

Advancing HPV Vaccine Delivery: 12 Priority Research Gaps

Paul L. Reiter, PhD^a, Mary A. Gerend, PhD^b, Melissa B. Gilkey, PhD^c,
Rebecca B. Perkins, MD^d, Debbie Saslow, PhD^e, Shannon Stokley, DrPH^f,
Jasmin A. Tiro, PhD^g, Gregory D. Zimet, PhD^h, and Noel T. Brewer, PhDⁱ

^a College of Medicine, The Ohio State University, Columbus, OH, USA

^b Feinberg School of Medicine, Northwestern University, Chicago, IL, USA

^c Harvard Medical School & Harvard Pilgrim Health Care Institute, Harvard University, Boston, MA, USA

^d School of Medicine, Boston University, Boston, MA, USA

^e American Cancer Society, Atlanta, GA, USA

^f National Center for Immunization and Respiratory Diseases, Centers for Disease Control and Prevention, Atlanta, GA, USA

^g University of Texas Southwestern Medical Center & Simmons Comprehensive Cancer Center, Dallas, TX, USA

^h School of Medicine, Indiana University, Indianapolis, IN, USA

ⁱ Gillings School of Global Public Health, University of North Carolina, Chapel Hill, NC, USA

Correspondence

Paul L. Reiter, PhD

Division of Cancer Prevention and Control

College of Medicine

The Ohio State University

1590 North High Street, Suite 525

Columbus, OH 43201 USA

614-366-4265 phone

614-366-5454 fax

Paul.Reiter@osumc.edu

Running Title: Advancing HPV Vaccine Delivery

Keywords: Human papillomavirus; HPV vaccine; Cancer

Acknowledgements: This paper reports findings from a meeting that was sponsored by the National HPV Vaccination Roundtable, which was established by the American Cancer Society and the Centers for Disease Control and Prevention. This publication was supported by the Grant or Cooperative Agreement Number 1H23IP000931-01 funded by the Centers for Disease Control and Prevention. Its contents are solely the responsibility of the authors and do not necessarily represent the official views of the above organizations or the Department of Health and Human Services.

Conflicts of Interest: P. L. Reiter has received research grants from Merck and Cervical Cancer-Free America, via an unrestricted educational grant from GlaxoSmithKline. G. D. Zimet has been an investigator on investigator-initiated HPV research funded by Merck and Roche and received travel support from Merck to present research findings at a scientific meeting. N. T.

Brewer has served on paid advisory boards for Merck and received research grants from Merck and Pfizer. The remaining authors have no conflicts of interest to report.

Word Count: 1100

Number of Tables: 1

Number of References: 9

Commentary

Human papillomavirus (HPV) vaccine has been available in the United States (US) for a decade, yet vaccination coverage remains modest. A recent review identified numerous interventions for increasing HPV vaccination,¹ but effects were small and evidence was often insufficient to identify best practices. The National HPV Vaccination Roundtable sponsored a one-day national meeting in 2016 on best and promising practices in HPV vaccine delivery, in part to identify important research gaps.

Meeting attendees were HPV vaccine delivery experts including scientists, clinicians, and other stakeholders. About 100 people attended in-person and about 400 additional people streamed the meeting online (livestream.com/ACS/events/5892004). Throughout the meeting, the meeting facilitators encouraged attendees to identify gaps that future research should address and write them on display boards (or send via email or Twitter). Facilitators did not provide attendees with a predefined list of gaps. Attendees identified a total of 33 gaps (Table 1). In-person attendees voted for up to five gaps they believed were top priorities. We categorized the gaps into themes. The 12 gaps that received the most votes generally fit into these themes: a) social media and vaccine confidence; b) healthcare provider interventions; or c) system-level approaches. Two gaps in the top 12 that did not fit these themes were determining **what interventions work in rural areas** (Gap 7) and **the impact of survivor testimonials** (Gap 9).

Social Media and Vaccine Confidence

Many attendees prioritized the gaps of **how to increase HPV vaccine confidence by intervening in social media** (Gap 1) and **how to address rumors about HPV vaccine spread via social media** (Gap 4). HPV vaccination has generated broad support as well as some

controversy since its introduction. Although not substantiated by evidence, stories about vaccine side effects and other misinformation have proliferated through anti-vaccination groups on social media.² Even if unfounded, this negative publicity can confuse and frighten parents, lead healthcare providers to incorrectly assume that parents may not value HPV vaccination, and create the perception among providers that conversations about HPV vaccination will be difficult. It is important to understand how best to leverage social media to counter the negative publicity and promote HPV vaccination. This includes determining which negative stories require a response, when and how the response should take place, and which organizations should issue the response.

Attendees prioritized the gap of **how to address parents' concerns and hesitancy about HPV vaccine** (Gap 8). Working groups at the World Health Organization and the US National Vaccine Advisory Committee have also identified this as a priority. However, relatively few interventions have been explicitly designed to address vaccine hesitancy and there is limited evidence on the effectiveness of such interventions.³

Healthcare Provider Interventions

Attendees prioritized several gaps involving healthcare providers, whose recommendations to vaccinate are central to increasing HPV vaccination. This included **how to encourage providers to attend in-clinic quality improvement interventions** (Gap 2), such as Assessment, Feedback, Incentives, and eXchange (AFIX) visits recommended by the Centers for Disease Control and Prevention. AFIX visits for adolescent vaccination are already in use nationally, but research is needed to optimize the delivery (including encouraging provider participation), impact, and sustainability of these programs.⁴

Consistent with the broader trend of team approaches to healthcare, attendees prioritized **how to intervene with the entire medical team** (Gap 6) as a research gap. Such interventions would engage the whole office, including physicians, mid-level providers, nurses, and front office staff, to create a culture supportive of HPV vaccination. Lastly, attendees prioritized the gap of **how to increase HPV vaccination during acute care visits** (Gap 10). Relatively few providers discuss HPV vaccination at visits that are not for preventive care (e.g., sick visits for patients with mild complaints).⁵ Medical visits for follow-up and non-serious acute illness or injury are missed opportunities for providers to recommend and administer HPV vaccine.

System-Level Approaches

Attendees prioritized several gaps concerning system-level approaches, which can have broad impact and may require less time, effort, and other costs than provider training. One system-level gap was identifying **best practices for health insurers and plans** (Gap 3). Health insurance plans can implement benchmark measures, making financial incentives and reimbursement contingent on meeting HPV vaccination goals. One widely used set of measures is the Healthcare Effectiveness Data and Information Set (HEDIS). Starting in 2017, HEDIS will have a single measure for adolescent vaccination: male and female adolescents receive all doses of HPV vaccine, the first dose of meningococcal vaccine, and tetanus booster vaccine by age 13.⁶ Assessing **the impact of quality standards** (Gap 12), such as HEDIS, will be important to future vaccination efforts.

Attendees prioritized determining **effective system-level changes in large health systems and hospitals** (Gap 11). These organizations have several promising tools at their disposal, including system-wide adoption of standing orders for HPV vaccination. Electronic

health record systems (EHRs) can automate reminder-recalls for patients due for HPV vaccination, generate reminder prompts for providers to administer the vaccine, and help facilitate nurse-only immunization visits and walk-in immunization hours that can make completion of the HPV vaccine series easier. Strategies such as reminder-recalls for patients and reminder prompts for providers have often, but not always, been successful at increasing vaccination,^{7,8} but implementation of these strategies is inconsistent. In addition, EHRs can generate reports to track the impact of strategies to increase HPV vaccination and potential procedural challenges during implementation (e.g., vaccine supply, parents refusing or delaying vaccination, etc.).

Attendees prioritized **the impact of connecting immunization information systems to EHRs and exchanging data bi-directionally** (Gap 5) as a research gap. Immunization information systems are population-based clinical information systems for specified geographic regions, typically states. Data exchange between immunization information systems and other clinical information systems, such as EHRs, can support the integration of scattered vaccination records. Bi-directional exchange can save providers time while increasing their confidence in the data informing patient care and quality improvement efforts. Any implementation of bi-directional exchange processes will have to be accomplished within the context of state policies, which may not require providers to use the registry, may require its use only for some doses (e.g., publicly funded doses), or may include data only for children of parents who opt in.⁹

Conclusions

National experts identified and prioritized research gaps that have promise for increasing HPV vaccination. Most of the prioritized gaps involved social media and vaccine confidence

(e.g., increasing vaccine confidence by intervening in social media), healthcare provider interventions (e.g., encouraging providers to attend in-clinic quality improvement interventions), or system-level approaches (e.g., best practices for health insurers and plans). It is critical to develop and evaluate interventions in each of these areas to close existing gaps and identify best practices for increasing HPV vaccination.

References

1. Smulian EA, Mitchell KR, Stokley S. Interventions to increase HPV vaccination coverage: a systematic review. *Hum Vaccin Immunother.* 2016;12(6): 1566-1588.
2. Dunn AG, Leask J, Zhou X, et al. Associations between exposure to and expression of negative opinions about human papillomavirus vaccines on social media: an observational study. *J Med Internet Res.* 2015;17(6): e144.
3. Sadaf A, Richards JL, Glanz J, et al. A systematic review of interventions for reducing parental vaccine refusal and vaccine hesitancy. *Vaccine.* 2013;31(40): 4293-4304.
4. Gilkey MB, Dayton AM, Moss JL, et al. Increasing provision of adolescent vaccines in primary care: a randomized controlled trial. *Pediatrics.* 2014;134(2): e346-e353.
5. Gilkey MB, Moss JL, Coyne-Beasley T, et al. Physician communication about adolescent vaccination: how is human papillomavirus vaccine different? *Prev Med.* 2015;77: 181-185.
6. National Committee for Quality Assurance. HEDIS[®] & performance measurement. 2016. Available at: <http://www.ncqa.org/hedis-quality-measurement>
7. Niccolai LM, Hansen CE. Practice- and community-based interventions to increase human papillomavirus vaccine coverage: a systematic review. *JAMA Pediatr.* 2015;169(7): 686-692.
8. Szilagyi PG, Serwint JR, Humiston SG, et al. Effect of provider prompts on adolescent immunization rates: a randomized trial. *Acad Pediatr.* 2015;15(2): 149-157.
9. Centers for Disease Control and Prevention. Survey of state immunization information system legislation. 2012. Available at: <https://www2a.cdc.gov/vaccines/iis/iissurvey/legislation-survey.asp>

Table 1. Gaps in HPV vaccination delivery research

| Gap | No. of Attendees Who Endorsed Gap as a Top Priority | <u>Theme</u> |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------|--------------------------------------|
| 1 How to increase HPV vaccine confidence by intervening in social media | 38 | <u>Social media & confidence</u> |
| 2 How to encourage providers to attend in-clinic quality improvement interventions (e.g., AFIX) | 36 | <u>Healthcare providers</u> |
| 3 What are best practices for health insurers and plans | 27 | <u>System-level</u> |
| 4 How to address rumors about HPV vaccine spread via social media | 25 | <u>Social media & confidence</u> |
| 5 What is the impact of connecting immunization information systems to electronic health records and exchanging data bi-directionally | 24 | <u>System-level</u> |
| 6 How to intervene with the entire medical team (e.g., physicians, mid-level providers, nurses, and front office staff) | 22 | <u>Healthcare providers</u> |
| 7 What interventions work in rural areas | 18 | <u>Diverse populations</u> |
| 8 How to address parents' concerns and hesitancy about HPV vaccine | 16 | <u>Social media & confidence</u> |
| 9 What is the impact of survivor testimonials | 14 | <u>Communication</u> |
| 10 How to increase HPV vaccination during acute care visits | 10 | <u>Healthcare providers</u> |
| 11 What are effective system-level changes in large health systems and hospitals | 10 | <u>System-level</u> |
| 12 What is the impact of quality standards (e.g., HEDIS) | 9 | <u>System-level</u> |
| 13 How to make tailored education interventions for parents sustainable and affordable | 7 | <u>Communication</u> |
| 14 How to optimize peer comparison interventions with providers (i.e., should comparisons be between providers, clinics, geographic regions, other recommended vaccines) | 7 | <u>Healthcare providers</u> |
| 15 How to conduct larger, multi-site randomized trials | 5 | <u>Intervention design</u> |
| 16 What interventions work in non-FQHC settings and non-minority groups | 5 | <u>Diverse populations</u> |

| | | | |
|----|-----------------------------------------------------------------------------------------------------------------------------------------|---|--------------------------------------|
| 17 | What interventions are feasible in primary care settings | 5 | <u>Healthcare providers</u> |
| 18 | What is the impact of financial incentives on HPV vaccination | 5 | <u>Other</u> |
| 19 | What works in the United States versus in global settings | 5 | <u>Diverse populations</u> |
| 20 | How to improve entry of HPV vaccine doses administered into immunization information systems (e.g., use of incentives versus penalties) | 4 | <u>System-level</u> |
| 21 | How to make HPV vaccination urgent | 4 | <u>Communication</u> |
| 22 | How to create a better definition of vaccine hesitancy and determine if there are different types | 3 | <u>Social media & confidence</u> |
| 23 | What longer-term follow-up data will reveal about lasting effects of interventions | 2 | <u>Intervention design</u> |
| 24 | Why HPV vaccination coverage is currently higher for many underserved and minority populations | 2 | <u>Diverse populations</u> |
| 25 | Which education messages work for parents with children age 13 and older | 2 | <u>Diverse populations</u> |
| 26 | How to optimize use of announcements as part of provider recommendations (e.g., when to use and for which patients) | 2 | <u>Healthcare providers</u> |
| 27 | What is the impact of saying HPV vaccine prevents cancer | 1 | <u>Communication</u> |
| 28 | How to intervene with younger versus older providers | 1 | <u>Healthcare providers</u> |
| 29 | What is the impact of Vaccine Information Sheets | 1 | <u>Communication</u> |
| 30 | Which interventions work best for which populations | 0 | <u>Diverse populations</u> |
| 31 | What is the cost of doing interventions | 0 | <u>Intervention design</u> |
| 32 | What is the impact of food on attendance at provider education sessions | 0 | <u>Healthcare providers</u> |
| 33 | Where do providers look for information about HPV vaccine | 0 | <u>Healthcare providers</u> |

Note. Meeting attendees endorsed up to five gaps they believed were the top priorities. HPV=human papillomavirus; AFIX=Assessment, Feedback, Incentives, and eXchange; HEDIS=Healthcare Effectiveness Data and Information Set; FQHC=Federally Qualified Health Center.