013

Incidence of in-situ carcinoma - Scotland



(1.0) (4.2) (35.6) (65.2) (69.3) (70.1) (86.5) ← (Vaccine coverage 3-doses)

https://www.hse.ie/eng/health/Immunisation/hcpinfo/conference/hpv173.pdf

HPV vaccine uptake summary

10 years after introduction, global HPV vaccine uptake remains slow

The countries that are most at risk for cervical cancer are the least likely to have introduced the vaccine

Several challenges to reaching adolescent girls and sustaining high coverage remain, including vaccine price and communication crises

When effectively implemented, benefits of HPV vaccination programmes are very apparent within 10 years

GACVS: Safety of HPV vaccines

GAVCS has reviewed evidence related to

- Syncope → Non-specific effect
- Anaphylaxis → Risk comparable to that of other inactivated vaccines
- Pregnancy outcomes, venous thromboembolism, auto-immune disease, Guillain-Barre syndrome, multiple sclerosis

➔ ***Large cohort studies did not demonstrate any association***

GACVS also examined concerns around

- CRPS and other chronic pain conditions, POTS
- The aluminum adjuvant used in HPV vaccines and cerebral vasculitis and death
- Findings of HPV L1 gene DNA fragments (consistent with manufacturing process) and VLPs

Summary of GACVS position

GACVS continues to closely monitor the safety of HPV vaccines

→ Based on a careful examination of the available evidence, GACVS continues to affirm that HPV vaccines benefit-risk profile remains favorable

The Committee is concerned by the
claims of harm that are being raised on the basis of anecdotal observations and reports in the absence of biological or epidemiological substantiation

The committee also remains concerned that
policy decisions based on weak evidence continue to cause real harm when, as a result, safe and effective vaccines cease to be used

HPV vaccines present a communications challenge, not a safety one

→ GACVS urges continued robust pharmacovigilance, as for all vaccines.

PAHO Technical Advisory Group on Vaccine-preventable Diseases (TAG) XXIV Meeting
12-14 July 2017 Panama City, Panama
Recommendations:

World Health Organization

TAG reiterates the importance of **prioritizing high coverage in adolescent girl** cohorts aged 9–14 years to ensure full protection against HPV and induce herd immunity among adolescent boy populations.

Currently available vaccines have **comparable safety profiles** and provide similar protection against cervical cancer.

TAG urges PAHO Member States to **carefully consider their approaches to communication around the HPV vaccine**, making sure to generate audience-specific messages.

Available in: http://www.paho.org/hq/index.php?option=com_content&view=article&id=1862&Itemid=2032

Part 4: Draft Action Plan for Cervcial Cancer Prevention and Control 2018-2030. Provisional Agenda Item at the 56th Directing Council, 70th Session of the Regional Committee of WHO for the Americas.

Pan American Health Organization
World Health Organization
REGIONAL OFFICE FOR THE Americas

56th DIRECTING COUNCIL

70th SESSION OF THE REGIONAL COMMITTEE OF WHO FOR THE AMERICAS

Washington, D.C., USA, 23-27 September 2018

Provisional Agenda Item 4.5

CD56/9
11 July 2018
Original: English

PLAN OF ACTION FOR CERVICAL CANCER PREVENTION AND CONTROL 2018-2030

Introduction

1. Cancer is the second leading cause of death in the Region of the Americas. In 11 countries, cervical cancer is the leading cause of cancer deaths and in 12 countries it is the second cause of cancer deaths among women.[1] Each year in the Americas an estimated 83,200 women are newly diagnosed and 35,680 women die from this disease, a significant proportion (52%) of them under 60 years of age *(1)*.

2. Cervical cancer is caused by persistent infection with high-risk types of human papillomavirus (HPV), a sexually transmitted infection. Cervical cancer is preventable through HPV vaccination and also with screening and treatment of precancerous lesions, It can be effectively treated if diagnosed in its early stages. Health promotion and sexual health and HIV/STI prevention programs also contribute to cervical cancer prevention. The HPV vaccine has been introduced in national immunization programs since 2006; cervical cancer screening programs have been instituted in almost all the countries of the Region beginning in the 1970s; and services for treating cervical cancer have been established in almost all the countries. As a result, notable progress has been observed in preventing and controlling the disease, as reported to the 29th Pan American Sanitary Conference in 2017 in the final report of the Regional Strategy and Plan of Action on Cervical Cancer Prevention and Control *(2)*.

3. Nonetheless, significant gaps and challenges persist in reducing incidence and mortality and paving the way toward the elimination of cervical cancer as a public health problem. This Plan sets forth a blueprint to guide Member States and the Pan American

[1] Cervical cancer is the leading cause of cancer deaths among women in Belize, Bolivia, Dominican Republic, El Salvador, Guyana, Haiti, Honduras, Nicaragua, Paraguay, Suriname, and Venezuela. It is the second cause of cancer deaths among women in Brazil, Dominica, Ecuador, Grenada, Guatemala, Jamaica, Panama, Peru, Saint Kitts and Nevis, Saint Lucia, Saint Vincent and the Grenadines, and Trinidad and Tobago.

Sanitary Bureau (PASB) in strengthening their capacity for evidence-based, innovative, and effective strategies that will accelerate reductions in cervical cancer incidence and mortality.[2]

Background

4. Unlike the situation with most other types of cancer, the cause of cervical cancer has been scientifically established and there are cost-effective tools available for its prevention and control *(3)*. HPV 16 and 18 are among the most prevalent types, responsible for approximately 70% of all cervical cancer cases. Since HPV infection also causes other cancers (anus, oropharynx, penis, rectum, vagina, and vulva), prevention strategies will also contribute to the reduction of these other HPV-related cancers. Cervical cancer develops slowly over time, beginning with HPV infection, which in some cases persists and advances to precancerous lesions that can evolve into invasive cancer if undetected and untreated. People who are immunocompromised, such as those living with HIV, are more likely to have persistent HPV infection and more rapid progression to cancer.

5. Screening asymptomatic women for precancerous lesions using the Papanicolaou (Pap) test has led to an average reduction of approximately 2.6% per year in cervical cancer mortality, in countries with robust health systems *(4)*. However, this approach has proven less effective in developing countries, mainly because of requirements for laboratory infrastructure, equipment, and logistic challenges associated with the screening process; as well as the performance of the Pap test itself, which has shown sensitivity of approximately 50% or less *(5)*. New technologies and approaches, including HPV vaccines, HPV tests,[3] and a "screen and treat" approach, have been developed and proven to effectively prevent cervical cancer *(6, 7)*. The cost-effectiveness of prevention strategies has been well documented, showing that HPV vaccination coupled with screening is more cost-effective than either strategy alone *(8-10)*. If implemented on a large scale, these new cost-effective interventions and approaches have the potential to accelerate reductions in cervical cancer mortality *(9)*.

6. Since adoption of the Regional Strategy and Plan of Action for Cervical Cancer Prevention and Control in 2008 *(11)*, Member States, with the collaboration of PASB, have strengthened their cervical cancer programs by introducing HPV vaccines and new approaches for screening, as well as improving the quality of cancer treatment, palliative care, and cancer registration. These commitments have been reinforced in three additional

[2] For the purpose of this Plan, Member States will identify priority populations based on their national context and epidemiological patterns of cervical cancer. They may include persons living under adverse social and economic circumstances, those residing in rural areas, medically underserved populations, indigenous and/or Afro-descendant populations, HIV-positive women and adolescents, sex workers, and/or migrants.

[3] There are a number of HPV tests available on the market, each with different characteristics. A summary of the various tests has been prepared to assist Member States in selecting the most suitable one(s) for their purposes. This summary is available on the PAHO website at: http://www.paho.org/hq/index.php?option=com_content&view=article&id=11925&Itemid=41948&lang=en.

PAHO plans of action for the Region: in 2013, the Plan of Action for the Prevention and Control of Noncommunicable Diseases (Document CD52/7, Rev. 1), which includes actions to improve cervical cancer screening *(12)*; in 2015, the Plan of Action on Immunization (Document CD54/7, Rev. 2), which includes HPV vaccination *(13)*; and in 2016, the Plan of Action for the Prevention and Control of HIV and Sexually Transmitted Infections (Document CD55/14), which addresses HPV infection *(14)*. Additionally, in 2017 the Regional Gender Agenda defined governmental agreements for sexual and reproductive health rights and gender equality, among other issues *(15)*. Recently, Member States reaffirmed their commitment to reduce morbidity, disabilities, and mortality from noncommunicable diseases, including cancer, in Goal 9 of the Sustainable Health Agenda for the Americas 2018-2030 (Document CSP29/6, Rev. 3).

7. Moreover, in 2017 the World Health Assembly adopted a resolution on cancer prevention and control in the context of an integrated approach, which, among other interventions, calls on Member States to develop and implement comprehensive cancer prevention and control plans with focus on cost-effective interventions, equity, and access *(16)*. In addition, the WHO Global Strategy for Women's, Children's and Adolescents' Health *(17)* emphasizes adolescent health and access to quality sexual and reproductive health services, and the WHO Global Health Sector Strategy on Sexually Transmitted Infections *(18)* calls for the scaling up of effective STI interventions and services, all of which support cervical cancer prevention.

8. Recently, with a view to strengthening cervical cancer initiatives, the UN Joint Global Programme on Cervical Cancer Prevention and Control *(19)* was established to provide Member States with coordinated technical cooperation across relevant United Nations programs to improve cervical cancer initiatives. Furthermore, a new global elimination strategy for cervical cancer is in the process of being developed by WHO and other United Nations partners, to be presented to the 2019 World Health Assembly. These global and regional plans, together with the present Plan, will contribute toward realization of the Sustainable Development Goals and, in particular, attainment of the following targets by 2030: 3.4, reduce by one-third premature mortality from noncommunicable diseases; 3.7, ensure universal access to sexual health care services; 3.8, achieve universal health coverage and 5.6, ensure universal access to sexual and reproductive health and reproductive rights *(20)*.

Situation Analysis

9. Cervical cancer rates vary widely in the Region, with large differences between lower and higher income countries (Annex A). For example, the cervical cancer mortality rate is 12 times higher in Bolivia than in Canada (21/100,000 women vs. 1.7/100,000 women, respectively). Similar variations are noted within countries, sometimes with marked differences between less and more developed areas. For example, in Argentina the cervical cancer mortality rate is four times higher in the province of Jujuy (15/100,000) than in the city of Buenos Aires (4/100,000) *(21)*. These differences have largely been attributed to variations in distribution of the determinants of health, particularly socioeconomic status, education, and income. HIV infection is also associated

with poorer outcomes. Furthermore, race can be a factor: indigenous and black women have a higher risk of developing invasive cervical cancer than the general population (*22, 23)*. In terms of trends, steady declines in the incidence of cervical cancer since 2000 have only been observed in a few countries (Argentina, Brazil, Canada, Chile, Costa Rica, Mexico, and the United States) *(24)*. Mortality is high and remains relatively unchanged in many countries of Latin America and the Caribbean *(24)*.

10. Three prophylactic HPV vaccines with relatively similar effectiveness in preventing cervical cancer are currently available—namely, the bivalent, quadrivalent, and nonavalent vaccines *(6)*. When HPV vaccines were first introduced, they were licensed and marketed using a three-dose schedule. However, the WHO Strategic Advisory Group of Experts (SAGE) recommended a two-dose schedule in 2014 and this change was approved the following year by the PAHO Technical Advisory Group on Immunization. To date, 31 countries and territories in the Region of the Americas have made HPV vaccines available in their national immunization programs (Annex A), a level higher than in any other region of the world. Data on HPV vaccination coverage were not available for the majority of countries. Where figures were available, coverage varied widely (Annex A). Coverage has been hampered in some countries by important public concerns about vaccine safety, following media coverage erroneously linking the HPV vaccine to adverse events *(25)*.[4] This situation underscores the need to ensure that health providers and the general public in all countries receive regular information and evidence on HPV vaccine safety and effectiveness from credible scientific sources. Reaching the estimated 37 million girls in the Region in the 9-14 year-old target population will be a challenge, as will be monitoring and consistent reporting on HPV vaccination coverage.

11. With regard to cervical cancer screening, almost all Member States report that such services are available. The Pap smear remains the most common test, although challenges continue to impede the effectiveness of screening services in many countries, including difficulties integrating it into HIV/STI programs, poor quality testing, long delays in providing women with their results, low population coverage, and poor follow-up treatment *(26)*. HPV testing, although it is a much more effective test to detect women at risk of developing cervical cancer, has not been widely incorporated into screening programs, with only nine Member States reporting that they have introduced this test. In these countries, relevant evidence has been generated showing that HPV testing is feasible in settings where resources are limited; it detects more disease than the traditional Pap test, and using this strategy can lead to significant improvements in screening coverage and treatment rates *(27–33)*. HPV testing can eliminate barriers related to accessing screening services, since the sample can be collected by the woman herself. HPV self-sampling has been implemented in a programmatic context in at least five countries of the Region *(32, 33)*,

[4] As of June 2017, over 270 million doses of HPV vaccine had been distributed worldwide. The Global Advisory Committee on Vaccine Safety has been reviewing the safety data since 2006. Anaphylaxis and syncope have been identified. The risk of anaphylaxis has been characterized as approximately 1.7 cases per 1,000,000 doses. Syncope has been established as a common anxiety- or stress-related reaction to the injection.

and in the case of a demonstration site in Argentina it resulted in a fourfold increase in screening coverage *(33)*.

12. In order to achieve program impact, screening coverage should reach at least 70% of the target population *(7)*. In the Americas, only seven countries report this level of coverage, so there is great need for improvement. Under a business-as-usual scenario, it will be impossible to reach the estimated 32 million women in the Region between 30 and 49 years of age who need to be screened in order to make an impact on the disease burden.[5] Several factors hinder better coverage: the majority of screening programs are not organized; they are mainly available in urban areas; and they are based on the Pap test, which has been shown to have low sensitivity, especially in limited resource settings, and requires multiple visits *(24, 34-36)*. But screening alone is not sufficient to prevent cervical cancer. Follow-up treatment of women with abnormal screening results is required, but it has been reported to be very low in most countries of the Region and continues to be a challenge *(26, 37)*.

13. Treatment services for invasive cervical cancer are available in almost all the countries, although there are significant gaps in access (Annex A). Access to palliative care also continues to be a challenge, with only 10 countries reporting that they offer palliative care services (Annex A). The overall trend for opioid availability in Latin America and the Caribbean has been increasing, but it is still well below a level that is adequate to meet the needs of cancer patients *(38)*. Far too many people continue to die in pain when very affordable and effective pain medication exists.

Proposal

14. This Plan envisions a future with the elimination of cervical cancer as a public health problem as a result of universal access to sexual health and STI prevention services, HPV vaccines, effective screening and precancer treatment services, treatment of invasive cervical cancer, and palliative care. It foresees that all women and girls, regardless of age, race, ethnicity, socioeconomic status, HIV status, or disability will have timely access to quality cervical cancer prevention, care, and treatment so that they can live in good health throughout the life course and enjoy the health-related human rights.

15. The Plan is based on the recognition of Member States' diverse contexts, priorities, and needs, while adapting the global mandates and initiatives relevant to cervical cancer to the regional context; and involves cooperating with Member States on the implementation of comprehensive strategies to strengthen cervical cancer programs in the Region. It calls for facilitating dialogue; implementing existing PAHO/WHO cervical cancer tools and resources (Annex B); and promoting synergies and coordinating efforts with existing partner initiatives (Annex C), including the RINC Cervical Cancer Prevention and Control Plan for South America *(39)*.

[5] The estimated total number of women in the Region of the Americas aged 30-49 who would benefit from cervical cancer screening. See: https://esa.un.org/unpd/wpp/DataQuery/.

16. The goal is to accelerate progress toward the elimination of cervical cancer as a public health problem in the Americas by reducing incidence and mortality rates by one-third by 2030. This goal is aligned with Target 3.4 of the Sustainable Development Goals.[6]

Goal	Impact indicator	Baseline (2012 latest year available)	Target (2030)
Reduce cervical cancer incidence and mortality in the Americas by one-third, by 2030	**1.** Cervical cancer incidence rate [a]	14.9/100,000 women [a]	10.0/100,000 women
	2. Cervical cancer mortality rate [a]	5.8/100,000 women [a]	3.9/100,000 women

a. Source: International Agency for Research on Cancer. Estimated cancer incidence, mortality, and prevalence worldwide, 2012 [cited Jan 4 2018]. Available from: http://globocan.iarc.fr/Pages/fact_sheets_population.aspx

Strategic Lines of Action

17. The Plan identifies the following four strategic lines of action:

a) Improve cervical cancer program organization and governance, information systems, and cancer registries;

b) Strengthen primary prevention through information, education, and HPV vaccination;

c) Improve cervical cancer screening and precancer treatment through innovative strategies; and

d) Improve access to services for cancer diagnosis, treatment, rehabilitation, and palliative care.

Strategic Line of Action 1: Improve cervical cancer program organization and governance, information systems, and cancer registries

18. Better organization of cervical cancer programs favors higher coverage for vaccination and screening, and contributes to increased follow-up of women with abnormal screening test results, all of which lead to greater impact on cervical cancer incidence and mortality. The following actions are important for improving the organization of cervical cancer programs:

a) Formulation/review and alignment of **national cervical cancer program strategies and plans**, with targets and milestones for 2030 in line with regional and global objectives for cervical and other HPV-related cancers, sexual and reproductive health, HIV/STIs, and health system plans.

[6] Sustainable Development target 3.4: By 2030, reduce by one-third premature mortality from noncommunicable diseases (cardiovascular diseases, cancer, diabetes, chronic respiratory diseases) through prevention and treatment and promote mental health and well-being.

b) Development/review of national cervical cancer **policies** based on the most up-to-date scientific evidence, with specific mention of HPV vaccination delivery strategies and target groups; screening method(s), including target groups and frequency; and referral mechanisms for diagnosis, treatment, and palliative care—all tailored to the needs of priority populations based on the local situation.

c) Creation/strengthening of the **managerial structure** in the Ministry of Health to ensure implementation, monitoring, and attainment of the national program's goals and targets, with coordinating mechanisms to ensure effective interprogrammatic coordination between different programs, such as immunization, sexual and reproductive health, HIV/STI, and other HPV-related cancers, as well as multisectoral coordination and the active participation of women, relevant civil society organizations, and indigenous/Afro-descendant networks and communities.

d) Strengthening of comprehensive **health information systems** that permit data generation and monitoring of cervical cancer programs across the continuum of prevention, care, and treatment services from a programmatic perspective, to include reporting on HPV vaccination coverage, cervical cancer screening coverage, and treatment rates with increased granularity of data by age group and equity variables, as well as the creation/strengthening of **population-based cancer registries** that generate regular up-to-date reports on incidence and mortality, including data on cervical and other HPV-related cancers.

e) Sustained allocation of sufficient **financial resources** for information and education initiatives and HPV vaccination, screening, diagnosis, treatment, and palliative care.

Objective	Indicator	Baseline (2017)	Target (2030)
1.1 Develop and update comprehensive national cervical cancer plans aimed at reducing cervical cancer incidence and mortality in alignment with related global and regional plans	**1.1.1** Number of countries and territories with current comprehensive cervical cancer plans [a]	10	25
1.2 Improve monitoring and evaluation of cervical cancer programs, including screening coverage, treatment rates, and cervical cancer incidence and mortality	**1.2.1** Number of countries and territories producing routine monitoring reports on their cervical cancer program [b]	9	25
	1.2.2 Number of countries and territories with population-based cancer registries and published incidence and mortality statistics [c]	11	19

a. Source: PAHO. NCD Country Capacity Survey, 2017.
b. Source: Literature and desk review of national cervical cancer program reports.
c. Source: IARC. Cancer Incidence in Five Continents, 2017.

Strategic Line of Action 2: Strengthen primary prevention through information, education, and HPV vaccination

19. Community mobilization, health education and information, and universal HPV vaccination are essential primary prevention strategies. Health information and education campaigns need to be strengthened, depending on the specific information needs of individuals and communities, by communicating up-to-date scientific information and messages about HPV, HPV vaccines, cervical cancer, and behavior changes that can reduce risks and prevent cervical cancer, presented in simple gender-sensitive, culturally appropriate, understandable language. Sustained HPV vaccination programs also need to be implemented, in accordance with global guidelines for target age and dose, with a view to achieving greater than 80% national coverage of HPV vaccines as part of national immunization programs. To strengthen primary prevention efforts for cervical cancer, it will be necessary to:

a) Develop/strengthen and implement gender-sensitive **HPV and cervical cancer prevention education and awareness-raising initiatives** to inform people—in particular, girls and boys and priority populations with higher HPV prevalence and in situations of vulnerability—about HPV infection, cervical and other HPV-related cancers, and their causes and natural history; provide education on sexual health, tailored to age and culture, with a view to reducing high-risk sexual behavior; point out the link between HIV and STI prevention and increased access and use of condoms; provide details on HPV vaccine effectiveness and safety; address misinformation and rumors that inhibit acceptance of HPV vaccination; promote screening for age-eligible women; increase awareness of signs and symptoms of cervical cancer; and address ignorance, fear, embarrassment, and stigma related to HPV and cervical cancer.

b) Develop/review national **HPV vaccine guidelines** to ensure that they are based on the most recent scientific evidence, in alignment with WHO/PAHO recommendations and ethical standards, and tailored to the needs of key populations and others in situations of vulnerability, depending on the local cervical cancer burden. The target age may vary in different settings; it should be determined based on the likelihood of reaching the largest group of people at highest risk prior to initiation of sexual activity.

c) Begin/continue to implement **HPV vaccination strategies** with the aim of reaching greater than 80% national coverage with the recommended dose in the target female age group as set out in national guidelines, monitoring adverse events and coverage rates, and reporting annually on HPV vaccination coverage by age cohort as part of the routine immunization reporting mechanism.

Objective	Indicator	Baseline	Target (2030)
2.1 Develop and implement national education and information campaigns for HPV and cervical cancer prevention	**2.1.1** Number of countries and territories with ongoing HPV and cervical cancer education and information campaigns [a]	9 (2017)	25
2.2 Implement HPV vaccination in a sustainable manner as part of national immunization programs	**2.2.1** Number of countries and territories with greater than 80% HPV vaccine coverage in the target female age group according to national guidelines [b]	2[c] (2016)	15

a. Source: Literature and desk review of national cervical cancer program reports.
b. Source: WHO. Human papillomavirus vaccines: WHO position paper. May 2017.
c. Source: WHO, Joint Reporting Form, July 2017.

Strategic Line of Action 3: Improve cervical cancer screening and precancer treatment through innovative strategies

20. Cervical cancer can be prevented by screening asymptomatic women in the target age group at risk of developing cervical cancer and providing treatment for all those detected with precancerous lesions. The aim is to screen the largest possible proportion of women targeted by the national guideline and ensure appropriate management for all those who have an abnormal test result. Strategies for successfully establishing this crucial link between screening and treatment include both the classical approach of "screen, diagnose, and treat" and also "screen and treat" or "screen, triage, and treat." A number of effective screening tests are available, including HPV tests, visual inspection with acetic acid (VIA), and cytology. The options for treating precancerous lesions include cryotherapy, the loop electrosurgical excision procedure (LEEP), and cold knife conization, recommended by WHO *(10)*. However, the HPV test, given its superior performance, followed by cryotherapy treatment with or without VIA triage, is recommended over other screening tests and approaches whenever it is feasible *(10)*. Regardless of the screening test, treatment method, or approach adopted, health services need to be organized to ensure high screening coverage in the target group, a high treatment rate for women with abnormal test results, and high quality in testing and treatment.

21. To strengthen screening and precancer treatment services, it will be necessary to:

a) Review/update national **screening and precancer treatment protocols** to ensure that they are based on the most recent scientific evidence, adhere to WHO recommendations and ethical standards, and are tailored to the needs of priority populations, including those living with HIV who need more frequent screening. The target age may vary in different settings and should be determined based on the likelihood of reaching the largest group of women, focusing on those between the ages of 30 and 49 and expanding to younger and older age groups as resources permit with a view to attaining maximal coverage.

b) Assess health service capacity and needs with a view to **increasing equitable access,** screening coverage, and treatment rates through clinical outreach services as well as static health services, while tailoring the service delivery model to the needs of women living in vulnerable and disadvantaged communities. Consider ways to deliver screening and treatment services in fewer health service visits so as to reduce loss in follow-up care and maximize impact on cervical cancer mortality. Ensure that cervical cancer services are part of the essential benefits offered by health systems and services at the first level of care with a definite strategy for referrals to secondary and tertiary care.

c) Strengthen **integrated service delivery** to better address women's health, sexual and reproductive health, HIV co-infection, and the prevention of cancer and other noncommunicable diseases. This approach includes offering and performing HIV testing and counseling in cervical cancer screening services and HPV testing in sexual health and HIV/STI prevention, care, and treatment services in order to provide more comprehensive, person-centered, and better integrated screening and management of sexual health services.

d) Ensure that all **primary care providers are trained** and competent in carrying out the procedures for screening and precancer treatment, in assuring high-quality care for women, and in providing comprehensive care through multidisciplinary teams that include community health workers who have been trained to address the clinical, psychosocial, and gender needs of women with persistent HPV infections or cervical precancerous lesions, as well as the elimination of stigma and discrimination in the health services.

e) Assess infrastructure capacity and needs, including laboratory capacity to process screening tests in a timely and accurate manner, and **ensure provision of the necessary infrastructure, supplies**, and equipment, making use of the PAHO Strategic Fund as necessary, to enable timely screening and precancer treatment services, maximized coverage of the target population, reliable services, and minimal service interruptions as a result of a shortage of providers, malfunctioning equipment, stock out of supplies, etc.

Objective	Indicator	Baseline (2017)	Target (2030)
3.1 Increase equitable access to and coverage of cervical cancer screening and precancer treatment	**3.1.1** Number of countries and territories with at least 70% screening coverage among women aged 30-49 or according to national policies for screening by age group [a]	7	20
	3.1.2 Number of countries and territories with a treatment rate of at least 70% among women with abnormal screening test results [b]	No data available	10

a. Source: PAHO. NCD Country Capacity Survey, 2017.
b. Source: Literature and desk review of national cervical cancer program reports.

Strategic Line of Action 4: Improve access to services for cancer diagnosis, treatment, rehabilitation, and palliative care

22. Accurate diagnosis and prompt and appropriate treatment, including rehabilitative care, pain relief, and palliative care, can reduce mortality and improve outcomes and quality of life for women with cervical cancer. Pathology services are essential in order to accurately analyze and guide the diagnosis, treatment, and management of the woman's health. Cervical cancer treatment options include surgery or radiation therapy with or without chemotherapy. The most effective treatment services are those that are: provided in an equitable, human-rights based, and sustainable manner; associated with accurate diagnosis and staging; treated according to evidence-based standards of care; and linked to rehabilitative services as well as palliative care. It is important to address barriers that limit access to safe, quality, effective, and affordable cancer services by working towards universal health access and coverage that include diagnosis, treatment, rehabilitation, and palliative care. Cancer treatment can exert a significant psychosocial and financial impact on women and their families, a factor that should be taken into account when improving access and coverage of cervical cancer services.

23. To strengthen diagnosis, treatment, and palliative care services, it will be necessary to:

a) Develop/update and implement evidence-based **protocols** for cervical cancer treatment and palliative care based on current scientific evidence.

b) Improve **equitable access** to pathology, radiation therapy, surgery, chemotherapy, rehabilitation, and palliative care services by ensuring that they are part of universal coverage schemes; adapting service delivery approaches based on people- and community-centered care through integrated health service networks; and integrating palliative care into primary care and community- and home-based care.

c) Ensure that there are sufficient numbers of **trained health care** workers in place—especially pathologists, oncology nurses, gynecologist-oncologists, radiologists, and medical physicists, among others—with the appropriate competencies and skills for cervical cancer control through appropriate human resources planning, recruitment, continuing education and training, deployment, and retention strategies, including career development opportunities.

d) Strengthen the supply of quality-assured and essential **cancer diagnostics, medicines, and treatment technologies,** making use of the PAHO Strategic Fund as necessary, and strengthen supply chain management structures and processes (forecasting, procurement, warehousing, and distribution) as well as radiation protection policies and practices.

Objective	Indicator	Baseline (2017)	Target (2030)
4.1 Increase equitable access to cancer treatment and palliative care services	**4.1.1** Number of countries and territories with publically available cancer treatment services	27	30
	4.1.2 Number of countries and territories utilizing the PAHO Strategic Fund for essential cancer medicines	3	15
	4.1.3 Number of countries and territories with palliative care services included in primary care	10	20

Implementation

24. Implementation of this Plan will first require the development of biennial work plans aligned with the PAHO biennial planning cycle. It will also require multisectoral, multiagency, intercountry, and interprogrammatic cooperation and collaboration. Key partners include the International Atomic Energy Agency (IAEA), the International Agency for Research on Cancer (IARC), and other United Nations partners; the South American Network of Cancer Institutes (RINC); the United States National Cancer Institute; NGOs, including the American Cancer Society, the Union for International Cancer Control, and Cervical Cancer Action; and other relevant sectors.

Monitoring and Evaluation

25. Monitoring and evaluation of this Plan will be aligned with the Organization's results-based management framework and its performance monitoring and assessment processes. A series of progress reports will be submitted to the PAHO Governing Bodies: the first in 2022, the second in 2026, and a final report in 2031.

Financial Implications

26. An average of US$ 3 million per year will be required for PAHO technical cooperation on cervical cancer prevention and control over the period 2018-2030. It is also to be noted that cervical cancer prevention and control will require substantial external and domestic resources to scale up efforts and shift away from small demonstration projects to population-based interventions that achieve high vaccination, screening, and treatment coverage in order to significantly reduce the number of cervical cancer cases and deaths and ultimately eliminate cervical cancer as a public health problem.

Action by the Directing Council

27. The Directing Council is requested to review the information provided in this document and consider adopting the proposed resolution found in Annex D.

Annexes

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Annex A

Overview of the Situation and Capacity for Cervical Cancer Prevention and Control in Countries and Territories in the Region of the Americas

Country/ territory	Cervical cancer burden (a,b)			HPV vaccination (c, d)			Screening (e)			Cancer treatment and palliative care (f,g)			Cancer registration (f)	
	Incidence rate (ASR per 100,000)	Mortality rate (ASR per 100,000)	5-year survival rate (%) 2005-2009	Year of introduction	Target age group	Coverage 2nd dose/3rd dose - 2016	Screening test used	Target age group	Screening coverage (%) (latest year)	Cancer treatment available	Radiotherapy – number of centers	Palliative care services available in primary care	Cancer registry exists	Hospital or population-based registry
Anguilla	--	--	--	5/2016	9-13 year-olds females	35%	--	--	--	No	NA	No	No	NA
Antigua & Barbuda	--	--	--	NI	NA	NA	Cytology	21-65 year-olds	--	Yes	1	Yes	No	NA
Argentina	20.8	8.3	50.6	10/2011	11 year-olds, both sexes (males 2017)	57%	Cytology/HPV test	30-64 year-olds	72 (2013)	Yes	81	No	Yes	Hospital-based
Aruba	--	--	--	11/2014	11 year-olds females	47%	--	--	--	Yes	--	Yes	No	NA
Bahamas	20.6	7.0	--	5/2015	9-10 year-olds, females	ND	Cytology	21-59 year-olds	--	Yes	1	No	Yes	Population-based
Barbados	25.4	7.2	--	2014	10-11 year-olds, both sexes	12%	Cytology	21-65 year-olds	--	Yes	1	No	Yes	Population-based
Belize	32.7	14.9	--	11/2016	9-13 year-olds, females	NA	Cytology/VIA	21-55 year-olds	37 (1999)	No	NA	No	No	NA
Bermuda	--	--	--	4/2007	9-15 year-olds, both sexes	30%	--	--	--	Yes	--	Yes	Yes	Population-based
Bolivia	47.7	21.0	--	4/2017	10-12 year-olds, females	NA	Cytology	25-64 year-olds	33 (2008)	Yes	6	No	Yes	Population-based
Brazil	16.3	7.3	61.1	3/2014	9-14 year-olds, both sexes (males 2017)	10%	Cytology	25-64 year-olds	82 (2014)	Yes	212	Yes	Yes	Population-based

Country/ territory	Cervical cancer burden (a,b)			HPV vaccination (c, d)			Screening (e)			Cancer treatment and palliative care (f,g)			Cancer registration (f)	
	Incidence rate (ASR per 100,000)	Mortality rate (ASR per 100,000)	5-year survival rate (%) 2005-2009	Year of introduction	Target age group	Coverage 2nd dose/3rd dose - 2016	Screening test used	Target age group	Screening coverage (%) (latest year)	Cancer treatment available	Radiotherapy – number of centers	Palliative care services available in primary care	Cancer registry exists	Hospital or population-based registry
Canada	6.3	1.7	66.8	2007-2009	9-13 year-olds (target age and sex vary by province)	73%	Cytology	21-69 year-olds	73 (2011)	Yes	54	Yes	Yes	Population-based
Cayman Islands	--	--	--	11/2012	9-15 year-olds, females	NR	--	--	--	Yes	--	Yes	Yes	Population-based
Chile	12.8	6.0	50.9	9/2014	9 year-olds females	78%	Cytology	25-64 year-olds	71 (2013)	Yes	26	No	Yes	other
Colombia	18.7	8.0	59.3	8/2012	9 -17 year-olds, females	NR	Cytology/VIA/HPV test	25-69 year-olds	67 (2005)	Yes	51	No	Yes	Hospital-based
Costa Rica	11.4	4.4	--	NI	NA	NA	Cytology	20 years and older	35 (2013)	Yes	4	Yes	Yes	Population-based
Cuba	17.1	6.7	64.0	NI	NA	NA	Cytology	25-64 year-olds	70 (1994)	Yes	9	Yes	Yes	Population-based
Dominica	--	--	--	NI	NA	NA	Cytology	18-65 year-olds	--	No	NA	No	No	NA
Dominican Republic	30.7	12.3	--	4/2017	9-10 year-olds, females	NA	Cytology	25-64 year-olds	66 (2003)	Yes	12	No	Yes	Hospital-based
Ecuador	29.0	14.0	61.7	2/2014	9-11 year-olds, females	86%	Cytology	21-65 year-olds	47 (2003)	Yes	12	Yes	Yes	Population-based
El Salvador	24.8	11.9	--	NI	NA	NA	Cytology /HPV test	30-59 year-olds	70 (2008)	Yes	4	No	Yes	Hospital-based
Grenada	--	--	--	NI	NA	NA	Cytology	21 years and older	--	No	NA	No	Yes	Hospital-based
Guatemala	22.3	12.2	--	NI	NA	NA	Cytology/VIA/HPV test	25-54 year-olds	40 (2003)	Yes	4	No	Yes	Population-based
Guyana	46.9	21.9	--	2011	9-13 year-olds, females	NR	Cytology/VIA	30-49 year-olds	17 (2012)	No	1	No	Yes	Population-based

Country/ territory	Cervical cancer burden (a,b)			HPV vaccination (c, d)			Screening (e)			Cancer treatment and palliative care (f,g)			Cancer registration (f)	
	Incidence rate (ASR per 100,000)	Mortality rate (ASR per 100,000)	5-year survival rate (%) 2005-2009	Year of introduction	Target age group	Coverage 2nd dose/3rd dose - 2016	Screening test used	Target age group	Screening coverage (%) (latest year)	Cancer treatment available	Radiotherapy – number of centers	Palliative care services available in primary care	Cancer registry exists	Hospital or population-based registry
Haiti	24.9	14.6	--	Pilot	NA	NA	Cytology/VIA	30 years and older	--	No	NA	No	Yes	Hospital-based
Honduras	29.4	14.1	--	5/2016	11 year-olds, females	55%	Cytology/HPV test	30-59 year-olds	31 (2002)	Yes	5	No	Yes	Hospital-based
Jamaica	26.3	11.9	--	10/2017	10-11 year-olds, females	NA	Cytology	25-54 year-olds	25 (2008)	Yes	3	No	Yes	Population-based
Mexico	23.3	8.0	--	10/2012	10-11 year-olds, females	96%	Cytology/HPV test	25-64 year-olds	64 (2003)	Yes	91	No	Yes	Population-based
Nicaragua	36.2	18.3	--	NI	NA	NA	Cytology/HPV test	25-64 year-olds	35 (2007)	Yes	1	No	No	
Panama	18.7	7.1	--	10/2008	10 year-olds, both sexes	56%	Cytology	25-59 year-olds	13 (2014)	Yes	4	Yes	Yes	Population-based
Paraguay	34.2	15.7	--	3/2013	10 year-olds, females	60%	Cytology/HPV test	25-49 year-olds	51 (2003)	Yes	4	No	No	
Peru	32.7	12.0	--	2/2015	9-12 year-olds, females	NR	Cytology/VIA	30-49 year-olds	54 (2013)	Yes	18	No	Yes	Hospital-based
Sint Maarten	--	--	--	9/2013	9-11 year-olds females	NR	--	--	NA	No	NA	No	No	NA
Saint Kitts and Nevis	--	--	--	NI	NA	NA	Cytology	18-55 year-olds	--	No	NA	No	No	NA
Saint Lucia	--	--	--	NI	NA	NA	Cytology	18-55 year-olds	--	No	NA	No	Yes	Hospital-based
Saint Vincent and the Grenadines	--	--	--	NI	NA	NA	Cytology	20-65 year-olds	--	No	NA	No	No	NA
Suriname	38.0	15.7	--	11/2013	9-13 year-olds, females	32%	Cytology/VIA	23-55 year-olds	--	Yes	1	Yes	Yes	Hospital-based

Country/ territory	Cervical cancer burden (a,b)			HPV vaccination (c, d)			Screening (e)			Cancer treatment and palliative care (f,g)			Cancer registration (f)	
	Incidence rate (ASR per 100,000)	Mortality rate (ASR per 100,000)	5-year survival rate (%) 2005-2009	Year of introduction	Target age group	Coverage 2nd dose/3rd dose - 2016	Screening test used	Target age group	Screening coverage (%) (latest year)	Cancer treatment available	Radiotherapy – number of centers	Palliative care services available in primary care	Cancer registry exists	Hospital or population-based registry
Trinidad and Tobago	24.5	12.0	--	2/2013	11-12 year-olds, both sexes	22%	Cytology	25-65 year-olds	--	Yes	3	No	Yes	Population-based
United States of America	6.6	2.7	62.8	6/2006	11-12 year-olds, both sexes	63% girls 50% boys	Cytology/HPV test	21-64 year-olds	81 (2013)	Yes	2,121	Yes	Yes	Population-based
Uruguay	18.9	7.1	--	4/2013	12 year-olds, females	41%	Cytology	21-69 year-olds	40 (2014)	Yes	10	Yes	Yes	Population-based
Venezuela	32.8	12.3	--	NI	NA	NA	Cytology	25-64 year-olds	35 (1994)	Yes	38	No	No	Hospital-based

Legend: ASR=age-standardized rate; -- = No data available; NI = No introduction; NA = Not applicable; NR = No report; VIA = Visual inspection with acetic acid.
Sources:
a. Globocan, 2012, http://globocan.iarc.fr/Default.aspx
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c. WHO/Joint Reporting Form (JRF), July 2017 and additional information provided to PAHO from the countries (with introduction at the end 2016 or 2017). Three territories have information as of year of introduction but no coverage data in JRF: Puerto Rico (6/2006); Saba (2013 = 1/3 of the Dutch municipalities) and Sint Eustatius (1/2013).
d. WHO/JRF, July 2017 and additional information provided to PAHO by the countries (with introduction at the end 2016 or 2017).
e. ICO HPV Information Center, 2017. http://www.hpvcentre.net/
f. PAHO, 2017. NCD Country Capacity Survey.
g. IAEA, 2017. Directory of Radiotherapy Centers. https://dirac.iaea.org/Query/Map2?mapId=0

Annex B

PAHO/WHO Tools for Cervical Cancer Prevention and Control

Comprehensive cervical cancer control: a guide to essential practice. WHO; 2014.

Available in English, Spanish, and Portuguese on the PAHO website: http://apps.who.int/iris/bitstream/handle/10665/144785/9789241548953_eng.pdf;jsessionid=A5E7480B867101AEBC6C5B1C35068450?sequence=1

Guidelines for screening and treatment of precancerous lesions for cervical cancer prevention. WHO, 2013

Available in English and Spanish on the WHO website: http://apps.who.int/iris/bitstream/handle/10665/94830/9789241548694_eng.pdf?sequence=1

Monitoring national cervical cancer prevention and control programmes. WHO, 2013

Available in English and Spanish on the WHO website: http://apps.who.int/iris/bitstream/handle/10665/79316/9789241505260_eng.pdf?sequence=1

Series of factsheets on HPV and cervical cancer. PAHO, 2015

Available in English, Spanish, and Portuguese on the PAHO website: https://www.paho.org/hq/index.php?option=com_content&view=article&id=11568&Itemid=40592&lang=en.

Integrating HPV testing in cervical cancer screening programs: a manual for program managers. PAHO, 2016

Available in English and Spanish on the PAHO website: http://www.paho.org/hq/index.php?option=com_content&view=article&id=12428&Itemid=40602&lang=en

PAHO Virtual Public Health Campus. Course on comprehensive cancer control. PAHO, 2018

Available in English and in Spanish on the campus website: https://mooc.campusvirtualsp.org/course/view.php?id=32

Annex C
Synopsis of Relevant Partner Initiatives on Cervical Cancer Prevention and Control

Initiative	Overview	Reference
Global initiatives		
UN Global Joint Program on Comprehensive Cervical Cancer	A global initiative of 7 United Nations agencies/programs to lead and coordinate technical assistance to governments with a view to building and sustaining high-quality national comprehensive cervical cancer control programs	http://www.who.int/ncds/un-task-force/un-joint-action-cervical-cancer-leaflet.pdf
Cervical Cancer Action	An international coalition of nongovernmental organizations that coordinates initiatives and leads global **strategic advocacy** efforts to inform policies, strengthen programs, and increase global funding for cervical cancer prevention and control	http://www.cervicalcanceraction.org/home/home.php
Cervical Cancer Prevention Initiative	A global initiative launched by Cervical Cancer Action in 2015 to promote multisectoral partnerships, spur investments in the health of adolescent girls and women, and build momentum for action on global cervical cancer prevention over five years (2015–2020)	http://www.cervicalcanceraction.org/initiative/
Pink Ribbon Red Ribbon	A global partnership of national governments, nongovernmental and multilateral organizations, foundations, and corporations with a shared goal of reducing deaths from cervical cancer and breast cancer in low- and middle-income countries	http://pinkribbonredribbon.org/about-cervical-breast-cancer/
International Cancer Control Planning Partnership	A group of international organizations engaged in cancer control planning efforts to support the development, implementation, and evaluation of national cancer control plans around the world	http://www.iccp-portal.org/
Regional initiatives		
RINC Cervical Cancer Plan Prevention and Control Plan for South America	Plan for cervical cancer developed under the aegis of the Network of South America National Cancer Institutes and Institutions (*Red de Instituciones Nacionales de Cáncer* – RINC), which includes cooperation in research and other areas	http://www2.rinc-unasur.org/wps/wcm/connect/rinc/site/home
IARC ESTAMPA project	A Latin American multicenter study on cervical cancer screening with HPV tests reaching out to 50,000 women in 10 Latin American countries	http://www.who.int/reproductivehealth/projects/HRX17_ESTAMPA.pdf
MD Anderson ECHO project for cervical cancer	A telementoring model used by MD Anderson with providers in Latin America to build capacity for the clinical management of cervical dysplasia	https://www.mdanderson.org/education-training/global-outreach/project-echo.html

Pan American Health Organization
World Health Organization
REGIONAL OFFICE FOR THE Americas

56th DIRECTING COUNCIL

70th SESSION OF THE REGIONAL COMMITTEE OF WHO FOR THE AMERICAS

Washington, D.C., USA, 23-27 September 2018

CD56/9
Annex D
Original: English

PROPOSED RESOLUTION

PLAN OF ACTION FOR CERVICAL CANCER PREVENTION AND CONTROL 2018-2030

THE 56th DIRECTING COUNCIL,

(PP1) Having examined the *Plan of Action for Cervical Cancer Prevention and Control 2018-2030* (Document CD56/9);

(PP2) Considering that the Plan is aligned with World Health Organization Resolution WHA70.12, Cancer Prevention and Control in the Context of an Integrated Approach, the WHO Global Health Sector Strategy on Sexually Transmitted Infections, the UN Joint Global Programme on Cervical Cancer Prevention and Control, the new WHO Global Strategy to Eliminate Cervical Cancer, and the Sustainable Development Goals (SDGs), and that this plan of action provides a clear long-term plan to reduce the cervical cancer burden in the Americas by 2030;

(PP3) Cognizant of the impact that this disease has on women, their families, and their communities throughout the Americas, especially among priority populations in situations of vulnerability;

(PP4) Acknowledging the need to decrease and eliminate the scourge of this disease, which is preventable through HPV vaccination, screening, and precancer treatment, and curable if detected at early stages of disease;

(PP5) Aware of the cost-effective and affordable interventions that are available to reduce cervical cancer incidence and mortality and the urgent action that is required to implement these interventions on a population-based scale, seeking to ensure equitable access to cervical cancer primary, secondary, and tertiary prevention,

RESOLVES:

(OP)1. To approve the *Plan of Action for Cervical Cancer Prevention and Control 2018-2030* (Document CD56/9).

(OP)2. To urge Member States, as appropriate and taking into account their national context and needs, to:

a) prioritize the prevention and control of cervical cancer in the national public health agenda;

b) formulate, review, and align national comprehensive cervical cancer strategies and plans with related global and regional strategies, plans, and targets, and regularly report on progress in this area;

c) strengthen governance, organization, and access to health services to ensure that comprehensive cervical cancer services are integrated across the relevant levels of care and that high coverage of HPV vaccination, screening, precancer treatment, and invasive cancer treatment is achieved;

d) strengthen cancer registries and information systems to monitor the coverage of HPV vaccination, coverage of screening, and treatment rates, and report regularly on these indicators;

e) implement high-impact interventions on a population-based scale along the continuum of health education and promotion, HPV vaccination, cervical cancer screening and diagnosis, and treatment for precancer and invasive cancer, with interventions tailored to the needs of priority populations in situations of vulnerability;

f) facilitate the empowerment and engagement of civil society organizations to provide a multisectoral approach to comprehensive cervical cancer prevention and control;

g) increase and optimize public financing with equity and efficiency for a sustainable response to cervical cancer, and progressively integrate prevention, screening, and treatment interventions into comprehensive, quality, and universal health services;

h) expand health services according to need and with a people-centered approach, noting that in most cases public expenditure of 6% of GDP for the health sector is a useful benchmark;

i) secure the uninterrupted supply of quality-assured and affordable HPV vaccines, screening tests, and evidence-based technologies for precancer and invasive cancer treatment, as well as palliative care medicines and other strategic commodities related to cervical cancer, while strengthening supply chain management structures and processes, including forecasting, procurement, warehousing, and distribution;

j) strengthen the technical capacity and competencies of the national health workforce, particularly at the primary level of care, to address cervical cancer prevention.

(OP)3. To request the Director to:

a) support implementation of this Plan of Action through a coordinated and interprogrammatic approach to technical cooperation for comprehensive cervical cancer prevention and control;

b) provide technical support to Member States to strengthen cervical cancer program coverage, quality, and effectiveness in coordination with the Network of National Cancer Institutes and Institutions (RINC)/UNASUR cervical cancer prevention and control plan for South America;

c) provide support for cancer registration and information systems in order to build country capacity to generate quality, complete, and up-to-date information, and regularly report on HPV vaccination coverage, screening coverage, treatment rates, and cervical cancer incidence and mortality;

d) provide technical support to Member States for the development and review of policies, norms, and guidelines for high-impact interventions along the continuum of cervical cancer prevention, screening, and diagnosis and treatment of precancer and invasive cancer, based on the latest WHO recommendations, while seeking to ensure quality and equity;

e) advocate for the empowerment of people and communities and their meaningful, effective, and sustainable engagement in the development and delivery of services for HPV vaccination and cervical cancer screening, treatment, and palliative care;

f) support capacity-building in the national health workforce, particularly at the primary care level, to provide good quality, accessible, equitable, and people-centered care in the health services;

g) provide support to Member States through the PAHO Regional Revolving Fund for Strategic Public Health Supplies or the PAHO Revolving Fund for Vaccine Procurement to improve the processes of procurement and supply management and distribution in order to ensure uninterrupted access to quality-assured and affordable HPV vaccines, HPV tests, and essential medicines for cancer and for palliative care in alignment with WHO prequalification;

h) mobilize resources, adhering to the rules and procedures of the Framework for Engagement with non-State Actors, to support Member States to increase investments in comprehensive cervical cancer prevention and control.

Pan American Health Organization

World Health Organization
REGIONAL OFFICE FOR THE Americas

CD56/9
Annex E

Report on the Financial and Administrative Implications of the Proposed Resolution for PASB

1. Agenda item: 4.5 - Plan of Action for Cervical Cancer Prevention and Control 2018-2030

2. Linkage to PAHO Program and Budget 2018-2019:

a) Categories:

Category 1- Communicable Diseases

Category 2- Noncommunicable Diseases and Risk \Factors

Category 4- Health Systems

b) Program areas and outcomes:

Program area 1.1: HIV/AIDS, STIs, and viral hepatitis (Outcome 1.1 - Increased access to key interventions for HIV and STI prevention and treatment)
Program area 1.5: Vaccine-preventable Diseases (Outcome 1.5 - Increased vaccination coverage for hard-to-reach populations and communities and maintenance of control, eradication, and elimination of vaccine-preventable diseases)

Program area 2.1: Noncommunicable Diseases and Risk Factors (Outcome 2.1 – Increased access to interventions to prevent and manage NCDs)

Program area 4.2: People-centered, Integrated, Quality Health Services (Outcome 4.2 – Increased access to people-centered, integrated, quality health services)

3. Financial implications:

a) Total estimated cost for implementation over the life cycle of the resolution (including staff and activities):

The estimated cost of this plan is US$ 3,000,000 per year. For the period 2018-2030, the total cost is US$ 36,000,000.

Areas	Estimated cost (US$)
Human resources	7,500,000
Training	10,500,000
Consultants/service contracts	5,500,000
Travel and meetings for program managers	5,000,000
Publications and communication materials	1,500,000
Supplies (e.g., HPV tests) and other expenses	6,000,000
Total	36,000,000

b) Estimated cost for the 2018-2019 biennium (including staff and activities):

The estimated cost for the biennium is US$ 3,000,000.

c) Of the estimated cost noted in *b),* what can be subsumed under existing programmed activities?

Staff currently funded through the PAHO Regular Budget, who will contribute between 25% and 50% of their time to implementation of this plan, will already be subsumed under existing programmed activities. Technical cooperation activities already included and budgeted in this biennial period will also be covered by the PAHO Regular Budget, as well as the PAHO-CDC cooperative agreement on NCDs and the OPEC Fund for International Development grant for NCDs. It is estimated that the total staff time and activity budget already covered for this Plan of Action in the current biennium is approximately US$ 750,000.

4. Administrative implications:

a) Indicate the levels of the Organization at which the work will be undertaken:

The work will be carried out at the country, subregional, and regional levels.

b) Additional staffing requirements (indicate additional required staff full-time equivalents, noting necessary skills profile):

For implementation of this Plan, it will be crucial to guarantee current technical staff strength at regional and subregional levels, as well as to ensure that NMH country office focal points set aside sufficient time for this Plan of Action in high-impact and priority countries.

c) Time frames (indicate broad time frames for implementation and evaluation):

The proposed plan will cover the time period 2018-2030 and require support from the Pan American Sanitary Bureau, Member States, and partner organizations. A series of progress reports will be submitted to the PAHO Governing Bodies: the first in 2022, the second in 2026, and a final report in 2031.

ANALYTICAL FORM TO LINK AGENDA ITEM WITH ORGANIZATIONAL MANDATES

1. **Agenda item:** 4.5 - Plan of Action for Cervical Cancer Prevention and Control 2018-2030

2. **Responsible unit:** Noncommunicable Diseases and Mental Health, Violence, and Injury Prevention (NMH/NV)

3. **Preparing officer:** Silvana Luciani, Adviser, Cancer Prevention and Control, NMH/NV

4. **Link between Agenda item and Sustainable Health Agenda for the Americas 2018-2030:**

   Goal 9: Reduce morbidity, disabilities, and mortality from noncommunicable diseases, injuries, violence, and mental health disorders

5. **Link between Agenda item and the Strategic Plan of the Pan American Health Organization 2014-2019 (Amended):**

   a) **Categories:**

   Category 1 - Communicable Diseases
   Category 2 - Noncommunicable Diseases and Mental Health
   Category 4 - Health Systems

   b) **Program areas and outcomes:**

   Program area 1.1: HIV/AIDS and STIs (Outcome 1.1 - Increased access to key interventions for HIV and STI prevention and treatment)

   Program area 1.5: Vaccine-preventable Diseases (Outcome 1.5 - Increased vaccination coverage for hard-to-reach populations and communities and maintenance of control, eradication, and elimination of vaccine-preventable diseases)

   Program area 2.1: Noncommunicable Diseases and Risk Factors (Outcome 2.1 – Increased access to interventions to prevent and manage NCDs)

   Program area 4.2: People-centered, Integrated, Quality Health Services (Outcome 4.2 – Increased access to people-centered, integrated, quality health services)

6. **List of collaborating centers and national institutions linked to this Agenda item:**

   Key partners with whom we will collaborate on the implementation of this Plan include but are not limited to the following:

   - World Health Organization
   - United Nations Population Fund
   - International Atomic Energy Agency

- International Agency for Research on Cancer
- South American Network of Cancer Institutes (RINC/UNASUR)
- United States National Cancer Institute
- United States Centers for Disease Control and Prevention
- American Cancer Society
- Union for International Cancer Control
- Cervical Cancer Action

7. Best practices in this area and examples from countries within the Region of the Americas:

a) National immunization programs, which have integrated HPV vaccines into their programs and are beginning to monitor coverage.

b) HPV testing, which has been introduced in selected countries to complement or substitute Pap testing and improve the quality and effectiveness of screening programs.

c) Information systems that permit the registration of women screened, their screening test results, and follow-up diagnosis and treatment in order to ensure complete quality of care.

d) Education and communication campaigns that have been implemented at the local and subnational level to raise awareness about HPV vaccination and cervical cancer prevention.

8. Financial implications of this Agenda item:

The estimated cost of this plan is US$ 3,000,000 per year. For the period 2018-2030, the total cost is US$ 36,000,000.

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