HPV VACCINATION ACCEPTABILITY AMONG IMMIGRANT AND ETHNIC MINORITIES IN THE UNITED STATES: SYSTEMATIC REVIEW

CERVICAL INTRAEPITHELIAL NEOPLASIA AND HPV VACCINATION WITHIN IMMIGRANT AND REFUGEE COMMUNITIES IN THE U.S.: COMPREHENSIVE REVIEW

A thesis submitted to the University of Arizona College of Medicine – Phoenix in partial fulfillment of the requirements for the degree of Doctor of Medicine

Bita Zahedi
Class of 2017

Mentor: Crista Johnson-Agbakwu, MD
Dedication

I would like to dedicate this work to my parents- Jila Zamanian and Dadras Zahedi for their unconditional love and support and believing in my dream of improving health care for all including the marginalized.
Acknowledgements

I would like to sincerely thank Dr. Crista Johnson for her mentorship and guidance in this project. I would also like to thank Dr. Mathew McEchron for his continuous support. Thank you for all your help and instruction, and allowing me to be a part of this research.
Chapter 1........................................................................................................................................pp 1-21
HPV Vaccination Acceptability Among Immigrant and Ethnic Minorities in the United States: Systematic Review

Chapter 2........................................................................................................................................ p22-35
Cervical Intraepithelial Neoplasia and HPV Vaccination within Immigrant and Refugee Communities in the U.S.: Comprehensive Review
Abstract

Objective. To systematically review all studies examining HPV vaccination acceptability among immigrant and ethnic minority parents and eligible individuals for cervical cancer prevention in the United States.

Materials and Methods. MEDLINE/PubMed, Cumulative Index to Nursing and Allied Health Literature, EMBASE, and Cochrane database searches were conducted searching for English language, US-based studies to examine immigrant and ethnic minority population’s acceptability of HPV vaccination. Thirteen of more than 3,098 potentially relevant articles were included in the final analysis.

Results. Latinos were statistically more likely to accept vaccination for both their daughters and sons. Foreign-born adult Latinas were more accepting of the vaccine than U.S.-born Latinas after controlling for other variables. Overall African American and Asian American parents were less likely to accept HPV vaccination for their daughters than Hispanic and White parents. Of the African American parents who intended to vaccinate their children the majority were significantly non-Baptist and had higher levels of education. The majority of Haitian immigrants intended to vaccinate daughters and the rest agreed that they would most likely have their daughters vaccinated if their daughters’ physicians recommended it.

Conclusion. More research is needed, particularly in the context of health care provider HPV vaccination recommendation to immigrant and ethnic-minority populations. Acceptance figures so far suggest that the vaccine is generally well received among Hispanic/Latin and Haitian immigrants, but details of ethnic variations among these groups and a qualitative understanding of lower rates of acceptability among African American and Asian American communities are still being awaited.
**Table of Contents:**

Introduction and Significance ................................................................. 8
Materials and Methods .............................................................................. 12
Results ........................................................................................................ 14
Discussion ................................................................................................... 20
Conclusions ................................................................................................. 23
References ................................................................................................... 24
Lists of Figures and Tables:

Figure 1 ................................................................................................................................. 13
Table 1 ...................................................................................................................................... 16
**Introduction and Significance:**

Invasive cervical cancer (ICC) remains a costly public health problem worldwide. In 2012, there were 12,900 new cases and 4,100 deaths due to the disease worldwide. ¹ Incidence and mortality rates declined by more than 75% since 1940, a decrease attributed to introduction and acceptance of ICC screening with cervical cytology (Pap) and treatment of precancerous lesions. With these advancements 84% of the burden of ICC cases remain in developing countries. Despite widespread availability of pap testing, disparities in cervical cancer incidence and mortality rates by race within the United States persist. African American women have the highest mortality rates of the disease and Hispanics have the highest incidence.²,³

A systematic review by Johnson in 2008 examined the sociocultural factors influencing cervical cancer screening among immigrant and ethnic minorities in the U.S. along the theoretical framework of the Health Belief Model and found commonly held beliefs across several immigrant and refugee populations that may deter them from seeking these interventions. Such beliefs include: fatalistic attitudes, lack of knowledge about cervical cancer, fear of Pap smears threatening one’s virginity, as well as beliefs that a Pap smear is only necessary if one is ill. Beliefs unique to specific cultural groups include: body-focused notions of childbirth, menses, sex and stress playing a role in one’s susceptibility to cancer for Hispanics; administrative processes in health care being a barrier to screening among African-Americans, and misconceptions of one’s susceptibility to cancer and stigmatization imposed by their community and providers among Asian-Americans.⁴

Human papillomavirus (HPV), a sexually transmitted infection, is related to almost 100% of cervical cancer cases with two strains, 16 and 18, accounting for approximately 70% of cervical cancer cases.⁵,⁶ In 2006, the first vaccine was approved by the U.S. Federal Drug Commission to prevent the spread of HPV. Currently, there are three HPV vaccines available in the U.S., varying slightly in protection, cost and target population. Gardasil®, produced by Merck, prevents infection of four strains of HPV: 6, 11, 16, and 18 and was approved by the FDA in 2006 for use in males and females ages 9-26. In December 2014, Gardasil® 9 was approved by the FDA, which protects against 9 strains of HPV: the four strains approved in the previous Gardasil vaccine, as well as 31, 33, 45, 52, and 58. ⁷ GlaxoSmithKline’s vaccine, Cervarix®, was
approved by the FDA in 2009 and protects against HPV strains 16 and 18. Cervarix® can only be administered to females and has been approved for females ages 10-25. 8,9

The current recommendation by the federal Advisory Committee on Immunization Practices (ACIP) is for all girls and boys get vaccinated at age 11 or 12, and that girls and women ages 13-26 and boys and men ages 13-21 be given a “catch-up” vaccination.10,11 The vaccine is recommended for use in men ages 22-26 if they have not been previously vaccinated, are immunocompromised, or engage in sexual activity with other men. ACIP recommended the vaccine for females in 2006 and added the recommendation for males in 2011. ACIP recommended the new HPV vaccine in February 2015 for females ages 9-26 and boys ages 9-15. Off label use for the new vaccine for males ages 16-21 is allowed, and a recommendation for this age group is expected to follow in the coming years.

HPV vaccination alone with 70% coverage of the target population (girls between 9 and 12) is expected to reduce the lifetime risk of cancer by 43%. At coverage rates of 100% the expected cancer reduction with vaccination alone would be as high as 61%. 12 The most important factors affecting the predicted coverage level include the cost, accessibility, and vaccinating girls prior to sexual activity. The decision to introduce new public health interventions to improve greater access to HPV vaccination must take into consideration multiple factors including the disease burden, effectiveness of the intervention, the financial costs required to initiate and sustain the program, the cost-effectiveness of the intervention, the programmatic capacity and infrastructure necessary to successfully deliver the intervention, and the likelihood of cultural acceptability, political will and public sector support.12 General estimates approximate the cost of each vaccination dose at $5 per preadolescent individual. Considering the cost effectiveness and wide availability of the vaccine in the U.S., the limiting factor remains proper education regarding vaccination and its cultural acceptance.

Prevalence of HPV has decreased significantly since the vaccine was made available, falling from 11.5% to 5.1% among girls ages 14-19 between 2003-2006 and 2007-2010. 13 Though awareness of the importance of HPV vaccine has grown, uptake and completion have been increasing slowly. Approximately four in ten (39.7%) adolescent girls aged 13-17 received all three doses of the vaccine in 2014 up from 37.6% in 2013.14 Furthermore women’s
perception that male vaccination is not as necessary has lead to lower acceptance of HPV vaccination among young boys attributing to the lower rates of vaccination completion among teen boys, which was 21.6% in 2014. Despite initiatives to educate about HPV infection and the link to cervical cancer, and mandates by some states, HPV vaccine lags behind other adolescent vaccines. In 2010, 91.6% of adolescents received 3 recommended doses of Hepatitis B vaccine, whereas only 32% of adolescent females received 3 recommended doses of HPV vaccine. 

Numerous barriers impeding HPV vaccine uptake have been identified. Among common individual barriers include perceived cost, safety, and the notion that vaccination is unnecessary if not sexually active. Parental knowledge, attitudes, and beliefs about the vaccine also influence uptake. Previous studies have shown that higher HPV literacy, such as knowledge about the disease and how it can be prevented, increases the likelihood of getting vaccinated. However a longitudinal cohort study of 360 predominantly African-American participants demonstrated that higher levels for knowledge was not associated with increase in likelihood to obtain vaccination for themselves or their daughters. Institutional/structural factors that influence vaccine initiation include cultural/linguistic differences, lack of health care access, and lack of physician recommendation. Among minority populations, language difficulties and navigating a complex health care system pose considerable challenges to vaccination. Poor access to health care services also negatively impacts vaccine uptake. Two studies indicate that physician recommendation of HPV vaccine is a key factor in vaccine initiation. A number of studies that examined pediatricians, family practice physicians and internists found that the majority of providers serving the highest risk populations for HPV infection and HPV-related cancers are not routinely recommending the HPV vaccine for their patients.

Though previous systematic reviews have examined HPV vaccine acceptability, none has focused on populations at greater risk namely immigrants and refugees as well as ethnic minorities. Given the high burden of invasive cervical cancer among immigrant and ethnic minority populations in the U.S. and sociocultural specific barriers to screening, HPV vaccination can be a promising strategy for the prevention of cervical cancer. The objective of this paper is
to systematically review U.S. based studies that examine HPV vaccination acceptability among immigrant and ethnic minority parents and eligible individuals for cervical cancer prevention in order to enhance our understanding of barriers specific to this group and focus on initiatives that address these issues, and reduce disparities in HPV vaccination, HPV infection and invasive cervical cancer.
**Materials and Methods**

We conducted a systematic review of the English-language literature to examine HPV vaccination acceptance attitudes and beliefs among immigrant and ethnic minorities in the United States. Articles from January 2007 to January 2017 in the following electronic databases were searched: MEDLINE/PubMed, Cumulative Index to Nursing and Allied Health Literature (CINAHL), EMBASE and Cochrane. A combination of the following keywords/phrases was used: “HPV vaccination”, “Papillomavirus Vaccine”, “U.S. immigrant population”, “immigrants”, “attitudes and beliefs” and “socio-cultural factors”. The initial search identified 3,098 relevant abstracts. Non-English, non-US-based studies and duplicates were excluded, along with reviews, letters and books. Peer-reviewed journal articles were included if they presented original research, examined knowledge, attitudes or acceptability related to HPV vaccination in parents or eligible individuals. Author names of relevant articles were searched in MEDLINE and PubMed for any related works on the same subject, which produced an additional 24 articles. Cross-checking of references with a reference librarian identified an additional 30 articles, leading to a total of 363 relevant abstracts and full-text articles. These studies were initially reviewed, followed by subsequent exclusion of 272 articles that did not meet strict inclusion criteria. Subsequently 91 full-text articles were reviewed in depth, which led to the exclusion of 78 articles that did not address acceptability and/or provide relevant data with respect to ethnicity or race, leading to a total of 13 articles, which were included for the final analysis.

All quantitative and qualitative study designs were examined, including focus groups, interviews, and mail/telephone surveys. The inclusion criteria included the following: English language, U.S.-based studies of sociocultural factors influencing HPV vaccination acceptability and knowledge across immigrant and ethnic minority populations: Hispanic/Latino (Mexican, Central and South American, Puerto Rican), African-American, Haitian immigrants, African Caribbean, and Asian. Study subjects included parents of eligible sons and daughters or adolescents or the general population that would be eligible for vaccination. The Newcastle-Ottawa quality assessment scale was used to determine the appropriateness of the studies and determine their quality by assessing each article’s selection, comparability and exposure; thereby resulting in 13 studies included in the final analysis. 3
Inclusion Criteria:
English, US Studies, Immigrant Populations, Ethnic Minorities, HPV Vaccination, Examination of Acceptability, Attitudes and Beliefs

Figure 1- Study eligibility Flow Diagram
Results

Thirteen U.S. based studies examined the acceptability of HPV vaccination with respect to the ethnicity and/or foreign-born status of subjects. To determine acceptability all studies exclude those who have already been vaccinated. The thirteen studies ascertained acceptability among 6,772 individuals- 4,532 parents and 2,240 adolescents within the following ethnic groups: Hispanic/Latin (9), African-American (8), White (5), Haitian immigrant (3) and Asian (2). Acceptability as an outcome was measured by intention to vaccinate, interest to vaccinate or agreement to vaccinate. Though some of the studies also determined knowledge level and barriers to initiating and completing the HPV vaccine series, this data was excluded to focus on the specific aims of this paper in order to devote attention to the attitudes and beliefs regarding acceptance of the HPV vaccine.

Four studies were conducted as an interview, and nine as surveys, taking into consideration the preferred language of communication for the participants. Eight studies examined parents’ attitude and beliefs, the majority of which were female parents, while four examined eligible young adolescents. One study included both parents and adolescent populations. Eight articles reviewed the acceptability of HPV vaccination for women, one focused on HPV vaccination for heterosexual men only, and four studies examined acceptability for both sexes. One study examined acceptability among foreign- born vs. U.S. born ethnic minorities and another study compared acceptability among Haitian immigrants vs. African-Americans. These results are displayed in table 1. 

The main study findings are that greater vaccine interest was observed among sexually active women, women with multiple sexual partners, and women who felt vulnerable to HPV infection irrespective of race. Knowledge about HPV and its association with cervical cancer were significantly associated with interest in getting the HPV vaccine. Findings also indicate that information regarding the severity of disease and the efficacy of the vaccine should be included in educational materials.

Ethnicity related findings display that the majority of parents/guardians were receptive toward vaccinating their sons against HPV. Systematic comparison by race/ethnicity revealed no differences in parents'/guardians’ views toward vaccinating their children. Despite low knowledge throughout all ethnic groups, the majority reported high levels of trust in physicians
and were willing to vaccinate if recommended by their physicians. 38 Misinformation about HPV was common and was associated with intention to get vaccinated among non-Hispanic white adolescents. 42 This study also found a relatively small proportion of unvaccinated Hispanic and non-Hispanic young adults intended to be vaccinated for HPV.

Data specific to the Hispanic/Latin population demonstrates that the majority of Hispanic/Latino parents accept STI vaccines for their adolescent children. 34, 21 Latinos were statistically more likely to accept vaccination for both their daughters and sons. 45 Interventions designed for Hispanics may be more effective if norms, rather than attitudes, are targeted. 39 Foreign-born adult Latinas were more accepting of the vaccine than U.S.-born Latinas after controlling for other variables. United States-born status was not associated with mothers’ vaccine acceptance for their daughters. 35

Overall African-American and Asian-American parents were less likely to accept HPV vaccination for their daughters than Hispanic and White parents. 21 Of the African-American parents who intended to vaccinate their children the majority were significantly non-Baptist and had higher levels of education. 44 Most African-Americans felt that vaccination fell within the parental role; whereas many Haitians felt uncomfortable vaccinating against STI because they felt children should not be having sex. The majority of African-American and Haitian immigrant parents intended to vaccinate their daughters. 37 Furthermore, the majority of Haitian mothers agreed that they would most likely have their daughters vaccinated if their daughters’ physicians recommended it. 43
Table 1- Summary of quantitative studies that have assessed ethnic differences in acceptability of HPV vaccination in the U.S.

<table>
<thead>
<tr>
<th>Article</th>
<th>Study Design</th>
<th>Study Population/ Demographic Characteristics</th>
<th>Ethnic BreakDown</th>
<th>Outcomes</th>
<th>Main Ethnicity Related Finding</th>
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</thead>
<tbody>
<tr>
<td>Bair et al. (2008)</td>
<td>Interview</td>
<td>Parents (90% female) (N=119)</td>
<td>Hispanics Only - 81% Mexican 16% central and S. American 3% Puerto Rican</td>
<td>Acceptability- Mean score of 85.6% on a scale of 0-100</td>
<td>Majority of Latino parents accept STI vaccines for their adolescent children. Findings indicate that information regarding the severity of disease and the efficacy of the vaccine should be included in the educational materials.</td>
</tr>
<tr>
<td>Barnack-Tavlaris et al. (2014)</td>
<td>Interview</td>
<td>US. Born and FB women ages 18-27 (N=1672) Mothers of vaccine-eligible girls (N=2994)</td>
<td>74.6% US born Mothers: 66.9% US born</td>
<td>Acceptability- Interest in getting the HPV vaccine Ages 18-27: Excluding 9.9% already vaccinated, 56.9% of women reported interest Mothers: excluding 16.6% whose daughters had received the vaccine, 57.6% reported interest</td>
<td>Foreign-born young adult Latinas were more accepting of the vaccine than U.S.-born Latinas after controlling for other variables. United States-born status was not associated with mothers’ vaccine acceptance for their daughters.</td>
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<tr>
<td>Study</td>
<td>Methodology</td>
<td>Participants</td>
<td>Acceptability</td>
<td>Notes</td>
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<td>Constantine et al. (2007)</td>
<td>Telephone Survey</td>
<td>Parents of eligible daughters (N=522)</td>
<td>White 40.5%</td>
<td>Hispanic Overall 75% would be willing to vaccinate a daughter &gt;13</td>
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<td>Hispanic 38.2%</td>
<td>Asian 7.7% AA 6.9%</td>
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<td>Hispanic parents were more likely to accept vaccination than were non-Hispanic parents, whereas AA and Asian-American parents were less likely</td>
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<td>Gerend et al. (2007)</td>
<td>Survey</td>
<td>Female university students ages 18-26 (N= 60)</td>
<td>AA 57%</td>
<td>Acceptability - 65% interested in receiving HPV vaccine</td>
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<td></td>
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<td></td>
<td>White 32%</td>
<td>Biracial 5% Asian 3% Latin 3%</td>
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<td></td>
<td>Greater vaccine interest observed among sexually active women, women with multiple sexual partners, and women who felt vulnerable to HPV infection irrespective of race</td>
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<td>Joseph et al. (2012)</td>
<td>Survey</td>
<td>Mothers of eligible girls (N=70)</td>
<td>Haitian 73%</td>
<td>Acceptability - 63% of AA and 75% of Haitians intended to vaccinate</td>
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<td>AA 27%</td>
<td>daughter</td>
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<td>Most African-Americans felt that vaccination fell within the parental role; whereas many Haitians felt uncomfortable vaccinating against STI because they felt children should not be having sex. Majority of both ethnic groups intended to vaccinate daughters.</td>
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<tr>
<td>Joseph et al. (2014)</td>
<td>Interview</td>
<td>Females ages 18-22 (N=132)</td>
<td>Haitian 36%</td>
<td>Acceptability - Intent to vaccinate 89% of AA 87% of Haitian 95% of</td>
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<td>AA 34%</td>
<td>Latina 15% White 15%</td>
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<td>Interventions designed for Hispanics may be more effective if norms, rather than attitudes, are targeted.</td>
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<td>95% of Latinas 95% of White</td>
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<td>Lechuga et al. (2011)</td>
<td>Survey</td>
<td>Mothers with eligible daughters (N=146)</td>
<td>AA 34%</td>
<td>Acceptability - Intent to vaccinate 50% of AA 55% of Hispanic 70% of</td>
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<td></td>
<td></td>
<td></td>
<td>Hispanic 34%</td>
<td>White 32%</td>
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<td>Interventions designed for Hispanics may be more effective if norms, rather than attitudes, are targeted.</td>
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<td>Study</td>
<td>Method</td>
<td>Sample Description</td>
<td>Acceptability</td>
<td>Acceptability Details</td>
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<tr>
<td>Perkins et al. (2013)</td>
<td>Interview</td>
<td>Parents/guardians of sons (N=120)</td>
<td>Acceptability</td>
<td>75% accept HPV vaccine for their sons across all racial/ethnic groups</td>
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<td>Majority of parents/guardians were receptive toward vaccinating their sons against HPV; systematic comparison by race/ethnicity revealed no differences in parents’/guardians’ views toward vaccinating their own children</td>
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<tr>
<td>Read et al. (2010)</td>
<td>Survey</td>
<td>Females aged 13-21 (N=174)</td>
<td>Acceptability</td>
<td>Interest in HPV vaccination</td>
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<td></td>
<td>34.6% of AA 54.1% of African Caribbean 64.7% Hispanic</td>
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<td>The level of acceptance of the HPV vaccine was overall lower than what has been reported among other racial/ethnic populations. Knowledge about HPV and its association with Cervical cancer were significantly associated with interest in getting the HPV vaccine.</td>
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<tr>
<td>Schmotzer et al. (2013)</td>
<td>Survey</td>
<td>Nursing college students (female and male) in the US-Mexico border region (N= 202) [34 male, 168 female]</td>
<td>Acceptability</td>
<td>Excluding 28.9% who had received the HPV vaccine, 22.8% had the intention to receive the vaccine</td>
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<td>Misinformation about HPV was common and was associated with intention to get vaccinated among non-Hispanic white students. Study found a relatively small proportion of unvaccinated Hispanic and non-Hispanic nursing students intend to be vaccinated for HPV</td>
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<tr>
<td>Study (Year)</td>
<td>Method</td>
<td>Sample Description</td>
<td>Sample Characteristics</td>
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<td>Stephens et al. (2013)</td>
<td>Survey</td>
<td>Low Income, urban mothers with eligible daughters (N=31)</td>
<td>All Haitian</td>
<td>The majority of mothers (68%) agreed that they would most likely have their daughters vaccinated if their daughters’ physicians recommended it</td>
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<tr>
<td>Thomas et al. (2012)</td>
<td>Survey</td>
<td>Rural parents with children (male or female) in elementary/middle school ages 9-13 (N=400)</td>
<td>All African-American Children gender: Female- 76.5% Male- 23.5%</td>
<td>Acceptability - Intend to vaccinate child with HPV vaccine: Male- 25.8% Female- 27.8%</td>
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<tr>
<td>Watts et al. (2009)</td>
<td>Survey</td>
<td>Mothers of eligible daughters and/or sons (N= 130)</td>
<td>Latina 60% Child gender: Male 46.5% Female 44.2% Non-Latina 40% Child gender: Male 17.7% Female 17.7%</td>
<td>Acceptability - Agreement to vaccinate child Latina-Child gender: Male 92.3% Female 97% Non Latina-Child gender: Male 76.9% Female 68.2%</td>
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Abbreviations: STI= sexually transmitted infections; FB= foreign-born; HPV= human papillomavirus; AA= African-American
Discussion

Despite lower awareness and knowledge of HPV infection and prevention among Hispanic/Latino communities, this population and Haitian immigrants have a higher acceptance rate than that of African American and Asian American communities. Foreign-born Latinos are more accepting of HPV vaccination than their U.S-born Latino counterparts. Despite, low knowledge throughout all ethnic groups, majority reported high levels of trust in physicians and were willing to vaccinate if recommended by their physicians.

This systematic review offers a unique perspective on HPV vaccination acceptability among ethnic minorities and immigrants in the United States. The most recent U.S.-based systematic review of HPV vaccine acceptability found that very few studies had Latina research participants, or women from rural areas, low-income and low-education categories. Interventions that aim to increase the rates of HPV vaccination need to specially take into consideration these segments of the population, as disparities in cervical cancer screening continue to exist among underserved immigrant and ethnic minority communities. Furthermore, sociocultural beliefs unique to each ethnic group further limit these communities from screening and early treatment.

Many studies that investigate HPV vaccination rates focus on participants’ knowledge level and its effects on adherence. A multitude of studies have shown that higher HPV literacy, such as knowledge about the disease and how it can be prevented, increases the likelihood of getting vaccinated. Other studies have shown that those with higher levels of knowledge were not more likely to obtain vaccination for themselves or their children. Similar to the latter, in the studies that were reviewed for the specific aim of this paper, Hispanics who have been found to have lower awareness and knowledge of HPV proved to accept HPV vaccination at higher rates than other ethnic groups. Furthermore, since there is no strong evidence to recommend any specific educational intervention for widespread implementation, it is crucial to determine the barriers for this population’s uptake and completion of HPV vaccine series.

Among racial/ethnic minorities, when comparing the foreign-born to U.S. born, and controlling for personal characteristics such as gender and health insurance coverage, the foreign-born initiate HPV vaccination at lower rates than their U.S. born counterparts.
Individuals of African descent, regardless of country of origin, also had lower rates of HPV vaccine initiation compared to U.S. born Whites. In this study factors associated with higher HPV vaccine uptake included college education, which lends support to the notion that lack of education may be a barrier to HPV vaccination. Lack of health insurance coverage and lack of a usual place to seek care were also associated with lower rates of uptake. Thus, nuances emerge when one considers foreign-born status, socioeconomic status and education. Moreover, the concept of preventative health care is not embedded in norms of well-being which may play a significant role in persistent disparities in HPV vaccination among foreign-born individuals.  

Irrespective of patient demographics, high-quality recommendations by health care providers are strongly associated with HPV vaccination behavior. However only about one-third of parents receive such recommendations. 49 Without physician endorsement, even mothers who had a strong conviction to immunize become confused or skeptical about the HPV vaccine and delay immunization. In a study conducted by Hamlish in 2012, four out of five instances of such delay resulted in a missed opportunity to vaccinate, even when the daughters were sexually active and were using birth control. Similarly, multivariable logistic modeling of data from the (NIS)-Teen for 2008-2012 demonstrates that health care providers making a clear, unambiguous recommendation; irrespective of individual demographic factors, is strongly associated with HPV vaccination behavior. 51, 52 Furthermore, racial/ethnic minorities, low-income and immigrant patient populations are less likely to receive a recommendation on HPV vaccination. 53 A recent study by Burdette demonstrates that racial and ethnic disparities in provider recommendations and HPV vaccinations have waned over time among males and females though there is still greater room for improvement. 54

There were a number of limitations in this systematic review, the primary of which being the heterogeneity across subpopulations and ethnic minority groups. There were also a greater number of studies examining Hispanic/Latin and African-American minorities with only two studies considering Asian immigrants and none considering Native American, Middle Eastern, and African populations. Furthermore there were variations among immigrants, with some groups displaying greater acculturation than others.
Despite the heterogeneity across populations, this systematic review does not support the hypothesis that ethnic minorities are less accepting of HPV vaccination. Studies to date conclude that while Hispanic/Latino communities as well as Haitian immigrants have high acceptability rates of HPV vaccination, African-American and Asians have lower acceptability rates. Given, the lower rates of HPV vaccination recommendation provided by health care professionals to these groups specifically, there is a need for more research that explores barriers to health care providers recommending HPV vaccines to immigrant and ethnic minorities.
Conclusion

We know relatively little about HPV acceptability among sub-groups of ethnic minorities and immigrants in the United States. Findings seem to suggest that despite lower awareness and knowledge of HPV infection and prevention, Hispanic/Latino communities and Haitian immigrants have a higher acceptance rate than African-American and Asian-American communities. Furthermore, foreign-born Latino adolescents are more accepting of HPV vaccination than their U.S-born Latino counterparts. Furthermore, despite low knowledge throughout all ethnic groups, the majority reported high levels of trust in physicians and were willing to vaccinate if recommended by their physicians. The majority of these studies examined ethnicity as just one of many factors, limiting the ethnic sub-populations and a more in depth understanding of the role of ethnicity in acceptance of HPV vaccination. It is important to include ethnic minorities in cancer prevention research to ensure that ethnically specific barriers are identified and potential ethnic inequalities are addressed. Considering this, a culturally competent vaccination program is a promising avenue to decrease the overwhelming burden of invasive cervical cancer in these populations. More research is needed, particularly in the context of health care provider HPV vaccination recommendation to immigrant and ethnic-minority populations.
References
11. Centers for Disease Control and Prevention. ACIP recommends all 11-12 year old males get vaccinated against HPV, 2011.


CERVICAL INTRAEPITHELIAL NEOPLASIA AND HPV VACCINATION WITHIN IMMIGRANT AND REFUGEE COMMUNITIES IN THE UNITED STATES: COMPREHENSIVE REVIEW

A thesis submitted to the University of Arizona College of Medicine – Phoenix
In partial fulfillment of the requirements for the degree of Doctor of Medicine

Bita Zahedi
Class of 2017

Mentor: Crista Johnson-Agbakwu, MD
Abstract

Despite advances in cervical cancer screening rates in the US, cervical cancer remains disproportionately high among low-income immigrant and minority women, making this subgroup particularly vulnerable to disparities in screening and its detection. The purpose of this study is to examine the qualitative aspects of institutional and community level interventions of Cervical Intraepithelial Neoplasia (CIN) within the immigrant and refugee populations and the use of HPV vaccination as a prevention method. Combinations of the following keywords/phrases will be used: CIN- Cervical Intraepithelial Neoplasia, Cervical diseases, Cervical dysplasia, Refugees, Pap smear, Cervical Cancer Screening, HPV- Human Papillomavirus, HPV vaccination, Ethnic minorities, Immigrants. Independent reviews of each article will be conducted to assess the study quality and confirm the accuracy, completeness, and consistency of the abstracted data.
Introduction and Background

*Cervical intraepithelial neoplasia (CIN) or Cervical dysplasia* is the abnormal growth of cells in the surface of the cervix and is a premalignant condition. The surface of the cervix that is visualized on vaginal speculum examination is known as the ectocervix and is covered in squamous epithelium, while the cervical canal or endocervix is covered with glandular epithelium. CIN refers to the squamous abnormalities and glandular cervical neoplasia include adenocarcinoma in situ and adenocarcinoma.¹

CIN is considered to be a precancerous condition caused by a sexually transmitted infection with the Human Papillomavirus strains 6, 11, 42 (HPV). Cervical dysplasia can lead to cervical cancer if undetected and unmanaged, while with proper management and treatment, the condition may revert or improve before becoming cancerous.²

Historically, premalignant squamous changes of the cervix were described as mild, moderate or severe cervical dysplasia. A new terminology was developed in 1988 known as the Bethesda system, which has since been revised in 1991 and 2001.³⁻⁵ Cytologic findings were described in terms of “Squamous Intraepithelial Lesion (SIL)” and histologic changes were described in terms of “Cervical Intraepithelial Neoplasia (CIN)”. CIN has three degrees of severity: 1, 2 and 3 being the highest grade lesion. Women with low grade CIN have a low potential for developing cervical malignancy, while those with high-grade lesions are at high risk of progression to malignancy.

In 2012, the Lower Anogenital Squamous Terminology (LAST) project of the College of American Pathology and The American Society for Colposcopy and Cervical Pathology revised the above mentioned terminology by describing the histological cervical findings in the same terminology of that used in cytology:³⁻⁷
### Terminology and histology of cervical intraepithelial neoplasia

#### Notes for the table above:

- **LSIL** (Low-grade squamous intraepithelial lesion): early changes in the size and shape of the cells; often resolving in women with intact immune systems without intervention within 18-24 months (LSIL can also be called mild dysplasia).
- **HSIL** (High-grade squamous intraepithelial lesion): cells appearing very different from normal cells. HSIL is more severe than LSIL and may be called moderate or severe dysplasia. Treatment of HSIL involves the removal of the abnormal tissue, which can be done in several ways such as Loop Electrosurgical Excision Procedure (LEEP) or Cold Knife Cone.
- **CIN 2** is stratified according to p16 immunostaining to identify precancerous lesions. CIN 2 has poor reproducibility and is likely a heterogeneous mix that includes lesions that could be called CIN 1 or 3. Specimens that are p16-negative are referred to as LSIL and those that are p16-positive are referred to as high-grade squamous intraepithelial lesions (HSIL).
Significance, and Rationale

Globally, cervical cancer accounts for an estimated 530,000 new cancer cases worldwide and for 275,000 deaths [globocan 2008]. 86% of new cervical cancer cases will be seen in developing countries. 14 Worldwide, the mortality rate from cervical cancer is 52 percent. 14,15 Global incidence and mortality rates depend upon the presence of screening programs for cervical precancer and cancer and of human papillomavirus vaccination, which are most likely to be available in developed countries. Due to these interventions, there has been a 75 percent decrease in the incidence and mortality of cervical cancer over the past 50 years in developed countries. 16,17

In developed countries in 2008, cervical cancer was the tenth most common type of cancer in women (9.0 per 100,000 women) and ranked below the top ten causes of cancer mortality (3.2 per 100,000). In contrast, in developing countries it was the second most common type of cancer (17.8 per 100,000) and cause of cancer deaths (9.8 per 100,000) among women. On the continent of Africa and in Central America, cervical cancer is the number one cause of cancer-related mortality among women. 14

In the United States, over 12,000 new cases of invasive cervical cancer and approximately 4000 cancer-related deaths occur each year. 18 Cervical cancer is the third most common cancer diagnosis and cause of death among gynecologic cancers in the United States, with lower rates than uterine corpus or ovarian cancer. Cervical cancer estimates are higher for certain racial and ethnic groups: whites (incidence: 7.7/100,000 and mortality: 2.2/100,000); Hispanics/Latinos (12.5/100,000 and 3.1/100,000); African-Americans (10.7/100,000 and 4.4/100,000); and American Indians and Alaska Natives (9.7/100,000 and 3.4/100,000). 18

The estimated annual incidence in the United States for CIN among women who undergo cervical cancer screening is 4% for CIN I and 5% for CIN 2 and 3. CIN affects between 250,000 and one million women throughout the U.S every year. Though, women of any age can develop cervical dysplasia, it most frequently occurs in women between the ages of 25 and 35. 19
Cervical Cancer Screening

Screening for cervical cancer includes cervical cytology and testing for oncogenic subtypes of HPV. Cervical cytology is the standard screening for cervical cancer and premalignant cervical lesions including. Cytology includes a Papanicolaou smear (Pap smear) or a liquid-based, think layer preparation (ThinPrep, SurePath). In a Pap smear, cells are scraped from the opening of the cervix and examined microscopically for the detection of abnormal cells. Though Pap smear and the newer method of ThinPrep are similar in detection of abnormal cells, ThinPrep liquid-based cervical cytology tends to be more sensitive and specific than conventional Pap smears and results in increased cytologic diagnosis of cervical dysplasias.

In the United States, a Pap smear is recommended in conjunction with a pelvic exam as part of a well-woman exam in women older than age 21 on a biannual basis. After age 30, pap smears are generally recommended every three years, or every five years. Certain risk factors lead physicians to recommend more-frequent Pap smears, regardless of age. These risk factors include:

- Diagnosis of cervical cancer or previous Pap smears showing precancerous cells
- Exposure to diethylstilbestrol (DES*) before birth

*DES is a synthetic nonsteroidal estrogen, classified as an endocrine disruptor and its human exposure occurred through dietary ingestion from supplemented cattle feed and medical treatment for certain conditions, including breast and prostate cancers. During 1940-1971 DES was mistakenly prescribed to pregnant women to reduce the risk of pregnancy complications and losses. Subsequent to the link of DES and vaginal tumors in women exposed to this drug in utero, the US FDA withdrew its use in pregnant women.

- HIV infection
- Weakened immune system due to organ transplant, chemotherapy or chronic corticosteroid use

A number of organizations have recommendations regarding when and how frequently women should have Pap smears. In general, organizations agree that the first Pap smear is
recommended at age 21. These guidelines differ slightly as each organization takes various sets of factors into consideration.

<table>
<thead>
<tr>
<th>Age</th>
<th>ACS American Cancer Society</th>
<th>ACOG American Congress of Obstetricians and Gynecology</th>
<th>USPSTF U.S. Preventive Services Task Forces</th>
<th>ICSI Institute for Clinical Systems Improvement</th>
</tr>
</thead>
<tbody>
<tr>
<td>21-29</td>
<td>Every 3 years</td>
<td>Every 3 years</td>
<td>Every 3 years</td>
<td>Every 2 years</td>
</tr>
<tr>
<td>30 and older</td>
<td>Every 3 years, or every 5 years when Pap smear is combined with an HPV test</td>
<td>Every 3 years, or every 5 years when Pap smear is combined with an HPV test</td>
<td>Every 3 years, or every 5 years when Pap smear is combined with an HPV test</td>
<td>Every 3 years if patient has had 3 negative tests in a row</td>
</tr>
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</table>

*women at high risk may need to be screened more often

In certain situations women can decide to end Pap smear testing:

- After a total hysterectomy (the removal of the uterus as well as the cervix) only if the total hysterectomy was done due to noncancerous conditions such as uterine fibroids
- Older age
  - ACS and USPSTF guidelines suggest women older than 65 can stop having regular screening
  - ICSI guidelines recommend women between the ages of 65 and 70 may consider stopping Pap smear testing if their last three tests have been negative and they've had no abnormal tests in 10 years
  - ACOG guidelines recommend women between the ages of 65 and 70 may consider stopping Pap smear testing if the patient has had a negative result for
three tests performed within the last 10 years or two consecutive negative Pap tests combined with negative HPV tests in the last 10 years, with the most recent test performed within the past 5 years.\textsuperscript{10,11}

When a Pap smear shows abnormal changes, further testing is necessary. For minor cell changes, physicians recommend having another Pap smear in 6-12 months and in other cases a Colposcopy and HPV test will be performed. A Colposcopy utilizes a Colposcope, an instrument that uses magnifying lenses to allow the physician to examine the cervix closer and more clearly. Upon the application of a weak solution of acetic acid to make the abnormal cells easier to view, a biopsy can be performed if necessary which will then be examined by a pathologist leading a potential diagnosis of CIN.\textsuperscript{12,13}

Infection and cervical dysplasia are generally asymptomatic, and can only be recognized with regular gynecological visits including pelvic exam and Pap smears. Though in some cases, the body clears itself of HPV infection, in others it can turn into cancer and require medical management. Though CIN is asymptomatic, invasive cervical cancer can accompany symptoms such as abnormal bleeding, in between the menstrual cycle or during and after sexual intercourse or pelvic exam. Other symptoms may include: heavier menstrual bleeding, bleeding after menopause, increased vaginal discharge and pain during intercourse.

Risk factors associated with a person’s chance of cervical cancer include: cigarette smoking or exposure to it, having multiple sexual partners, compromised immune systems (ie: HIV patients, transplant recipients or those taking immunosuppression drugs)
HPV Vaccination

Well-organized screening and early treatment can be effective in reducing cervical cancer mortality, but difficult to implement in low-resource settings such as in the case of immigrants and refugees. Alternatively HPV vaccination can be a cost-effective prevention method, which is less dependent on existing health system infrastructure.

The currently available HPV vaccines are a quadrivalent vaccine administered in three doses that protects against sexually transmitted HPV types 6, 11, 16, 18 or a bivalent vaccine protecting against HPV types 16, 18. HPV vaccination alone with 70% coverage of target population (girls between 9 and 12) is expected to reduce the lifetime risk of cancer by 43%. At coverage rates of 100% the expected cancer reduction with vaccination alone would be as high as 61%. 21

The most important factors affecting the predicted coverage level include the cost, accessibility, and vaccinating girls prior to sexual activity. The decision to introduce new public health interventions to improve greater access to HPV vaccination must take into consideration multiple factors including the disease burden, effectiveness of the intervention, the financial costs required to initiate and sustain the program, the cost-effectiveness of the intervention, the programmatic capacity and infrastructure necessary to successfully deliver the intervention, and the likelihood of cultural acceptability, political will and public sector support. 21 The general estimates approximate the cost of each vaccination dose at $5 per preadolescent individual. Considering the cost effectiveness and wide availability of the vaccine in the US, the limiting factor remains proper education regarding vaccination and its cultural acceptance.
Conclusion

Although screening for cervical cancer has been developed and in use for more than half a century, it is the third leading cause of cancer death in women and in the U.S. cervical cancer remains the sixth most commonly diagnosed cancer. Despite advances in cervical cancer screening rates in the US, cervical cancer remains disproportionately high among low-income immigrant and minority women, making this subgroup particularly vulnerable to disparities in screening and therefore detection of CIN. The greatest burden of cervical cancer is found in underserved, resource-poor population of women: eighty percent of all incident cervical cancer and related mortality occurring in this population.

Considering that immigrant and refugee women emigrate from developing countries that lack precancer, cancer screening and HPV vaccination, they are at a higher risk for CIN. NIH estimates that half of the women who receive cervical cancer diagnoses have never been screened for cervical cancer and more than half of all cervical cancer deaths in the US have been reported to occur in foreign-born women. Barriers to implementing cervical cancer screening programs in developing countries include competing health care demands. The principal health care issues that compete with cervical cancer prevention in developing countries include infectious diseases: Tuberculosis, Malaria, and HIV. Furthermore, scarcity of health care resources shifts the focus to curative rather than preventive. In addition to the social and political conditions of low resource countries, other factors involved in impeding cervical cancer screening programs include the lack of reliable and affordable modes of communication and transportation, lack of education, literacy and information about interventions such as cervical cancer screening.

In addition to environmental and financial barriers, cultural barriers play a great role in preventing the immigrant and refugee population from receiving cervical cancer screening and HPV vaccinations. Commonly held beliefs across several immigrant and refugee groups that may deter them from seeking these interventions include: fatalistic attitudes, lack of knowledge about cervical cancer, fear of Pap smears threatening one’s virginity, as well as beliefs that a Pap smear is only necessary if one is ill. Beliefs unique to specific cultural groups include: 

20
Hispanics: body-focused notions as childbirth, menses, sex and stress being considered to play a role in one’s susceptibility to cancer

African-Americans: administrative processes in health care being considered as a barrier to screening

Asian: misconceptions of one’s susceptibility to cancer and stigmatization imposed by their community and providers.

Furthermore, other risk factors more prominent in the immigrant and refugee populations such as early age at first birth (younger than 20 years old) and increasing parity (3 or more full term births) have been associated with increased risk of cervical cancer. Though, these associations may be due to the increase in likelihood of exposure to HPV through sexual intercourse. The possibility of a direct relationship can be contributory. ¹⁵

Early detection of CIN will allow for better treatment and will avoid its progression to invasive cervical cancer. CIN is both detectable and quantifiable which presents many opportunities for evaluation or early treatment, intervention and eventually, for cancer prevention. It is especially important to take into consideration the environmental, financial and cultural barriers that place immigrant and refugee populations at a greater risk for CIN. Some strategies to increase screening among targeted high risk and vulnerable populations include:

- Increased availability of female health care providers
- Providing education in the population’s respective language targeting varying levels of education with regards to cervical screening and its implications
- Cost reduction of cervical screening and HPV vaccination
- Presenting patients with the opportunity to discuss other health matters during cervical screening visits
- Receiving Pap smear results via means such as postal mail, over the phone or electronically without an appointment to avoid additional cost and transportation hassles

In the high burden population of refugee and immigrant women with limited financial resources, HPV vaccination can be a promising strategy for the prevention of cervical cancer.
To deliver this intervention, the likelihood of cultural acceptability and proper education regarding the vaccine can be studied to examine the successful delivery and implementation of HPV vaccination as a cost effective method of cervical cancer prevention.
References


