Impact of the HPV Vaccination Program in the United States

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HPV vaccine impact monitoring

- Impact on cancers will not be observed for decades
- More proximal outcomes being evaluated and impact on these outcomes has been reported
  - HPV infection

    Australia, Denmark, Sweden, UK, US
  - Genital warts

    Australia, Denmark, Germany, New Zealand, Canada, Sweden, US
  - Cervical precancer lesions

    Australia, Canada, Denmark, Sweden, US

Systematic review and meta-analysis: Population-level impact and herd effects following HPV vaccination programs

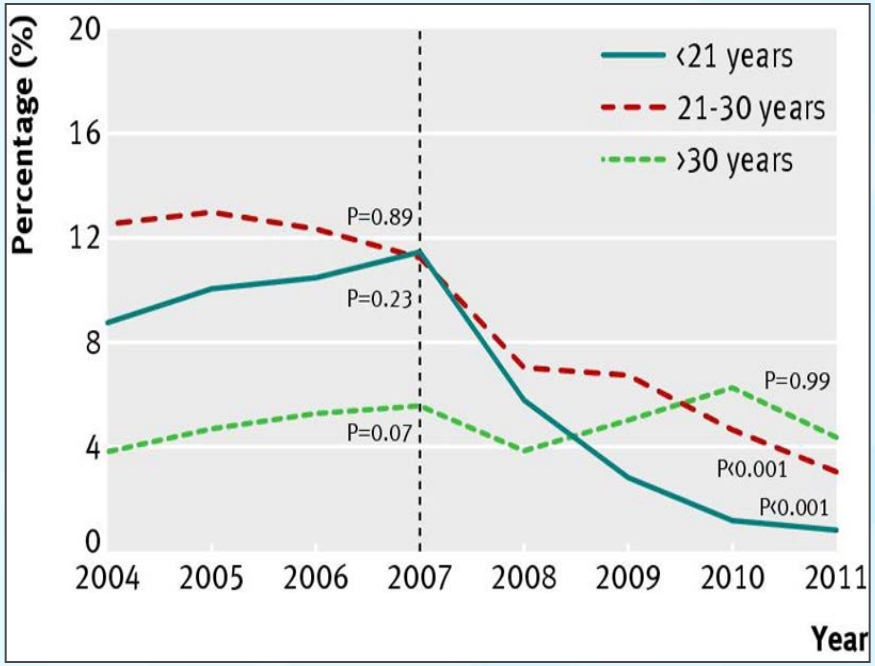
- Review of 20 studies in 9 high income countries within 4 years of vaccine introduction
- In countries with ≥ 50% coverage, among females < 20 yrs
  - HPV 16/18 prevalence decreased at least 60%
  - Anogenital warts decreased ~ 60%
  - Evidence of herd effects with decreases in anogenital warts among older females and in males
  - Some evidence of cross protection against other types
- In countries with < 50% coverage
  - Smaller decreases in vaccine type prevalence and anogenital warts
- No significant increase in non vaccine types

Drolet et al. Lancet Infect Dis 2015;15:565-80

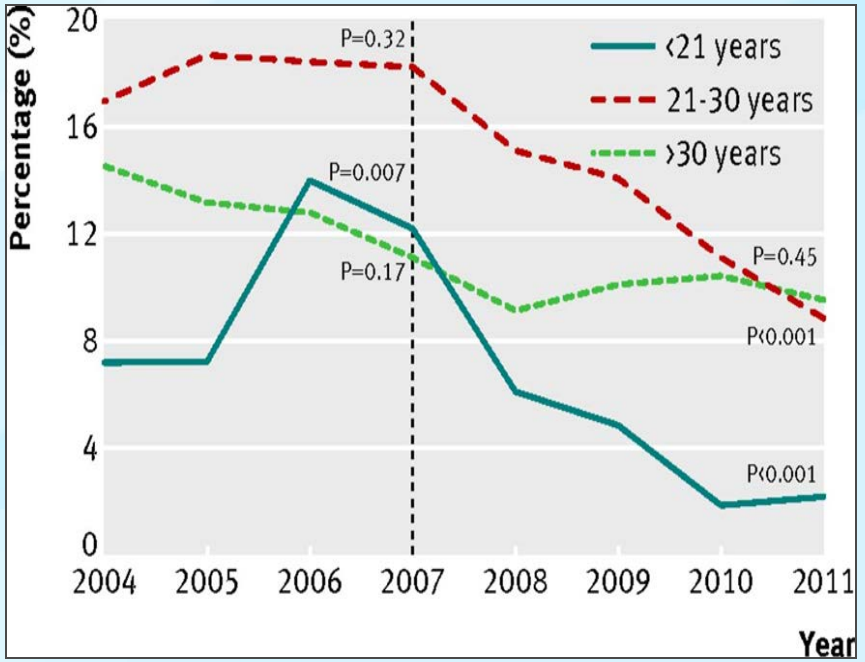
Impact of HPV vaccination in Australia

Proportion of Australian born females and males diagnosed as having genital warts at first visit, by age group, 2004-11

Females



Heterosexual Males

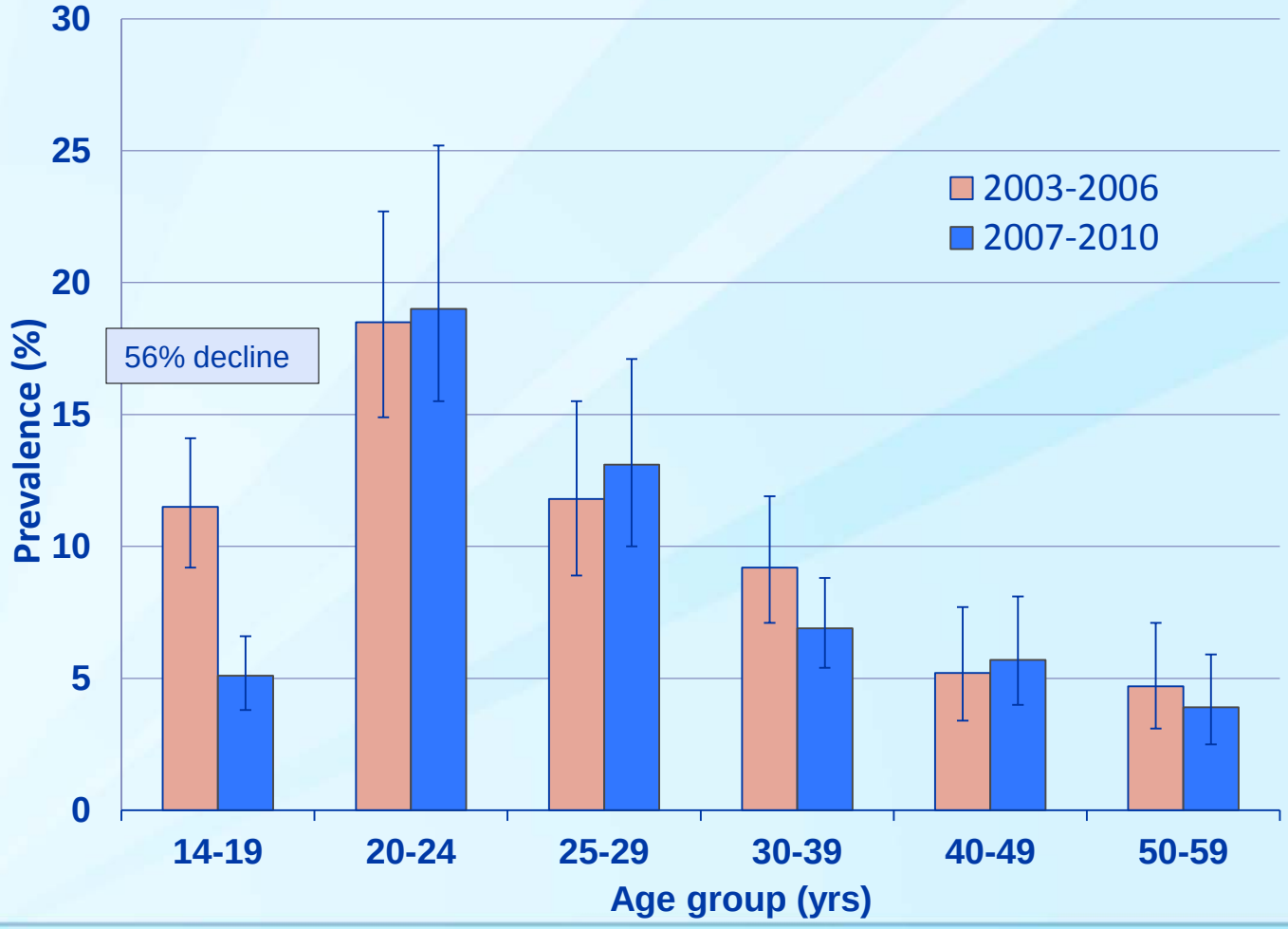


Ali et al. BMJ 2013

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 NHANES 2003-2006 and 2007-2010



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

HPV prevalence among women 20-29 years undergoing cervical cancer screening

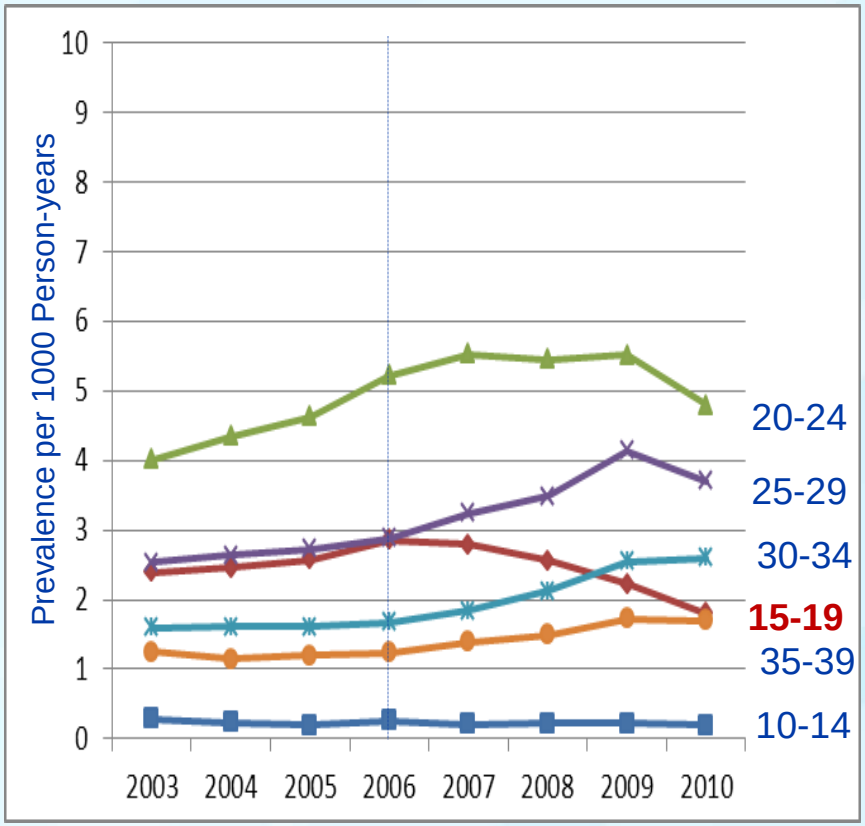
- Cervical specimens tested for HPV in 2007 and 2012-2013*
- Vaccination status in 2012-2013
  - 21% received 3 doses of HPV vaccine; 32% received at least 1 dose
- HPV 6,11,16,18 prevalence
  - Between 2007 and 2012-2013: decreased from 10.6% to 6.2%
  - In 2012-2013: 3.2% in vaccinated[+] and 7.6% in unvaccinated

*~4000 women in each time period; Northwest, U.S.

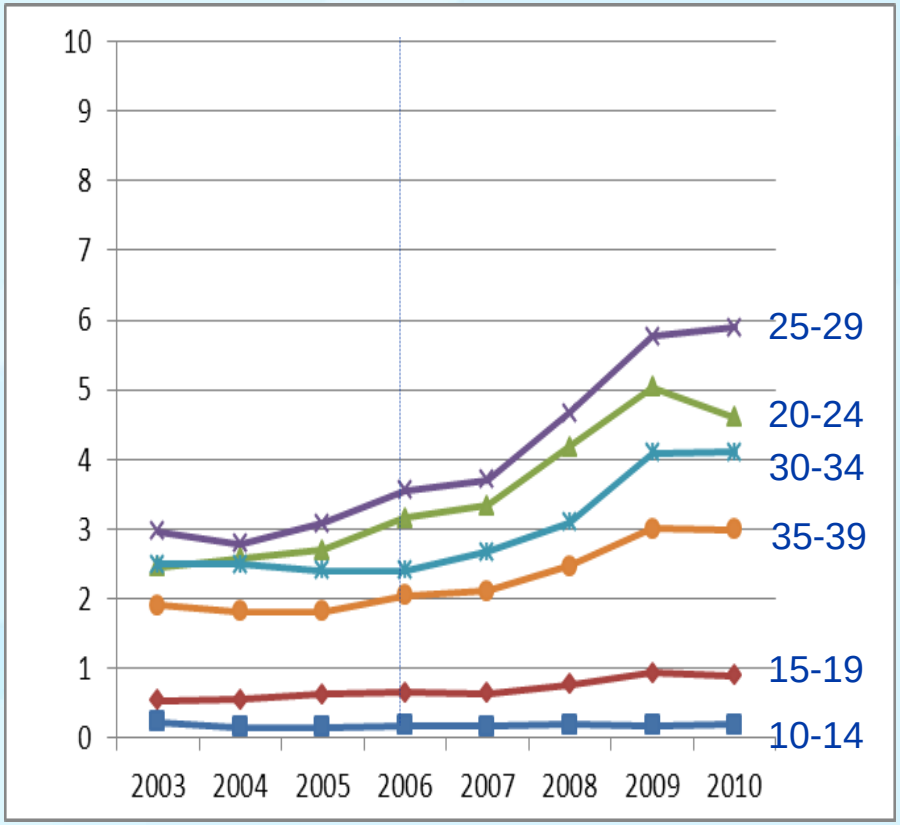
[+]at least one dose

Dunne et al. JID 2015

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
- Changes in screening recommendations
  - 2009 – ACOG recommended to start at age 21; less frequent
  - 2012 – Multiple groups recommended to start at age 21*
- Lack of cervical cancer screening registries
- Incomplete linkages with vaccination registries

*ACOG Practice Bulletin 2012 Saslow et al. Am J Clin Path 2012 Moyer. Ann Intern Med 2012

Detection of cervical cancer precursors and associated HPV in the United States: HPV-IMPACT

- Capitalize on infrastructure of Emerging Infections Program
- Collect CIN2+ in women ≥18 yrs in catchment area
- Determine HPV types in lesions from subset of women 18-39 yrs, vaccine history
- Estimate population level cervical cancer screening

Monroe County, NY
New Haven County, CT
Davidson County, TN
8-City Area (Alameda County), CA
28-Zipcode Area (Portland metro), OR

CIN2+, cervical intraepithelial neoplasia grade 2 or 3 and adenocarcinoma in situ

Population-based rates of CIN2+ in the early HPV vaccine era

CIN2+ diagnosis rates* by age and site

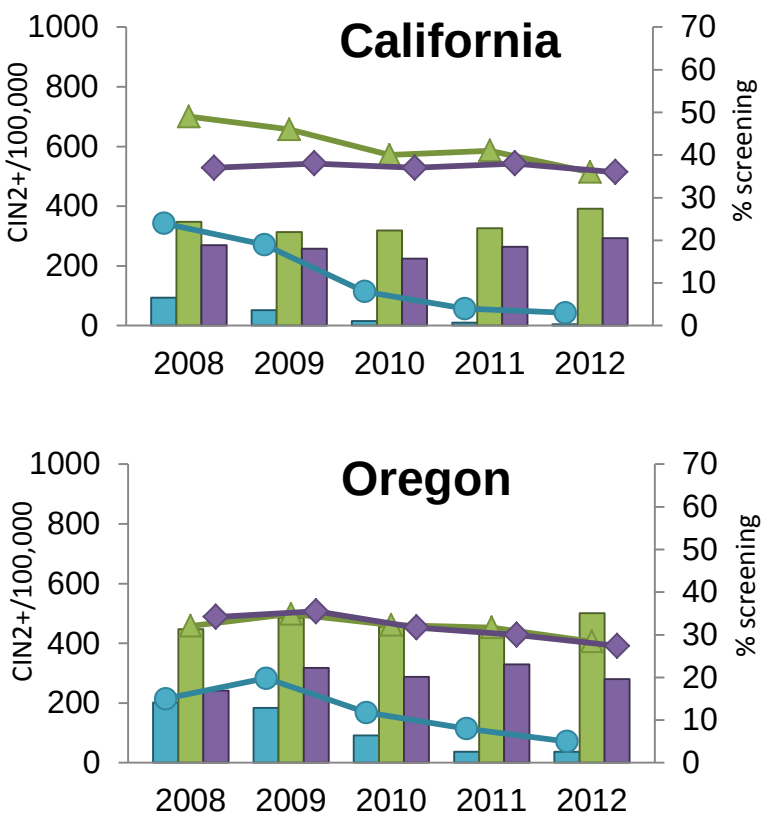
Age, years	2008		2012		% change
	N	(Rate)	N	(Rate)	% (95% CI)
18-20					
California	18	(94)	1	(5)	-94 (-99, -58)
Connecticut	87	(450)	11	(57)	-87 (-93, -76)
New York	56	(299)	8	(43)	-86 (-93, -70)
Oregon	22	(202)	4	(37)	-82 (-94, -47)
21-29					
California	192	(348)	216	(392)	13 (-7, 37)
Connecticut	397	(762)	307	(589)	-23 (-33, -10)
New York	363	(770)	219	(465)	-40 (-49, -29)
Oregon	232	(447)	260	(501)	12 (-6, 34)
30-39					
California	160	(270)	174	(293)	9 (-12, 35)
Connecticut	198	(368)	185	(343)	-7 (-24, 14)
New York	142	(321)	144	(325)	1 (-20, 28)
Oregon	137	(241)	159	(280)	16 (-8, 46)

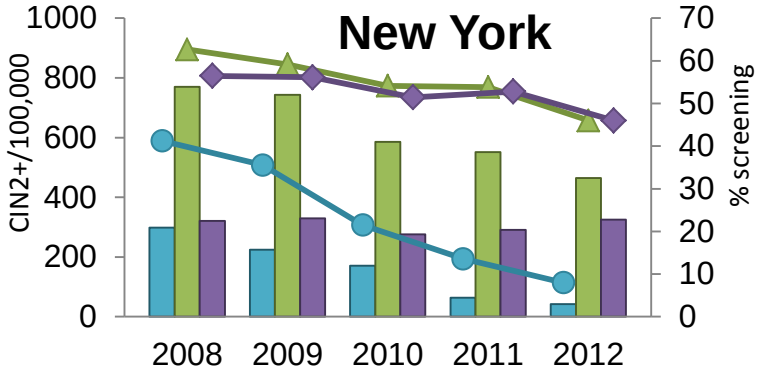
*Rates per 100,000 based on 2010 US Census

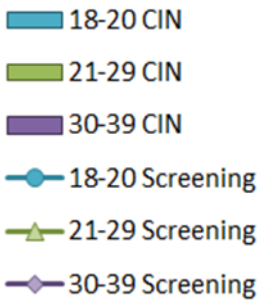
Hariri et al. Cancer 2015;121:2775-81

Population-based trends in CIN2+ lesions and % cervical cancer screening, 2008-2012

CIN2+ incidence (per 100,000) and % screened by age and year

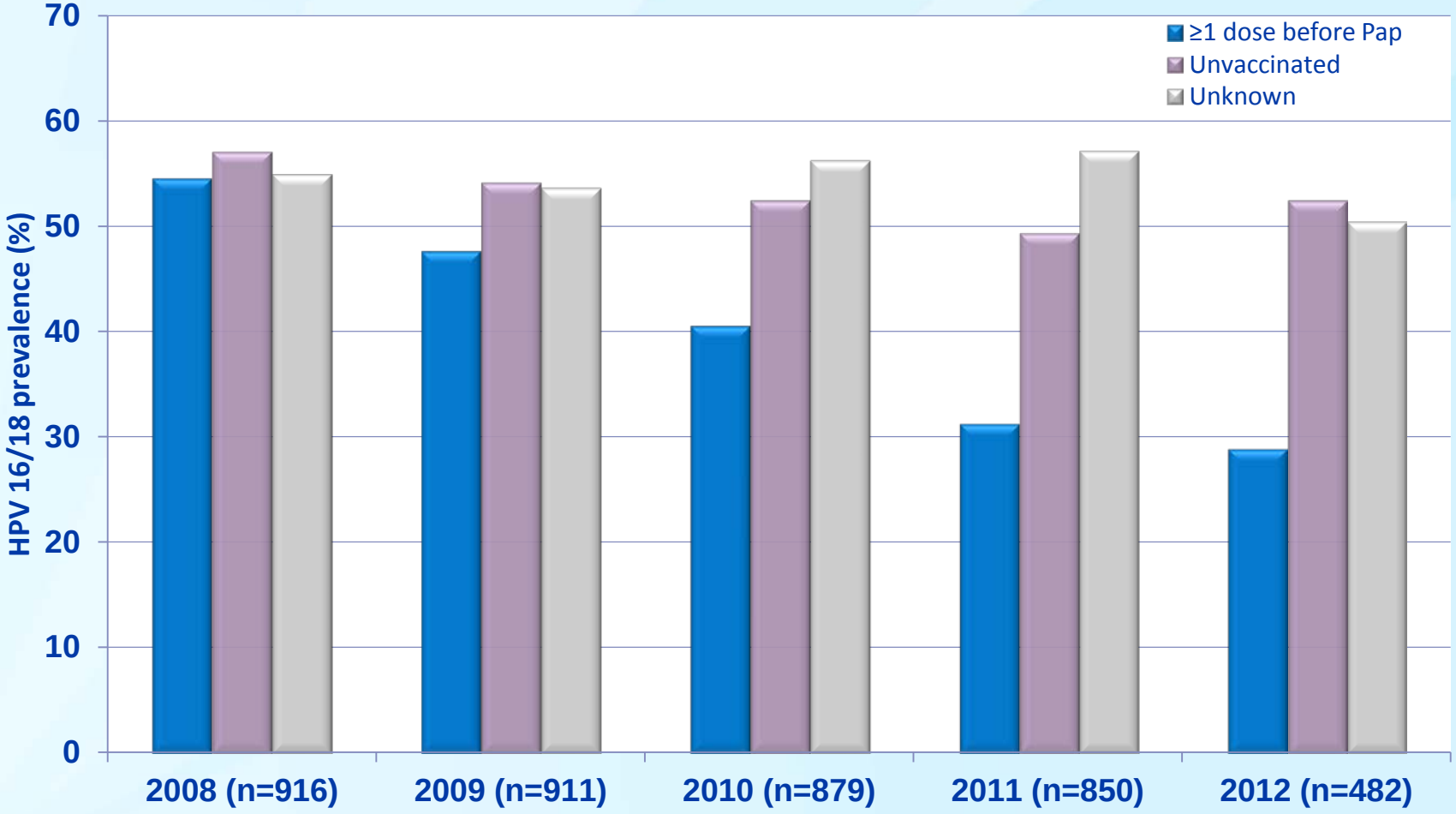






Hariri et al. Cancer 2015;121:2775-81

HPV 16/18 associated CIN2+ among women age eligible for vaccination, by year and vaccination status United States, 2008-2012



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

Limited to women age eligible for vaccination

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

Vaccine effectiveness: % CIN3/AIS 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	427	69.8	Ref
Vaccinated <30 days/after screening test	132	67.2	0.99 (0.87 – 1.13)
Vaccinated before screening test			
1-12 months	40	80.0	1.17 (0.97 – 1.40)
13-24 months	41	65.9	0.92 (0.74 – 1.14)
25-36 months	32	75.0	1.02 (0.83 – 1.25)
37-48 months	29	44.8	0.62 (0.41 – 0.93)
>48 months	10	40.0	0.55 (0.26 – 1.16)

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

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

Limited to women age eligible for vaccination

Other evaluations

- HPV prevalence among men who have sex with men
- Additional analyses with administrative data
- Vaccine effectiveness by number of doses

Summary

- Available data from the U.S. and other developed countries show impact on HPV prevalence and other early HPV-associated outcomes
- As expected, the first impact in the U.S. was observed on HPV prevalence and genital warts among females 14-19 years and later among those in their 20s
- There are challenges in evaluating vaccine impact on incidence of cervical precancers in the U.S., but available data suggest early impact
- Further monitoring data are forthcoming
- Achieving higher vaccine coverage will lead to greater impact of the vaccination program

- Overview of 9-valent HPV vaccine introduction
- Future ACIP Work Group plans

9-valent HPV vaccine introduction, U.S.

- **Licensed by FDA, December 2014**
- **Recommended by ACIP, February 2015**
  - MMWR Policy Note published March 2015
- **Available through Vaccines For Children Program, April 2015**
  - By September 2015, 94% of CDC's 64 awardees had placed orders
  - In September 2015, 36% ordered 9vHPV only
- **Managed care and insurance***
  - >85% managed care plans decided to cover 9vHPV
- **Doses distributed in the U.S.**
  - 5M doses through September 2015

*Information provided by Merck & Co.

Future ACIP HPV Vaccines Work Group plans

- **Review data on reduced dose schedules**
  - 9-valent HPV vaccine 2- vs 3-dose immunogenicity trial*
  - Other immunogenicity data
  - Post licensure effectiveness studies
  - Cost effectiveness analyses
- **Present reduced dose data to ACIP**
  - Starting in February 2016

*Clinicaltrials.gov identifier NCT01984697

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Thank you

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