

There's Much Yet to be Done: Diverse Perspectives on HPV Vaccination

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Introduction

It has been over 10 y since the first HPV vaccines were licensed and introduced in a number of countries around the world. As only the second vaccine (after hepatitis B) that prevents an infection that can lead to the development of cancer, HPV vaccine occupies an important position in our armamentarium of vaccines yet remains underutilized. The number of national HPV vaccination programs has increased steadily; as of June 2017, 91 countries had introduced national HPV vaccination programs,¹ with that number now over 100. Over the past 10+ y, several modifications have been made to the vaccination regimen (e.g., moving from three to two doses if the first dose is administered before age 15 y), in the type of vaccine available (e.g., introduction of the 9-valent vaccine), and in the target of vaccination (e.g., many countries have shifted from female-only to gender-neutral vaccination). There is great variability across the globe in terms of HPV vaccination policies and accompanying barriers to the implementation and/or sustainability of programs. It is well known, for instance, that Japan's initial success with vaccination was undermined by several factors, leading to a precipitous drop in vaccination rates, with little subsequent recovery.² Other countries, such as the U.S.,³ have struggled to achieve vaccination goals, and still others have faced setbacks but with good recovery (e.g., Denmark and Ireland).^{4,5} At the same time, many countries, including China,⁶ still have not implemented national vaccination programs, with the cost of vaccines presenting a significant obstacle, particularly for those countries that are not eligible for reduced pricing through Global Alliance for Vaccines and Immunisation (GAVI) or other mechanisms. Other countries, such as Malaysia, Rwanda, Australia, and the U.K., have achieved sustained high levels of vaccination.^{7–10} Unwarranted fears about HPV vaccine and the proliferation of misinformation, particularly via social media, have proven to be significant and widespread obstacles to achieving and maintaining high vaccination rates.^{11,12}

This special issue of *Human Vaccines & Immunotherapeutics* brings together a number of timely articles covering several topic areas related to HPV vaccination. Included among these are papers focused on: social media and the Internet; vaccination policy; interventions to improve vaccination rates; new domains related to HPV vaccine knowledge, attitudes, and behaviors; alternative settings for vaccine delivery; HPV prevalence,

incidence, and type distribution among specific populations; HPV-related oropharyngeal cancers (OPC), vaccine characteristics; and cost-effectiveness modeling. The 68 papers in this special issue include research papers, reviews or policy pieces, short reports, and commentaries.

Social media and the Internet

As noted above, social media have enabled the spread of false information about HPV vaccination, presenting clinicians and researchers with difficult challenges.¹³ At the same time, social media also convey accurate information about vaccines and can (and should) be used by clinicians and researchers to counteract the proliferation of false information. Included in this special issue are several papers addressing social media and online information about HPV immunization. These include a systematic review examining how social media may affect attitudes about, and uptake of, HPV vaccine,¹⁴ as well as several research papers reporting on analyses of HPV-vaccine-related posts on Instagram,¹⁵ Facebook,¹⁶ and Twitter.^{17,18} Two additional articles examine the readability of online information¹⁹ and present a content analysis of online continuing medical education about HPV vaccination, respectively.²⁰

HPV vaccination policy

The ways in which countries, regions, and states craft public health policies about HPV vaccination have had an enormous effect on the success or failure of vaccination programs. Five articles in this special issue address varying aspects of policy. One paper involves a unique examination of U.S. states' statutes and regulations regarding HPV vaccination by using WestlawNext, a legal research database.²¹ A second paper points to the lower vaccination rates in rural areas of the U.S. and suggests policy strategies to improve vaccine uptake in these areas.²² A third paper examines, in detail, policy challenges and issues with the introduction of vaccines in China.⁶ Another paper addresses the challenges associated with implementing effective HPV vaccination programs for men who have sex with men,²³ and a final paper reviews the arguments for and against the implementation of policies to vaccinate female sex workers.²⁴

Interventions and pre-interventions to improve vaccination rates

There is a great need to continue to develop and evaluate interventions to increase HPV vaccination uptake. Eight articles in this special issue focus on pre-interventional and interventional research to improve vaccine initiation and series completion, including a review of technology-based interventions (e.g., text messaging and electronic health record reminders) designed to improve vaccination rates.²⁵ Three papers involve evaluations of a patient navigator program,²⁶ a quality improvement intervention,²⁷ and a tablet-based tailored messaging intervention,²⁸ respectively, in terms of their effects on vaccine initiation and series completion. An additional article reports on the acceptability to caregivers of the patient navigator program.²⁹ Another research report³⁰ examines secondary outcomes from a previously reported multi-component intervention designed to improve health-care provider (HCP) communication about HPV vaccination.³¹ Still another paper evaluates vaccine-related community-clinical linkages and addresses the implications for vaccine intervention efforts.³² A final research study looks at the effects on knowledge about HPV due to an educational intervention targeted to undergraduate students in Italy.³³

Knowledge, attitudes, and behaviors

There are 23 research reports, 2 review articles, and 1 commentary addressing different aspects of HPV vaccine knowledge, attitudes, and behaviors. An enormous amount of past research has addressed knowledge and attitudes about HPV vaccination. However, the articles in this special issue make some unique contributions to the literature. One paper reports on a systematic review of literature on the determinants of vaccine hesitancy in Europe,³⁴ and another offers practical guidance to HCPs in how to refute HPV vaccine myths.³⁵ Meanwhile, a commentary summarizes consensus messages to strengthen parental confidence in HPV vaccination that were generated at the U.S. National HPV Vaccination Roundtable meetings.³⁶ Other papers address provider, parent, and patient issues specific to understudied countries, such as China, India, and Italy, as well as areas of vaccine hesitancy and/or low vaccination uptake in the U.S. and Canada.^{37–44} Another research report found that few providers in a U.S. regional health plan administered vaccine in a way that was consistent with Healthcare Effectiveness Data and Information Set benchmarks.⁴⁵ Two articles explore issues of trust among African American parents and how this impacts vaccination.^{46,47} Two additional papers examine issues of risk compensation post-vaccination in the U.S. and in China, respectively.^{48,49} Still other articles involve a latent-class analysis of parental worries,⁵⁰ adolescents' perspectives on vaccination,⁵¹ college students' lack of awareness of HPV diseases and vaccination,⁵² knowledge and attitudes of caregivers of childhood cancer survivors,⁵³ HCPs' recommendation profiles and perceptions of barriers to vaccination,^{54,55} and perspectives on vaccination among boys in Sweden.⁵⁶ Finally, articles in this section apply the Precaution Adoption Process Model to a study of parental vaccine hesitancy,⁵⁷ examine preferences for a vaccine-related mobile health tool among young men

who have sex with men,⁵⁸ and report on the association between vaccination history in women and the HPV vaccine status of their 11–14-y-old children.⁵⁹

Alternative settings for HPV vaccine delivery

In countries like the U.S. that have not implemented school-located HPV vaccination programs, efforts have been made to expand promotion and/or delivery of vaccines beyond traditional pediatric or family practice office settings. Seven articles in this special issue consider such alternative settings, with papers addressing pharmacies and pharmacists as vaccine providers^{60,61} and gynecological providers.⁶² Two articles examine the potential role that dentists and dental practices can play in promoting HPV vaccination,^{63,64} and one additional paper considers barrier and facilitators of vaccination at school-based health centers.⁶⁵ A final study in this section used Veterans Affairs Medical Center data to identify missed opportunities for vaccination among young adult men and women who were military veterans.⁶⁶

HPV prevalence, incidence, and type distribution – implications for vaccination

Five articles in this special issue focus on HPV infection and disease in specific populations, which has implications for HPV vaccination programs. Two papers examine HPV genotype distribution among women in Changzhou,⁶⁷ China and among women with cervical cytological abnormalities in Xinjiang, China, respectively.⁶⁸ The Changzhou study found the most prevalent types in women with cervical cancer to be 16, 52, and 58. Similarly, the Xinjiang study identified types 16, 58, and 52 as the most prevalent types. Of note, types 52 and 58 are not covered by the bivalent and quadrivalent vaccines, only by the nonavalent vaccine. Another article looks at genital HPV prevalence among adult immigrants living in the U.S., finding that high-risk HPV prevalence was lower among this population compared to those born in the U.S.⁶⁹ An additional paper evaluated incident genital HPV infections in adult women living with HIV/AIDS, reporting that 35% of incident infections could have been prevented by the 9-valent vaccine.⁷⁰ A final article examined the hypothesis that obesity status might be associated with greater risk of HPV infection in the anal canal due to an increased associated risk of micro and macro tears in the epithelium.⁷¹ Results were mixed but certainly support universal gender-neutral HPV vaccination.

Oropharyngeal HPV

The incidence of HPV-related OPC has increased significantly over the last 15 y in the U.S. and in other high-income countries, particularly among men.⁷² Although HPV vaccines are not yet indicated for the prevention of HPV-related OPC, there is indirect evidence that vaccination may be effective.^{73–75} Three articles address aspects of HPV-related OPC. One paper reviews the epidemiology of OPC, as well as approaches to prevention and emerging technologies for screening.⁷⁶ In a commentary, there is a discussion of the roles that otolaryngologists can play in promoting vaccination.⁷⁷ A final study

examined whether sex differences in immune response may explain the significantly lower incidence of OPCs among women compared to men.⁷⁸

Other topics related to HPV and HPV vaccination

Seven articles in this special issue cover a variety of key issues central to HPV vaccination. One reports on the impact of updated medical costs on cost-effectiveness estimates for HPV vaccination in the U.S.,⁷⁹ while another estimates the epidemiological impact and cost-effectiveness of the 9-valent vaccine in Spain.⁸⁰ An additional paper finds evidence for cross-protection, but no evidence for type replacement 11 y after the introduction of HPV vaccine in the U.S.⁸¹ A study involving a 10-y follow-up of 10–14-y-old girls vaccinated with the bivalent vaccine found strong sustained antibody levels, with no severe adverse events attributable to the vaccine.⁸² Another report looked at the effect of long intervals between doses of HPV vaccine on immune response, finding that intervals of several years do not negatively impact the immune response to the second dose.⁸³ Also in this section, there is an article involving evaluation of the feasibility of using a combined approach to HPV vaccination and screening (also known as FASTER) in Mexico.⁸⁴ The final article in this section reports on the important effort to overcome barriers to implementation in low- and middle-income countries related to the need for continuous refrigeration during transport. Using a mouse model, they show immunogenicity and protective efficacy of the 9-valent vaccine after it had undergone a spray drying and stabilizing process.⁸⁵

Conclusions

Despite the availability of HPV vaccine in many locales for over 10 y, there remain substantial barriers to adequate coverage in many countries and regions. Reasons for poor rates of vaccination include attitudinal and behavioral barriers, system barriers, logistical challenges, and political and policy barriers. The 68 papers in this issue reflect the richness and diversity of research and thinking around HPV vaccination. Our hope is that the kind of work represented here will help in the global effort to move the dial on HPV vaccination to increased utilization of this very important disease-prevention method so that future suffering and deaths from HPV-related diseases can be minimized and the goal of HPV-cancer elimination can eventually become a reality.

Disclosure of potential conflicts of interest

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