2019

Cervical Cancer Screening and Prevention in Central America

Madeline Jensen
Augsburg University

Cervical Cancer Screening and Prevention in Central America

By

Madeline Jensen

Dr. Holly Levine

Paper Submitted in Partial Fulfillment

Of the Requirements for the Degree

Of Master of Science

Physician Assistant Studies

Augsburg University

Table of Contents

Abstract

Cervical cancer is the fourth most frequent cancer in women around the world. In the Central American region, it is a leading cause of mortality for young women due to inadequate preventive and screening measures. The disease is slow-growing and caused by the human papillomavirus, which is transmitted via sexual contact. The HPV vaccination was created in order to prevent the disease, and there are a variety of quality screening methods to quickly identify progression. The most common screening methods include the Papanicolaou (Pap) test and visualization by acetic acid (VIA). While frequent screening is common in developed countries, rates are much lower in Central American countries primarily due to financial and educational constraints. In order to prevent cases of cervical cancer in this region, current educational assistance programs should be expanded, and financial assistance must be procured. In terms of screening, VIA should be preferred over Pap testing in Central America due to its cost effectiveness and lesser training requirements.

Introduction

According to the World Health Organization, cervical cancer is currently the fourth most frequent cancer in women across the globe.[1] In comparison to other malignancies, it is a slow-growing disease, but it can be deadly if not caught and treated in a timely manner. In 2018, there were approximately 311,000 women who lost their lives to the disease.[2] Of these women, over 85% resided in a less-developed or middle-income country.[1-2] In the Latin American region in particular, cervical cancer is the most common cause of mortality due to malignant neoplasm in women 20-40 years of age.[3] These statistics are alarming, given that with adequate screening and intervention methods, cervical cancer is a preventable and treatable disease.

The vast majority of cervical cancer is caused by infection of the human papillomavirus (HPV), which is a group of non-enveloped double stranded DNA tumor viruses.[4] HPV is the most common sexually transmitted infection (STI), and can be spread during vaginal, anal, or oral sex with an infected person, as well as through skin-to-skin genital contact.[5] There are more than 100 different types of HPV, but only a select few cause disease. As the virus infects the skin and mucosa, some types can manifest as benign warts, whereas others will result in no symptoms at all. It can take weeks, months, or even years after infection for warts to develop after the initial infection.[6] Persistent and untreated infection of types 6, 11, 16, and 18 have been identified to cause nearly all cervical cancers in addition to some vaginal, vulvar, and anal cancers.[2,4] HPV was not determined to be the essentially exclusive cause until the 1980's, and the discovery has allowed researchers to develop extremely effective preventative and screening recommendations for the public as well as providers. Similar to warts, cancers can take years to develop after an HPV infection. Around the world, annual cancer cases attributable to HPV number 570,000 in women and 60,000 in men.[7] Without effective screening methods, it is nearly impossible to identify and treat these cancers in their earliest stages.

Because cervical cancer does not evolve as rapidly as some other cancers, the HPV infection commonly follows a fairly predictive course. The progression begins with a sexually transmitted HPV infection that occurs shortly after sexual activity. It is more common for a male partner to pass the virus to a female partner, but transmission occurs both ways. Contracting HPV is so common that researchers estimate that almost every person who is sexually active will get HPV at some point if they are not vaccinated.[5] In the majority of patients, the body clears the virus without trouble, and there is no further disease progression. Two years after acquisition, 90% of infections will have cleared without any intervention.[2] However, if the infection consists

of one of the known carcinogenic strains, the abnormal cells are more likely to persist and grow. It is clear that action should be taken in these cases, but there can be limitations to consider. Depending on the region of the world, financial and geographical strains may prevent access to healthcare. Patients in less-developed or lower income countries are much less likely to have access to preventative care than if they resided in a developed country. In addition, there is a lack of effective programs to raise awareness about HPV and to bring in proper training in many Central American communities.

Ultimately, the prevalence of global HPV transmission identifies a prominent public health issue that requires evaluation of screening and preventative measures. According to the Centers for Disease Control and Prevention (CDC) in the United States, 93% of cervical cancers could have been prevented with either vaccination or screening.[5] This identifies a prominent gap in healthcare services for those in developing countries or without access to healthcare. The countries within Central America are in varying stages of political, economic, and social development and can provide insight into the challenges of implementing the ideal approaches. As cervical cancer is the leading cause of cancerous mortality for women in this area, it is imperative to find plausible ways to prevent these unnecessary deaths. This paper will explore the current methods in Central America, and identify opportunities to implement further action.

Background

Cervical Cancer Progression

The cervix itself contains two types of cells. The endocervix is covered with glandular cells, and the ectocervix contains squamous cells. Both cell types come together in an area of metaplastic tissue between the endocervical canal and the vagina, called the transformation zone. Although any epithelial tissue can be infected by HPV, the transformation zone is the most

susceptible area for progression to precancers and cancers to occur. According to the American Cancer Society, 90% of cervical cancers are squamous cell carcinomas, and the majority of the others are adenocarcinomas from the glandular cells.[8]

As previously mentioned, nearly all cervical cancers begin with a sexually-transmitted HPV infection. While these infections are very common, there are some factors that can put a patient at higher risk for STIs, including HPV. Having unprotected sex, sexual contact with multiple partners, and abusing drugs and alcohol all put a person at higher risk for contracting an STI. For HPV in particular, researchers have determined an increased risk in those who are immunocompromised, have had other STIs, have had many children, have been on long term oral contraceptives, and who engage in smoking tobacco.[2,9] Following a minority of cases of infection, evidence of abnormal cellular morphology is detected. These findings are usually labeled by laboratories as "atypical squamous cells of undetermined significance (ASC-US)" or "low-grade squamous intraepithelial lesions (LSIL)." These abnormalities are transient, with over 50% naturally clearing in one year, and 90% by two years.[8]

Unfortunately, cellular abnormalities can only be detected if the patient is seen in a healthcare setting for a pelvic exam. If the abnormal cells are not identified and treated at this point, there is a small chance that an unresolved low-grade lesion could progress to a high-grade squamous intraepithelial lesion (HSIL). In these cases, further cellular changes may continue, and there is potential for the abnormal morphology to fully develop into cervical cancer cells. Though not all high-grade lesions will become cancerous, they are considered "pre-cancerous" in nature. The majority of women with precancerous lesions will not display any symptoms of the underlying disease. Cells are most likely to progress to malignancy if the initial HPV infection

was high-risk, such as with HPV types 16 and 18.[10] Cancer development occurs after cell dysplasia has been ongoing for as many as 10-15 years.

When advanced dysplasia is allowed to advance without intervention, malignancy can occur. At this point, the cancer can be classified as either a squamous cell carcinoma or an adenocarcinoma. These early stages of cancer are when most women begin to experience symptoms. Patients may notice irregular vaginal bleeding or abnormal vaginal discharge. As with any cancer, cells can break away and travel through the bloodstream or the lymph system and form new tumors. Nearby lymph nodes are usually affected first, but cancer can spread to the vagina, bladder, rectum, and walls of the pelvis. At this stage, there is a 56% 5-year survival rate for women.[8] In later stages, the cancer has spread to distant lymph nodes, lungs, bones, or liver. When metastatic disease is present, women may recognize changes in urination or defecation, fatigue, and weight loss.[9] The 5-year survival rate drops to 17% in these cases.[8] The slow-growing nature of cervical cancer allows for many opportunities to identify and treat the lesions in their early stages. Women cannot rely on presenting symptoms to seek healthcare. At the time of symptom presentation, the cancer may already be metastatic.

Global Recommendations for Prevention and Screening

Since the 1940s, the methods for screening and prevention of cervical cancer have developed substantially. With better technology and methodology, rates of incidence and mortality of cervical cancer have decreased dramatically. The first screening option created was the Papanicolaou (Pap) test, which involves collecting cells from the transition zone of the cervix and performing cytology to assess the morphology. Implementation of this method allows for abnormal lesions to be caught and treated before they progress to symptomatic and dangerous

cancers. The International Agency for Research on Cancer (IARC) found that the occurrence of invasive cervical cancer could be reduced by 80% or more with Pap-based screening programs.[11] The World Health Organization (WHO) recommends that women with positive cytology results (ASCUS, LSIL, HSIL) should either repeat cytology in a year or undergo further testing such as HPV testing, colposcopy, and biopsy to further characterize the lesions.[12] Alternatively, women who test negative on cytology (Pap) should be routinely screened every three to five years.[12] While the Pap test is widely used, the results must be examined under microscopy, and there is potential for human error.

While not as widely recommended in developed countries, another screening technique frequently used is visual inspection by acetic acid (VIA). This is an inexpensive test in which acetic acid is applied directly to the cervix, allowing precancerous lesions to become visibly white to the naked eye.[11] This method has a greater margin for error and is not as accurate in identifying the severity of the lesions. However, it requires little equipment and training to perform.

When HPV was determined to be the cause of nearly all cervical cancers in the 1980's, a preventative vaccine as well as screening tools were developed. In 2007, the first prophylactic vaccine for HPV became widely available.[13] In the four years following introduction, HPV infections in teen girls decreased by 56%.[14] There are currently three options for vaccination, each covering various high-risk strains (quadrivalent Gardasil/Silgard, bivalent Cervarix, nonvalent Gardasil 9). All three vaccines cover high-risk strains 16 and 18, but none protect against all HPV types.[13] The CDC in the United States recommends routine vaccination at 11 or 12 years of age, as children ideally should be vaccinated before any exposure to the human papillomairus.[14] Both males and females should be vaccinated, as both genders can transmit the

virus. Long-lasting immunity can be generated with 2-3 doses of the non-infectious recombinant vaccine.[15]

The vaccine is a great option for those who are able to receive it before HPV exposure, but it is not therapeutic. To identify the virus after contraction has occurred, patients can undergo an HPV screening test. This detects the DNA of the virus itself, rather than the cellular changes that cytology detects. HPV testing is highly sensitive and allows for longer screening intervals – done every five years rather than three with cytology alone. A negative HPV test indicates the patient is not infected with an HPV type that is linked to cervical cancer, whereas a positive test indicates there is a presence of cancer-linked HPV.[16] A positive test does not indicate the presence of cancer, but instead identifies at risk patients. HPV testing can conveniently be completed with the same sample obtained for cytologic testing. These tests are almost always completed together, deemed "co-testing" to providers and patients. The combination of the test results allows providers to gain a more complete understanding of HPV presence and disease progression. If the two tests do not correspond, further testing with colposcopy may be indicated. HPV tests also produce a large number of false positives, which may lead to unnecessary testing.[11]

Prevention and screening methods are largely based on the peaks of acquisition at each stage of the disease. For example, the peak age group that women contract the HPV virus is in adolescence and early adulthood. The goal of the vaccination is to prevent infection before exposure occurs. Because researchers have found that the vast majority of infections are cleared naturally in young women, it is not recommended to screen with cytology until 21 years of age.[16] With predictive progression, the peak of HSIL lesions has been found to be around 25-30 years of age. In accordance with this data, it is advised that women are screened every three years with

cytology from ages 21-29. From ages 30-65, women may be screened with an HPV co-test (Pap + HPV test).[16] Because the HPV test is more sensitive to high-grade persistent lesions, it is not recommended for women under 30 who are more likely to have a transient infection. Studies have shown that the peak of cervical cancer in women is not until 45-60 years of age. This highlights the large window of intervention time before a high-grade lesion advances to cancer.

Although these screening practices can be very effective, they are only useful if women have the ability to access and afford follow-up visits and treatment. The WHO mentions that successful programs are designed in order to reach the largest amount of women at risk with quality screening and treatment.[15]

Prevention and Screening in Central America

Women in developing countries are disproportionately affected by cervical cancer. While the incidence of cervical cancer has consistently decreased in many areas, the same cannot be said for underdeveloped and low income nations. Technological advances that could allow prevention of the disease are not available to a large number of women. In the years after the invention of the HPV vaccine, only 3% of 10-20 year old females in less developed countries had received a dose.[17] Throughout Central America, the incidence and mortality rates of cervical cancer vary considerably. In terms of cancer-related deaths, it is the leading cause in El Salvador, and the sixth most in Costa Rica.[18]

In terms of prevention, there are some programs focused on administering HPV vaccinations in some areas of Central America. In 2015, Panama was the only Central American country with a national vaccination schedule in place.[19] Unfortunately, there are many challenges that must be overcome before the vaccine can become widely available. The vaccine is expensive, requires more than one dose, and implementation strategies are currently ineffective.

Additionally, the vaccine does not help women who have already been infected with HPV or who are beyond the recommended age range. This leaves many women in need of adequate screening strategies rather than prevention.

Pap testing is the most common method of screening around the world, but it requires an office visit every three years, trained providers, and microscopic analysis. Despite years of attempts to implement cytologic testing across Central America, rates of cancer still remain high in most areas.[19] In well-equipped laboratories in developed countries, there is about 50% sensitivity in detecting high-grade lesions cervical lesions. Comparatively, sensitivity ranges between 22-42% in Central American countries, indicating that the majority of lesions are missed.[20] A large number of programs in Central America are underfunded, and frequently lose patients to follow up. The few organized programs that do exist are located in major urban centers, which are inaccessible to a large portion of the population. Furthermore, a pelvic exam is required to collect specimens for Pap tests, and many people in this region are apprehensive due to cultural reasons.[20]

As previously discussed, HPV testing allows for less frequent testing, and more accurate screening. Costa Rica, the most politically stable and economically developed country in Central America, was the first in the region to begin HPV testing. The Costa Rican Ministry of Health conducted a large scale, long-term project called "The Guanacaste Project." Women in this area had the highest cervical cancer rates in the country. After introduction of a multimethod screening effort including HPV testing, there was a 31% cancer incidence reduction.[21] Many years later in 2011 the Nicaraguan government launched *care*HPV, which allows women the option to self-collect vaginal samples for HPV testing. While not as sensitive as a provider collected specimen, more than 80% of women agreed to the self-collected sample. In addition,

this collection method had a higher sensitivity for lesions in comparison to cytologic testing.[20] With the results of these studies, El Salvador, Guatemala, Honduras, and Nicaragua all began to introduce HPV testing to their pre-existing cytology programs.

Another technique commonly used in low-resource settings is visual inspection by acetic acid (VIA). As previously mentioned, this test is inexpensive and allows precancerous lesions to become visibly white to the naked eye.[11] Because of the nature of the test, results are immediately available, preventing the need for many follow up visits. This method requires little training, and few resources. It is much more widely accepted across communities, and still produces 80% sensitivity and 92% specificity.[22]

At this point in time, thousands of women in underserved parts of Central America do not have access to screening measures. There is a lack of organized programs and access to both funds and resources. Lack of services results in women seeking care when the disease has become invasive, and treatment options are either expensive or nonexistent.

Methods

The PubMed and Google Scholar databases were utilized to complete literature searches related to cervical cancer screening and prevention across the world, and specifically in Central America. PubMed search terms included: cervical cancer prevalence, cervical cancer prevention, cervical cancer screening Central America, HPV vaccination, and HPV testing. Google Scholar search terms included: WHO HPV recommendations, cervical cancer prevention, cervical cancer screening Central America, HPV vaccination, and HPV testing.

In addition to online research, in-person interviews were conducted in Costa Rica to gain additional understanding of the topic. Providers and locals were asked about screening and prevention practices currently used, opinions and attitudes related to methods, and access to care

(See Appendix A). Interviews were conducted in various locations in Costa Rica, including San Jose, Boruca, and Longo Mai. It is important to note that interviews were completed with Costa Rican locals alone. Information from other Central American countries was inquired about, and was also extrapolated from online resources.

Discussion

Ideally, the most current and up-to-date technologies should be available to all patients receiving healthcare. Unfortunately, there are many barriers to providing even the most basic healthcare necessities to large groups of people. As aforementioned, research on the preventative and screening methods of cervical cancer has increased dramatically in the last 50 years. Because of the nature of the disease, it is essential that HPV infections and precancerous lesions are identified and treated before they are allowed to progress to cancer. The WHO and the Pan American Health Organization (PAHO) have determined the most effective strategies, and have created guidelines for optimal practice. However, Central American societies do not always have the means to execute them. It is important to take financial, geographical, and cultural matters into account to determine the best methods in this part of the world.

In the developed world, the HPV vaccine is utilized for prevention, and screenings include Pap and/or HPV testing, followed by potential colposcopy, biopsy, or excisional procedures. Screening as a whole has been proven to reduce the incidence of cancer, decrease the rates of progressive disease, and save lives. While these techniques have been proven successful, they are expensive and require trained professionals, high-level equipment, and multiple clinic visits.

Primary prevention with the HPV vaccine is uncommon in most Central American countries. Although there are many explanations for low vaccination rates, a prominent issue is simply a

lack of public awareness. In 2013, over 600 mothers were interviewed in Honduras, and while nearly all of them had been educated about cervical cancer, only 13% had heard of the HPV vaccination.[24] Despite worldwide support for the vaccine, most health systems do not cover vaccination, meaning many patients could not afford to purchase it. Additionally, multiple doses are required, which demands multiple visits to a clinic.

Frequency of visits required is also a considerable obstacle when using Pap tests for screening. Screening requirements state that women should be tested every three years, yet the necessary equipment if often not available locally. When there are a lack of resources, less women receive care. If Pap tests cannot reach populations at the highest risk of developing cancer, such as those in rural areas, there is little chance of positive change. Countries able to screen 50-70% of women with a Pap test every 3-5 years have death rates of 4 in 100,000 women, whereas countries with more than 70% coverage see less than 2 in 100,000 deaths per year.[23] Even when screening is completed, lack of training or education in clinicians commonly results in inadequate samples or interpretation.

HPV DNA testing is one of the most accurate screening methods, but comes with considerable financial cost. In comparison to Pap tests alone, HPV co-testing would be more efficient than cytology alone in less developed countries. Co-testing can allow patients to decrease the time interval between screenings to five years rather than three.

In interviews, both residents and medical providers in Costa Rica recognized cervical cancer as a prevalent problem for women. Pap screening was the most commonly used diagnostic test for providers in both urban and rural areas. Even in Boruca, a small rural community in Costa Rica, there were informative infographics and notices for screening with pap tests (Figure 1). Pap test frequency recommendations were consistent with the WHO recommendations in these

communities. While screening was seen to be very prevalent across the country, preventative HPV vaccinations were absent from the required schedules (Figure 2). In regards to more advanced cancer care, it was stated that access to colposcopy and further treatment is not easily accessible. Many patients do not receive care due to the geographical distance to these facilities.

Even without these measures widely available, death rates in Costa Rica remain significantly lower than in other Central American countries such as El Salvador. The main reason for Costa Rica's comparative success is the funding available for universal healthcare. In 1974, Costa Rica implemented a social security program—the Caja Costarricense de Seguro Social (CCSS or Caja)—with the medical services offered by the Ministry of Health.[25] The single-payer model is funded by employers, employees, and the government. Using this method, nearly 90% of the population has access to quality care.[25] Unfortunately, other Central American countries do not have the financial stability to put such a program in motion. As a result, the quality of healthcare and access for patients is inadequate.

In order to reduce the incidence and mortality rate of cervical cancer in all Central American countries, there are options to assist with outreach and access. For example, in 2003 Dr. Sanjeev Arora created Extension for Community Healthcare Outcomes (ECHO®). It has been implemented to improve cancer care by connecting providers in high resource areas with providers in lower resource areas. It is a low cost intervention that allows healthcare professionals to "telementor" in order to share knowledge, guidance, and feedback.[18] The project has been introduced in twelve regions of Central and South America regarding cervical dysplasia. In this way, healthcare providers can become confident and skilled to provide screening cares in their own communities. Higher numbers of properly trained clinicians equates to increased patient care throughout the country.

In addition to the ECHO® educational outreach, there are training programs such as the Central America Gynecologic Oncology Education Program (CONEP). Volunteer gynecologic oncologists travel to Latin America to provide instruction on hands-on screening and treatment methods.[26] While these types of programs are invaluable, it is important to recognize the need for consistency and follow up to ensure the continuity of education.

It is also important to address the cost of services. Patients living in low-income, rural areas are extremely unlikely to seek care if it is unaffordable. Currently, PAHO and the Global Alliance for Vaccines and Immunizations (GAVI) financially supports HPV vaccines at a discounted price.[23] With government or organizational assistance from programs in each individual country, vaccines could be made affordable or free of cost to the general public. In terms of administration, many countries have found success in school-based vaccination programs. This would help to cover nearly all young girls, particularly rural girls who might not otherwise have access to healthcare.

When considering access to secondary prevention measures, adult women also have difficulty finding access to frequent care. It has been suggested that mobile HPV screening programs could help bridge the gap in access to care, but this would require a great deal of planning and support. It is unclear whether these programs would be able to employ enough well-trained staff to make a difference. Some countries around the world have also attempted to introduce HPV testing in the form of self-collection, aiming to decrease stigma and increase participation. While this may be true, the testing itself is still a costly option. Furthermore, if HPV testing is administered without cytology, 15% of invasive cancers can be missed.[23]

Financial burden on both systems and patients is also a large concern for both systems and patients. VIA is already commonly used in low-resource settings due to its low cost,

simplicity, and acceptance. One study found that VIA costs $3,198 per case in comparison to $36,802 with cytologic screening.[27] Given the financial constraints of many Central American countries, this method is likely a leading approach to decrease cervical cancer incidence.

Conclusion

Ultimately, cervical cancer is a preventable disease with many opportunities to diagnose and treat lesions before malignancy occurs. In developed countries with ample resources, prevention and screening programs have decreased rates of incidence and mortality by at least 50%.[8] However, the majority of countries within Central America have ineffective screening programs due to lack of infrastructure and healthcare resources. Therefore, cervical cancer is one of the leading causes of death in women of Central America.

HPV vaccinations are not widely administered, but should be a priority for the prevention of disease in young girls. In terms of access to care, HPV co-testing with cytology is the most accurate method to screen for precancerous and cancerous lesions. However, there are financial and geographic challenges in reaching large populations of women in Central America with this method.

There are several strategies that could help to provide both prevention and screening measures to the masses of people living in urban and rural Central America. Expanding programs such as ECHO® and CONEP can aid in bridging the educational gap. If funding assistance can be procured from various worldwide organizations, the HPV vaccine can be administered at low costs. The vaccination should be targeted towards young girls prior to the onset of sexual activity, ideally in a school-based program.

In order for these programs to succeed, national recognition from the Ministries of Health and governing bodies in Central America are required. Partnerships with health systems across

the globe in combination with new initiatives have the potential to increase HPV vaccination rates, improve access to services, as well as the quality of screening and treatment.

Currently, the most effective method in screening for cervical cancer is HPV co-testing with cytology. However, with the barriers in low-resource areas in Central America, the best option is likely visual inspection by acetic acid (VIA). It is a cost effective, well-recognized strategy that requires little training of the clinician. With time and assistance, Central America will move towards HPV co-testing, but the central focus should be providing accurate screening to as many women in Central America as possible. Early detection and intervention could save countless lives.

References

1. WHO | Cervical cancer. https://www.who.int/cancer/prevention/diagnosis-screening/cervical-cancer/en/. Accessed June 1, 2019.
2. WHO | Human papillomavirus (HPV) and cervical cancer. https://www.who.int/en/news-room/fact-sheets/detail/human-papillomavirus-(hpv)-and-cervical-cancer. Published January 24, 2019. Accessed June 1, 2019.
3. Negrin LGC. Epidemiology of cervical cancer in Latin America. *Ecancermedicalscience.* 2015;9:577. doi:10.3332/ecancer.2015.577
4. Handisurya A, Schellenbacher C, Kirnbauer R. Diseases caused by human papillomaviruses (HPV). *J Dtsch Dermatol Ges.* 2009;7(5):453-66. doi:10.1111/j.1610-0387.2009.06988
5. CDC | HPV Fact Sheet. https://www.cdc.gov/std/hpv/stdfact-hpv.htm. Updated November 16, 2017. Accessed June 3, 2019.
6. FDA | HPV (human papillomavirus). https://www.fda.gov/consumers/women/hpv-human-papillomavirus. Updated May 29, 2019. Accessed June 3, 2019.
7. DeMartel C, Plummer M, Vignat J, et al. Worldwide burden of cancer attributable to HPV by site, country, and HPV type. *Int.J.Cancer.* 2017;141:664-670. doi:10.1002/ijc.30716
8. ACA | What is Cervical Cancer? https://www.cancer.org/cancer/cervical-cancer/about/what-is-cervical-cancer.html. Updated Dec 5, 2016. Accessed June 6, 2019.
9. Schiffman M, Wentzensen N. Human papillomavirus (HPV) infection and the multi-stage carcinogenesis of cervical cancer. *Cancer Epidemiol Biomarkers Prev.* 2013;22(4):553-560. doi:10.1158/1055-9965. EPI-12-1406
10. Khieu M, Butler SL. High Grade Squamous Intraepithelial Lesion (HSIL). *StatPearls*. 2019;1. Available from: https://www.ncbi.nlm.nih.gov/books/NBK430728/.
11. Chrysostomou AC, Stylianou DC, Constantinidou A, et al. Cervical Cancer Screening Programs in Europe: The Transition Towards HPV Vaccination and Population-Based HPV Testing. *Viruses.* 2018;10(12):729. doi10.33390/v10120729
12. WHO | WHO Guidelines for screening and treatment of precancerous lesions for cervical cancer prevention. https://who.int/iris/bitstream/handle/10665/94830/9789241548694_eng.pdf. Accessed June 13, 2019.
13. Drolet M, Benard E, Boily MC, et al. Population-level impact and herd effects following human papillomavirus vaccination programmes: a systematic review and meta-analysis. *Lancet Infect Dis.* 2015;15(5):565-580. doi:10.1016/S1473-3099(14)71073-4
14. CDC | HPV Vaccine Recommendations. https://www.cdc.gov/vaccines/vpd/hpv/hcp/recommendations.html. Updated Dec 15, 2016. Accessed June 16, 2019.

15. WHO | Screening for cervical cancer. https://www.who.int/cancer/detection/cervical_cancer_screening/en/. Updated 2019. Accessed June 16, 2019.
16. CDC | Screening Recommendations and Considerations. https://www.cdc.gov/cancer/knowledge/providereducation/cervical/recommendations.htm. Updated Sep 13, 2018. Accessed June 16, 2019.
17. Campos NG, Tsu V, Jeronimo J, et al. Evidence-based policy choices for efficient and equitable cervical cancer screening programs in low-resource settings. *Cancer Med.* 2017;6(8):2008-2014. doi:10.1002/cam4.1123
18. Lopez MS, Baker ES, Maza M, et al. Cervical cancer prevention and treatment in Latin America. *J Surg Oncol.* 2018;115(5):615-618. doi:10.1002/jso.24544
19. Murillo R, Almonte M, Pereira A, et al. Cervical cancer screening programs in Latin America and the Caribbean. *Vaccine.* 2008;26(11):37-48. doi:10.1016/j.vaccine.2008.06.013
20. Jeronimo J, Holme F, Slavkovsky R, et al. Implementation of HPV testing in Latin America. *Virology.* 2016;76(1):69-73. doi:10.1016/j.jcv.2015.11.035
21. Rodriguez AC, Avila C, Herrero R, et al. Cervical cancer incidence after screening with HPV, cytology and visual methods: 18-year follow up of the Guanacaste cohort. *IJC.* 2017;140:1926-1934. doi:10.1002/ijc.30614
22. Sauvaget C, Fayette JM, Muwonge R, et al. Accuracy of visual inspection with acetic acid for cervical cancer screening. *Int J Gynaecol Obstet.* 2011;113(1):14-24. doi:10.1016/j.ijgo.2010.10.012
23. Bychovsky BL, Ferreyra ME, Strasser-Seippl K, et al. Cervical cancer control in Latin America: A call to action. *Cancer.* 2015;122(4):502-514. doi:10.1002/cncr.29813
24. Blake KD, Ottenbacher AJ, Finney Rutten LJ, et al. Predictors of human papillomavirus awareness and knowledge in 2013: gaps and opportunities for targeted communication strategies. *Am J Prev Med.* 2015;48:402-410. doi:10.1016/j.amepre.2014.10.024
25. Ugalde A, Homedes N. Health and Equity in Latin America. https://www.americasquarterly.org/node/980. Updated October 2009. Accessed July 17, 2019.
26. Schmeler KM, Ramirez PT, Reyes-Martinez CA, et al. The Central America Gynecologic Oncology Education Program (CONEP): improving gynecologic oncology education and training on a global scale. *Gynecol Oncol.* 2013;129:445-447. doi:10.1016/j.ygyno.2013.03.013
27. Perkins RB, Langrish SM, Stern LJ, et al. Impact of patient adherence and test performance on the cost-effectiveness of cervical cancer screening in developing countries: the case of Honduras. *Womens Health Issues.* 2010;20(1):35-42. doi:10.1016/j.whi.2009.09.001

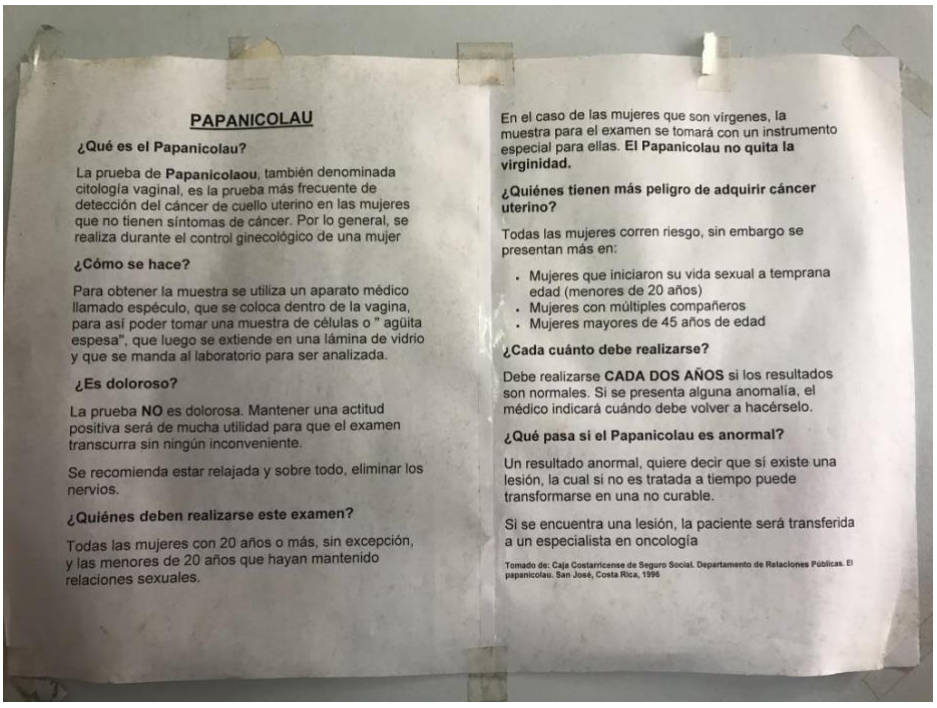
Appendices

Appendix A:

Interview Questions

1. Is the HPV vaccine available at this location?
2. Is the HPV vaccine commonly given?
3. Are there any methods currently in place at this location to screen for cervical cancer? If so, what are they?
4. Do you find that the screening methods are effective?
5. What do you think is the biggest barrier to cancer screening?

Appendix B: Figures



PAPANICOLAU

¿Qué es el Papanicolau?

La prueba de **Papanicolaou**, también denominada citología vaginal, es la prueba más frecuente de detección del cáncer de cuello uterino en las mujeres que no tienen síntomas de cáncer. Por lo general, se realiza durante el control ginecológico de una mujer

¿Cómo se hace?

Para obtener la muestra se utiliza un aparato médico llamado espéculo, que se coloca dentro de la vagina, para así poder tomar una muestra de células o " agüita espesa", que luego se extiende en una lámina de vidrio y que se manda al laboratorio para ser analizada.

¿Es doloroso?

La prueba **NO** es dolorosa. Mantener una actitud positiva será de mucha utilidad para que el examen transcurra sin ningún inconveniente.

Se recomienda estar relajada y sobre todo, eliminar los nervios.

¿Quiénes deben realizarse este examen?

Todas las mujeres con 20 años o más, sin excepción, y las menores de 20 años que hayan mantenido relaciones sexuales.

En el caso de las mujeres que son vírgenes, la muestra para el examen se tomará con un instrumento especial para ellas. **El Papanicolau no quita la virginidad.**

¿Quiénes tienen más peligro de adquirir cáncer uterino?

Todas las mujeres corren riesgo, sin embargo se presentan más en:

- Mujeres que iniciaron su vida sexual a temprana edad (menores de 20 años)
- Mujeres con múltiples compañeros
- Mujeres mayores de 45 años de edad

¿Cada cuánto debe realizarse?

Debe realizarse **CADA DOS AÑOS** si los resultados son normales. Si se presenta alguna anomalía, el médico indicará cuándo debe volver a hacérselo.

¿Qué pasa si el Papanicolau es anormal?

Un resultado anormal, quiere decir que sí existe una lesión, la cual si no es tratada a tiempo puede transformarse en una no curable.

Si se encuentra una lesión, la paciente será transferida a un especialista en oncología

Tomado de: Caja Costarricense de Seguro Social. Departamento de Relaciones Públicas. El papanicolau. San José, Costa Rica, 1996

Figure 1: Papanicolau test information displayed in a small clinic in rural Boruca, Costa Rica.

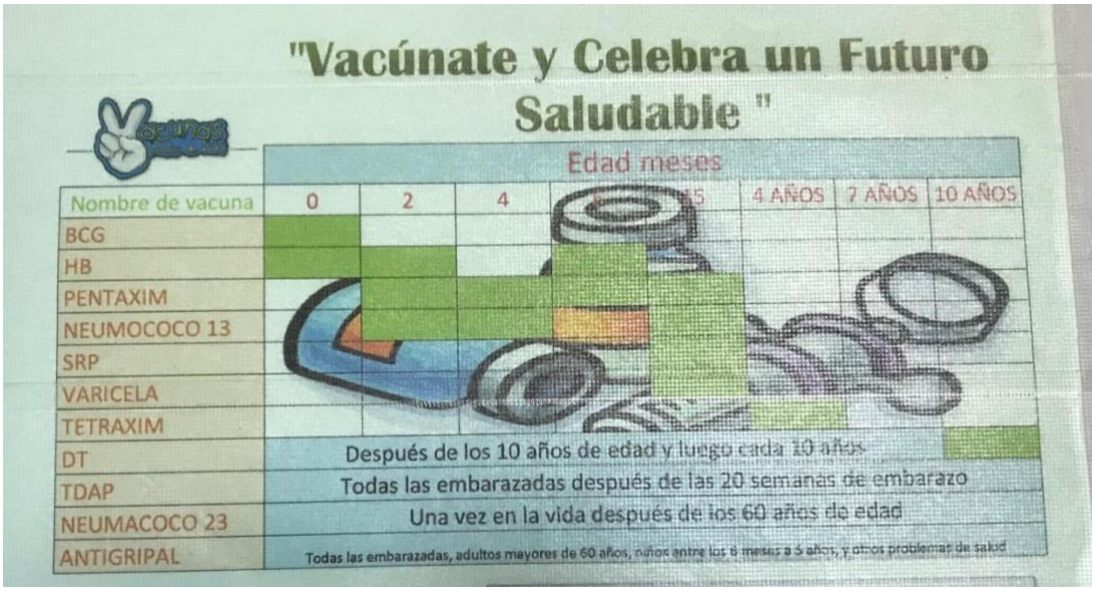


Figure 2: Vaccination schedule displayed in a small clinic in rural Boruca, Costa Rica.

AUGSBURG UNIVERSITY

Augsburg University Institutional Repository Deposit Agreement

By depositing this Content ("Content") in the Augsburg University Institutional Repository known as Idun, I agree that I am solely responsible for any consequences of uploading this Content to Idun and making it publicly available, and I represent and warrant that:

- I am *either* the sole creator or the owner of the copyrights in the Content; or, without obtaining another's permission, I have the right to deposit the Content in an archive such as Idun.
- To the extent that any portions of the Content are not my own creation, they are used with the copyright holder's expressed permission or as permitted by law. Additionally, the Content does not infringe the copyrights or other intellectual property rights of another, nor does the Content violate any laws or another's right of privacy or publicity.
- The Content contains no restricted, private, confidential, or otherwise protected data or information that should not be publicly shared.

I understand that Augsburg University will do its best to provide perpetual access to my Content. To support these efforts, I grant the Board of Regents of Augsburg University, through its library, the following non-exclusive, perpetual, royalty free, worldwide rights and licenses:

- To access, reproduce, distribute and publicly display the Content, in whole or in part, to secure, preserve and make it publicly available
- To make derivative works based upon the Content in order to migrate to other media or formats, or to preserve its public access.

These terms do not transfer ownership of the copyright(s) in the Content. These terms only grant to Augsburg University the limited license outlined above.

Initial one:

_x_ I agree and I wish this Content to be Open Access.

___ I agree, but I wish to restrict access of this Content to the Augsburg University network.

Work (s) to be deposited

Title: Cervical Cancer Screening and Prevention in Central America

Author(s) of Work(s): Madeline Jensen

Depositor's Name (Please Print): Madeline Jensen

Author's Signature: Madeline Jensen Date: 8/26/19

If the Deposit Agreement is executed by the Author's Representative, the Representative shall separately execute the Following representation.

I represent that I am authorized by the Author to execute this Deposit Agreement on the behalf of the Author.

Author's Representative Signature: _____ Date: _____