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Review

Overcoming the barriers to HPV vaccination in high-risk populations in the US[☆]Levi S. Downs Jr.^{a,*}, Isabel Scarinci^b, Mark H. Einstein^c, Yvonne Collins^d, Lisa Flowers^e^a Division of Gynecologic, The University of Minnesota, Minneapolis, MN, USA^b Division of Preventive Medicine, University of Alabama, Birmingham, AL, USA^c Division of Gynecologic Oncology, Albert Einstein College of Medicine, USA^d Division of Gynecologic, University of Illinois Chicago, Chicago, IL, USA^e Division of Gynecologic Oncology, Emory and Montefiore Medical Center, Bronx, NY, USA

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ABSTRACT

Objectives. To review populations of women in the United States at high risk for cervical cancer, assess known reasons for existing outcome disparities, and discuss potential strategies to reduce barriers to HPV vaccination and current strategies for cervical cancer prevention.

Methods. An expert forum conducted September 12–13, 2008, by the Society of Gynecologic Oncologists including 56 experts in cervical cancer and titled "Future strategies of cervical cancer prevention: what do we need to do now to prepare?"

Results. Although epidemiological data is useful and necessary to identify populations at high risk for cervical cancer, an understanding of the knowledge and attitudes regarding HPV and cervical cancer prevention of racial/ethnic groups and sub-groups within racial/ethnic categories is critical for the implementation of effective targeted and effective educational efforts. Inequities in cervical cancer screening, diagnosis and treatment and HPV vaccination may arise from a number of barriers including access to healthcare, cultural beliefs, and limited awareness of options.

Conclusions. Initiatives to promote uptake of prophylactic HPV vaccination that target high-risk women need to be implemented before existing disparities widen. Although acceptability of HPV vaccination is promising, uptake is still low among low-income populations and specific racial/ethnic minorities. To address limited vaccine uptake it may be beneficial to establish national/state guidelines as well as culturally relevant interventions at the individual and community levels. The successful implementation of multiple integrated initiatives on HPV awareness, knowledge, and vaccination will diminish existing disparities in cervical cancer incidence and mortality.

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[☆] On September 12–13, 2008, the Society of Gynecologic Oncologists convened a symposium of 56 cervical cancer experts titled "Future strategies of cervical cancer prevention: what do we need to do now to prepare?" to discuss evidence-based strategies in cervical cancer prevention and control, including HPV vaccination. This paper is the third in a series of manuscripts which highlight concepts, information, obstacles and approaches discussed during the Forum's sessions and focuses on the issue of barriers to HPV vaccination in high-risk populations in the United States and initiatives to overcome these barriers.

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Introduction

Despite a wealth of resources aimed at prevention, over 11,000 new cases of cervical cancer were diagnosed in the US in 2009, and 4000 deaths are attributed to cervical cancer annually [1]. Significant disparities exist among women with cervical cancer, in incidence rates by race, ethnicity, geography, income, and education. The fact that disparities in cervical cancer incidence and mortality continue to

exist for a largely preventable and treatable disease is indicative of larger health system deficiencies, including the lack of a national screening program, and underscores the need for aggressive public health interventions [2].

This review will focus on HPV vaccination in US Women at high risk for cervical cancer. Specifically, women with lower income, with lower education and racial/ethnic minorities: African Americans and Hispanics. Often, these high-risk populations do not have adequate access to preventative health care, or they may have access but, for various reasons, choose not to utilize available services. Although HIV positive women are at increased risk for cervical cancer, there are no large, randomized trials that demonstrate vaccine efficacy in HIV infected women. We do not discuss HPV vaccination of HIV infected women in this review.

Cervical cancer screening programs have been largely responsible for substantial decrease in the incidence of cervical cancer and recently developed prophylactic HPV vaccines will likely further reduce incidence rates [3]. It is plausible that successful implementation of widespread HPV vaccination will diminish disparities in populations where screening is currently underutilized [4]. However, women who currently do not get regular cervical screening may also be less likely to receive an HPV vaccine and less likely to vaccinate their daughters. Culturally-relevant behavioral interventions aimed at increasing HPV awareness, informing the public about the benefits of HPV vaccination, and promoting behavior change may help to minimize current disparities that exist in high-risk populations. This review will discuss known reasons for existing disparities in the populations described above and discuss potential challenges as well as strategies to reduce barriers to HPV vaccination and other forms of cervical cancer prevention. This content was developed at the 2008 Cervical Cancer Forum held by the Society for Gynecologic Oncologists and is the consensus of the authors who were the leaders/facilitators of this portion of the conference and who have developed the content of this manuscript based on our research and interpretations of the discussion among conference attendees.

Populations at high risk for cervical cancer

Cervical cancer incidence is a marker of poverty in the US and across the globe. United States women living below the poverty line are 3 times more likely to be infected with a high-risk strain of HPV than those who are not poor [5]. In addition, cancer incidence in areas where >20% of residents are living below the poverty level is greater than in areas with <10% of residents under the poverty level [6]. High rates of cervical cancer morbidity and mortality disproportionately affect poor minority women [7]. Higher than average cervical cancer mortality rates have been observed in African American women in the South, Hispanic women along the Texas–Mexico border, white women in Appalachia, American Indians of the Northern Plains, Vietnamese-American women, and Alaskan Natives [8].

Data from the Surveillance Epidemiology and End Results (SEER) database (2001 to 2005) reveal that among racial/ethnic groups in the US, Hispanics have the highest incidence rate of cervical cancer (13.2/100,000) (Fig. 1) [8]. Demographic projections for the year 2050 predict that among girls 10–14 years of age, Hispanics are likely to have the largest population growth rate compared to other racial/ethnic groups, more than doubling their current numbers [9]. This suggests that the disproportionately high incidence of cervical cancer in Hispanics may be exacerbated in coming decades. Multiple factors contribute to the higher cervical cancer incidence rate in Hispanic women, including lower Pap test rates and a lower likelihood of adherence to follow-up recommendations after diagnoses of precancerous lesions [10,11]. Differences in high-risk sexual behavior may also contribute to an increase in HPV transmission in both Hispanic and African American women. In the CDC's 2007 Youth Risk Behavior Survey, Hispanic and African American high school students were

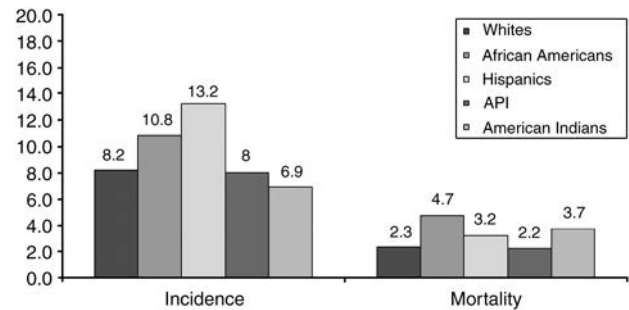


Fig. 1. Cervical cancer incidence and mortality by race. Cervical cancer incidence and mortality rates from 2001 to 2005. From the Surveillance Epidemiology and End Results (SEER) database [8].

more likely to report engaging in high-risk sexual behaviors compared to white students [12].

Interestingly, African American women participate in cervical screening at a high rate (88% received at least 1 Pap test between 2003 and 2006), yet still exhibit the highest cervical cancer mortality rate (4.7/100,000), and the second highest incidence rate (10.8/100,000) [8]. This paradoxical result may be related to poor adherence to post-screening follow-up recommendations and disparate management of abnormal cytology, cervical dysplasia and cervical cancer [13]. For example, studies have identified that African American women with cervical cancer are more likely to receive radiation therapy alone or no treatment, as opposed to surgery, compared to white women [14]. Although surgery as a treatment option may be associated with improved survival, African American women are less likely than white women to receive surgery. This is because they are less likely to have surgery recommended by their physician, more likely to have comorbid conditions that increase surgical risk, and more likely to decline recommended surgery [15,16].

Epidemiological data is necessary to identify high risk populations but we must understand the sub-groups within racial/ethnic categories to implement targeted and effective prevention and treatment efforts in these high-risk populations. For example, although McCracken et al. report that Asian-American/Pacific Islanders have shown the lowest mortality rates from cervical cancer, incidence rates in women of Vietnamese Americans are approximately 2.5 times that of Chinese Americans [17]. There are likely other sub-population disparities that have not yet been identified because within our current categories of race and ethnicity there is significant heterogeneity [17–19].

Barriers to HPV vaccination

Inequities in preventive care may arise from a number of barriers including access to healthcare, cultural beliefs, and lack of communication and education regarding preventive care options [20].

Most studies have described health care access as having a regular source of care; others focus on utilization of health services, and others on having health insurance coverage. Penchansky and Thomas proposed an alternative view. They identified five dimensions of access: availability (volume and type of services from which patients can choose), accessibility (location of health services vs. location of clientele), accommodation (the ease of obtaining appointments), affordability (cost and perceived ability to pay for care), and acceptability (perceptions about practice characteristics) [21]. Scarinci et al. examined the unique contribution of an array of socioeconomic indicators and race to health care access among healthy white and African American women. They found that family income was the strongest predictor of total health care access, and there was a

significant interaction between occupation and race for total health care access. Occupation significantly predicted accessibility, median income by zip code significantly predicted accommodation, and family income significantly predicted affordability [22].

Other studies have shown that women who live in poverty access healthcare less frequently than mainstream populations; their visits are typically only for urgent or emergent care, with limited participation in preventive care such as cervical cancer screening [23]. Impoverished women often live in regions with a high incidence of many diseases, like breast cancer and cerebrovascular disease, in addition to cervical cancer. Similar to cervical cancer, there are effective screening programs and prevention strategies for most of these diseases, yet disease burden remains high [2]. This suggests either a lack of access to or underutilization of proper preventive care.

Cultural beliefs may also inhibit some women from seeking preventive care. Surveyed Hispanic women displayed fatalistic beliefs that cancer is 'bad luck', and many fear this diagnosis and would prefer not to know if they have cancer [24]. Language barriers between the healthcare provider and the patient may also present difficulties. For example, Spanish-speaking women are less likely to undergo Pap testing when seen by clinicians who do not speak Spanish than when seen by Spanish-speaking clinicians [25].

There is also a wide range of awareness and knowledge about the risks of HPV infection and its link to cervical cancer [26]. Among Hispanic immigrant women in Alabama, HPV awareness was only 51% in 2007 (Scarinci, unpublished data). In a review of the literature, Klug et al. found that HPV awareness differed by attained education, and gender, with women being more knowledgeable than men [27]. However, many women do not perceive themselves as being at risk for HPV infection and HPV-related disease. In fact, among women polled in the 2005 Health Information National Trend Survey, only 40% of women had ever heard of HPV and less than 50% knew that HPV was associated with cervical cancer [28].

Although parents have been shown to generally be in favor of HPV vaccination for their daughters, some parents may be uncomfortable with the perceived implications of vaccination [29]. Some fear that HPV vaccination will promote sexual activity, and alternatively, others decline immunization because they believe their daughters are not sexually active and therefore at low risk for HPV infection [29]. In addition, as with any new drug or technology, many women simply do not know enough about HPV vaccines, the rationale for vaccination before sexual debut, or the benefits of vaccination. The lack of knowledge about HPV and HPV vaccination promotes misinformation about the risks of infection, the need for protection, and is contributing to existing disparities in cervical cancer outcomes.

Approaches to enhance vaccine uptake

Although a number of studies have examined acceptability of the HPV vaccine [30–33] there is a need for more studies examining factors associated with vaccine uptake, particularly among high risk populations. It is important to consider both acceptability and uptake in future research. Acceptability refers to willingness to get vaccinated while uptake or vaccination rates are more useful measurement endpoints. Studies have shown that intention to engage in a particular healthy behavior does not necessarily mean that the individual will engage in such behavior. For example, Scarinci et al. have found that 78.7% of Latina immigrants between 19 and 26 years of age would be willing to get the HPV vaccine (Scarinci unpublished data). However, data from the CDC's 2007 National Immunization Survey estimate that only 10% of all females and only 1% of Hispanic women between 18 and 26 received at least one HPV vaccine dose [29]. This discrepancy suggests that acceptability and uptake as well as the factors associated with each may be different, and further research is needed. Regional or national vaccine registries may be an important and useful tool to identify where current disparities in HPV vaccine uptake exist.

Educational programs that promote acceptance of HPV immunization are needed [33]. Studies have shown that successful strategies may not be the same across sub-populations. For example, Scarinci et al. found that although African American women and Latina immigrants expressed willingness to be vaccinated, the barriers and motivators were not the same in these two sub-populations. Both groups indicated side effects, cost, and lack of information about HPV infection and its link with cervical cancer, as well as lack of information about the vaccine as barriers. However, Latina immigrants tended to focus mostly on cost and African Americans focused on unknown long-term side effects and mistrust of the health care system. With regard to motivators, African American women reported education/information, affordable prices, good results with the vaccine, and knowing people who had been vaccinated. Latina immigrants were emphatic in saying that, in order to encourage HPV vaccination, more than one credible source of information is needed (educational talks, doctor's office, television, churches, and advice from other women that know about HPV) [33].

It is important to understand perceived barriers so that educational initiatives can be designed to convert these barriers to motivators. For example, some continue to question the relationship between HPV vaccination and promiscuity. Although HPV can be transmitted through sexual contact, any notion of a causal link between vaccination and increased sexual activity should be dispelled by primary care providers and community public health leaders. HPV vaccination should instead be viewed as a positive step towards protecting one's body and preventing cancer. Changing private and public perceptions about the implications of HPV vaccination potentially could diminish the incidence of cervical cancer in high-risk populations.

Further, behavioral and/or educational interventions should be tailored to underserved populations with culturally relevant messaging and messengers. For instance, in the US, some Hispanic women may be afraid of anti-immigrant attitudes and prefer information from a trusted source such as church leaders or community health advisors. Similarly, African Americans have expressed a distrust of government agencies, and have suggested that an African American spokesperson would be most effective [33].

Another influential vaccination motivator is physician recommendation [34]. Incentives for physicians to recommend HPV vaccination like pay for performance mechanisms could be considered in order to increase compliance. One model that could be followed is from the 2007 Physician Quality Reporting Initiative, initiated by the Centers for Medicare and Medicaid Services. Over a 6-month period, physicians who participated in the program were eligible to receive a 1.5% reimbursement bonus of their total allowed charges for recording whether or not specific procedures were carried out on at least 80% of their patients [35]. In a recent editorial, Goff proposed that if this program were applied to cervical cancer screening and HPV vaccination, the appropriate agency could reimburse physicians for successful adherence to screening and HPV vaccine guidelines in at least 80% of eligible women [36]. Vaccination reminder systems for physicians may also be helpful in this regard.

Mandatory vaccination would improve the likelihood of achieving widespread vaccination among high-risk populations. However, there are many controversies surrounding mandatory HPV vaccination. Legislators may be hesitant to intrude on parental autonomy and some believe that opt-out provisions are unfair to those opposed to HPV vaccination [37]. Vaccinologists believe that mandates with opt-out clauses defeat the purposes of the mandates and ultimately lower the chance of herd vaccination. There is a need for open discussions between proponents on both sides of this controversial topic. This process should include parents, community leaders, patient advocates, clinicians, public health officials and government representatives. As shared values are identified and as we learn more about HPV vaccination, controversy surrounding policies regarding mandatory

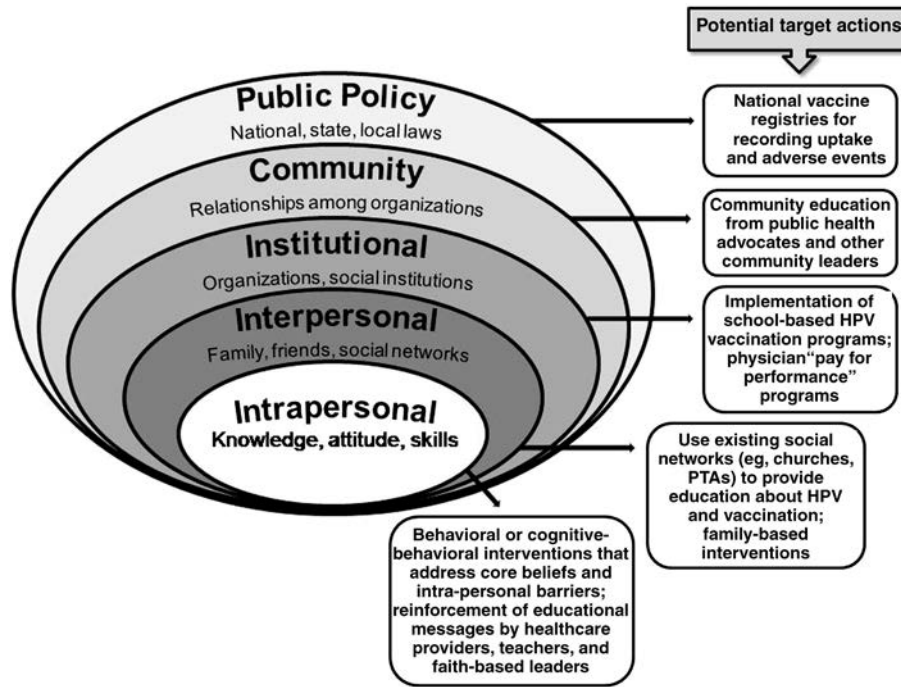


Fig. 2. The socio-ecological model that could be used to structure initiatives to overcome barriers to HVP vaccination.

HPV vaccination will likely diminish. From a socio-ecological perspective these discussions need to occur on many levels: public policy, communities, institutions/organizations, social networks (e.g., families, religious organizations), and individuals (Fig. 2). Further, lessons can be learned from initiatives that promote cervical cancer screening regarding the importance of a consistent message across each of these levels. We have summarized the recommendations from the discussions at the forum in Table 1.

Conclusions

There is increasing data about the perceptions, attitudes, HPV knowledge, and vaccination acceptance and initiation rates of US women but more research is needed urgently on this topic, particularly for high-risk populations. There is a need to target vaccination to high-risk groups before existing disparities widen. Although acceptance of HPV vaccination is promising, uptake is still low among low-income populations and particular racial/ethnic minorities that are at highest risk for cervical cancer incidence and mortality. Barriers to screening, such as lack of access and cultural influences may be the same barriers

to vaccination uptake. Further studies are needed to identify the sociocultural barriers and motivators to vaccine uptake. Knowledge of HPV, cervical dysplasia and cervical cancer is a first step to the effective uptake and acceptance of the HPV vaccine [38]. In order to increase access to education, healthcare providers in underserved areas must be given culturally relevant educational materials, and be educated on how best to change patient behavioral patterns. In addition to person-to-person education, informing whole at-risk communities about HPV may require innovative pilot programs. It will also be important to link vaccination programs to sex education, and involve community leaders and religious-based organizations in the initiatives.

With growing prospective evidence of vaccine efficacy and safety, it is likely that widespread HPV vaccination will be achieved. The continued implementation of integrated initiatives focusing on HPV awareness, knowledge, and vaccination will diminish existing disparities in cervical cancer incidence and mortality.

Conflict of interest statement

The authors have the following conflicts to disclose:
 Levi S Downs Jr., research support and honoraria from Merck Corporation and GSK.
 Isabel Scarinci, none.
 Mark H Einstein:
 Montefiore has received grant funding for research-related costs of clinical trials that Dr. Einstein has initiated or been the Montefiore PI from GSK, Merck, Hologic, Nventa Biotechnologies and Tigris Pharmaceuticals. Dr. Einstein has advised, consulted or participated as a speaker, but does not receive an honorarium from the following companies: Merck, GSK, Roche, Tigris, Nventa, PDS Biotechnology, Qiagen (Digene) and Hologic.
 Yvonne Collins, honoraria from Merck Corporation and GSK.
 Lisa Flowers has served as an advisor to GSK and Merck.

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Table 1

Summary of Recommendations
Research on cervical cancer outcomes in sub-populations of traditional racial/ethnic categories will enhance our ability to design education initiatives that target high-risk women
There is an urgent need for additional research on vaccine uptake in high risk populations
Similarities and differences between high-risk populations should be considered when designing targeted interventions
Additional research is needed to identify perceived barriers to vaccination this will foster creative interventions that convert barriers to motivators
Behavioral and educational interventions must promote culturally relevant messages and messengers
Incentives for physicians to recommend HPV vaccination, like pay for performance, should be implemented
There is a need for open discussions about mandatory vaccination between supporters and opponents of this controversial approach
There is a need to integrate HPV vaccination with cervical cancer screening

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