HPV prevention and control: Overview of activities, accomplishments and challenges in the United States

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Centers for Disease Control and Prevention

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Outline

- **Areas of CDC working on HPV issues**
- **Evolution of U.S. HPV vaccine recommendations**
- **U.S. HPV vaccination program**
  - Coverage
  - Vaccination challenges
  - Vaccine safety monitoring
- **HPV vaccine impact monitoring in the U.S.**

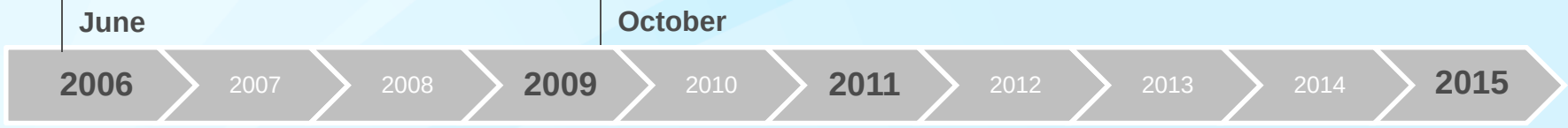
CDC HPV Workgroup

- **Immunization Program Activities**
  - Domestic
  - Global
- **Immunization Safety Office**
- **Sexually Transmitted Diseases**
- **Cancer Prevention**
- **HPV Laboratory**
- **Global HIV Program – Pink Ribbon Red Ribbon**

Evolution of recommendations for HPV vaccination in the United States

Quadrivalent
Routine, females 11 or 12 yrs* and 13-26 yrs not previously vaccinated

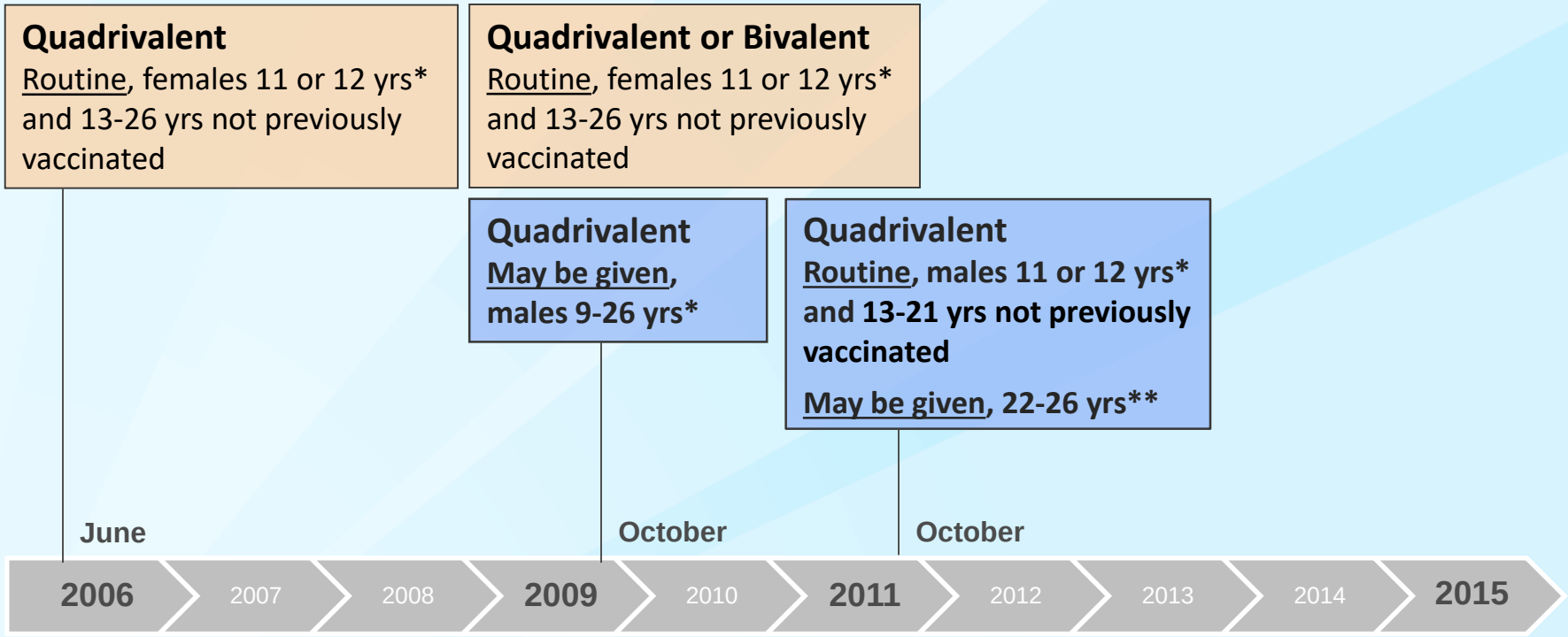
Quadrivalent or Bivalent
Routine, females 11 or 12 yrs* and 13-26 yrs not previously vaccinated



Quadrivalent (HPV 6,11,16,18) vaccine; Bivalent (HPV 16,18) vaccine

* Can be given starting at 9 years of age; ** For MSM and immunocompromised males, quadrivalent HPV vaccine through 26 years of age

Evolution of recommendations for HPV vaccination in the United States



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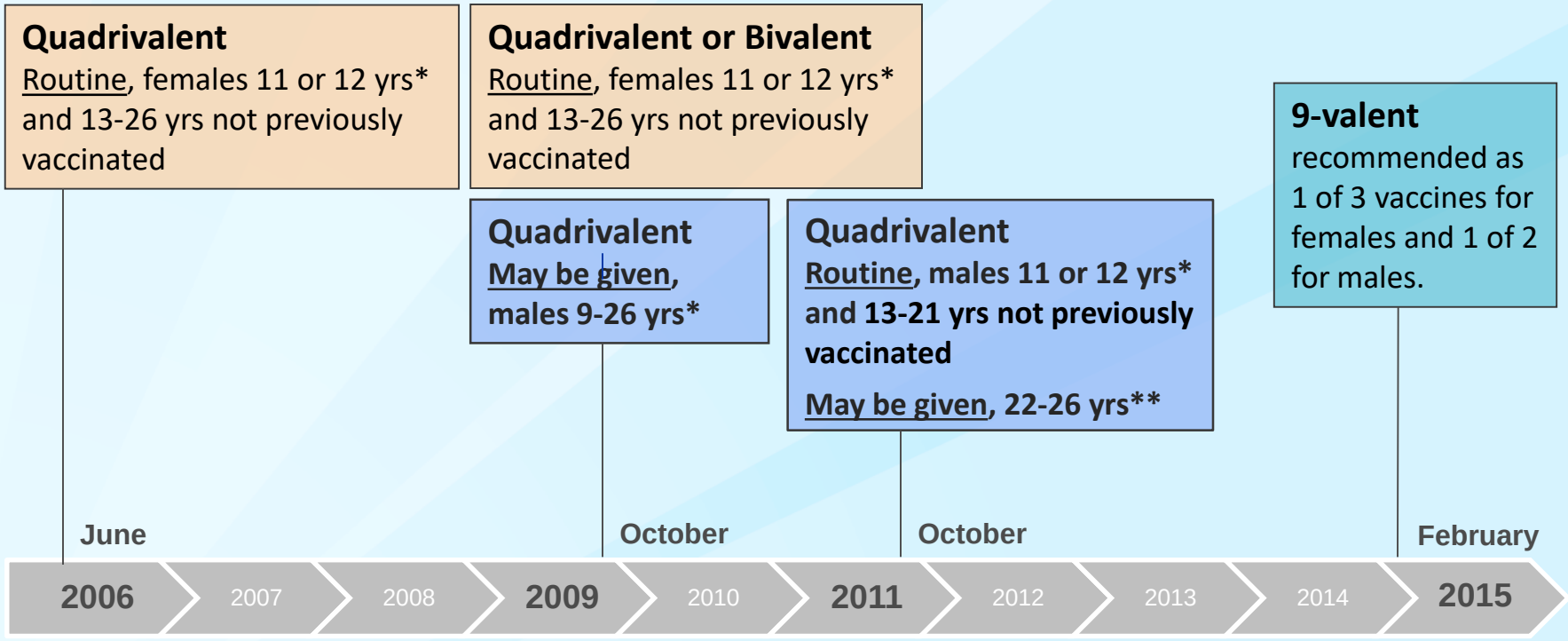
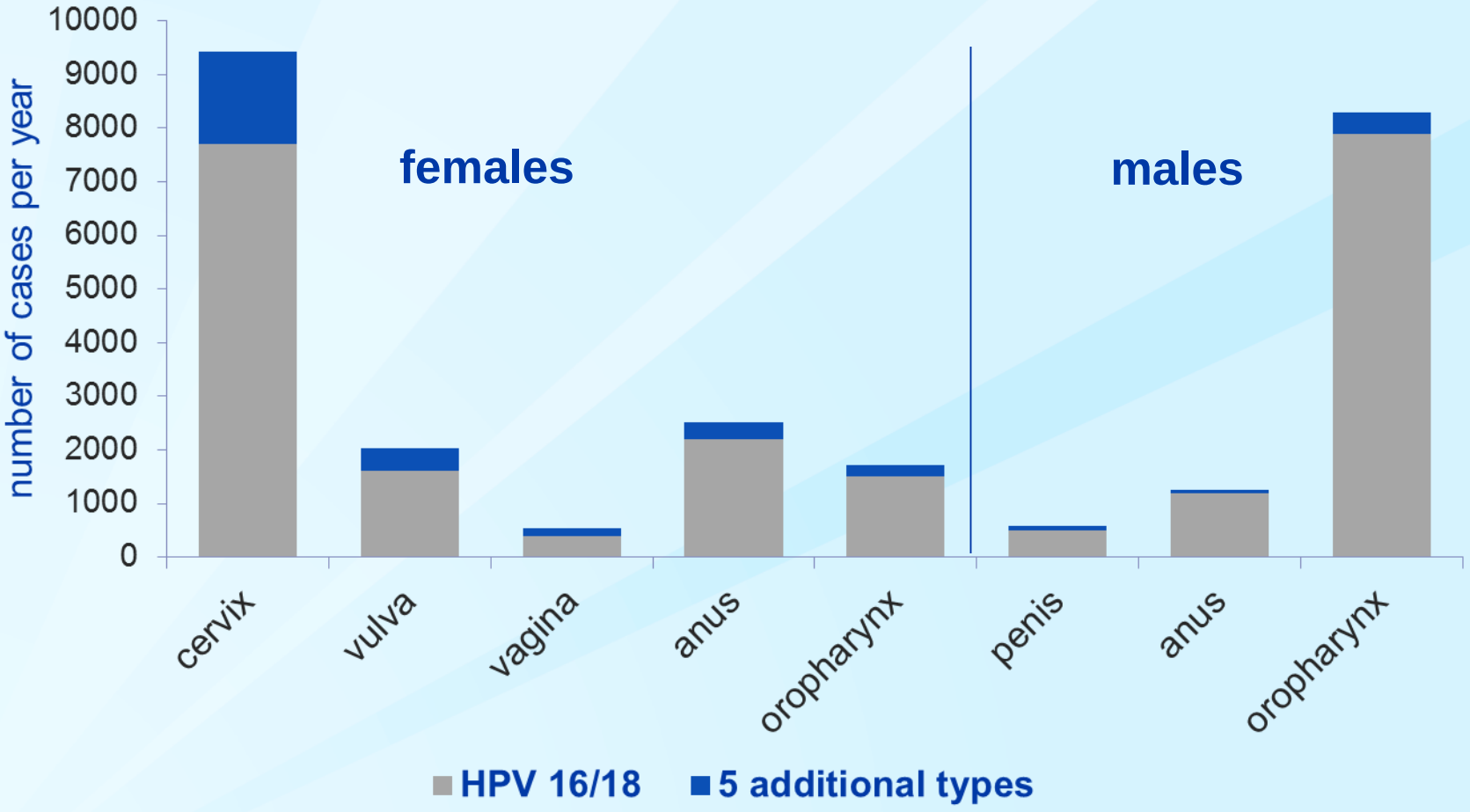


Quadrivalent (HPV 6,11,16,18) vaccine; Bivalent (HPV 16,18) vaccine; 9-valent (HPV 6,11,16,18 31.33, 45, 52, 58) vaccine

* Can be given starting at 9 years of age; ** For MSM and immunocompromised males, quadrivalent HPV vaccine through 26 years of age

Estimated numbers of HPV-associated cancers attributable to HPV 16/18 and 5 additional types in 9-valent vaccine, U.S.*



*Based on years 2006-2010 http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6349a11.htm and data from Saraiya et al. JNCI 2015

Cost-effectiveness of 9-valent HPV vaccination in the United States

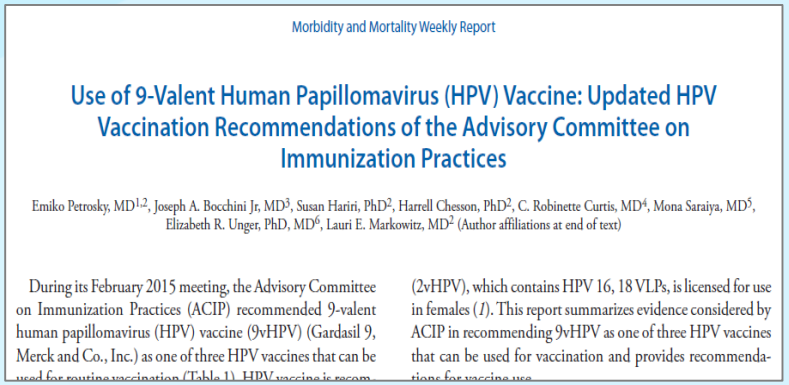
- 9-valent vaccine for both sexes is likely cost-saving compared to quadrivalent for both sexes
  - Of most benefit in females
  - Cost saving in most scenarios
    - < $25,000 in all scenarios

Base case assumption that 9-valent HPV vaccine costs $13 more per dose than quadrivalent HPV vaccine
QALY: quality-adjusted life year

Brisson et al. JNCI 2015

Updated recommendations for HPV vaccination in the United States, 2015

- Routine vaccination at age 11 or 12 years*
- Vaccination recommended through age 26 for females and through age 21 for males not previously vaccinated
- Vaccination recommended for immunocompromised persons (including persons HIV-infected) and for men who have sex with men through age 26
- 3-dose schedule (0, 1-2 and 6 months)
- Vaccines
  - 2vHPV, 4vHPV or 9vHPV for females
  - 4vHPV or 9vHPV for males



Morbidity and Mortality Weekly Report

Use of 9-Valent Human Papillomavirus (HPV) Vaccine: Updated HPV Vaccination Recommendations of the Advisory Committee on Immunization Practices

Emiko Petrosky, MD[1,2], Joseph A. Bocchini Jr, MD[3], Susan Hariri, PhD[2], Harrell Chesson, PhD[2], C. Robinette Curtis, MD[4], Mona Saraiya, MD[5], Elizabeth R. Unger, PhD, MD[6], Lauri E. Markowitz, MD[2] (Author affiliations at end of text)

During its February 2015 meeting, the Advisory Committee on Immunization Practices (ACIP) recommended 9-valent human papillomavirus (HPV) vaccine (9vHPV) (Gardasil 9, Merck and Co., Inc.) as one of three HPV vaccines that can be used for routine vaccination (Table 1). HPV vaccine is recom-

(2vHPV), which contains HPV 16, 18 VLPs, is licensed for use in females (*1*). This report summarizes evidence considered by ACIP in recommending 9vHPV as one of three HPV vaccines that can be used for vaccination and provides recommenda-tions for vaccine use.

*The vaccination series can be started at age 9 years

MMWR 2015;64:300-4

Summary: 9-valent HPV vaccine

- Licensed by FDA in December 2014
- Recommended by ACIP in February 2015
- Targets 5 additional high risk types
  - Overall 14% of HPV-associated cancers in females; 4% in males attributable to these 5 types
  - 15% of cervical cancers attributable to these 5 types
- One of 3 HPV vaccines that can be used for routine vaccination of females and one of 2 for males
- Doses distributed in the U.S.
  - 5 million through September 2015

Regulatory considerations for 2-dose HPV vaccination schedules in the U.S. (status in 2014)

- 2vHPV – no plans for submission to FDA
- 4vHPV – no plans for submission to FDA
- 9vHPV
  - No data on 2-dose schedules in BLA under consideration by FDA
  - Trial comparing 2-dose and 3-dose schedules initiated by manufacturer

BLA, Biologics License Application

9-valent HPV vaccine 2- vs 3-dose trial

- Immunogenicity trial
- Start date: Dec 2013; last visit: July 2015
- 5 arms (N=1500)

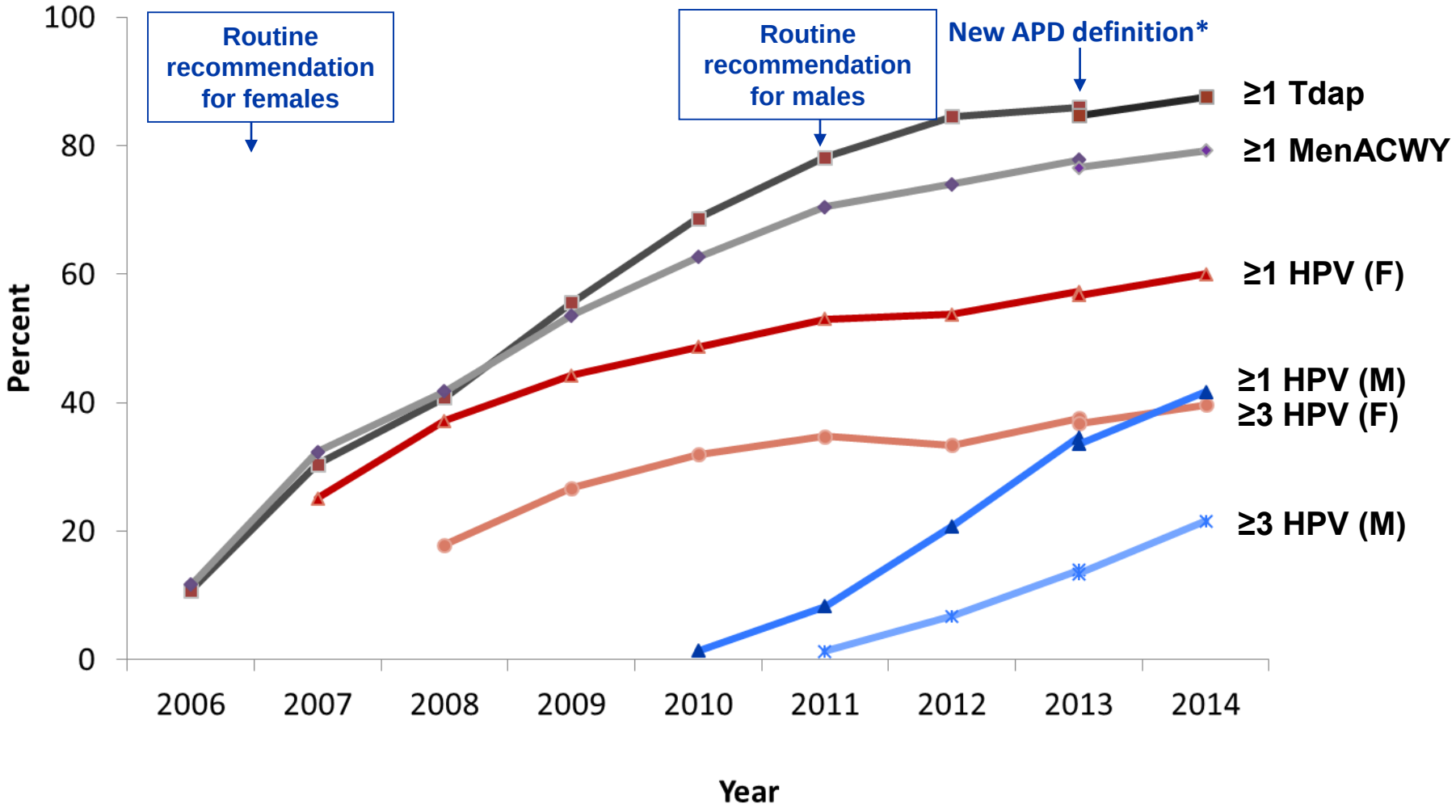
Number of doses	Dose interval (mos)	Age groups
2	0,6	9-14 yr old girls
2	0,6	9-14 yr old boys
2	0,12	9-14 yr old girls and boys
3	0,2,6	9-14 yr old girls and boys
3	0,2,6	16-26 yr old women

Clinicaltrials.gov identifier NCT01984697

U.S. HPV vaccination program

- Target age group 11 or 12 years
- One of several vaccines recommended for adolescent age group
  - Tetanus, diphtheria, and acellular pertussis vaccine (Tdap), meningococcal (MCV4), annual influenza
- Vaccinations funded through public program (Vaccines for Children) for those eligible and through private insurance
- Vaccine delivered mainly by primary care providers

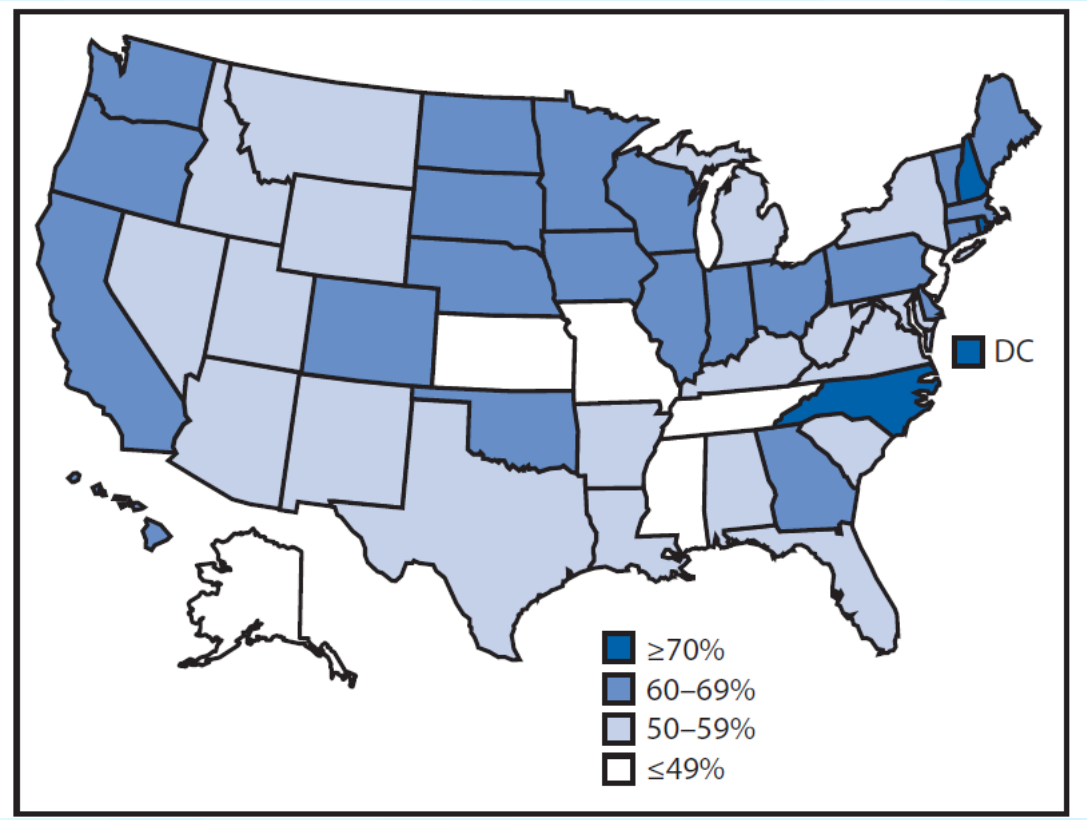
National estimated vaccination coverage among adolescents 13-17 Years, NIS-Teen 2006-2014



MMWR 2015;64:784-792

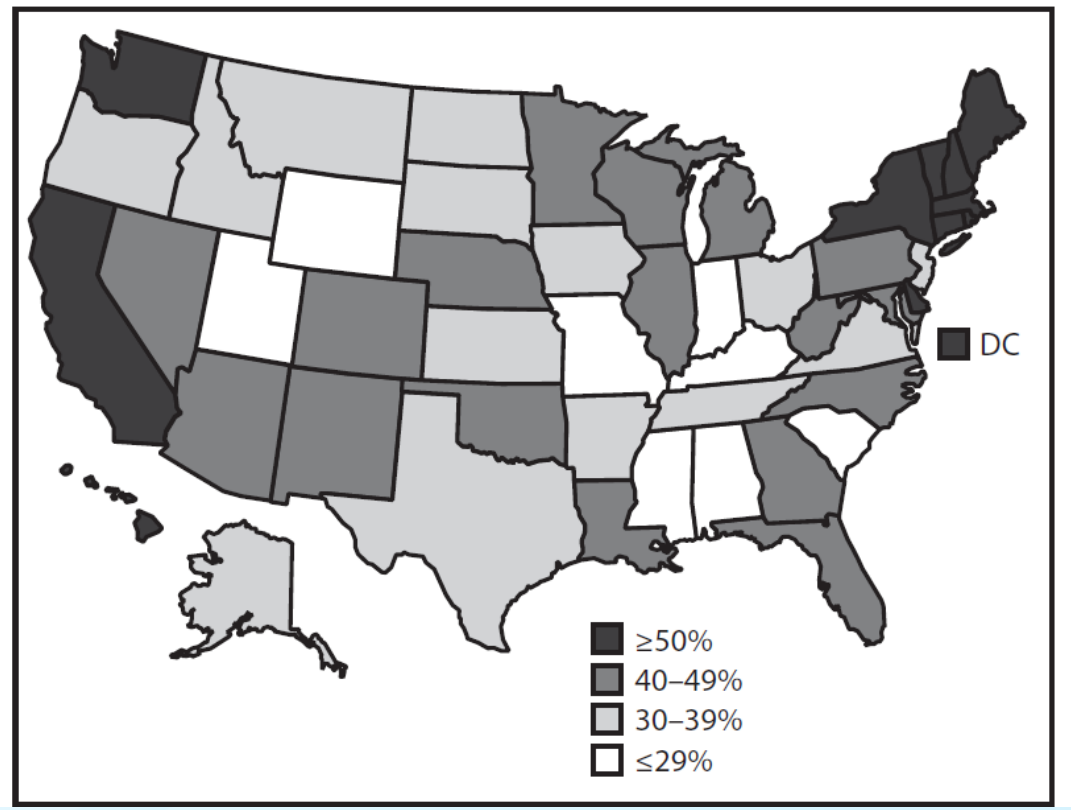
* APD = Adequate provider data

Estimated coverage with ≥ 1 dose HPV vaccine among females 13-17 years by state, NIS-Teen 2014



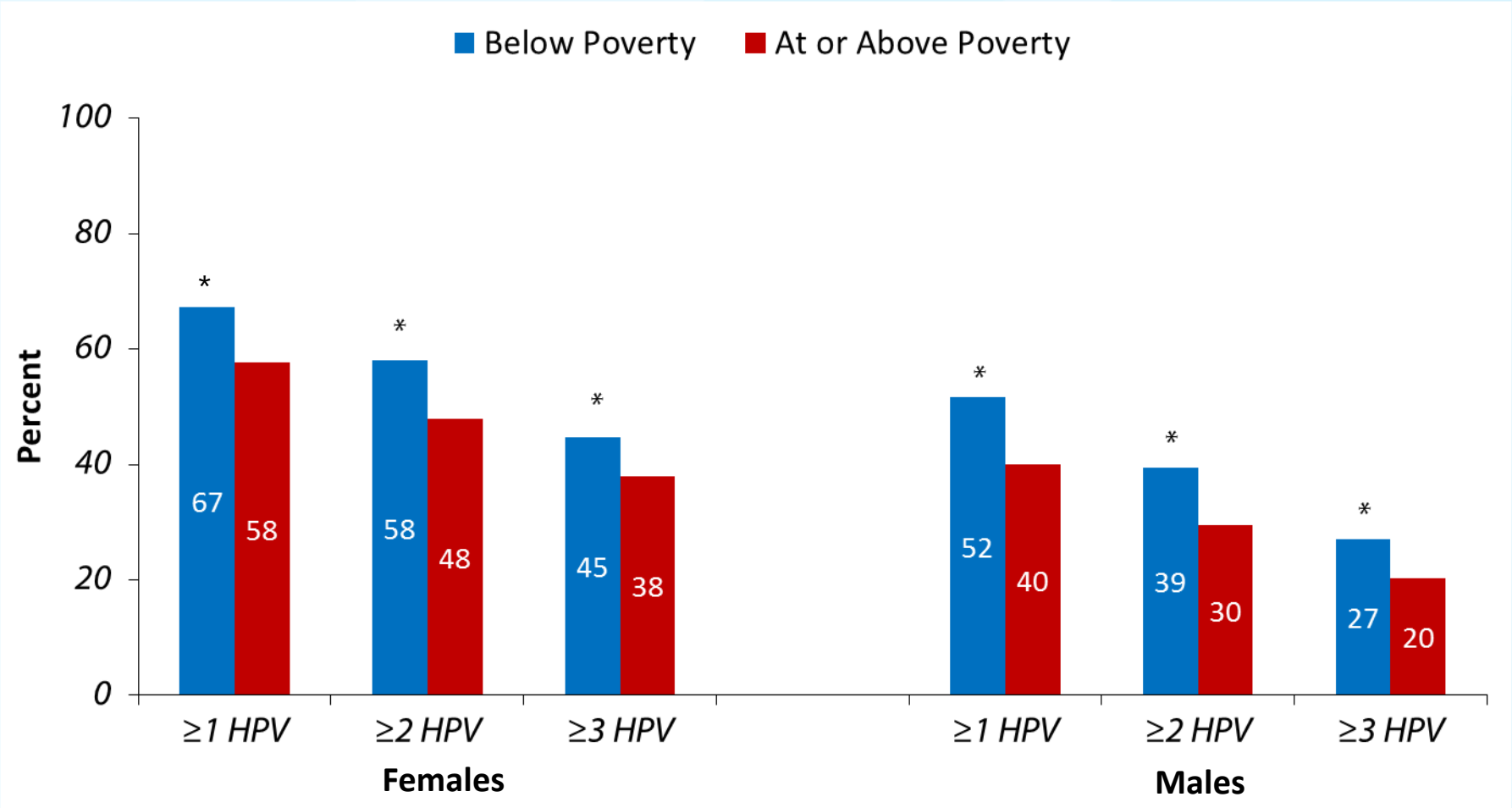
MMWR 2015;64:784-792

Estimated coverage with ≥ 1 dose HPV vaccine among males 13-17 years by state, NIS-Teen 2014



MMWR 2015;64:784-792

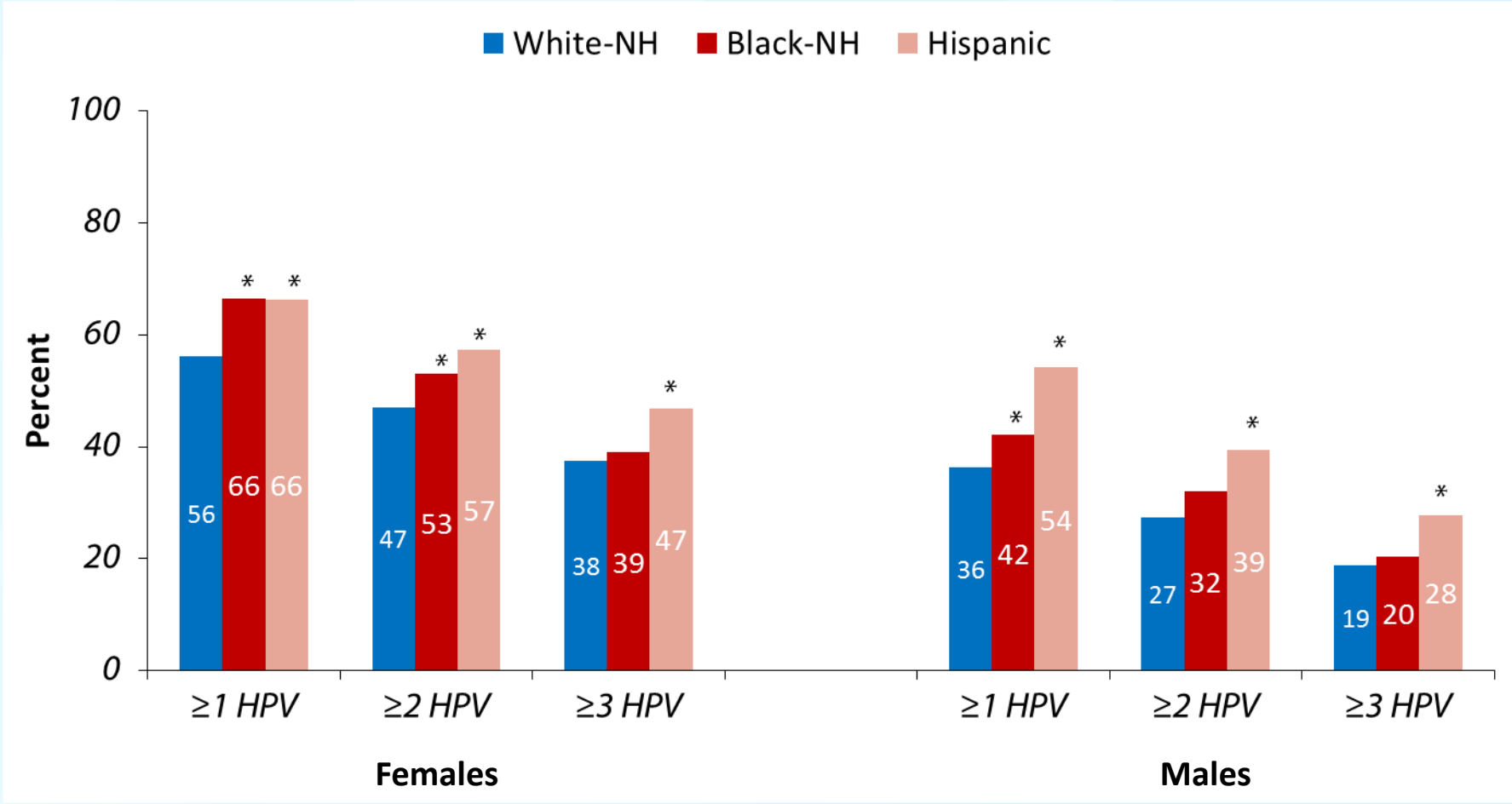
HPV vaccination coverage among adolescents aged 13-17 years by poverty status NIS-Teen, United States, 2014



* Statistically significant difference compared with adolescents at or above the poverty level ($p<0.05$).

MMWR 2015;64:784-792

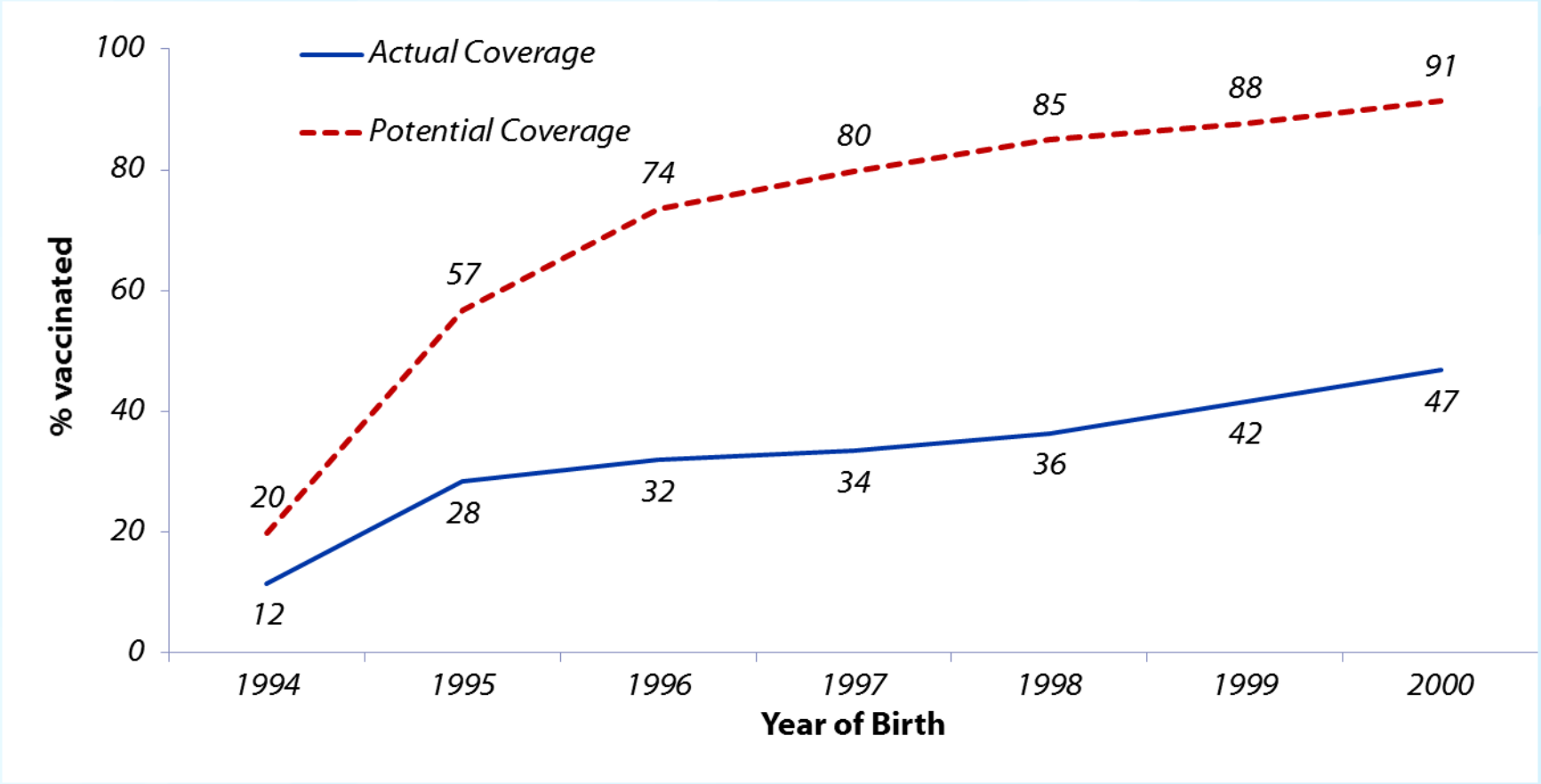
HPV vaccination coverage among adolescents aged 13-17 years by race/ethnicity NIS-Teen, United States, 2014



* Statistically significant difference compared with White-NH adolescents ($p<0.05$).

MMWR 2015;64:784-792

Actual and potentially achievable vaccination coverage of ≥1 HPV vaccine doses by age 13 among adolescent girls if missed opportunities* were eliminated, NIS-Teen 2007-2013 combined



*Missed opportunity defined as having a healthcare encounter where at least one vaccine was administered but HPV vaccine was not

MMWR 2014;63:620-4

Top 5 reasons for not vaccinating daughter, among parents with no intention to vaccinate in the next 12 months, United States, 2013

Lack of knowledge	15.5%
Not needed or necessary	14.7%
Safety concern/side effects	14.2%
Not recommended by provider	13.0%
Not sexually active	11.3%

Source: National Immunization Survey-Teen; MMWR 2014;63:620-4

Key challenges for HPV vaccination in the U.S.

- **No or weak recommendation from the provider**
  - #1 reason for not receiving vaccine
  - Present vaccine as optional
- **Providers more likely to recommend HPV vaccine for:**
  - Older teens compared to 11-12 year olds
  - Girls compared to boys
- **Missed vaccination opportunities common**
- **Gaps in parental knowledge**
  - Safety concerns
  - Child is not sexually active – does not need vaccine

CDC strategies to increase HPV vaccination coverage

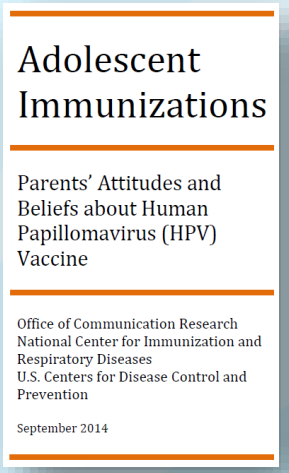
- Support state and local immunization programs
- Mobilize partners and stakeholders
- Strengthen provider commitment
- Improve and utilize reminder systems
- Increase public awareness

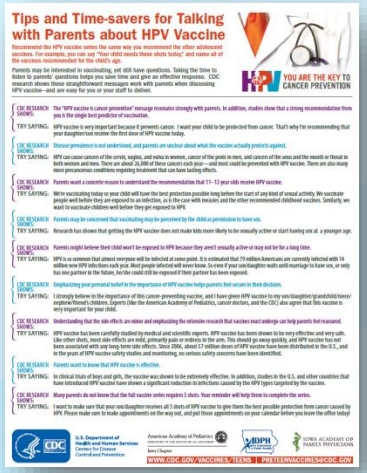
Strategies based on research with healthcare professionals

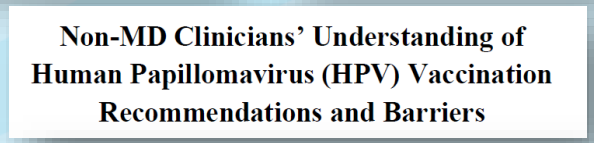
- Provide HCPs with strategies for how to give a strong HPV vaccine recommendation
- Assist HCPs in answering questions about HPV vaccine
- Share information with HCPs on systems that can help improve HPV vaccine coverage (reminder/recall, prompts, feedback loops, etc)

Communication efforts to increase HPV vaccine coverage, U.S.

- HPV core messages
- *You Are the Key* clinician slide deck
- Provider Tip Sheet
- Provider Portal for HPV







CDC Partnership cooperative agreements focused on increasing HPV vaccination

- Initially funded in late 2014
- Multiple national partners:
  - American Academy of Pediatrics
  - American Cancer Society
  - Academic Pediatric Association
  - National Area Health Education Center Organization
  - National Association of County and City Health Officials

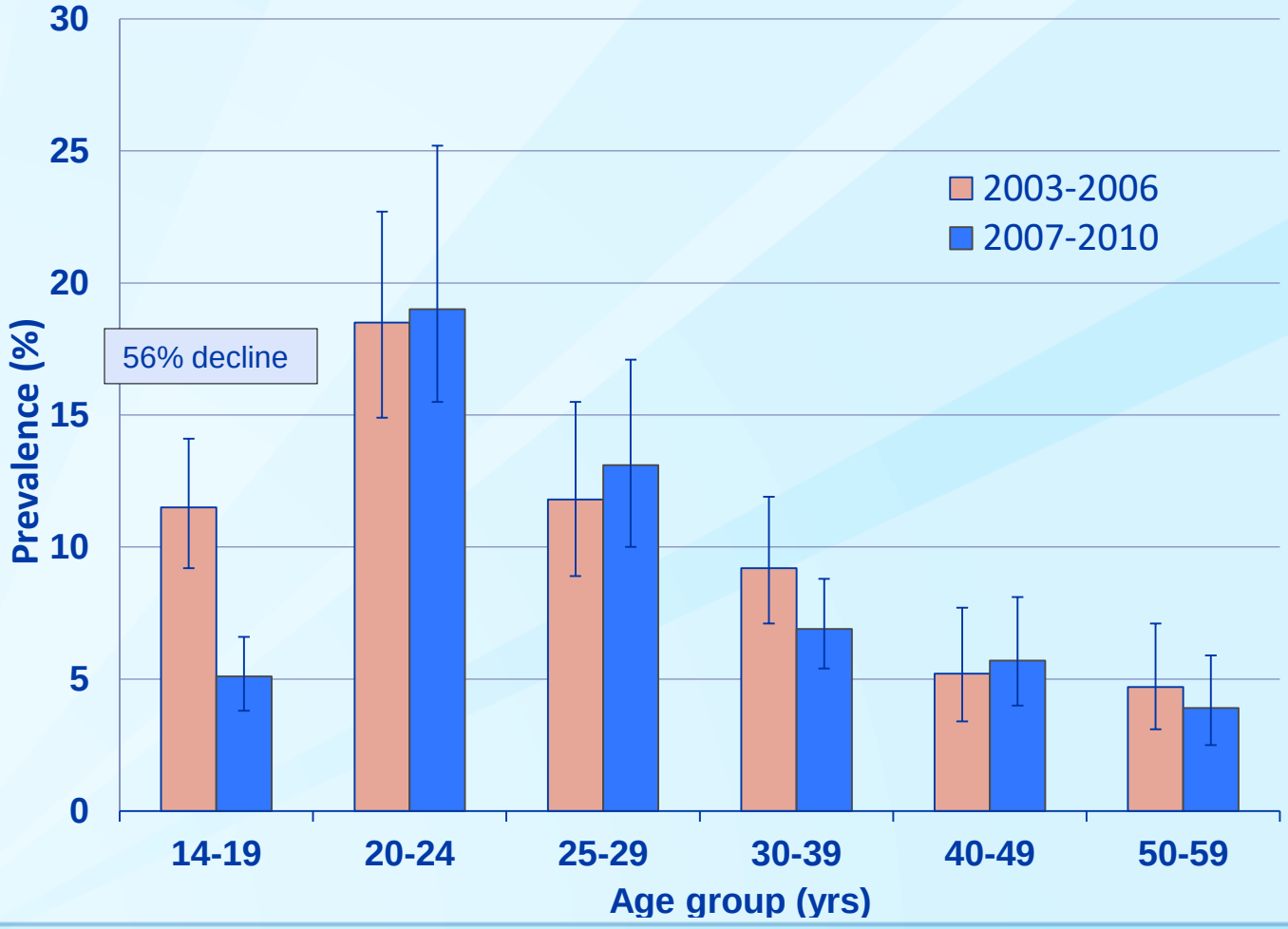
Post-licensure vaccine safety monitoring infrastructure in the US

System	Collaboration	Description
Vaccine Adverse Event Reporting System (VAERS)	CDC and FDA	US frontline spontaneous reporting system to detect potential vaccine safety problems
Vaccine Safety Datalink (VSD)	CDC and 9 Managed Healthcare Plans	Large linked database system used for active surveillance and research ~9.2 million members (~3% of US pop.) -Conducts monitoring & evaluation -Rates & risk estimates can be calculated
Clinical Immunization Safety Assessment (CISA) Project	CDC and 7 Academic Centers	Expert collaboration that conducts individual clinical vaccine safety assessments and clinical research

HPV vaccine impact monitoring in the US

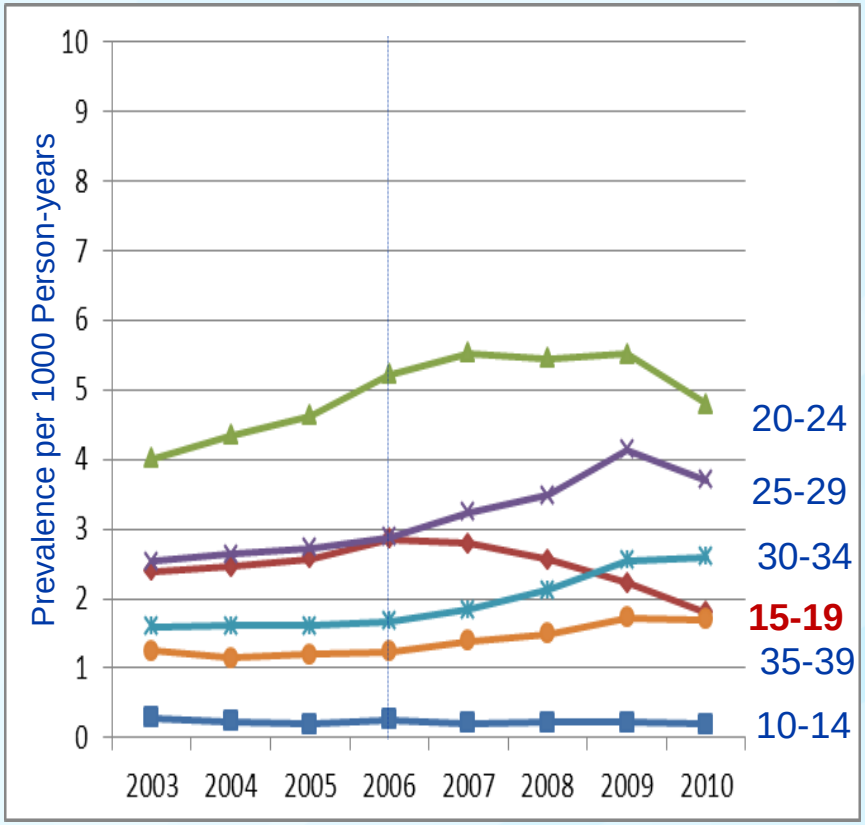
- HPV prevalence
  - National surveys (NHANES)
  - Women screened for cervical cancer
  - Clinic based populations
- Genital warts
  - STD clinics
  - Administrative data
- Cervical precancers
  - Population based sentinel sites
  - Administrative data
- Cancer
  - Cancer registries

Prevalence of HPV 6,11,16,18 in cervicovaginal swabs, by age U.S., 2003-2006 and 2007-2010

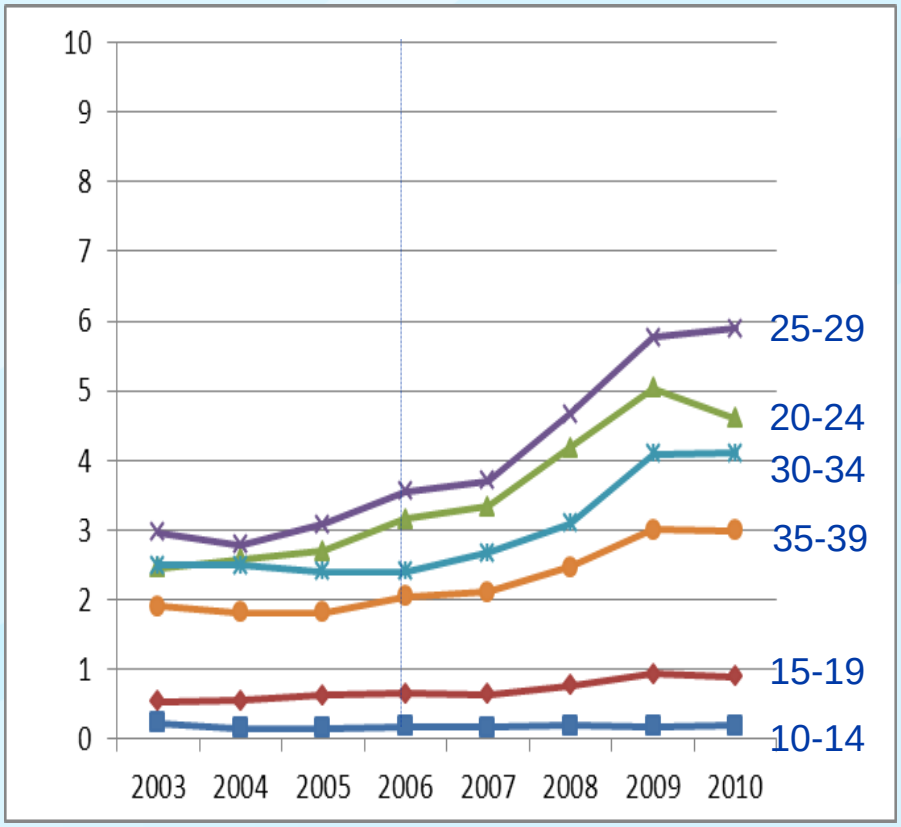


Markowitz et al. JID 2013;208:385-93

Anogenital wart prevalence per 1000 person-years, private insurance enrollees, U.S., 2003-2010



Females



Males

Flagg et al. AJPH 2013;103:1428–35

Challenges in monitoring HPV vaccine impact on cervical lesions

- Detected through cervical cancer screening
- Changing screening recommendations
- Lack of cervical cancer screening registries
- Incomplete linkages with vaccination registries

Vaccine effectiveness: % CIN2+ attributable to HPV 16/18 by timing of vaccination in relation to screening test, U.S.

Vaccination status and timing of vaccine initiation	N	% HPV 16/18	aPR* (95% CI)
Not vaccinated	1274	53.6	Ref
Vaccinated <30 days/after screening test	444	54.5	1.01 (0.92 – 1.10)
Vaccinated before screening test			
1-12 months	152	50.0	1.02 (0.87 – 1.19)
13-24 months	149	46.3	0.91 (0.77 – 1.08)
25-36 months	109	39.5	0.79 (0.63 – 0.99)
37-48 months	85	27.1	0.51 (0.36 – 0.72)
>48 months	54	13.0	0.28 (0.14 – 0.55)

aPR = adjusted prevalence ratio
*adjusted for race, site, insurance status, diagnosis grade

Hariri et al. Vaccine 2015;33:1608-13

Limited to women age eligible for vaccination

Summary

- HPV vaccine policy has changed since vaccine first licensed in 2006
- United States is one of the few countries to include boys as well as girls in the routine immunization program
- HPV vaccination coverage is still low and further efforts are needed to increase vaccine uptake
- Strong provider recommendation important for program with vaccination delivered by primary care providers
- Early impact of vaccination program on HPV-associated outcomes observed despite low vaccine uptake

Lessons learned from national HPV vaccine introductions globally

- **When implementing HPV vaccine, every country has an array of problems to solve**
- **Size and location of target population are often revised (upwards) after the 1st and even after the 2nd year of HPV vaccine use**
- **Delivery strategies often need modification, particularly to ensure that least advantaged populations are being reached**
- **Investments in information, education, and communication (IEC) are *critical* for HPV vaccine implementation**
- **HPV vaccine is a uniquely high profile vaccine receiving political attention and media scrutiny and has a broad array of stakeholders**
- **The extent of health systems strengthening required to sustainably introduce HPV vaccine nationally is *often underestimated***

Thank you

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.