Background – HPV Vaccines Session

Lauri Markowitz, MD
Division of Viral Diseases

Advisory Committee on Immunization Practices
June 26, 2019
Outline

- Background for policy issues being considered today
  - Harmonization of catch-up vaccination through age 26 years
  - Vaccination of adults older than age 26 years
- Global HPV vaccine landscape
Policy Issues
### HPV vaccines licensed in the United States

#### Before October 2018

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>HPV types</th>
<th>Manufacturer</th>
<th>Licensure ages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bivalent (2vHPV)</td>
<td>16,18</td>
<td>GlaxoSmithKline</td>
<td>Females 9–25 yrs</td>
</tr>
<tr>
<td>Quadrivalent (4vHPV)</td>
<td>6,11,16,18</td>
<td>Merck &amp; Co.</td>
<td>Females and males 9–26 yrs</td>
</tr>
<tr>
<td>9-valent (9vHPV)</td>
<td>6,11,16,18, 31,33,45,52,58</td>
<td>Merck &amp; Co.</td>
<td>Females and males 9–26 yrs</td>
</tr>
</tbody>
</table>

**Availability**

- Since end of 2016, only 9vHPV has been distributed in the United States
### HPV vaccines licensed in the United States

**October 2018**

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>HPV types</th>
<th>Manufacturer</th>
<th>Licensure ages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bivalent (2vHPV)</td>
<td>16,18</td>
<td>GlaxoSmithKline</td>
<td>Females 9–25 yrs</td>
</tr>
<tr>
<td>Quadrivalent (4vHPV)</td>
<td>6,11,16,18</td>
<td>Merck &amp; Co.</td>
<td>Females and males 9–26 yrs</td>
</tr>
<tr>
<td>9-valent (9vHPV)</td>
<td>6,11,16,18, 31,33,45,52,58</td>
<td>Merck &amp; Co.</td>
<td><strong>Females and males 9–45 yrs</strong></td>
</tr>
</tbody>
</table>

**Availability**

- Since end of 2016, only 9vHPV has been distributed in the United States

**Vaccine licensure and use in adults in other countries**

- HPV vaccines have been licensed through age 45 years or older in other countries
- No country has a public health vaccination program targeting adults older than 26 years
Current recommendations for HPV vaccination

- **Routine vaccination**
  - Age 11 or 12 years
  - Vaccination can be started at age 9 years

- **Catch-up vaccination**
  - Females through age 26 years
  - Males through age 21 years
  - Certain populations through age 26 years*

- **Males aged 22 through 26 years may be vaccinated**

*Men who have sex with men, transgender persons, and persons with certain immunocompromising conditions

MMWR 2014;63 (RR-05)  MMWR 2015;64:300-4  MMWR 2016;65:1405-8
HPV vaccination recommendations and vaccine use in the United States

Recommendation for Females
Routine: 11 or 12 years
Catch-up: through 26 years
3-dose schedule

Recommendation for Males
Routine: 11 or 12 years
Catch-up: through 21 years
3-dose schedule

2-dose schedule
if first dose age <15 years

HPV vaccination recommendations and vaccine use in the United States

**Recommendation for Females**
- **Routine:** 11 or 12 years
- **Catch-up:** through 26 years
- **3-dose schedule**

**Recommendation for Males**
- **Routine:** 11 or 12 years
- **Catch-up:** through 21 years
- **3-dose schedule**

**2-dose schedule if first dose age <15 years**

- **2006**
- **2007**
- **2008**
- **2009**
- **2010**
- **2011**
- **2012**
- **2013**
- **2014**
- **2015**
- **2016**
- **2017**
- **2018**
- **2019**

**Quadrivalent Vaccine**

**Bivalent Vaccine**

**9-valent Vaccine**
Estimated HPV vaccination coverage among adolescents aged 13–17 years, NIS-Teen, United States, 2006–2017

Adapted from Walker et al. MMWR 2018; NIS-Teen, National Immunization Survey-Teen; UTD, Up-to-date
Note: Revised definition of adequate provider data in 2013
HPV vaccination for males

- Considered by ACIP
  - After 4vHPV licensed for use in males and data available on vaccine efficacy for prevention of anal precancers in males
  - Using GRADE, including health economic analyses
    • Inclusion of males less cost-effective than female vaccination
    • Vaccination becomes less cost-effective with increasing age at vaccination

- Vaccination recommended at age 11 or 12 years; catch-up through age 21
  - ACIP considered health economic data when recommending age for catch-up

GRADE: Grading of Recommendations, Assessment, Development and Evaluation
Recommendations on the use of quadrivalent human papillomavirus vaccine in males — Advisory Committee on Immunization Practices (ACIP), MMWR 2011;60:1705-8
Harmonization of catch-up HPV vaccination through age 26 years

- Increasing interest from partners and stakeholders in harmonizing catch-up recommendations across genders

- In 2017–2018, before CDC awareness of the manufacturer application to FDA for the 9vHPV expanded age range
  - ACIP Work Group was considering harmonization of catch-up recommendations

- Work Group delayed consideration of harmonization
  - FDA agreed to an expedited review for the expanded age application, April 2018
  - Unclear what health economic analyses would show for adult vaccination; wanted to avoid multiple recommendation changes in one year
  - Health economic analyses more challenging than anticipated
Vaccination of adults older than age 26 years

- ACIP HPV Vaccines Work Group
  - Considered vaccination of adults older than age 26 years harmonized across genders
  - Reviewed wide range of data: clinical trials, epidemiology, and natural history
    - Uncertainty about some aspects of natural history
  - Considered results from 5 health economic models
    - 3 models initially; 2 additional models included after October 2018
    - 4 of 5 models predict high cost per QALY for expanding catch-up age

QALY, quality-adjusted life year
Presentations today

- Summarize data presented to ACIP over past year
  - Evidence to Recommendations presentation

- The only new data today
  - Some of the health economic modeling data
  - Data from a 9vHPV immunogenicity and safety trial
Licensure of 9vHPV for use in expanded age range
FDA Summary Basis for Regulatory Action

- Results of a randomized, double-blind, placebo-controlled trial (base study) of 4vHPV that included women aged 27–45 years
- Observational follow-up through 10 years in a subset of women in the base study
- A cross-study immunogenicity analysis showing statistical non-inferiority of immune responses to 4vHPV in males aged 27–45 years vs aged 16–26 years
- Extrapolation of data to 9vHPV in individuals aged 27–45 years


GRADE for vaccination of 27–45 year-old adults

- GRADE presented to ACIP in October 2018
  - Evidence tables included data for 2vHPV and 4vHPV immunogenicity, efficacy and safety in adults aged 27–45 years*

- Work Group updated GRADE tables in June 2019
  - To include data from 9vHPV immunogenicity and safety trial in women aged 27–45 years†

GRADE: Grading of Recommendations, Assessment, Development and Evaluation
[https://www.cdc.gov/vaccines/acip/recs/grade/about-grade.html](https://www.cdc.gov/vaccines/acip/recs/grade/about-grade.html)
*Meites, presentation at October 2018 ACIP meeting;
*Luxembourg, presentation at June 2019 ACIP meeting
Global Landscape – HPV Vaccines
Countries with HPV vaccine in the national immunization program, 2019

- Introduced (Includes partial introduction) to date (96 countries or 49%)
- Not Available, Not Introduced/No Plans (96 countries or 51%)
- Not applicable
Current global HPV vaccine demand/supply imbalance

- **World Health Organization recommendations**
  - 2009 - HPV vaccination of girls for single age cohort of girls
  - 2016 - Multi-age cohort vaccination (age 9-14 years in first year)
    - Increased vaccine demand

- **Gavi funding for HPV vaccination**
  - Started in 2012

- **HPV vaccine demand/supply imbalance**
  - Projected to last 3-5 years
  - Delay introduction in some countries
  - Prevent multi-age cohort vaccination

- **No HPV vaccine shortage anticipated in United States**

Global HPV vaccine supply: World Health Organization SAGE meeting report, October 2018

“Concerned about the impact of a constrained HPV vaccine supply forecast until at least 2024, SAGE urged that a globally more equitable distribution of the available doses be encouraged to ensure optimal global public health access to the vaccine.

Countries that currently implement extended vaccination strategies (including target groups of boys, cohorts of different ages and older age groups) may consider rationalizing their vaccine use in order to make urgently needed vaccine available in countries with a high burden of disease.

Additionally, SAGE called for: (i) collaboration with all current and future manufacturers to expedite increases in the vaccine supply and (ii) comprehensive evaluation of the options for best use and allocation of the limited vaccine supply...”
Current global HPV vaccine demand/supply imbalance

- Reasons presented to ACIP today
  - General awareness
  - Some Work Group members considered this in discussions of policy options for vaccination of adults older than 26 years
Policy issues being considered today

- Harmonization of catch-up vaccination through age 26 years
- Vaccination of adults older than age 26 years
ACIP HPV Vaccines
Work Group

ACIP Members
Peter Szilagyi (Chair)
Jose Romero
Kevin Ault

Ex Officio Members
Jeff Roberts (FDA)
Joohee Lee (FDA)

CDC Lead
Lauri Markowitz

Liaison Representatives
Shelley Deeks (NACCI)
Linda Eckert (ACOG)
Sandra Fryhofer (ACP)
Amy Middleman (SAHM)
Chris Nyquist (AAP)
Sean O’Leary (PIDS)
Robin O’Meara (AAFP)
Patricia Whitley-Williams (NMA)
Jane Zucker (AIM)

Consultants
Joseph Bocchini
Tamera Coyne-Beasley
John Douglas
Allison Kempe
Aimee Kreimer (NCI)
Debbie Saslow (ACS)
Rodney Willoughby
Rachel Winer

CDC Contributors
Harrell Chesson
Julianne Gee
Elissa Meites
Jeanne Santoli
Mona Saraiya
John Su
Shannon Stokley
Lakshmi Panagiotakopulos
Elizabeth Unger
Charnetta Williams
Thank You

For more information, contact CDC
1-800-CDC-INFO (232-4636)

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.