

Scholarship application. Details below.

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Degree:

PhD

Project Title:

Acceptability of HPV vaccine in Female Sex Workers

Category:

practice

Acceptability of HPV vaccine in Female Sex Workers

Faculty advisor: Neal Halsey

Introduction/Importance:

Persistent human papillomavirus (HPV) infection is found in nearly all 500,000 cases of cervical cancer each year worldwide¹. HPV prevalence in Peru is approximately 17.7%, much higher than the worldwide prevalence of 10.4%, while cervical cancer is the leading cause of cancer death in Peruvian women (17%)^{2,3}. A low proportion of Peruvian women are screened for cervical infections and cancer precursors, because a Pap test is more than one day's pay for a family already in poverty⁴.

Recent studies have shown HPV vaccines to be effective in decreasing the burden of cervical cancer precursor incidence among women in the general population. HPV vaccine is currently approved for use in Peru, but with the current cost of \$375 for 3 doses, it is not possible for the majority of women to receive this life saving medicine. In addition, studies have not included women of higher age and experience, mainly due to opinions of prior exposure. The FDA is considering increasing the recommended oldest age of HPV vaccination from 26 to 49 years, because data show that women who are older and HPV exposed, even with one of the four vaccine subtypes may also benefit from this vaccine. HPV types 16, 18 are present in 20% of HPV infections, and it is unlikely that women would be exposed to both of these cancer causing subtypes protected with vaccine^{5,6}. In fact, infection with both subtypes in a sexually active female college student population in Lima, Peru was only 0.3%, showing promise for our study (new results). While it may not be financially possible to vaccinate all women in Lima, a focus on high risk populations may be achievable.

Female sex workers (FSWs) are at higher risk of HPV infection and cervical cancer due to multiple partners in their occupation and the resulting exposure to multiple HPV types^{7,8}. Compared to women in the general population, HPV prevalence in FSWs was found to be approximately 14.4%-75% in several studies^{8,9}. Registered FSWs in Peru undergo sexually transmitted infection (STI) testing at clinics every 3 months, making completion of a modified HPV vaccine schedule at this time more feasible¹⁰.

Methods:

The primary objectives of the research are to determine the acceptance and potential for the effective use of HPV vaccine in FSWs of different ages. We will also be obtaining data on HPV prevalence in this population, which is lacking in the academic literature. As a result, this is a public health practice project. To accomplish these objectives, we will employ two different study designs:

- 1. A cross-sectional study of HPV prevalence and cervical infection in female sex workers*
- 2. A prospective open label randomized trial of the acceptance of HPV vaccine at different schedules.*

This study will take place in Lima, Peru at the non-governmental organization Via Libre over the course of 11 months. We estimate 250 women will be screened and 200 women will be included in the protocol. At baseline, HPV prevalence and cytology will be measured among participating females attending Via Libre with a physician administered Pap smear and collection of serum antibody. Correlation of HPV infection with history of sexual partners will be examined. Participants will be randomized to receive HPV vaccine according to the standard schedule (0, 2, 6 months) or the modified schedule (0, 3, 6 months) which matches their required STI testing visits at the clinic. The vaccine will be provided at no charge to study participants. Antibody to HPV types 6, 11, 16 and 18 will be measured among FSWs at baseline and one month after the third dose (month seven). A behavioral survey will be administered at baseline and follow-up to collect information on awareness of HPV, and other relevant information.

Work in this project will be overseen by Professor Neal Halsey, with whom I have received partial funding through Merck pharmaceuticals. The IRB application is complete and we are preparing to begin the project in late April. We are currently working on the application to the Peruvian NIH. In preparation for the trial,

we recently completed a baseline survey of 319 women on acceptability of HPV vaccine and barriers to acceptance. We will soon submit results of this study to Sexually Transmitted Infections.

Significance:

This trial includes several novel innovations. This will be the first trial which studies the immune response of a licensed HPV vaccine in female sex workers. It will also explore the acceptability of the three dose regimen in this population, while examining the benefit of employing a schedule more suitable for FSWs in Peru.

Participants in our study will be offered a Pap smear at baseline. For many women this will be their first and only exam in their lifetime. Systematic screening for abnormal cervical cells has been shown to be cost effective compared to treating cancer cases, and efficient in reducing death rates from cervical cancer by 70% or more¹¹. Women with any abnormal cytology will be referred to an OB/GYN on site, and peer health educators will be available for necessary counseling. Women will have blood analyzed for high cervical cancer risk HPV infection on two occasions.

As the subtypes protected by HPV vaccine are found among approximately 60% of women with cervical cancer cases in Latin America, and FSWs are a high risk population, the burden of cervical cancer may be substantially decreased through early and widespread vaccination efforts this study population. Vaccination may not only help prevent cervical cancer in the FSWs, but it would help prevent infection by subtypes 16 and 18 to other sex partners of men who frequent brothels in Lima for sex work. Benefits may include protecting wives, girlfriends and significant others from chronic HPV infection, genital warts, and cervical cancer. FSWs as a group may benefit from the modified (0, 3, 6 months) schedule due to their mandatory presentation to STI clinics every 3 months. Our study will help determine the practicality of HPV vaccination in FSWs as well as evaluate the effectiveness of administering HPV vaccine at the more convenient schedule.

In summary, this study will help increase HPV awareness among FSWs, provide already globally recommended cervical screening, as well as provide potential evidence for worldwide early vaccination of female sex workers to prevent cervical cancer in this high risk population. Mathematical modeling has shown that high vaccination coverage over many decades can decrease type specific cervical cancer incidence by as much as 91%¹². We hope to make a contribution to reaching this goal.

ITEMIZED BUDGET PLAN

Funding received from the Delta Omega Scholarship will be used to purchase crucial items which are necessary to undertake our study but not covered by other funding sources. We will purchase 200 pregnancy tests (and relevant collection materials) to ensure that women meet our inclusion criteria and are able to receive the study vaccine. Study information cards will be created to give potential participants information about the study including the location of the study site. Outreach materials will be purchased to ensure our participants don't forget to return for additional visits. Funds will also be used to pay for the hefty registration of this study with the Peruvian NIH, which is a requirement for clinical trials being conducted in Peru. In total, we are applying for \$1000. The following is a brief breakdown of these funds:

200 pregnancy tests	\$310
Study information cards	\$50
Outreach materials to ensure retention	\$100
Registration fee for clinical trial with Peruvian NIH	\$540
Total Amount	\$1000

Additional funding sources include:

*Merck Pharmaceuticals-vaccine provision and HPV testing grant

*Training Grant in International Maternal and Child Health (T32 HD046405)-tuition and living stipend

References

- ¹ IARC, Monographs on the evaluation of carcinogenic risks to humans: human papillomaviruses. 2005, Vol 90: Lyon: International Agency for Research on Cancer.
- ² de Sanjose S, Diaz M., Castellsague X, et al. Worldwide prevalence and genotype distribution of cervical human papillomavirus DNA in women with normal cytology: a meta-analysis. *Lancet Infectious Diseases*, 2007;7(7): 453-9.
- ³ Ferlay J, Bray F, Pisani P, et al. GLOBOCAN 2002: Cancer Incidence, Mortality and Prevalence Worldwide [database online]. IARC CancerBase No. 5. version 2.0, IARCPress, Lyon, 2004.
- ⁴ Jeronimo J, Morales O, Horna J, et al. Visual inspection with acetic acid for cervical cancer screening outside of low-resource settings. *Pan American Journal of Public Health*, 2005; 17(1): 1-5.
- ⁵ Santos, C., Munoz, N., Klug, S., et al. HPV types and cofactors causing cervical cancer in Peru. *British Journal of Cancer*, 2001. 85(7): p. 966-71.
- ⁶ Clifford, G., Gallus, S., Herrero, R., et al. Worldwide distribution of human papillomavirus types in cytologically normal women in the International Agency for Research on Cancer HPV prevalence surveys: a pooled analysis. *Lancet*, 2005. 366(9490): p. 991-8.
- ⁷ Calhoun B. Feasibility of a Community-based Voluntary HIV Counseling and Testing Program in Commercial Sex Venues in Lima, Peru, in Third Annual Poster Presentation at Puget Sound Partners for Global Health Lecture, 2005: Puget Sound, Washington.
- ⁸ Mak R, Renterghem LV, Cuvelier C. Cervical smears and human papillomavirus typing in sex workers. *Sexually Transmitted Infections*, 2007; 80: 118-120.
- ⁹ Juarez-Figueroa L, Wheeler CM, Uribe-Salas FJ, et al. Human papillomavirus: a highly prevalent sexually transmitted disease agent among female sex workers from Mexico City. *Sexually Transmitted Diseases*, 2001; 28(3): 125-130.
- ¹⁰ Peru: Country Report on Human Rights Practices. [Government human rights website]. 2005. Available at: <http://www.state.gov/g/drl/rls/hrrpt/2005/61738.htm>. Accessed January 20, 2007.
- ¹¹ Kitchener HC, Castle PE, and Cox JT. Chapter 7: Achievements and limitations of cervical cytology screening. *Vaccine*, 2006; 24(S3): 63-70.
- ¹² Barnabas, R., Laukkanen, P., Koskela, P., et al. Epidemiology of HPV 16 and cervical cancer in Finland and the potential impact of vaccination: mathematical modelling analyses. *PLOS Medicine*, 2006. 3(5): p. e138.