Dr. Anna R. Giuliano

DISCLOSURE OF CONFLICTS OF INTEREST

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THE FACULTY REPORTED THE FOLLOWING FINANCIAL RELATIONSHIPS OR RELATIONSHIPS TO PRODUCTS OR DEVICES THEY OR THEIR SPOUSE/LIFE PARTNER HAVE WITH COMMERCIAL INTERESTS RELATED TO THE CONTENT OF THIS CME ACTIVITY:

DR. ANNA GIULIANO HAS DISCLOSED THE FOLLOWING RELEVANT FINANCIAL RELATIONSHIPS WITHIN THE PAST 12 MONTHS:

Consultant/Independent Contractor: Merck
Grant/Research Support: Merck
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Speaker's Bureau: Merck

Communicating an Integrated HPV Message

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Disclosure

- Dr. Giuliano: Grants/Research Support: Merck & Co., Inc.; Consultant: Merck & Co., Inc.; Speakers Bureau: Merck & Co., Inc.

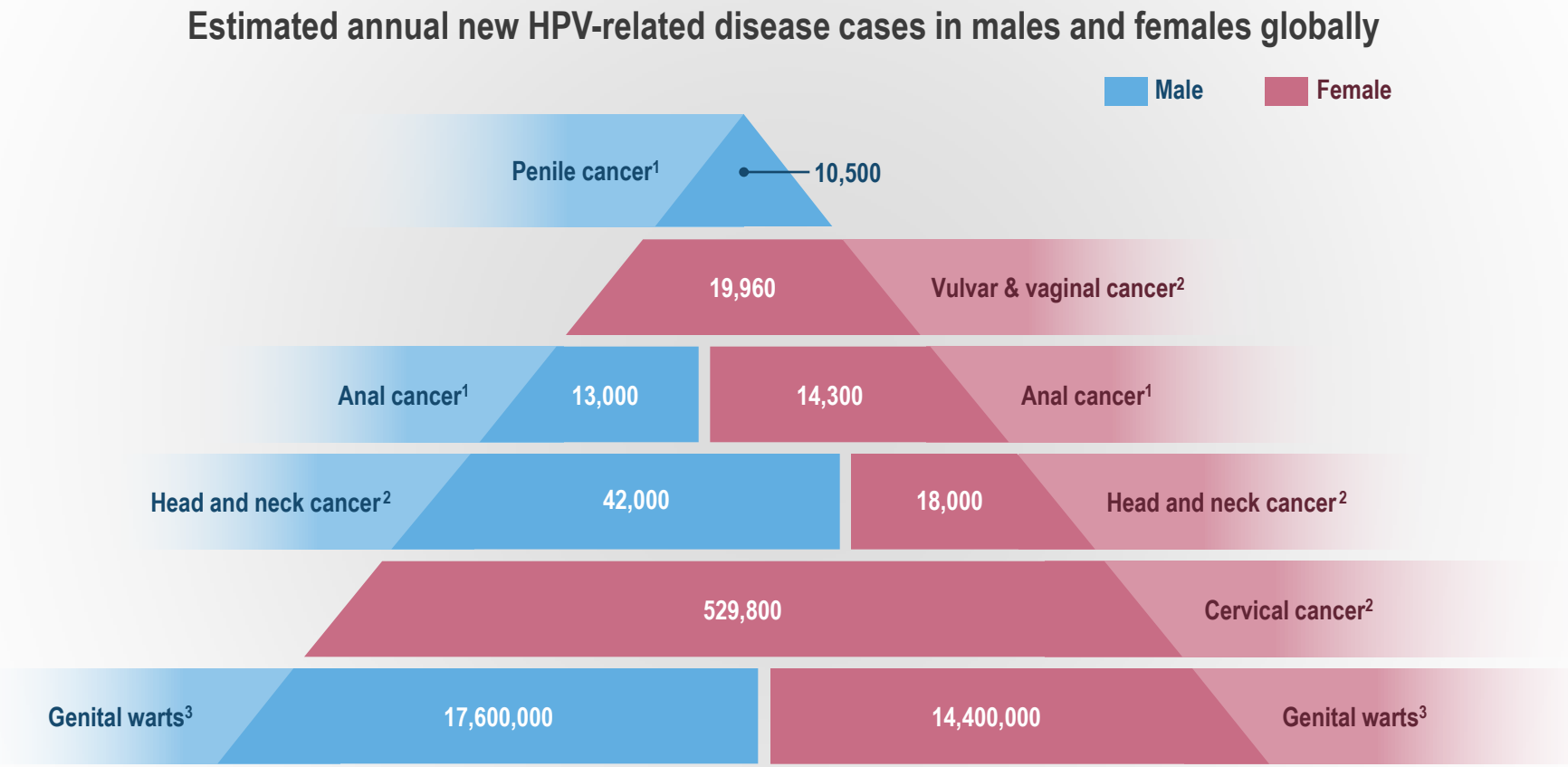
“Knowledge is not enough; we must apply. Willing is not enough; we must do.”

Johann Wolfgang von Goethe

HPV is a Necessary Cause of Cervical Cancer

- Association of cervical neoplasia with sexual activity
- In the mid-1970's Professor zur Hausen identified HPV as a likely viral candidate in cervical neoplasia.
- ~100% of cervical cancer and majority of HgSIL contain HPV DNA
- Strong and consistent associations between HPV and cervical cancer (OR=9 to >100)
- HPV infection precedes onset of disease
- ~50% of cervical tumors contain HPV 16 DNA, an additional ~20% of tumors contain HPV 18, and an additional 20% HPV 31, 45, 33, 52, 58 DNA

There Is a High HPV Disease Burden Among Males and Females Globally



Published HPV prevalence rates were applied as follows: Parkin D et al. *Vaccine*. 2006 (penile, vulvar, anal, cervical cancers); WHO/ICO 2010 (head and neck cancer); De Vuyst H et al. *Int J Cancer.* 2009 (vaginal cancer); Greer CE et al. *J Clin Microbiol.* 1995 (genital warts).

1. Parkin DM et al. *Vaccine.* 2006;24(Suppl 3):S3/11–S3/25. **2.** WHO/ICO Information Centre on HPV and Cervical Cancer (HPV Information Centre). Human Papillomavirus and Related Cancers in World. Summary Report 2010. http://www.who.int/hpvcentre/en/. Accessed June 21, 2012. **3**. World Health Organization (WHO). Executive summary: the state of world health. 1995. http://www.who.int/whr/1995/media_centre/executive_summary1/en/index3.html#. Accessed June 7, 2012.

Disease Endpoints Evaluated in Women

Disease Endpoint	GARDASIL™	Cervarix™
Immediate Cervical Cancer Precursors[1]		
HPV 16/18-related CIN 3	✓	
HPV 16/18-related AIS	✓	
Immediate Vulvar Cancer Precursor[2]		
HPV 16/18-related VIN 2/3	✓	
Immediate Vaginal Cancer Precursor[2]		
HPV 16/18-related VaIN 2/3	✓	
High-grade Cervical Dysplasia[1,3]		
HPV 16/18-related CIN 2/3	✓	✓
HPV 16-related CIN 2/3	✓	✓
HPV 18-related CIN 2/3	✓	✓
Low-grade Cervical Dysplasia[3-5]		
HPV 16/18-related CIN 1	✓	✓
HPV 6/11-related CIN 1	✓	
External Genital Lesions[4]		
Genital warts	✓	

Gardasil Vaccine Efficacy

Per-Protocol Populations

Population	HPV 6/11/16/18-Related Endpoints	Per Protocol Efficacy (%)	95% CI
16-26 year-old women	CIN 2/3	98	93, 100
	VIN 2/3	100	67, 100
	VaIN 2/3	100	55, 100
	Genital warts	99	96, 100

FDA Approval and CDC routine vaccination recommendation for females in 2006

Kjaer et al., *Cancer Prev Res* 2009; The FUTURE I/II Study Group, *BMJ* 2010

9-Valent HPV Vaccine in Final Year of Phase III Testing in Females

Burden of HPV-Related Disease in Males

- Genital warts
- Recurrent respiratory papillomatosis

>90% caused by HPV 6 & 11[1,2]

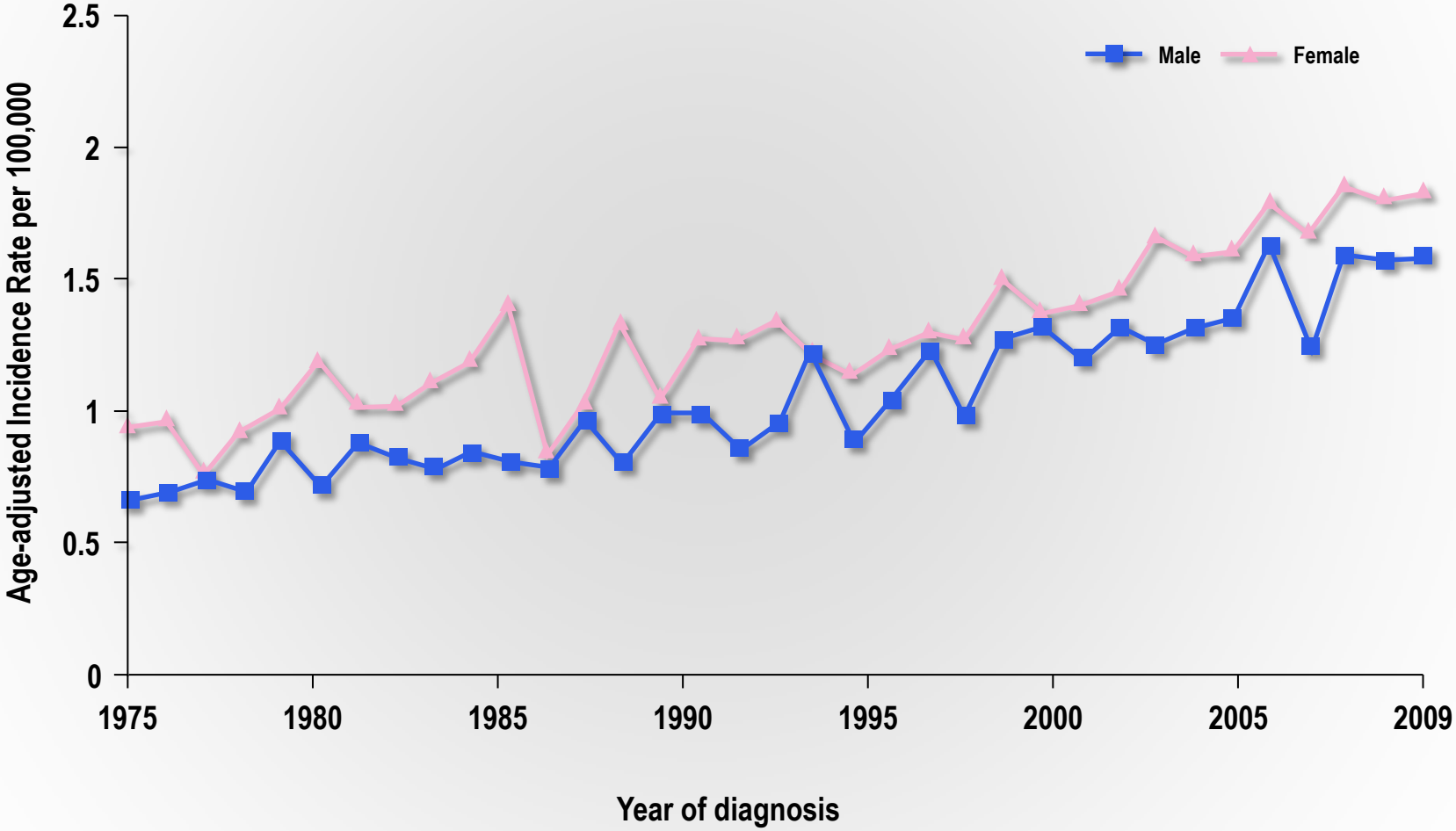
- Anal cancer
- Penile cancer
- Oropharyngeal and oral cavity cancers

~30%–90% caused by HPV 16 & 18[3-5]

There are no routinely available reliable screening methods for cancers caused by HPV in men

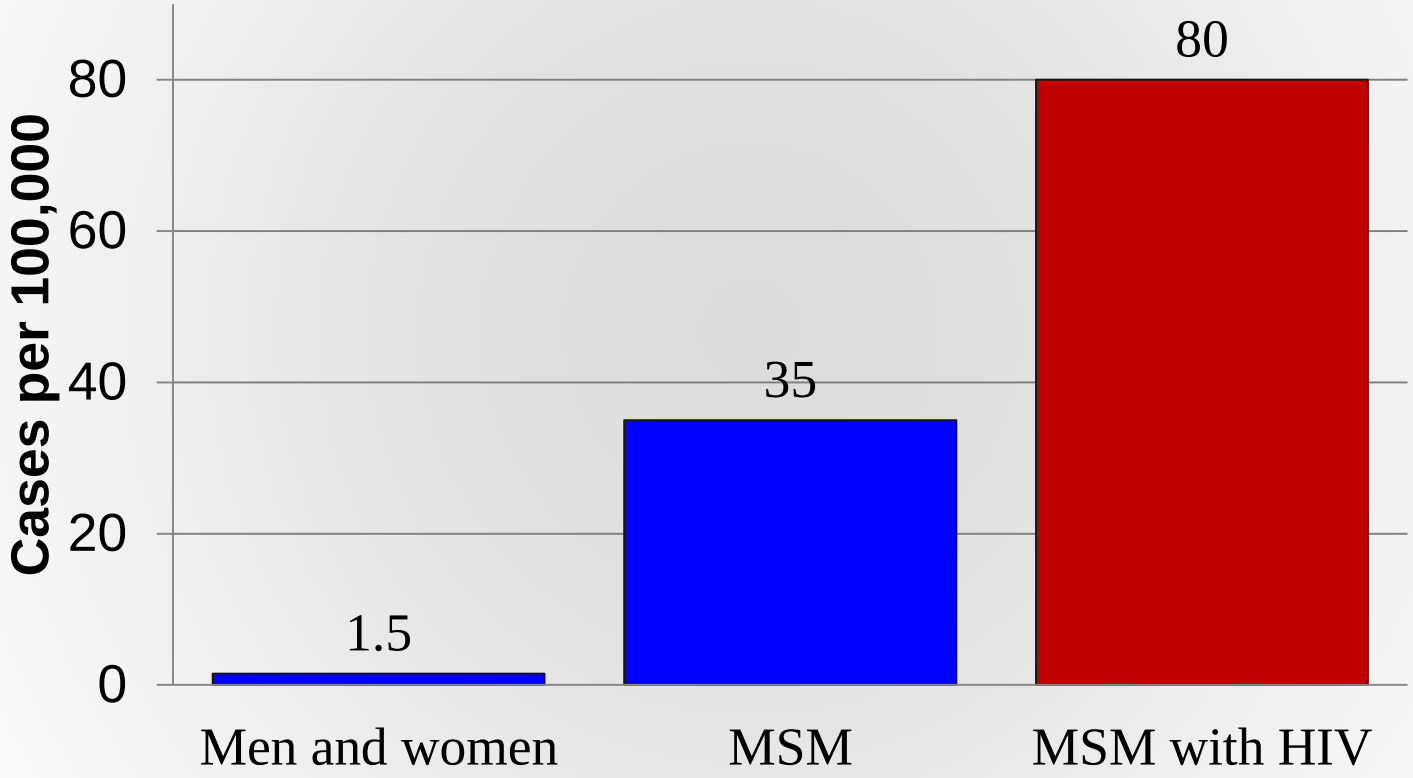
1. Greer CE et al. *J Clin Microbiol*. 1995;33:2058–2063. **2.** Freed GL et al. *Int J Pediatr Otorhinolaryngol*. 2006;70:1799-1803. **3.** De Vuyst H et al. *Int J Cancer*. 2009;124:1626-1636. **4.** Miralles-Guri C et al. *J Clin Pathol*. 2009;62:870-878. **5.** Kreimer AR et al. *Cancer Epidemiol Biomarkers Prev*. 2005;14:467-475.

Age-Adjusted Incidence of Invasive Anal Cancer by Gender and Year of Diagnosis: United States



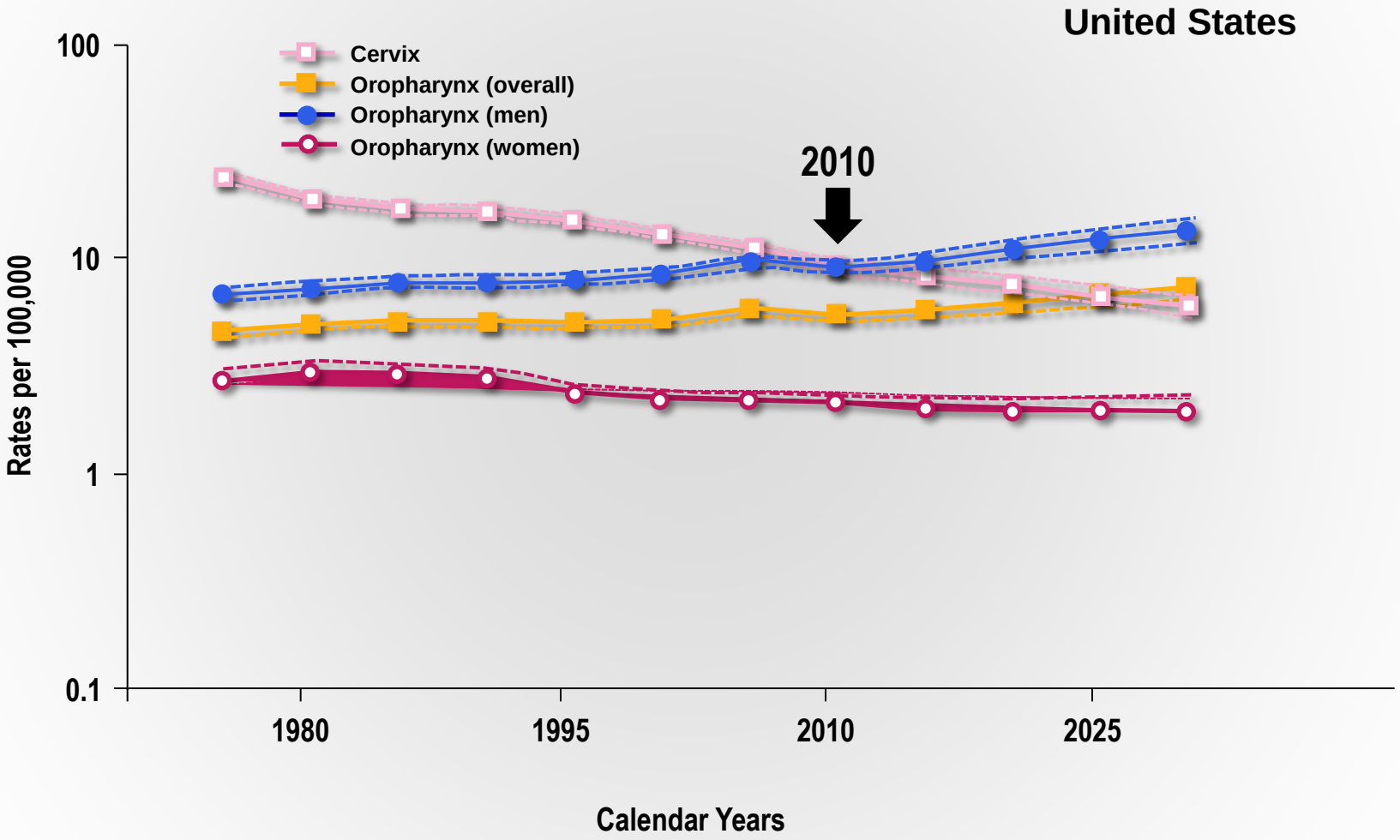
Howlader N et al. (eds). SEER Cancer Statistics Review, 1975-2009 (Vintage 2009 Populations). http://seer.cancer.gov/csr/1975_2009_pops09/. Accessed June 21, 2012.

US Annual Incidence of Invasive Anal Cancer



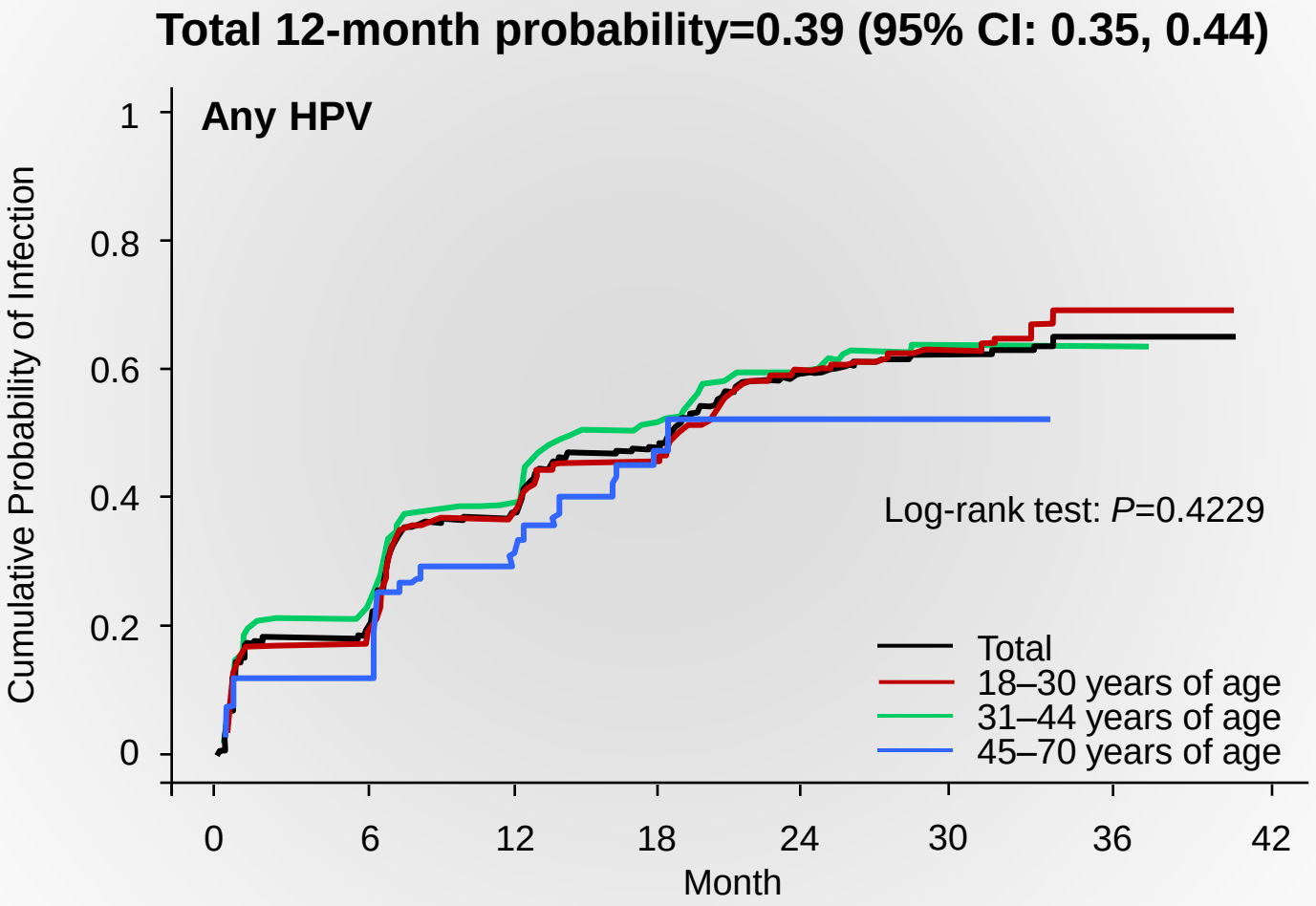
Joseph et al., 2008; Cress et al., 2003, Frisch, 2003; Daling et al., 1982; Chin-Hong et al., 2002

Observed and Projected Incidence Rates for Oropharyngeal Cancers and Cervical Cancer



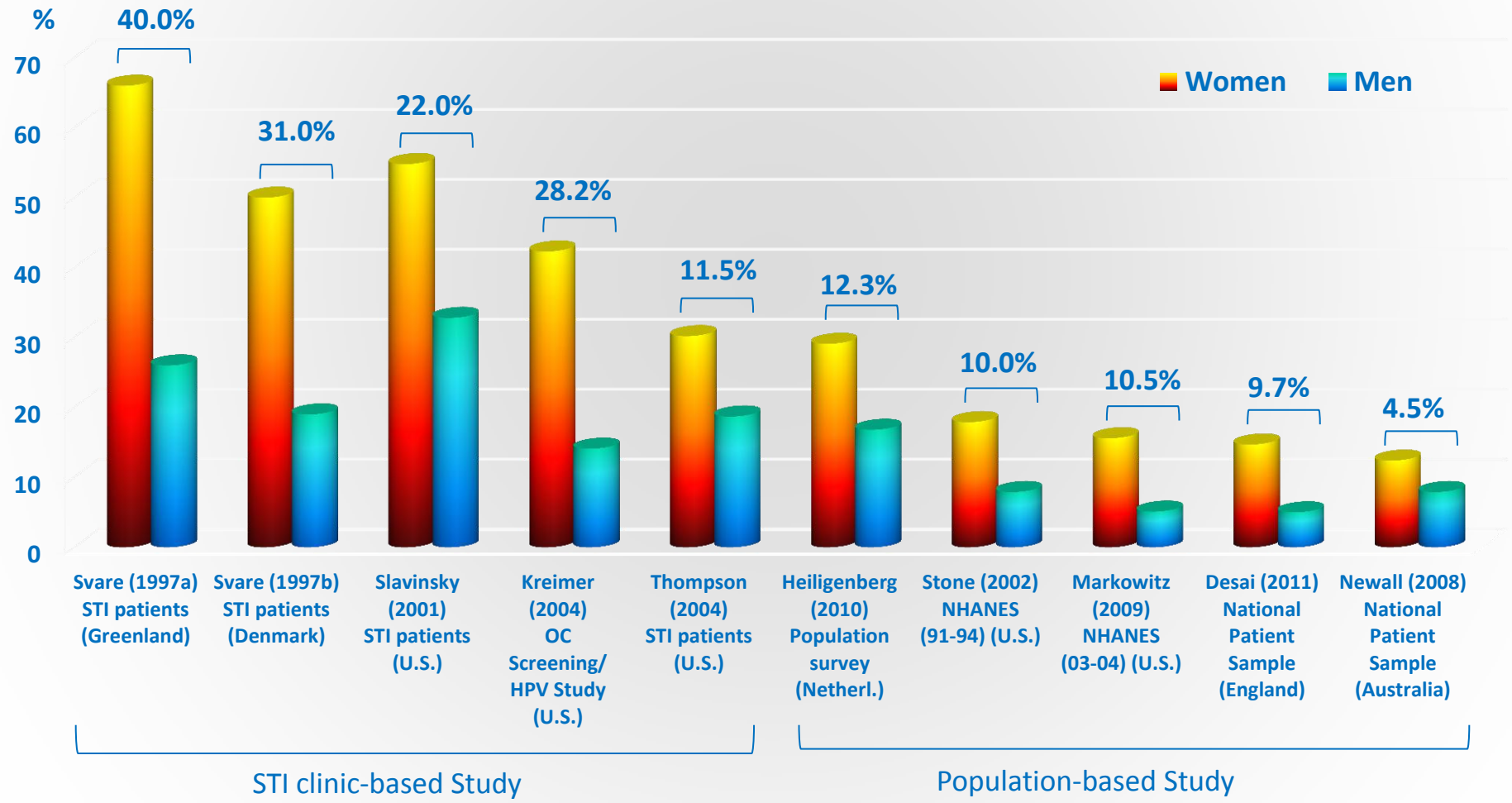
Chaturvedi AK et al. *J Clin Oncol*. 2011;29:4294–4301.

Risk of Acquiring an HPV Infection in Males Does Not Differ by Age

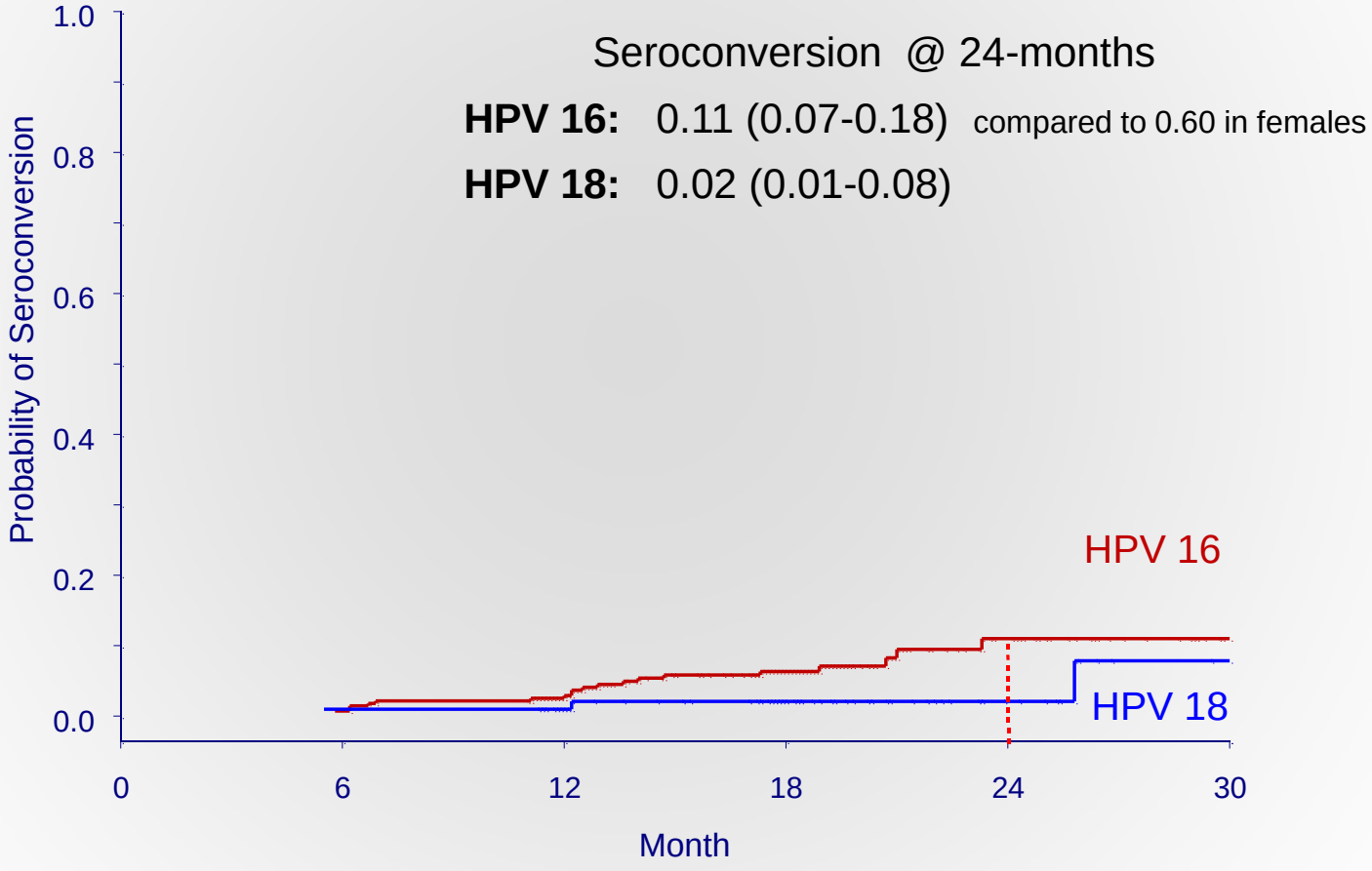


Giuliano AR et al. *Lancet.* 2011;377:932–940.

Gender Gaps in HPV 16 Seroprevalence



Low Seroconversion Following HPV HPV 16 and 18 DNA Detection



Lu B, et al, Presented at *International Papillomavirus Meeting*, November 2012

HPV VACCINATION OF MALES REDUCES DISEASE BURDEN

Efficacy Against HPV 6/11/16/18 Related External Genital Lesions (EGL)

Per-protocol population

	qVaccine (n = 1,397)		Placebo (n = 1,408)				
Endpoint	Cases	Inc. per 100 PY	Cases	Inc. per 100 PY	% Efficacy	95% CI	p-value
All subjects	3	0.1	31	1.1	90.4	69.2, 98.1	<0.001

EGLs include external genital warts, penile/perianal/perineal intraepithelial neoplasia (PIN), penile, perianal, or perineal cancer; case counting began after month 7.

Giuliano AR, Palefsky J, et al. *N Engl J Med* 2011.

Efficacy Against HPV 6/11/16/18–Related Anal Disease Among MSM

Per-protocol population

	qHPV vaccine (n=299)		Placebo (n=299)				
Endpoint	Cases	Inc. per 100 PY	Cases	Inc. per 100 PY	% Efficacy	95% CI	*P* value
All subjects	5	1.3	24	5.8	77.5	39.6–93.3	<0.001

- Anal intraepithelial neoplasia
- Case counting began at month 7

Palefsky JM , Giuliano AR et al. *N Engl J Med.* 2011;365:1576–1585.

Vaccine Indications in Men in Several Countries

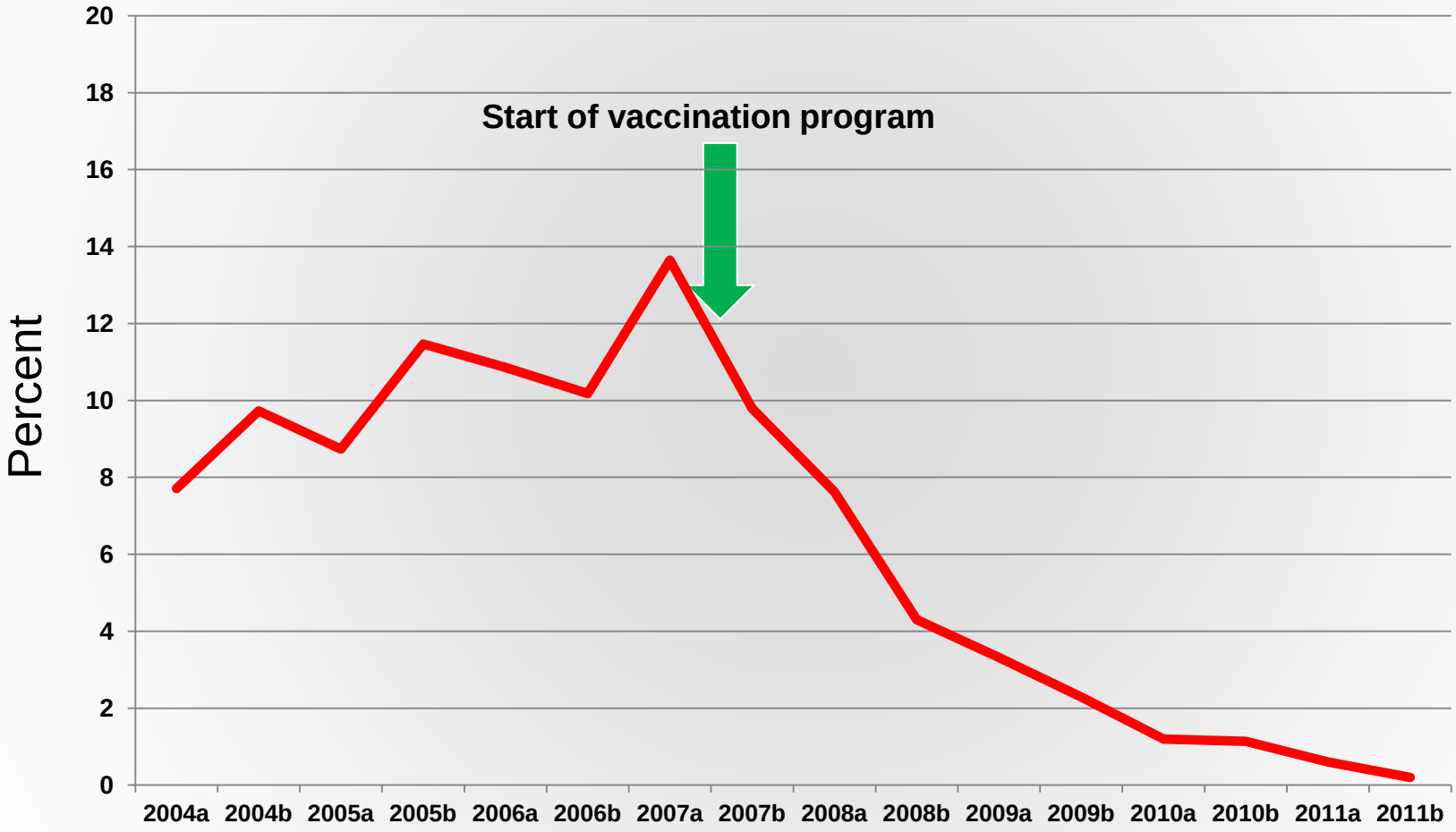
- Prevention of genital warts - 2009
- Anal cancer prevention (males and females) – 2010

US ACIP approved **routine vaccination** of males - 2011

HMO coverage

MDs advised to actively recommend vaccine to boys as well as girls

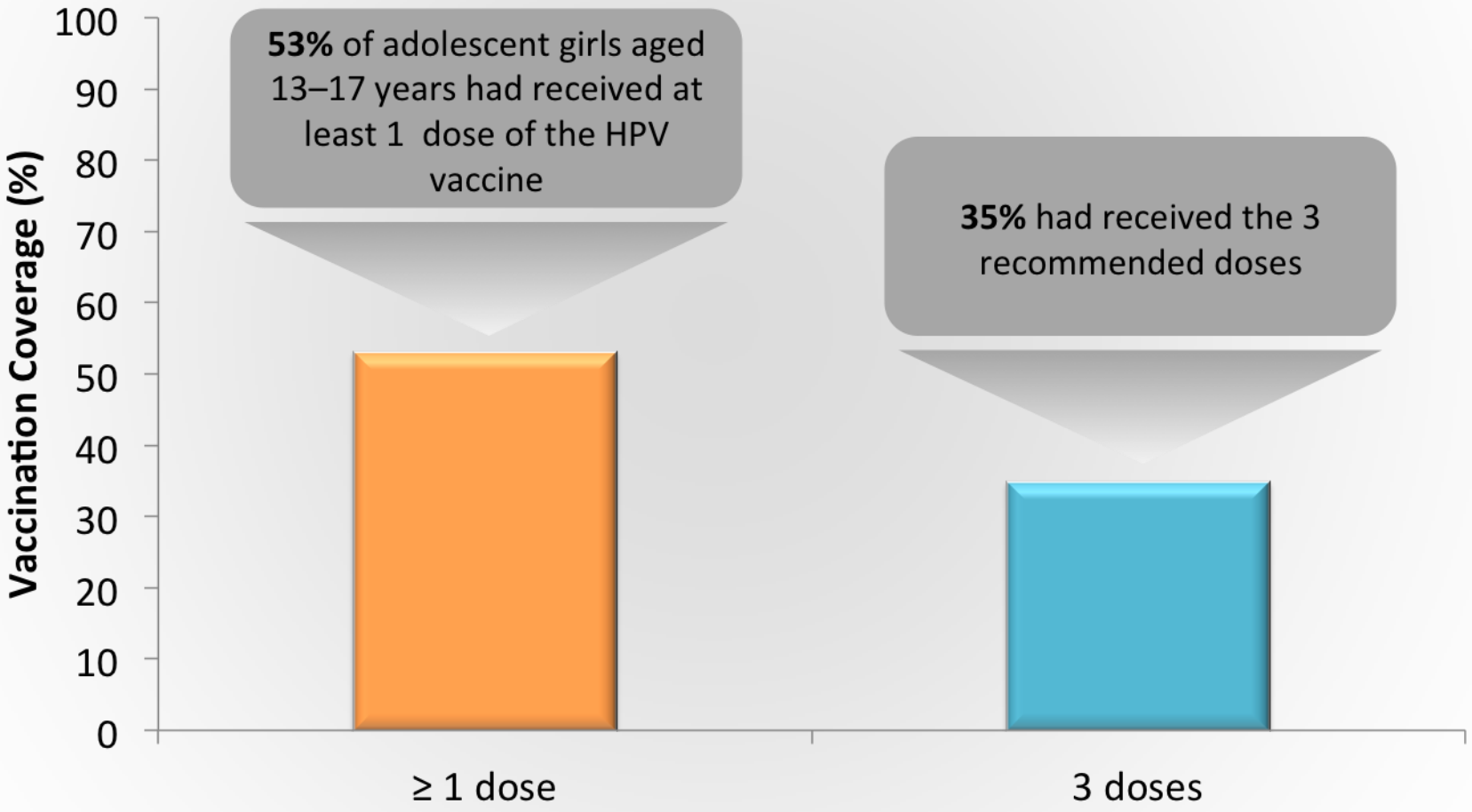
Proportion of Australian born women under 21 years with genital warts, 2004-2011



Slide courtesy of Andrew Grulich, MD

US HPV Vaccination† Coverage

2011



† Quadrivalent or bivalent vaccine

Source: National Immunization Survey (NIS) Teen, US, 2011

Summary

- HPV causes multiple diseases in females and males
- Currently licensed and recommended 4-valent HPV vaccine will prevent in women:
  - Genital warts, cervical, vaginal, and vulvar cancers
- Currently licensed and recommended 4-valent HPV vaccine will prevent in men:
  - genital warts and anal cancer
- HPV vaccine dissemination in the US is <50% in females and <10% in males

Eliminating HPV related disease depends on dissemination of proven technologies

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HIM Study Team

USA

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Questions and Comments?