

## Learning Objectives

At the completion of this activity, participants will be better able to :

1. Assess the potential effect of HPV infection
2. Identify HPV serotypes associated with particular cancers and genital warts
3. Apply preventive strategies to reduce the prevalence of HPV-related disease

1

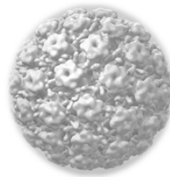
## Drug List

| Generic                     | Trade Name                             |
|-----------------------------|--|
| Bivalent HPV                | Cervarix                               |
| qHPV                        | Gardasil                               |
| gvHPV                       | Gardasil 9                             |
| HepB                        | Engerix-B, Recombivax HB               |
| MCV <sub>4</sub><br>MenACWY | Menactra, Menveo, Menomune, Meningovax |
| MMR                         | M-M-R II                               |
| Tdap                        | Adacel, Boostrix                       |

2

## HPV-Related Cancers and Diseases

- Worldwide, HPV causes ~5% of all new cancers occurring in males and females annually
- Globally, HPVs are responsible for:
  - Virtually 100% of cervical cancers
  - 75% of vaginal cancers
  - 69% of vulvar cancers
  - Almost all cases of genital warts and RRP
  - 91% of anal cancers
  - 63% of penile cancers
  - 70% of oropharyngeal cancers



HPV=human papillomavirus; RRP=recurrent respiratory papillomatosis.

1. Forman D et al. *Vaccine*. 2012;30 suppl 5:F12-F23; 2. Lacey CJ et al. *Vaccine*. 2006;24 suppl 3:S3/S5-S3/S41; 3. Bailey HH et al. *J Clin Oncol*. 2016;34(15):1803-1812. <http://jco.ascopubs.org/content/early/2016/04/07/JCO.2016.67.2014.full>. Accessed June 17, 2016; 4. American Cancer Society. *Cancer Facts & Figures 2015*. Atlanta: American Cancer Society; 2015.

**Approximately 80% of all people are infected by  $\geq 1$  type of HPV at some point in their lifetime**

1. Syrj nen K, Syrj nen S. *Scand J Infect Dis Suppl*. 1990;69:7-17; 2. Dunne EF et al. *JAMA*. 2007;297(8):813-819; 3. Human Papillomavirus. In: Atkinson W et al, eds. *Epidemiology and Prevention of Vaccine-Preventable Diseases*. 12th ed. Washington DC: Public Health Foundation/Centers for Disease Control and Prevention; 2011:175-186. <http://www.cdc.gov/vaccines/pubs/pinkbook/downloads/hpv.pdf>. Accessed September 29, 2016.

## Median Age at Cancer Diagnosis

- Breast Cancer 62 years
- Colon Cancer 68 years (men)  
72 years (women)
- Prostate Cancer 67 years
- Lung Cancer 72 years

National Cancer Institute. Surveillance, Epidemiology, and End Results Program. <http://seer.cancer.gov/>. Accessed January 22, 2016.

## HPV-Associated Cancers Affect Younger Adults Median Age at Diagnosis of HPV-Associated Cancers

- Cervical Cancer 47 years
  - More than 14% before age 35
- Oropharyngeal Cancer 62 years
  - 30% before age 50 years
  - HPV-related cancers typically <50 years
- Anal Cancer 60 years
  - More than 30% before age 55

1. National Cancer Institute. Surveillance, Epidemiology, and End Results Program. <http://seer.cancer.gov/>. Accessed January 22, 2016; 2. Marur S et al. *Lancet Oncol*. 2010;11(8):781-789; 3. Chaturvedi AK et al. *J Clin Oncol*. 2008;26(4):612-619.

## Vaccine Composition

- Pseudovirion-based vaccines
  - Based on L1 (capsid) protein
  - Highly immunogenic
- Bivalent vaccine
  - HPV 16, HPV 18 pseudovirions
  - ASO<sub>4</sub> adjuvant
    - Combination of aluminum hydroxide and monophosphoryl lipid A
- Quadrivalent vaccine
  - HPV 6, HPV 11, HPV 16, HPV18 pseudovirions
  - Amorphous aluminum hydroxyphosphate sulfate adjuvant
- 9-valent vaccine
  - HPV 6, 11, 16, 18, 31, 33, 45, 52, 58 pseudovirions
  - Amorphous aluminum hydroxyphosphate sulfate adjuvant

ASO<sub>4</sub>=Adjuvant System 04.

## qHPV Vaccine Efficacy (vaccine serotypes, PPE)

- In females
  - 98% for prevention of genital warts and for prevention of CIN2/3 and AIS
- In males
  - 90% for prevention of external genital lesions
  - 75% for prevention of AIN2/3

AIN=anal intraepithelial neoplasia; AIS=adenocarcinoma in situ; CIN=cervical intraepithelial neoplasia; PPE=paraneoplastic pneumococcal empyema; qHPV=quadrivalent human papillomavirus.

## Real-World Effectiveness of the 4-Valent HPV Vaccine and Prevention of Additional Disease With the 9-Valent HPV Vaccine

Anna R. Giuliano, PhD

Director  
Center for Infection Research in Cancer  
Moffitt Cancer Center

## Why is it Important to Monitor Real-World Effectiveness of the qHPV Vaccine?

- Provides evidence of vaccine effectiveness at local and regional levels, outside of the context of clinical trials
- Early indications of impact on short-term outcomes may suggest similar impacts will be seen on longer-term outcomes
- Opportunity to evaluate duration of protection, effectiveness by dose, herd protection, and potential cross-protection
- Provides information needed to inform:
  - Vaccination program policy decisions
  - Screening guidelines
  - Cost-effectiveness analyses








1. Crowe E et al. *BMJ*. 2014;348:g1458. 2. Flagg EW et al. *Am J Public Health*. 2013;103(8):1428-1435. 3. Brotherton JM et al. *Lancet*. 2011;377(9783):2085-2092. 4. Markowitz LE et al. *J Infect Dis*. 2013;208(3):385-393.

## Multiple Clinical End Points Are Used to Monitor Impact of qHPV Vaccination

- Short-term (months)
  - Prevalence of HPV infection
  - Incidence of genital warts (GW)
- Intermediate-term (years)
  - Incidence of precancerous or dysplastic cervical, vulvar, vaginal, or anal lesions
- Long-term (decades)
  - Incidence of cervical, vulvar, vaginal, or anal cancers

Brotherton JM, Gertig DM. *Expert Rev Anti Infect Ther*. 2011;9(8):627-639.

## qHPV Vaccination Programs Among Countries With Reported Effectiveness Data

|   |  |  |  |  |  |  |  |
|---|---|---|---|---|---|---|---|
| Program Started                                 | 2007 <sup>1</sup>   | 2008 <sup>2</sup>   | 2008 <sup>3,4</sup>   | 2009 <sup>5,6</sup>   | 2009 <sup>7</sup>   | 2009 <sup>8</sup>   | 2009 <sup>9,10</sup>  |
| Type of Program                                 | School and clinic based <sup>1</sup>  | School and clinic based <sup>2</sup>  | Clinic based <sup>3,4</sup>   | School and clinic based <sup>5</sup>  | Clinic based <sup>6</sup>   | Clinic based <sup>7</sup>   | School based <sup>9,10</sup>  |
| Routine <sup>a</sup> Cohort (Age, Years)        | M & F: 12-13 <sup>1</sup>   | F: 12 <sup>2</sup>  | F: 12 <sup>3,4</sup>  | F: 10-12 <sup>5</sup>   | M & F: 11-12 <sup>6</sup>   | F: 9-14 <sup>7</sup>  | F: 9-13 <sup>9,10</sup><br>M: 9-26 <sup>10</sup>                                      |
| Catch-Up Cohort (Age, Years)                    | M: 14-15 through 2014 <sup>1</sup><br>(F: 14-18 ended in 2008) <sup>1</sup>         | F: 13-18 <sup>2</sup>   | F: 13-17 (2008-2009) <sup>3,4</sup>   | F: 13-18 <sup>5</sup>   | M: 13-21 <sup>6</sup><br>F: 13-20 <sup>6</sup>  | F: 15-17 <sup>7</sup>   | F: 14-26 <sup>9,10</sup><br>(2008-2014)   |
| HPV Vaccination Coverage Rates <sup>b</sup> (%) | F: 71 (aged 15, 2012) <sup>11</sup>   | F: 40 <sup>2</sup>  | F: 81-85 <sup>3</sup>   | F: 18 (aged 13-17, 2006-2010) <sup>6</sup>  | F: 38 (aged 13-17, 2013) <sup>6</sup>   | F: 40 <sup>7</sup>  | F: 51-85 <sup>9,10</sup>  |
| Male Vaccination                                | Universal: 2013 <sup>1</sup>  | None  | None  | None  | Permissive: 2009; Universal: 2011 <sup>6</sup>  | None  | Universal: 2010 <sup>12</sup>   |

<sup>a</sup>One hundred percent covered by national health programs except in the United States. <sup>1,3,5,11</sup> Full 3-dose completion. <sup>1,3,4,6,11,12</sup> Varies by region/province. <sup>8</sup>Opportunistic vaccination for females began in October 2004 and has been partially subsidized for girls 13 to 17 years old since May 2007. HPV vaccination in Sweden is now school based. <sup>3</sup> Males 22 to 24 years old may be vaccinated. <sup>9</sup>

<sup>b</sup>Female: Mmale.

References available in corresponding slide notes.

## Effectiveness of HPV Vaccination Programs



*Results from a Meta-Analysis*

Drolet M et al. *Lancet Infect Dis.* 2015;15(5):565-580.

## Population-Level Effectiveness of HPV Vaccination Against HPV and Related Diseases

### Objective:

- Assess population-level impact of HPV vaccination programs – report trends in HPV-related disease and infection pre- and post-vaccine implementation

### Methods:

- Retrospective database searches between January 1, 2007 and February 28, 2014
- Studies compared incidence or prevalence between pre- and post-vaccine programs
  - Infection
  - Genital warts
  - CIN 2+
- Analyses stratified by age and sex
- Rate ratios were used to compare effectiveness measures across studies

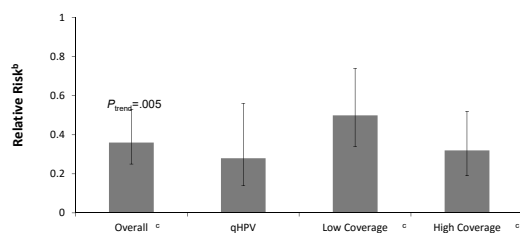
### End Point:

- Relative risk estimates of the population-level changes in trends of HPV-related end points pre- and post-HPV vaccine implementation

CIN 2+=cervical intraepithelial neoplasia grade 2 or higher.

Drolet M et al. *Lancet Infect Dis.* 2015;15(5):565-580.

## 72% Lower HPV 16/18 Infection Prevalence Following HPV Vaccination in Girls Aged 13-19 Years



<sup>a</sup>Data from 20 studies in 9 countries (United States, Australia, England, Scotland, New Zealand, Sweden, Denmark, Canada, and Germany).

<sup>b</sup>Compared to pre-vaccination period.

<sup>c</sup>Includes both quadrivalent and bivalent HPV vaccines.

Drolet M et al. *Lancet Infect Dis.* 2015;15(5):565-580.

## Population-Level Reductions of HPV Disease Due to HPV Vaccination

- Report represents >140 million person-years of follow-up data
- Results strongly suggest reductions in HPV-related outcomes due to HPV vaccination
- Reinforce the need for early vaccination and high vaccination coverage to maximize population-level effectiveness
- Evidence from the meta-analysis supports the role of HPV vaccination in decreased HPV-related disease outcomes based on:
  - Large, statistically significant reductions in disease outcomes seen in the vaccination target age group (girls aged <20 years)
  - Dose-response association between population coverage and reduction in HPV 16/18 infection in girls and genital warts in both women and men
  - Consistency between countries with similar levels of vaccination coverage

Drolet M et al. *Lancet Infect Dis.* 2015;15(5):565-580.

## Effectiveness of qHPV Vaccination Programs

### High-Grade Cervical Lesions



*Results from Individual Studies*

## Determining Impact of qHPV Vaccination on Precancerous Cervical Lesions in the United States

### Objectives:

- Describe the HPV vaccination status of females with CIN 2+
- Examine HPV vaccination impact on HPV 16/18-related precancerous cervical lesions

### Methods:

- Indirect cohort study using data collected from HPV-IMPACT project from 2008 to 2011: females aged 18 to 39 years with a CIN 2+ diagnosis residing in 5 states
  - Analysis restricted to those aged 18 to 31 years at the time of CIN 2+ diagnosis because they were age-eligible for HPV vaccination prior to or during the study period
- HPV vaccination data were collected
- Females with HPV 16- and 18-related CIN 2+ compared with females with CIN 2+ caused by nonvaccine-type HPV
- Abnormal Pap test date immediately prior to CIN 2+ diagnosis, referred to as "trigger Pap," collected from pathology reports or medical charts
- Archived diagnostic tissue from HPV-IMPACT project used for HPV genotyping

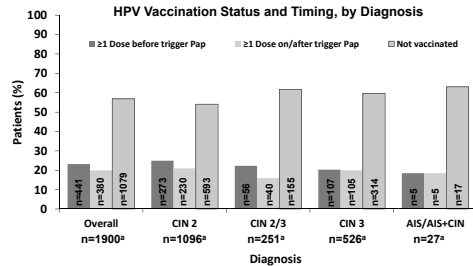
### End Points:

- Vaccination status in women diagnosed with CIN 2+
- Impact of HPV vaccination on precancerous cervical lesions caused by HPV 16/18

Powell SE et al. *Vaccine.* 2012;31(11):109-113.

## qHPV Vaccination Reduced the Number of Precancerous Cervical Lesions Among Women in the United States

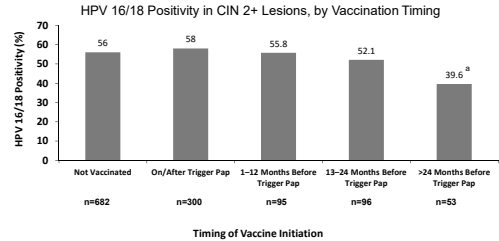
Fewer diagnoses of CIN 2+ seen in vaccinated (with ≥1 dose) than in unvaccinated women



\*Includes cases with known vaccination and trigger Pap dates.

Powell SE et al. *Vaccine*. 2012;31(11):109-113.

## Fewer HPV 16/18-Positive CIN 2+ Lesions in Women Vaccinated With qHPV Vaccine >24 Months Prior to Abnormal Pap Test



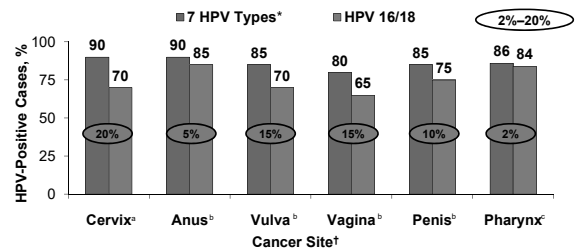
<sup>a</sup>aPR=0.67 (95% CI: 0.48-0.94) compared to unvaccinated women; data were normalized for project site and race/ethnicity.

aPR=adjusted prevalence ratio; CI=confidence interval.

Powell SE et al. *Vaccine*. 2012;31(11):109-113.

## Additional Protection With 9-Valent HPV Vaccine

## Relative Contribution of 7 and 2 HPV Types to HPV-Positive Cancers By Site

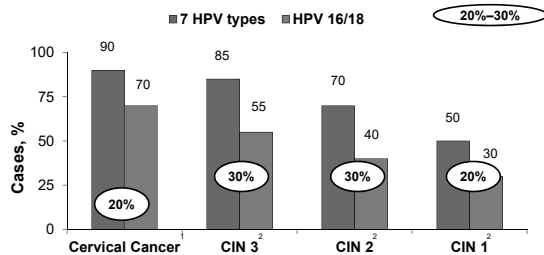


\*HPV 6/11/16/18/31/33/45/52/58

<sup>†</sup>Overall contribution of HPV in cases of cervical cancer (100%), anal cancer (88%), vulvar cancer (25%), vaginal cancer (70%), penile cancer (30%), and oropharyngeal cancer (26%).

<sup>a</sup> Serrano B et al. *Infect Agent Cancer*. 2012;7(1):38; <sup>b</sup> Merck data on file; <sup>c</sup> Castellague X, et al. Presented at: 28th International Papillomavirus Conference; November 30-December 6, 2012; San Juan, PR.

## Relative Contribution of 7 and 2 HPV Types to HPV-Positive Cervical Cancer and Precancerous Lesions

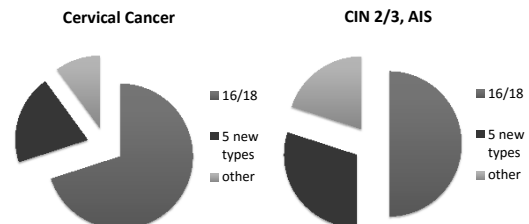


a. HPV 6/11/16/18/31/33/45/52/58

b. Overall contribution of HPV in cases of CIN 1 (73%), CIN 2 (86%), CIN 3 (93%), cervical cancer (100%)<sup>3,4</sup>

1. Serrano B et al. *Infect Agent Cancer*. 2012;7(1):38; 2. Merck data on file; 3. Guan P et al. *Int J Cancer*. 2012;131(10):2349-2359; 4. Forman D et al. *Vaccine*. 2012;30 suppl 5:F12-F23.

## Rationale for Multivalent Vaccine



De Sanjose 2010, Hariri 2011, Serrano 2012, Joura 2014.

## 9-Valent HPV Vaccine Trials

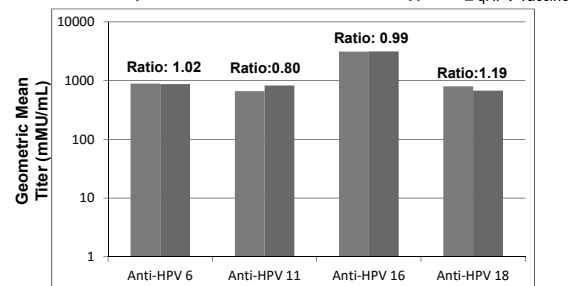
- **V503-001**
  - Efficacy, immunogenicity, and safety study of the 9vHPV vaccine in **young women, aged 16 to 26 years** (N~14,000)
  - Subjects equally randomized to 9vHPV vaccine and qHPV vaccine\* (3-dose regimen)
- **V503-002**
  - Immunogenicity and safety study of 9vHPV vaccine in **adolescent girls (N~1800) and boys (N~600), aged 9 to 15 years**, with a comparison to young women, aged 16 to 26 years (N~400)
  - All subjects received 9vHPV vaccine (3-dose regimen)

9vHPV=9-valent human papillomavirus vaccine.

## Anti-HPV 6, 11, 16, 18 GMTs

Month 7

Non-inferiority criterion was met for all 4 HPV types



GMT=geometric mean titer; mMU=milli Merck units.

Joura EA et al; Broad Spectrum HPV Vaccine Study. *N Engl J Med.* 2015;372(8):711-723.

## HPV 31/33/45/52/58 Vaccine Efficacy

Per-Protocol Efficacy Population

| End Point                    | 9vHPV<br>n | qHPV<br>n  | VE                        |
|------------------------------|------------|------------|---------------------------|
| CIN, VIN, VaIN               | 3 / 6016   | 103 / 6017 | <b>97.1%</b> (91.8, 99.2) |
| CIN2, VIN2/3, VaIN2/3        | 1 / 6016   | 30 / 6017  | <b>96.7%</b> (80.9, 99.8) |
| 6-month Persistent infection | 35 / 5939  | 810 / 5953 | <b>96.0%</b> (94.4, 97.2) |

VaIN=vaginal intraepithelial neoplasia; VIN=vulvar intraepithelial neoplasia;

Joura EA et al; Broad Spectrum HPV Vaccine Study. *N Engl J Med.* 2015;372(8):711-723.

## HPV 31/33/45/52/58 Vaccine Efficacy

Per-Protocol Efficacy Population

| End Point    | 9vHPV<br>Vaccine<br>n | qHPV<br>Vaccine<br>n | Vaccine Efficacy          |
|--------------|-----------------------|----------------------|---------------------------|
| CIN 1+       | 2 / 5948              | 88 / 5943            | <b>97.7%</b> (92.2, 99.6) |
| CIN 2+       | 1 / 5948              | 27 / 5943            | <b>96.3%</b> (79.5, 99.8) |
| VIN, VaIN    | 1 / 6009              | 16 / 6012            | <b>93.8%</b> (61.5, 99.7) |
| VIN/ VaIN 2+ | 0 / 6009              | 3 / 6012             | <b>100.0%</b> (71.5, 100) |

Joura EA et al; Broad Spectrum HPV Vaccine Study. *N Engl J Med.* 2015;372(8):711-723.

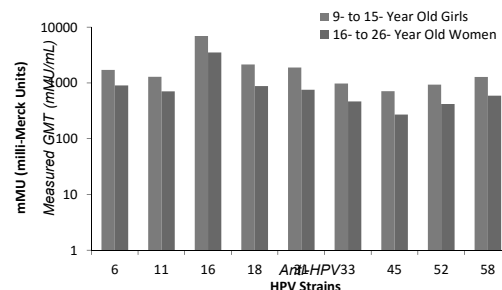
## Reduction of HPV 31/33/45/52/58 Related Procedures

Per-Protocol Efficacy Population

|                    | 9vHPV<br>n | qHPV<br>n  | Risk Reduction (%)       |
|--------------------|------------|------------|--------------------------|
| Biopsy             | 7 / 6016   | 222 / 6017 | <b>96.9</b> (93.6, 98.6) |
| External Genital   | 2 / 6009   | 22 / 6012  | <b>90.9</b> (65.7, 98.5) |
| Cervical Biopsy    | 6 / 6012   | 208 / 6014 | <b>97.2</b> (93.9, 98.8) |
| Definitive Therapy | 4 / 6012   | 32 / 6014  | <b>87.5</b> (65.7, 96.0) |

Giuliano, Joura, & V503-001 study team, manuscript in preparation 2016

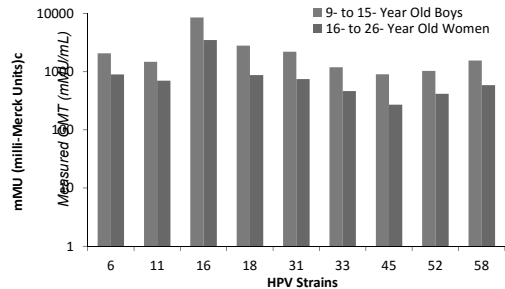
## Month 7 cLIA GMT in Girls vs Women 9vHPV Vaccine



cLIA=competitive Luminex immunoassay.

Van Damme & V503-002 study team *Pediatrics* 2015

## Month 7 cLIA GMT in Boys vs Women 9vHPV Vaccine



Van Damme & V503-002 study team Pediatrics 2015

## Safety Assessments

- **Vaccination Report Card (VRC)-aided surveillance**
  - Elevated temperatures (days 1 to 5 following any vaccination)
  - Injection-site and systemic AEs (days 1 to 15 following any vaccination)
- **Serious adverse experiences (SAEs)**
  - SAEs regardless of causality (day 1 through 180 days post-dose 3)\*
  - Vaccine-related SAEs and deaths (day 1 to end of study)

\*This generally represents the period from day 1 through month 12.

AEs=adverse events.

## Adverse Event Summary

Days 1 to 15 Following Any Vaccination

|  | 9vHPV Vaccine<br>n (%) | qHPV Vaccine<br>n (%) |
|--|------------------------|-----------------------|
| Subjects in population                               | 7071                   | 7078                  |
| With 1 or more AEs                                   | 6640 (93.9)            | 6419 (90.7)           |
| Injection-site                                       | 6423 (90.8)            | 6023 (85.1)           |
| non-injection site                                   | 3948 (55.8)            | 3883 (54.9)           |
| With no AE   | 431 (6.1)              | 659 (9.3)             |
| <b>With vaccine-related* AEs</b>                     | <b>6519 (92.2)</b>     | <b>6200 (87.6)</b>    |
| Injection-site                                       | 6422 (90.8)            | 6023 (85.1)           |
| non-injection-site                                   | 2086 (29.5)            | 1929 (27.3)           |
| With SAEs  | 25 (0.4)               | 17 (0.2)              |
| With serious vaccine-related AEs                     | <b>2 (0.0)</b>         | <b>1 (0.0)</b>        |
| Who died   | 1 (0.0)                | 1 (0.0)               |
| Discontinued** because of an AE                      | 7 (0.1)                | 3 (0.0)               |
| Discontinued because of a vaccine-related AE         | 5 (0.1)                | 3 (0.0)               |
| Discontinued because of a serious AE                 | 2 (0.0)                | 0 (0.0)               |
| Discontinued because of a serious vaccine-related AE | <b>1 (0.0)</b>         | <b>0 (0.0)</b>        |

Giuliano AR, on behalf of the v503-001 and 002 study teams. Presented at: EUROGIN 2013; November 3-6, 2013; Florence, Italy.

## Injection-Site AEs Intensity Appears Higher for 9 vs 4-Valent Vaccine

Days 1 to 5 Following Any Vaccination Visit – All Vaccinated Subjects

|   | 9vHPV Vaccine<br>(N=7071) | qHPV vaccine<br>(N=7078) |
|---|---------------------------|--------------------------|
|   | %                         | %                        |
| Injection site pain                     | 89.9                      | 83.5                     |
| Mild                                    | 53.1                      | 57.1                     |
| Moderate                                | 32.5                      | 23.8                     |
| Severe                                  | <b>4.3</b>                | <b>2.6</b>               |
| Injection site erythema                 | 34.0                      | 25.6                     |
| Mild (≤1 inch [2.5 cm])                 | 27.2                      | 22.0                     |
| Moderate (>1 to 2 inches [2.5 to 5 cm]) | 5.2                       | 2.8                      |
| Severe (>2 inches [5 cm])               | <b>1.6</b>                | <b>0.8</b>               |
| Injection site swelling                 | 40.0                      | 28.8                     |
| Mild (≤1 inch [2.5 cm])                 | 27.7                      | 22.5                     |
| Moderate (>1 to 2 inches [2.5 to 5 cm]) | 8.4                       | 4.7                      |
| Severe (>2 inches [5 cm])               | <b>3.8</b>                | <b>1.5</b>               |

Giuliano AR, on behalf of the v503-001 and 002 study teams. Presented at: EUROGIN 2013; November 3-6, 2013; Florence, Italy.

## Vaccine-Related\* Systemic AEs (≥1% in Any Group) Appear Similar

Days 1 to 15 Following Any Vaccination Visit

|                    | 9vHPV Vaccine<br>N=7071 | qHPV Vaccine<br>N=7078 |
|--------------------|-------------------------|------------------------|
| Headache           | 1031 (14.6)             | 969 (13.7)             |
| Pyrexia            | 357 (5.0)               | 301 (4.3)              |
| Nausea             | 311 (4.4)               | 261 (3.7)              |
| Dizziness          | 211 (3.0)               | 197 (2.8)              |
| Fatigue            | 166 (2.3)               | 150 (2.1)              |
| Diarrhea           | 87 (1.2)                | 71 (1.0)               |
| Oropharyngeal pain | 73 (1.0)                | 40 (0.6)               |
| Myalgia            | 69 (1.0)                | 48 (0.7)               |

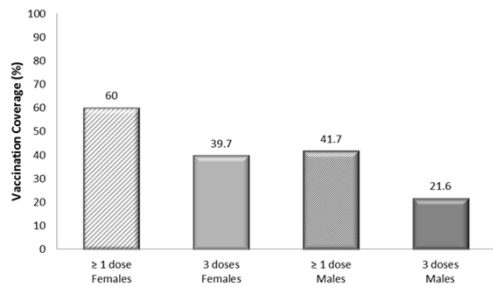
Giuliano AR, on behalf of the v503-001 and 002 study teams. Presented at: EUROGIN 2013; November 3-6, 2013; Florence, Italy.

## Conclusions

- **V503-001**
  - Acceptable safety profile in young women, aged 16 to 26 years
  - Frequencies of clinical adverse experiences generally comparable between 9vHPV vaccine and qHPV vaccine
  - Differences with respect to injection-site swelling
    - Higher frequency of injection-site AEs with 9vHPV vs qHPV vaccine
    - Majority of injection-site AEs are mild-moderate intensity with both vaccines
- **V503-002**
  - Acceptable safety profile in all 3 demographic groups
    - Similar frequencies of severe injection-site AEs among the 3 groups
  - Safety profile similar or slightly more favorable in boys vs girls and women
    - Similar to previous findings with qHPV vaccine



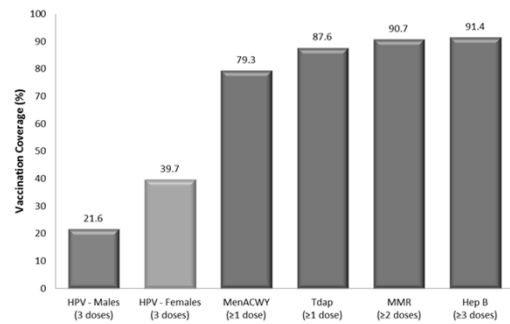
## US HPV Vaccination Coverage, 2014



† Quadrivalent or bivalent vaccine

Centers for Disease Control and Prevention. 2014 National Immunization Survey Teen. [http://www.cdc.gov/nchs/nis/data\\_files\\_teen.htm](http://www.cdc.gov/nchs/nis/data_files_teen.htm). Accessed September 30, 2016.

## Vaccine Coverage, 13-17 years, 2014



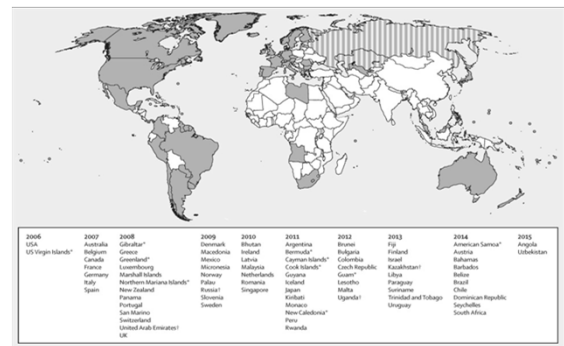
Centers for Disease Control and Prevention. 2014 National Immunization Survey Teen. [http://www.cdc.gov/nchs/nis/data\\_files\\_teen.htm](http://www.cdc.gov/nchs/nis/data_files_teen.htm). Accessed September 30, 2016.

## National HPV Vaccine Meeting

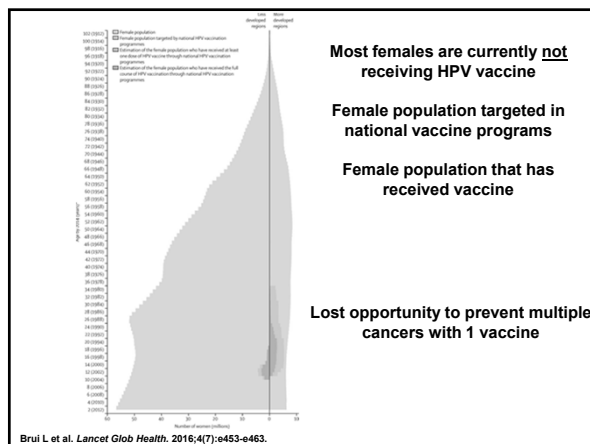
### Increasing HPV Vaccination in the United States: A Collaboration of NCI-funded Cancer Centers

- Discussion of national strategy, common goals and approaches
- 76 representatives from 37 cancer centers
- Top-level representatives from the NCI, CDC, ACS, and US Congress

## Countries With Publicly Funded National HPV Vaccine Programs Since 2006



Brui L et al. *Lancet Glob Health*. 2016;4(7):e453-e463.



Brui L et al. *Lancet Glob Health*. 2016;4(7):e453-e463.

## Acknowledgments

Thanks to all patients and study contributors

**Investigators:** M. Akin, E. Andersen, R. Andrade, E. Andruczyk, K. Ault, N. Balcazar, S. Bagshaw, D. Bartholomew, S. Block, C. Bouchard, K. Brody, R. Cabello, R. Cestero, C. Chen, T. Cheung, C. Cho, T. Chu, H. Chou, C. Cruz, E. Fedrizzi, M. Ferguson, D. Ferris, S. Gall, A. Giuliano, K. Greven, A. Guevara, H. Hanashi, K. Hesla, O. Iversen, E. Joura, N. Khemapech, Y. Kim, B. Kim, S. Kim, S. Koonlerkit, J. Kratzer, M. Lally, E. Lazcano, C. Lee, R. Lewis, A. Linden-Hirschberg, R. Lotocki, A. Lukes, J. Luna, I. Maldonado, C. Mao, M. Mayrand, S. McNeil, J. Mehlsen, H. Mogesen, H. Moi, D. Money, E. Moreira, Y. Ngan, C. Nicholson-Uhl, C. Nossa, S. Olsson, L. Panther, L. Petersen, S. Pilis, P. Pitisuttithum, M. Plata, S. Pinjaroen, O. Poblete, O. Reich, S. Reid, J. Restrepo, F. Revollo, K. Rhein, G. Riis-Johannessen, H. Roberts, B. Romanowski, J. Romaguera, A. Ruiz, H. Ryu, M. Sakamoto, M. Santiago, M. Scutella, M. Shew, A. Silva, T. Soerdal, Y. Song, D. Soper, H. Stacey, J. Stapleton, G. Stuart, E. Suarez, N. Takeshima, Y. Takeuchi, K. Trosterud, L. Trujillo, W. Tsunezawa, N. Twu, A. Vachon, M. Varman, A. Victoria, D. Wiley, S. Wilailak, L. Woelber, Y. Yang, M. Yardley, M. Yu, P. Zedler

**Merck:** A. Luxembourg, R. Haupt, O. Bautista, J. Chen, I. Chan, E. Moeller, M. Ritter, S. Vuocolo



### New ACIP Recommendations for Use of the 9-Valent HPV vaccine (parallel to recommendations for quadrivalent vaccine)

- The 9-valent HPV vaccine is recommended for routine vaccination of 11- and 12-year-old males and females
- As with the quadrivalent vaccine, immunization may be initiated as young as age 9 years
- The ACIP also recommended catch-up immunization with the 9-valent vaccine for females aged 13-26 years and for males aged 13-21 years
- Immunization is also recommended for males aged 22-26 years if immunocompromised or MSM

MSM=men who have sex with men.

Petrosky E et al; Centers for Disease Control and Prevention (CDC). *MMWR Morb Mortal Wkly Rep.* 2015;64(11):300-304.

49

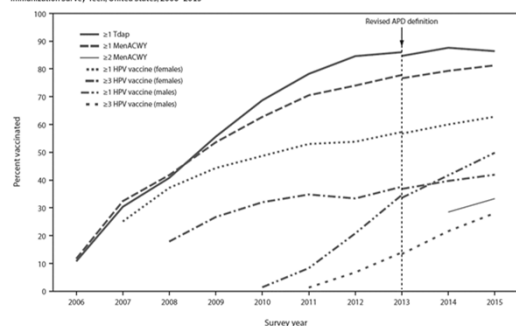
### What to do with people who have started, but have not yet completed, the 3-dose series?

- For females, the ACIP does not make a preference among the 2-valent, 4-valent, or 9-valent vaccines
- For females, a 3-dose series with any of the vaccines is recommended
- For males, a 3-dose series with either the 4-valent or 9-valent is recommended

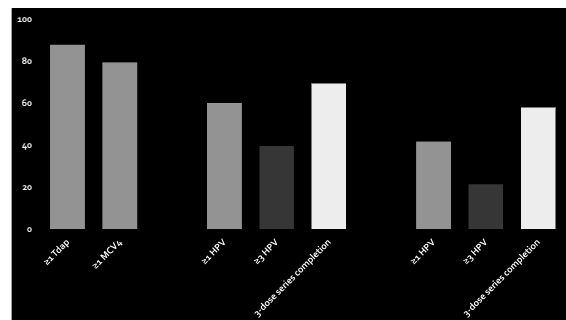
Petrosky E et al; Centers for Disease Control and Prevention (CDC). *MMWR Morb Mortal Wkly Rep.* 2015;64(11):300-304. Supplemental guidance can be found at <http://www.cdc.gov/hpv/downloads/9vHPV-guidance.pdf>. Accessed September 30, 2016.

50

FIGURE 1. Estimated vaccination coverage with selected vaccines and doses\* among adolescents aged 13–17 years, by survey year — National Immunization Survey–Teen, United States, 2006–2015†

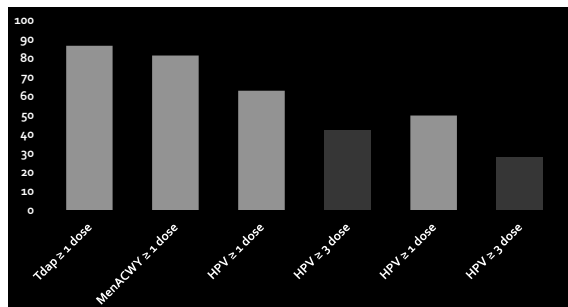


### Estimated Vaccination Coverage Among Adolescents Aged 13 to 17 Years, United States, National Immunization Survey–Teen, 2014



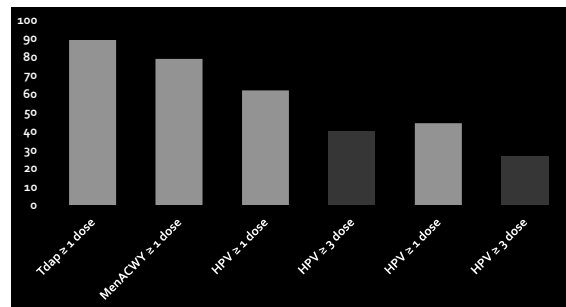
Reagan-Steiner S et al. *MMWR Morb Mortal Wkly Rep.* 2015;64(29):784-792.

### Estimated Vaccination Coverage Among Adolescents Aged 13 to 17 Years, Illinois, National Immunization Survey–Teen, 2015



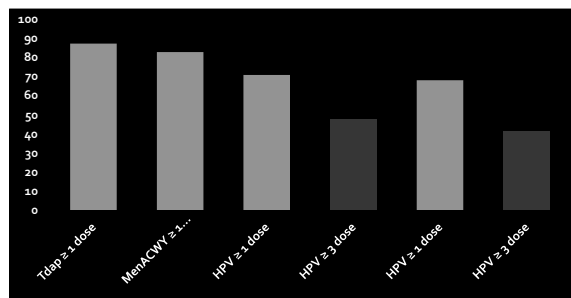
Morbidity and Mortality Weekly Report (MMWR) 65(33):850–858 (2016)

### Estimated Vaccination Coverage Among Adolescents Aged 13 to 17 Years, Illinois, National Immunization Survey–Teen, 2015



Morbidity and Mortality Weekly Report (MMWR) 65(33):850–858 (2016)

### Estimated Vaccination Coverage Among Adolescents Aged 13 to 17 Years, Chicago, National Immunization Survey–Teen, 2015



Morbidity and Mortality Weekly Report (MMWR) 65(33):850–858 (2016)

### Do we undervalue HPV immunization?

- National sample of 776 US physicians (53% pediatricians, 47% family medicine physicians)
- Assessed physicians' perceptions and communication practices related to recommending adolescent vaccines for 11- and 12-year-old patients

Gilkey MB et al. *Prev Med*. 2015 ;77:181-185.

### Do we undervalue HPV immunization?

- For patients aged 11 to 12 years:
  - 95% of physicians reported recommending tetanus, diphtheria, and acellular pertussis (Tdap) as highly important
  - 87% of physicians reported recommending meningococcal conjugate vaccine (MCV4) as highly important
  - 73% of physicians reported recommending HPV vaccine as highly important

Gilkey MB et al. *Prev Med*. 2015 ;77:181-185.

### Do we undervalue HPV immunization?

- 13% of physicians perceived HPV vaccine as being highly important to parents (74% for Tdap, 62% for meningococcal vaccine)
- Among physicians with a preferred order for discussing adolescent vaccines, 70% discussed HPV vaccine last

Gilkey MB et al. *Prev Med*. 2015 ;77:181-185.

### Each year in the United States...

- Pertussis kills approximately 20 people per year, mostly young infants
- Meningococcal infections kill approximately 100 people each year.
- By vaccinating adolescents with Tdap and MCV4 vaccines, we are working to prevent approximately 120 fatalities per year

1. Centers for Disease Control and Prevention. 2014 Final Pertussis Surveillance Report. <http://www.cdc.gov/pertussis/downloads/pertuss-surv-report-2014.pdf>. Accessed September 30, 2016; 2. Centers for Disease Control and Prevention. Active Bacterial Core Surveillance (ABCs). <http://www.cdc.gov/abcs/reports-findings/surv-reports.html>. Accessed September 30, 2016.

### And yet, each year in the United States...

- Approximately 4000 women die of cervical cancer, another 1900 die of vaginal and vulvar cancer, 1000 men and women die of anal cancers, and at least 1700 die of HPV-associated oropharyngeal cancers
- Taken together, timely HPV vaccination could prevent as many as 8000 to 10,000 HPV-associated cancer deaths

American Cancer Society. *Cancer Facts & Figures 2015*. Atlanta: American Cancer Society; 2015. <http://www.cancer.org/acs/groups/content/@editorial/documents/document/acspc-044552.pdf>. Accessed September 30, 2016.

**Who are the best physicians to  
immunize adolescents against HPV?**

**Pediatric/Family Medicine providers  
or  
Obstetrician/Gynecologists?**

**Why Pediatricians and  
Family Medicine?**

**Why can't the Obstetrician/Gynecologists do this  
(especially for HPV)?**

**Why Pediatricians and Family Medicine?**

- Adolescents need medical homes with providers who understand adolescent issues
- The vaccine works best when given at a younger age
  - Obstetrician/Gynecologists do not care for early teens
- Obstetrician/Gynecologists do not see males
- Obstetrician/Gynecologists are poor immunizers
- Pediatric providers are vaccine enthusiasts
- Caring for teens is good business

**Pediatricians and Family Physicians know how  
to talk with adolescents and their parents.**

**Parents make decisions,  
not on the basis of facts,  
but on the basis of experience**

**When we speak provider-to-provider,  
we use the language of epidemiology**

**...We talk about risk**

**...We use statistics**

**...Proven facts matter**

**The prospective, double-blinded, placebo-  
controlled trial is the standard we demand**

How we talk about HPV immunization  
with our patients and in the community  
must differ from  
how we speak with one another

**To best serve our patients,  
we must be translators.**

**When we talk to patients  
and in the community,  
we must be less scientific  
and more emotional**

**We must tell compelling stories.**

**Each year in the United States,  
because of our low HPV  
immunization rates,  
non-immunizing providers condemn  
approximately 2200 women  
to die of vaccine-preventable  
cervical cancer**

2200 women/year dying of preventable cervical cancer =  
One 747 crash every 3 months

### **Two Approaches...**

- HPV stands for human papillomavirus
- HPV causes genital warts and cervical cancer
- HPVs are transmitted sexually
- Many adolescents become sexually active by age 13 years
- Do you want this vaccine for your 11-year-old?

***My child is not  
(and never will be)  
sexually active!***

### Two Approaches...

- Has anyone that you care about had cancer?
  - What was it like for him or her?
  - What was it like for you?
- We can reduce the chances of your son or daughter having a cancer experience
- Do you want to reduce your child's risk for cancer?

## HPV Tdap meningococcal flu

### When talking with parents about immunization, parents want to know 3 things:

1. Does it work?
2. Is it safe?
3. What is your recommendation?

### Talking With Parents About Immunization

#### 1) Does it work?

##### Yes!

Vaccine efficacy is high for prevention of cervical disease, genital warts, and anal malignancies.

The vaccine may also protect against some head and neck cancers.

### Talking With Parents About Immunization

#### 2) Is it safe?

##### Yes!

Large clinical trials and extensive postmarketing surveillance have identified sore arms, and the occasional headache and fever, as the only vaccine-associated side effects.

### Talking With Parents About Immunization

#### 3) What is your recommendation?

**Use Every Opportunity to Immunize**

**Nothing you do for children  
is ever wasted.**

*Garrison Keillor*