HPV Vaccination in Male Cohorts: Immunogenicity and Efficacy

Anna R Giuliano, PhD
Director, Center for Immunization and Infection Research in Cancer
Senior Member, Cancer Epidemiology
President, International Papillomavirus Society (IPVS)

MOFFITT CANCER CENTER

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.

Outside of Bahrain, Canada, Hong Kong, Kuwait, Mauritius, Philippines, Qatar, Taiwan, Thailand, UAE and the US currently no HPV vaccines are approved for the prevention of oropharyngeal cancer and other head and neck cancers. No HPV vaccines are not approved for the prevention of recurrent respiratory papillomatosis and penile cancer.

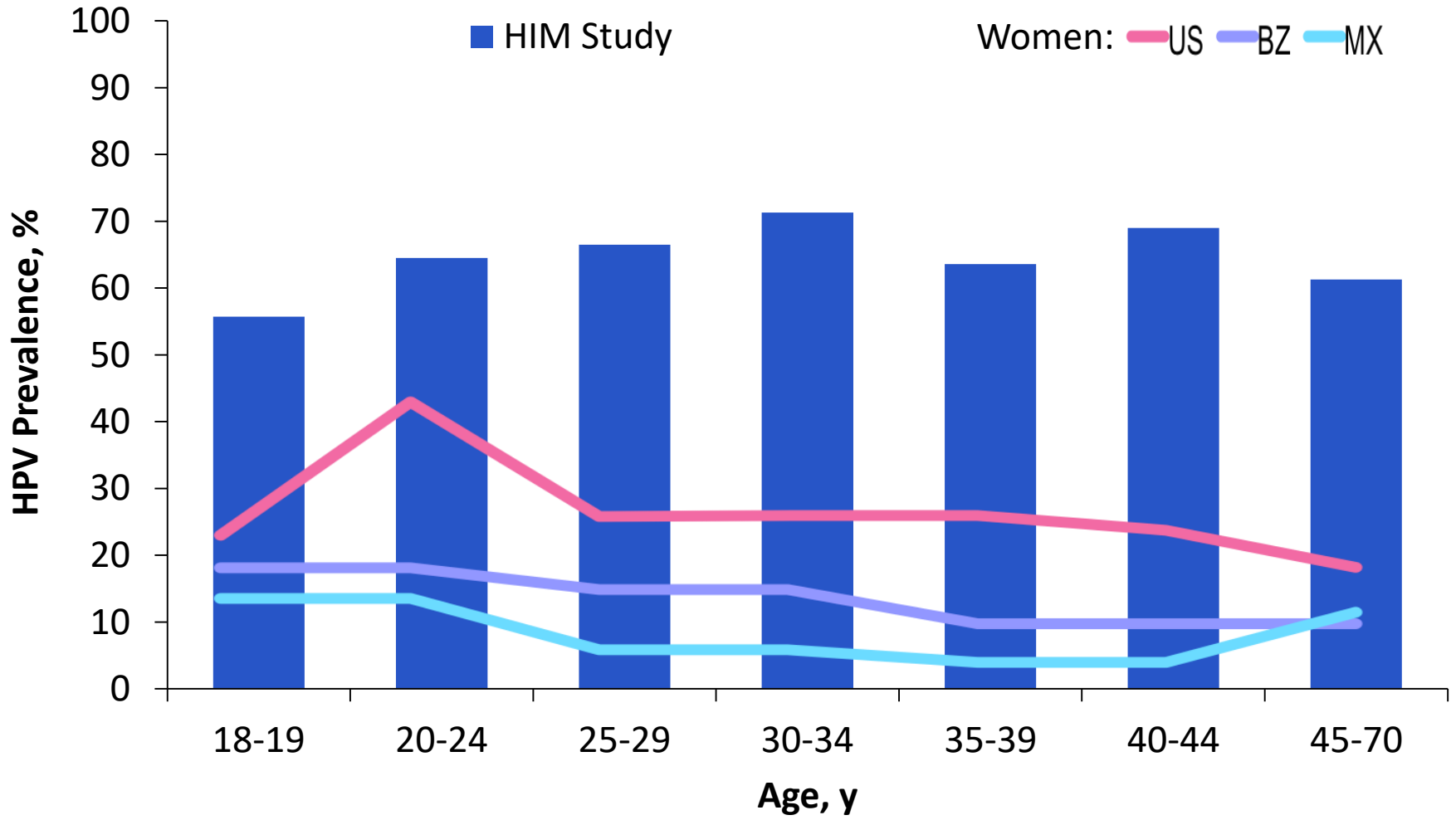
Sites of HPV-Related Cancers and Causal Types

Cancer Site	HPV Types that Cause Cancer	HPV Types with Limited Evidence for Carcinogenicity
Cervical	16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59	26, 53, 66, 67, 68, 70, 73, 82
Vagina	16	
Vulva	16	18, 33
Penis	16	18
Anus	16	18, 33
Oral cavity	16	18
Tonsil and Pharynx	16	

Most HPV-related cancers are caused by type 16 and 18

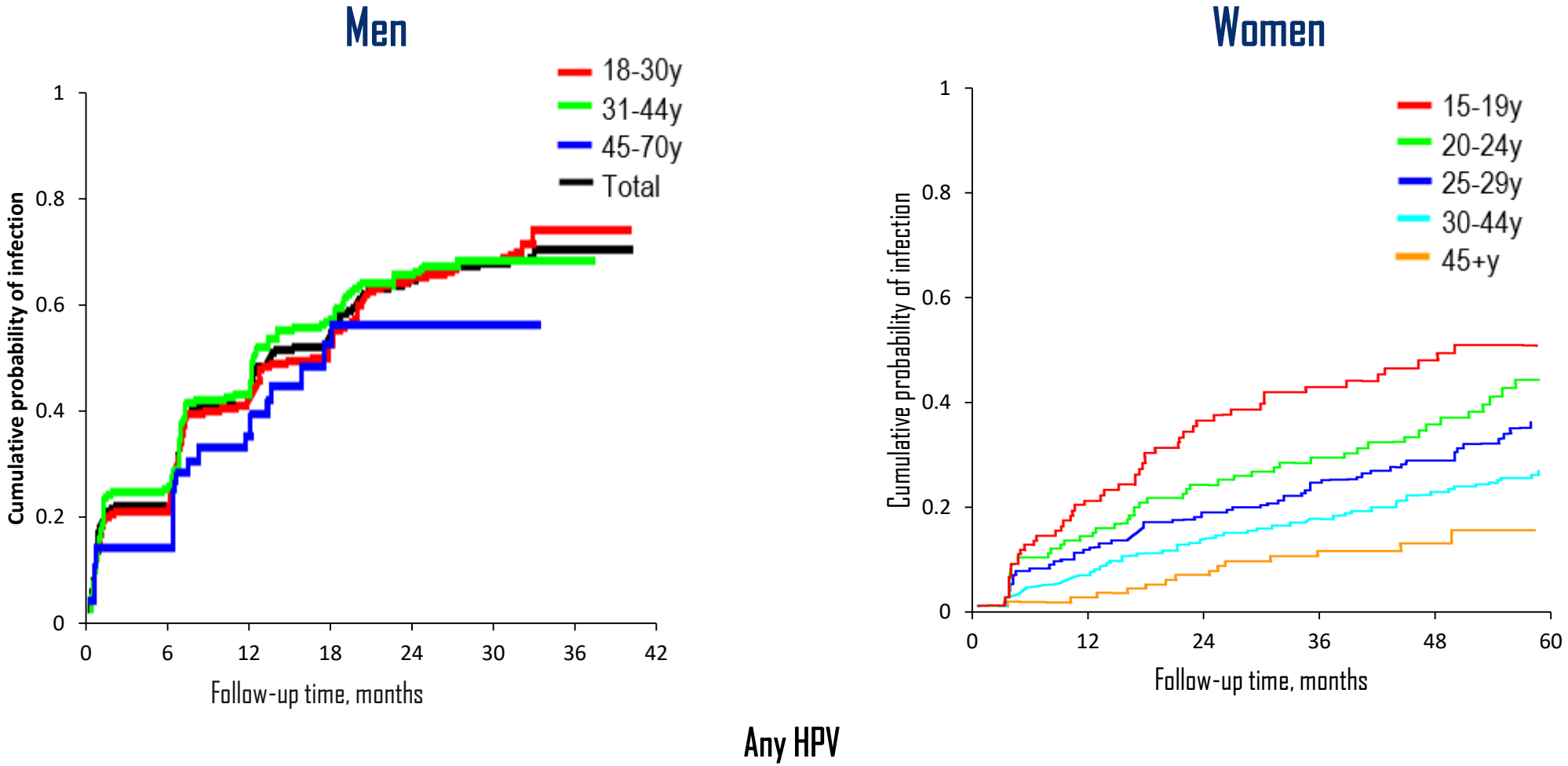
International Agency for Research on Cancer, https://monographs.iarc.who.int/wp-content/uploads/2019/07/Classifications_by_cancer_site.pdf, Accessed 04.26.21

Genital HPV Prevalence is Higher in Men than Women and Does Not Vary with Age



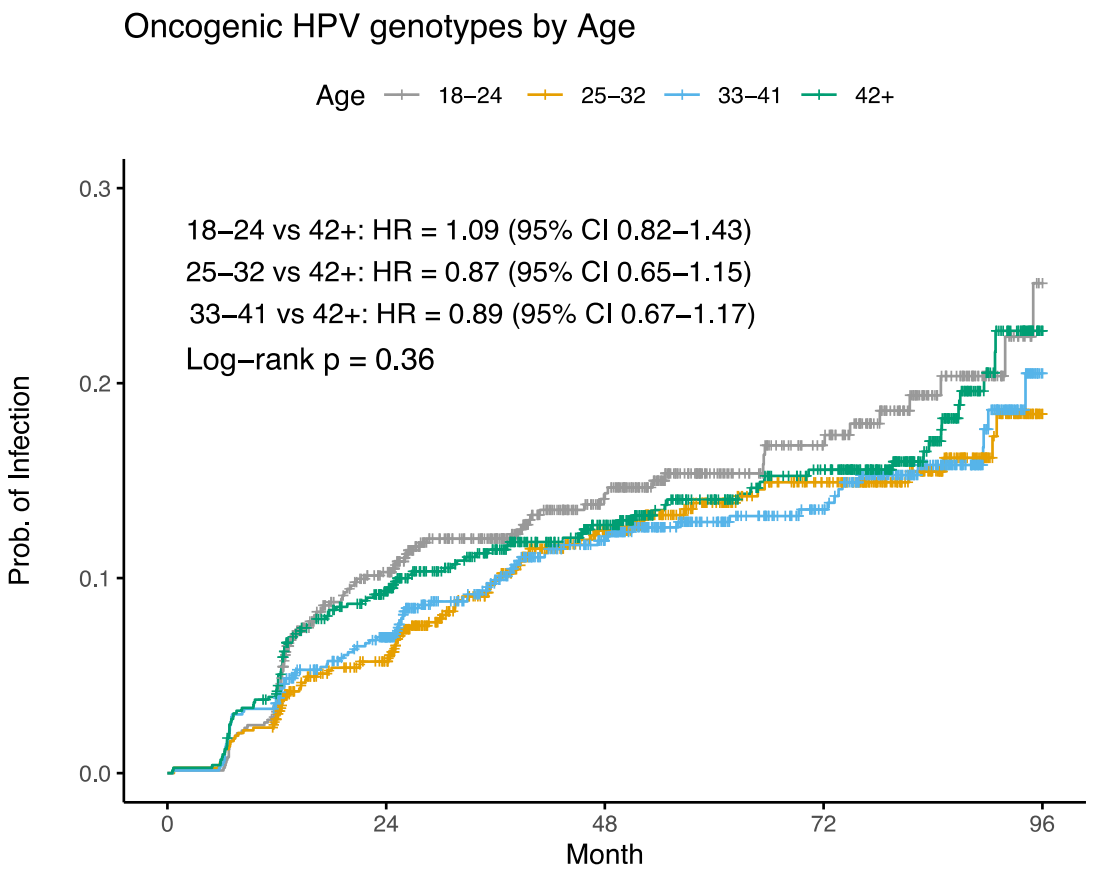
Giuliano AR et al., *CEBP* 2008;17:2036–43; Dunne E et al., *JAMA* 2007;297:813-819; WHO/ICO Information Centre on HPV and Cervical Cancer.

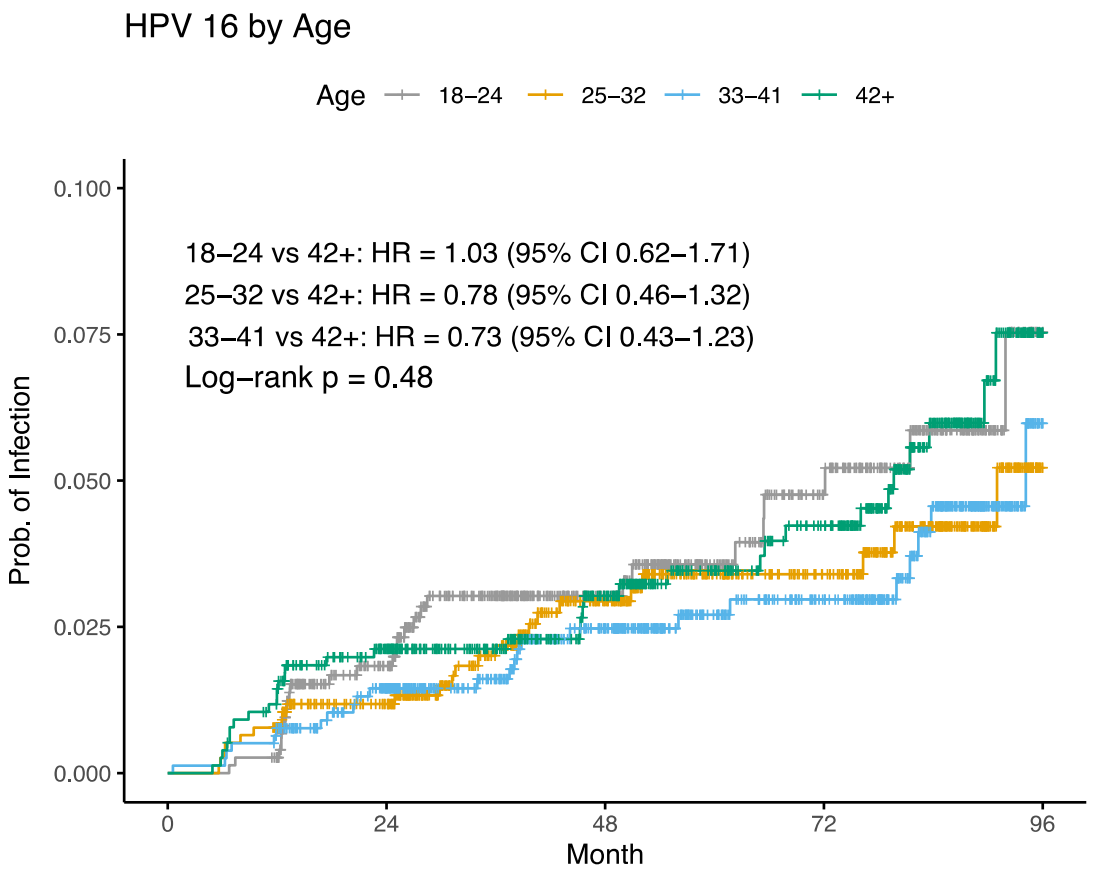
Genital HPV Incidence Lowest in Older Women but Does NOT Vary with Age in Men



Giuliano AR et al., *Lancet,* 2011; Muñoz N et al., *JID,* 2004.

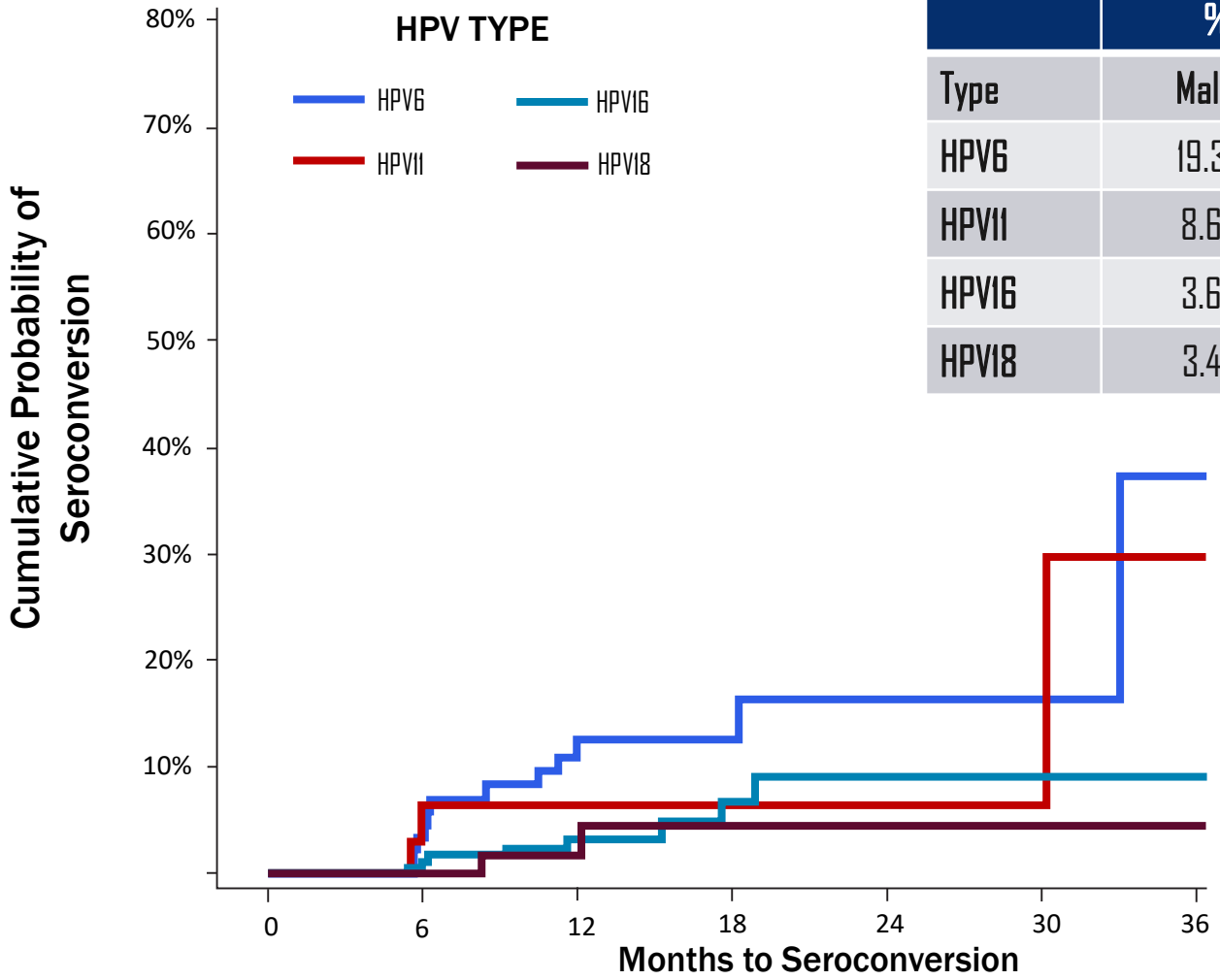
Oral Oncogenic and HPV 16 Acquisition Does Not Differ by Age Group





Mandishora RSD...Giuliano AR, *Nat Microbiolo*/2024

Men Have Low Rate of Seroconversion Following Genital HPV Infection



	% Seroconversion	
Type	Males[1]	Females[2]
HPV6	19.3%	68.8%
HPV11	8.6%	
HPV16	3.6%	59.5%
HPV18	3.4%	54.1%

1. Giuliano AR et al., *PVR* 2015; 2. Carter JJ et al., *J Infect Dis* 2000

Antibodies to Natural Infection Do Not Protect Against New Infections in Men, except for HPV18

	Seropositive n / N	Seronegative n / N	Crude HR (95% CI)
6-month persistent infection			
HPV 6	7 / 283	100 / 3105	0.80 (0.37-1.72)
HPV 11	2 / 513	37 / 3132	0.33 (0.08-1.35)
HPV 16	21 / 420	120 / 2912	1.25 (0.79-1.99)
HPV 18	2 / 391	74 / 3202	0.22 (0.05-0.91)

n: number of infections; N: number of men

Seropositivity is not associated with decreased anal or oral HPV 16 incidence

Pamnani SJ et al., *Cancer Res* 2016;76:6066-75

HPV Transmission is Higher from Female to Males than from Males to Females

	Women to Men		Men to Women	
	Number of infections	Incidence (95% CI)	Number of infections	Incidence (95% CI)
Any HPV type	18	12.9 (7.6 - 20.3)	10	5.9 (2.8 - 10.9)
Oncogenic types	4	9.4 (2.6 - 24.0)	3	3.9 (0.8 - 11.5)
Nononcogenic types	14	14.4 (7.9 - 24.2)	7	7.5 (3.0 - 15.5)

Nyitray A, et al *JID* 2014; 209: 1007-15

Men Remain Susceptible to HPV Throughout Their Lifetime

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

	qVaccine (n = 1,397)		Placebo (n = 1,408)			
Endpoint	Cases	Inc. per 100 PY	Cases	Inc. per 100 PY	% Efficacy	95% CI
Genital Warts	3*	0.1	28	1.0	89.4	65.5, 97.9
PIN 1	0	0.0	2	0.1	--	--
PIN 2/3	0	0.0	1	0.0	--	--
Penile/perineal/perianal cancer	0	0.0	0	0.0	--	--

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

HPV vaccines are not approved for the prevention of PIN or penile cancer.

4v HPV Vaccine Prevents Anal HPV Infections & Lesions

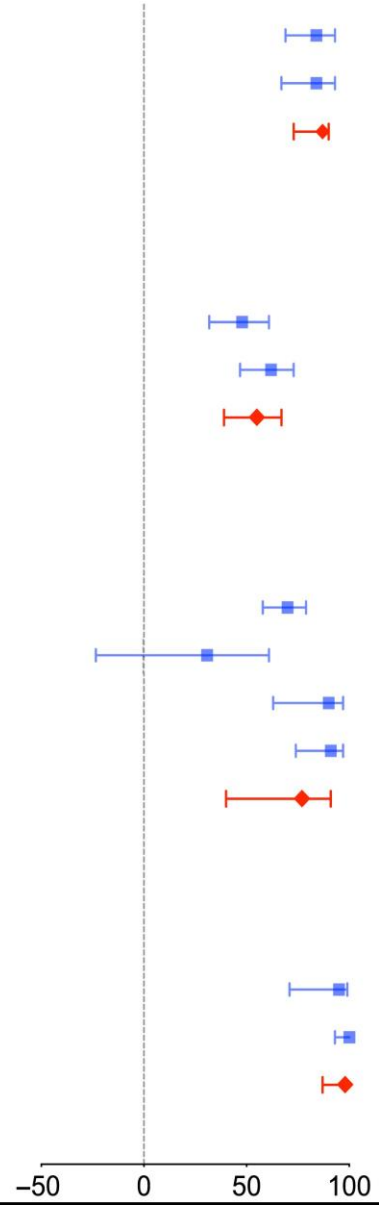
Efficacy against persistent anal infection with 4v types at any time in per-protocol efficacy population

	qHPV Vaccine		Placebo		ObsOerved Efficacy % (95% CI)
	No. in Analysis	Events per 100 PY at risk	No. in Analysis	Events per 100 PY at risk	
Persistent Infection HPV 6, 11, 16, or 18	193	8.8	276	21.6	59.4 (43.0-71.4)
AIN Grade 1	194	1.0	208	3.9	73.0 (16.3-93.4)
AIN Grade 2	194	0.5	208	2.2	75.8 (-16.9-97.5)
AIN Grade 3	194	0.5	208	1.4	63.7 (-103.0-96.4)
Anal Cancer	194	0.0	208	0.0	N/A

Palefsky J, Giuliano AR, et al., *NEJM* 2011

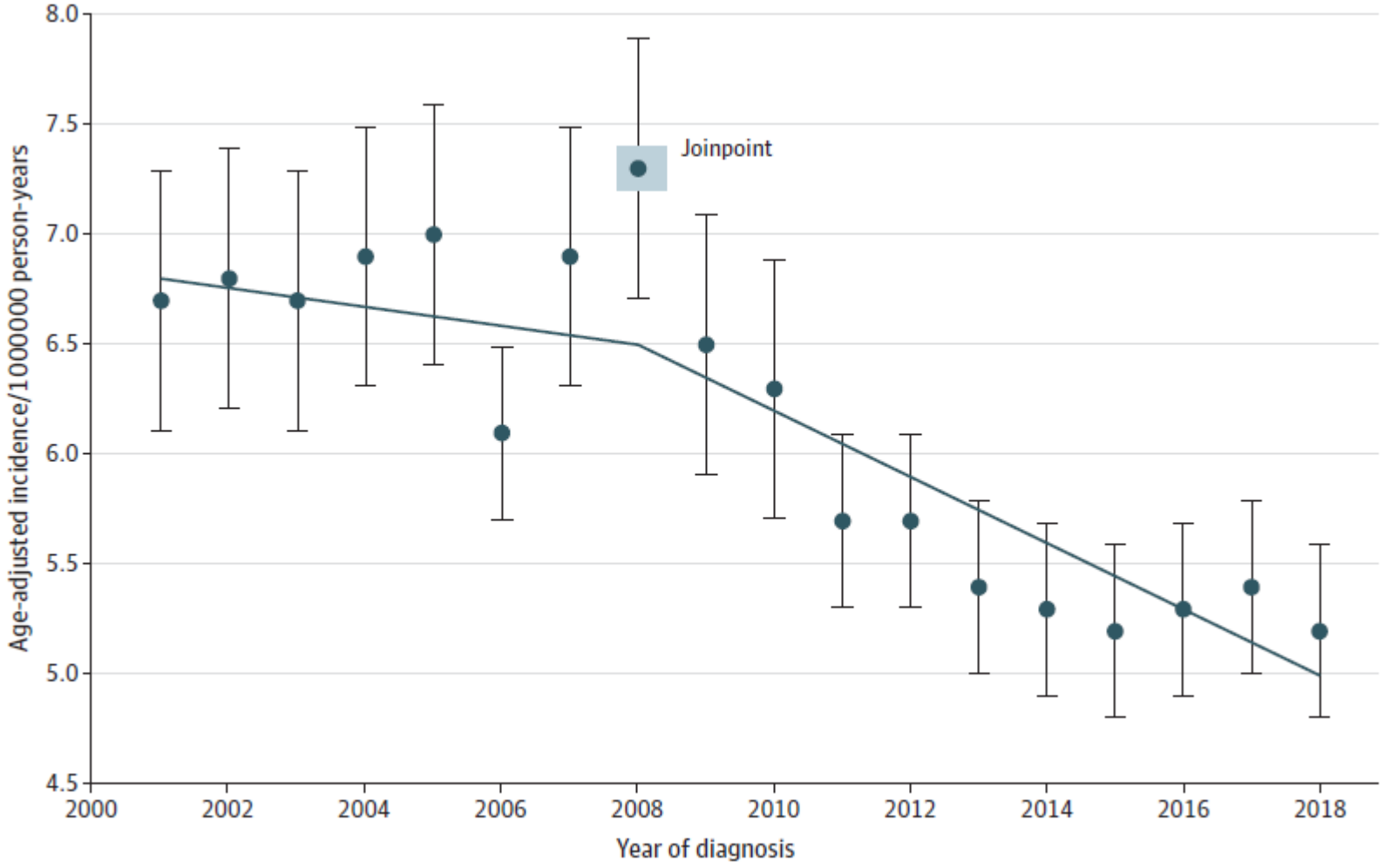
Pooled HPV Vaccine Efficacy Against Vaccine-Targeted Anal HPV

Study	Vaccine Group, No.		Nonvaccine Group, No.		VE (95% CI), %	Weight, %
	Event	Total	Event	Total		
Incident/prevalent anal HPV infection in PPE in clinical trials						
Palefsky et al (2011) [17]	10	193	61	208	84 (69 to 93)	50.6
Kreimer et al (2011) [16]	8	1003	48	986	84 (67 to 93)	49.4
Random-effects model					**84 (73 to 90)**	**100.0**
Heterogeneity: I^2 = 0%; P = .96						
Incident/prevalent anal HPV infection in ITT in clinical trials						
Palefsky et al (2011) [17]	85	275	147	276	48 (32 to 61)	50.5
Kreimer et al (2011) [16]	47	2103	124	2107	62 (47 to 73)	49.5
Random-effects model					**55 (39 to 67)**	**100.0**
Heterogeneity: I^2 = 46%; P = .17						
Incident/prevalent anal HPV infection in real-world studies						
Schlecht et al (2012) [21]	13	327	22	132	70 (58 to 79)	32.8
Meites et al (2020) [18]	471	704	465	687	31 (–23 to 61)	29.2
Woestenberg et al (2020) [19]	3	357	14	191	90 (63 to 97)	17.3
Chow et al (2021) [20]	4	144	54	193	91 (74 to 7)	20.8
Random-effects model					**77 (40 to 91)**	**100.0**
Heterogeneity: I^2 = 81%; P < .01						
Persistent anal HPV infection in PPE in clinical trials						
Palefsky et al (2011) [17]	2	193	39	208	95 (71 to 99)	53.6
Mikamo et al (2019) [23]	0	494	9	498	100 (93 to 100)	46.4
Random-effects model					**98 (87 to 100)**	**100.0**
Heterogeneity: I^2 = 32%; P = .22						



Wei F, et al., *JID*, 2023

HPV Vaccine Reduces Anal Cancer Incidence



Age-adjusted incidence among adults aged 20-44 in the U.S.

APR: 2001-2008: −0.6 (95%CI, −2.5 to 1.4);

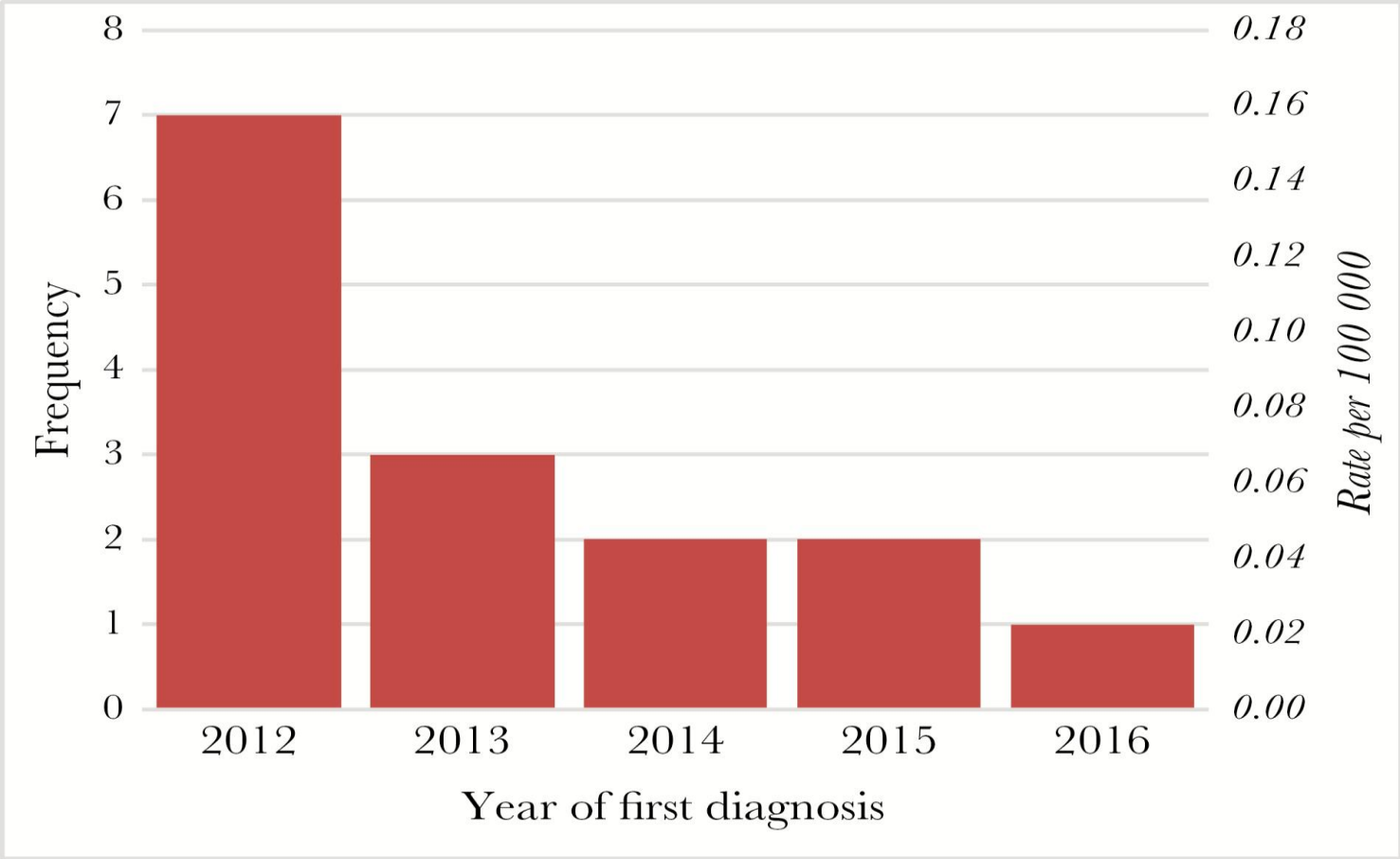
2008-2018: −2.7 (95%CI, −3.8 to −1.6,

Berenson A et al., *JAMA Onc*, 2022

HPV Vaccination Reduces Recurrent Respiratory Papillomatosis Incidence

Incident cases of juvenile onset recurrent respiratory papillomatosis notified in Australia per year 2012–2016.

Frequency and rates per 100,000 children aged 0–14 years

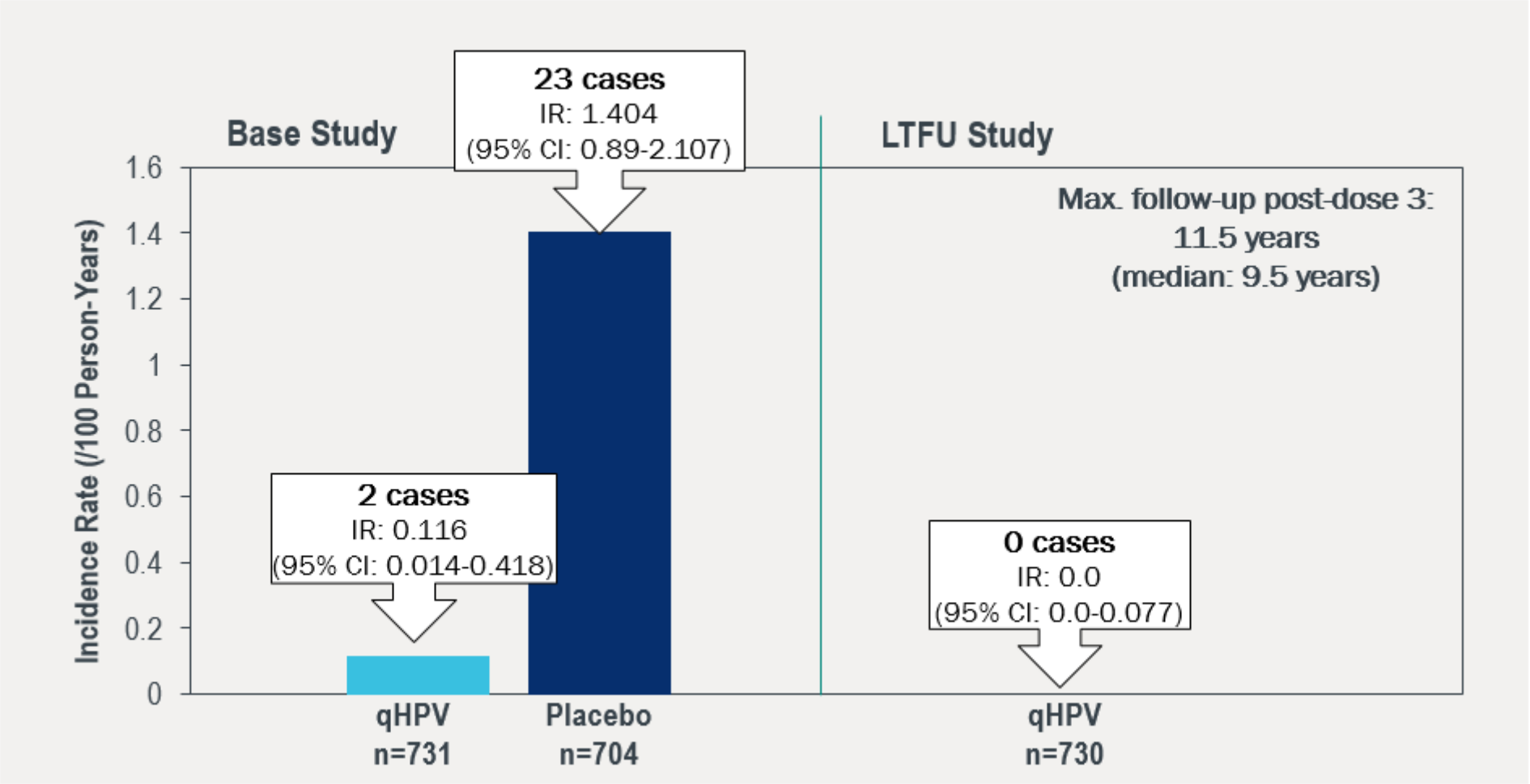


Novacovik et al., *JID* 2018

Difference between rate in 2012 and 2016 P = 0.036.

No HPV vaccines are indicated for the prevention of RRP. The effect of vaccination on the incidence reduction of JoRRP based on published observational studies has been added to section 5.1 of the EMA SmPC.

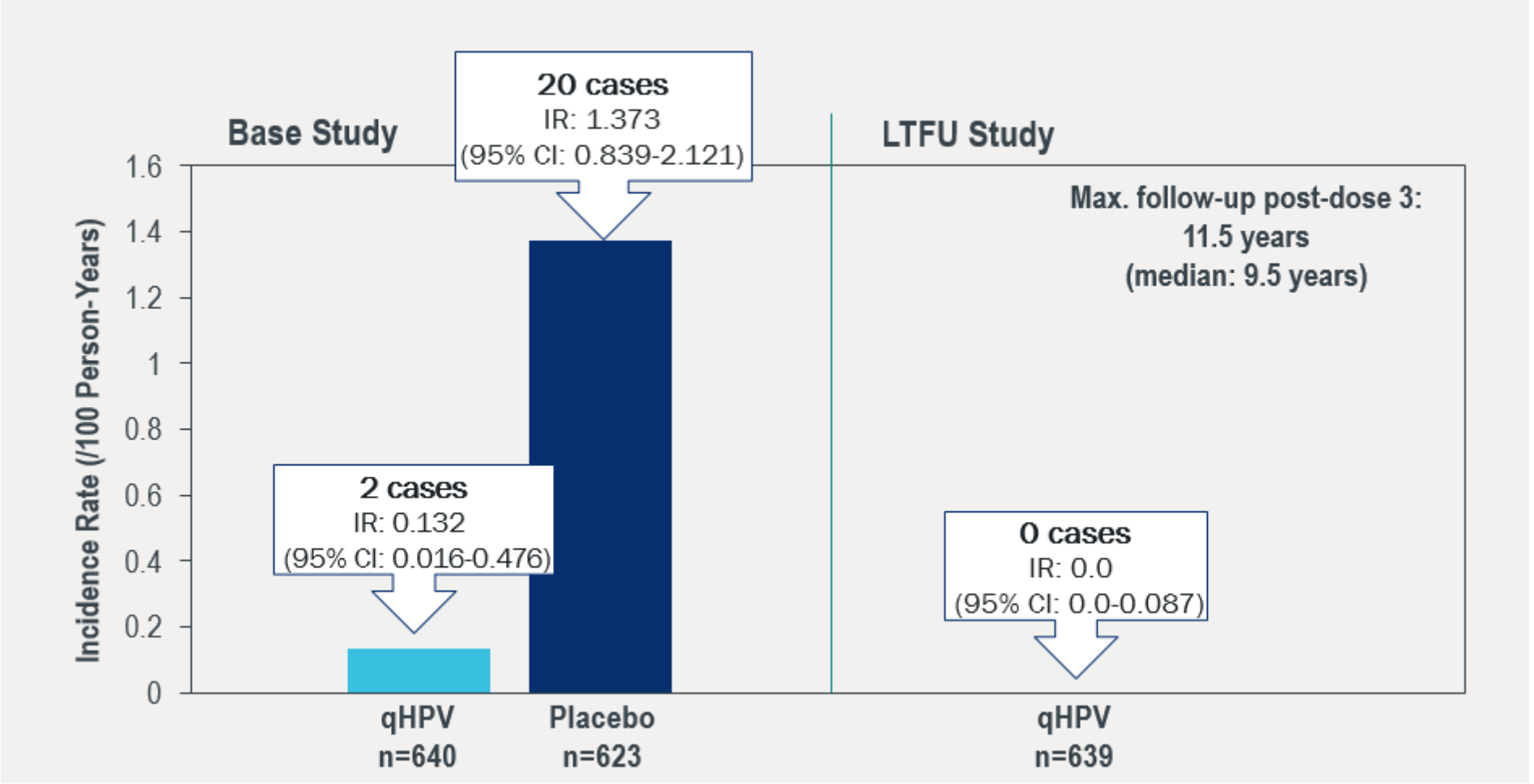
No New Cases of 4vHPV-Related External Genital Disease During LTFU of Men Ages 16-26 years



Per-protocol population (LTFU participants)
CI, confidence interval

Goldstone SE, Giuliano AR, et al. *Lancet Infect Dis*, 2022

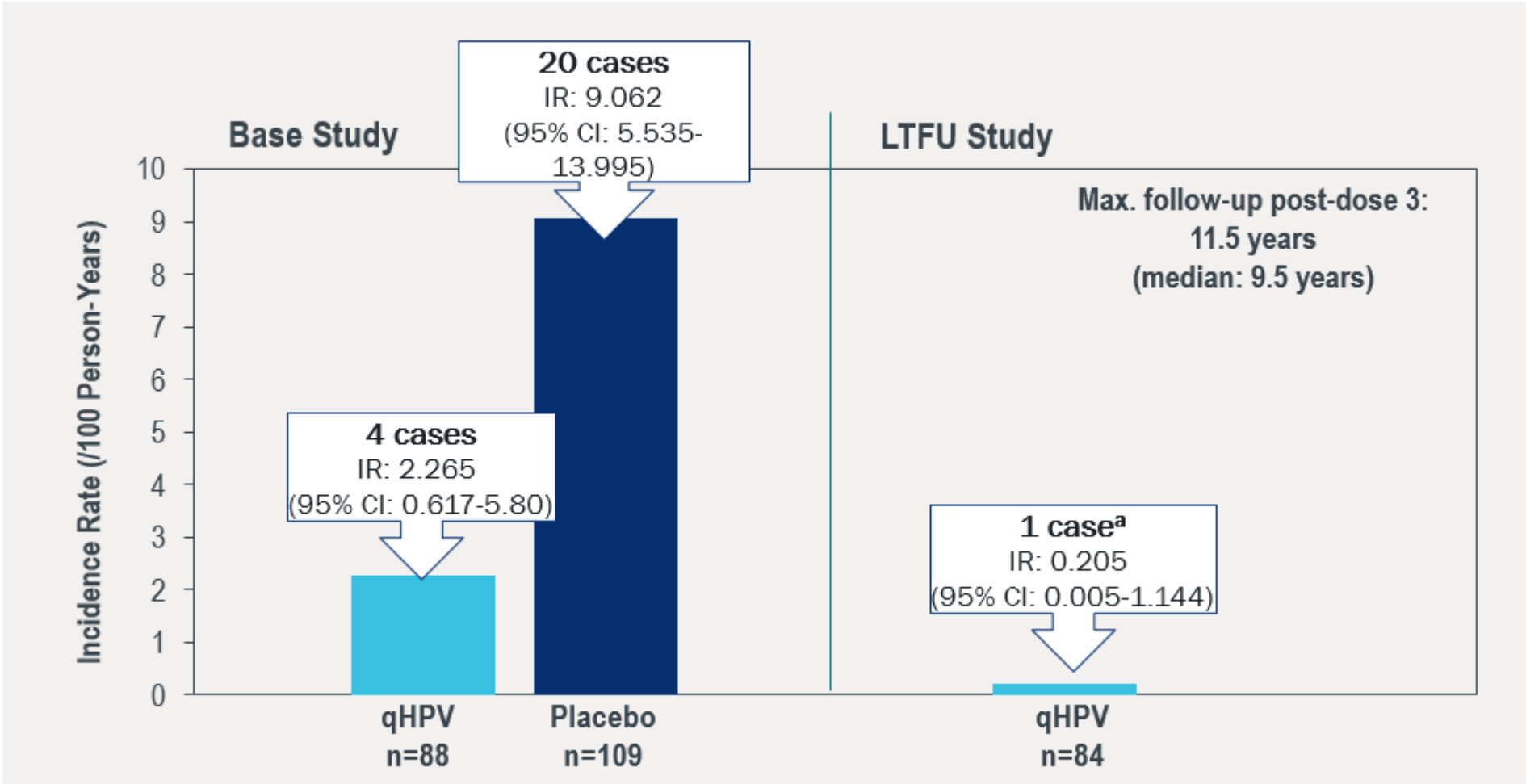
No New Cases of HPV6/11-Related External Genital Warts During LTFU of Men Ages 16-26 years



Goldstone SE, Giuliano AR, et al. *Lancet Infect Dis*, 2022

Per-protocol population (LTFU participants)

Low Rates of 4vHPV-Related AIN and Anal Cancer in MSM In LTFU Study of Men Ages 16-26 years



Per-protocol population (LTFU participants)

[a]HPV6-related AINI (HPV58 co-detected)

Goldstone SE, Giuliano AR, et al. *Lancet Infect Dis*, 2022

Persistent 4vHPV Vaccine Type Antibody Responses Over 10-year Follow-up Among Men Ages 16-26 years

GMT

- Peak at Month 7, sharp decrease through Month 24, and slower decrease after that

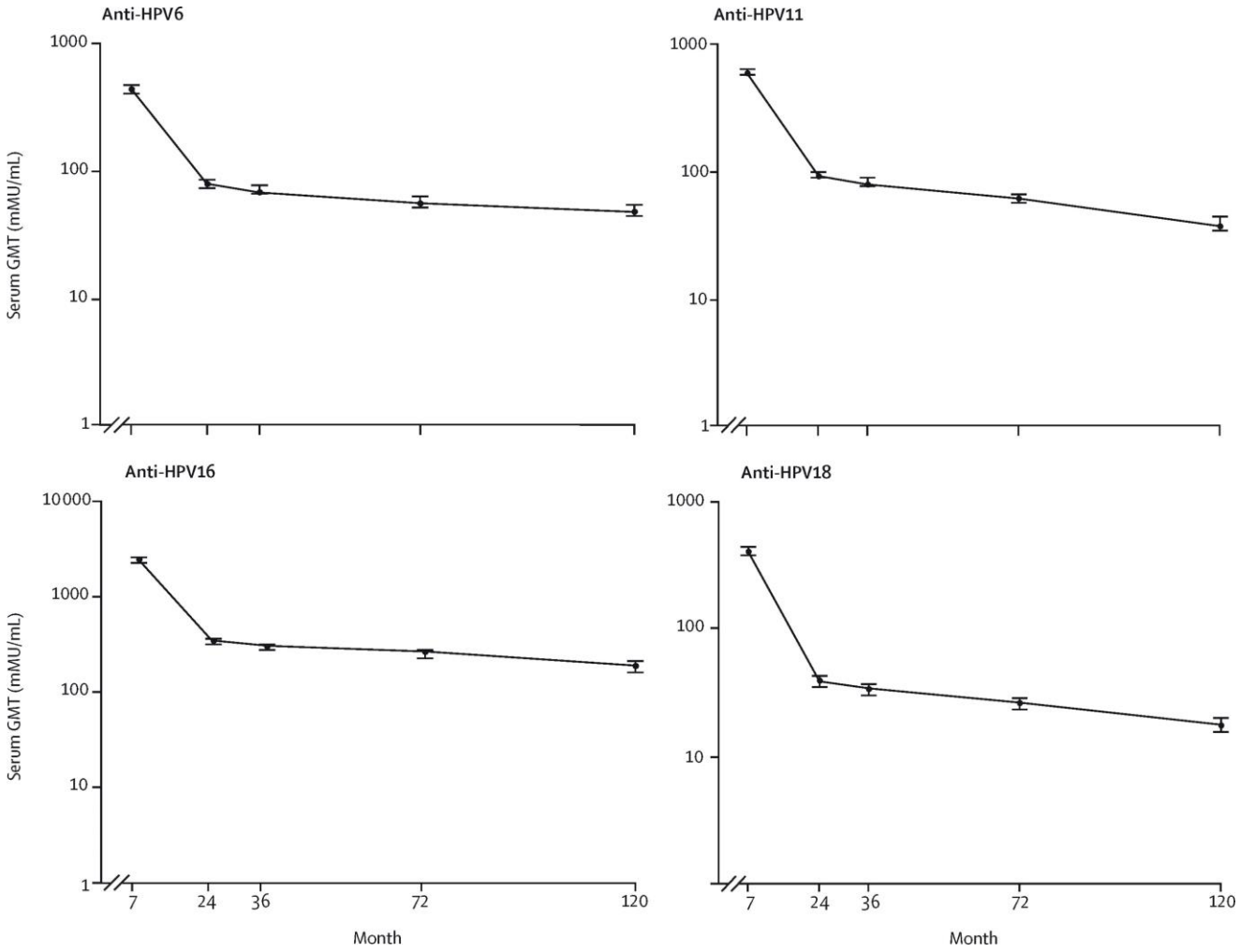
Seropositivity at Month 120

cLIA

- 79%, 80%, 95%, and 40% for HPV 6, 11, 16, and 18, respectively

IgG-LIA

- 92%, 92%, >99%, and 92% for HPV 6, 11, 16, and 18, respectively



Goldstone SE, Giuliano AR, et al. *Lancet Infect Dis,* 2022

Gardasil Efficacy Against Persistent Oral HPV Infection Among HIV+ Men Ages ≥27 years

Antibody titer response did not differ by age

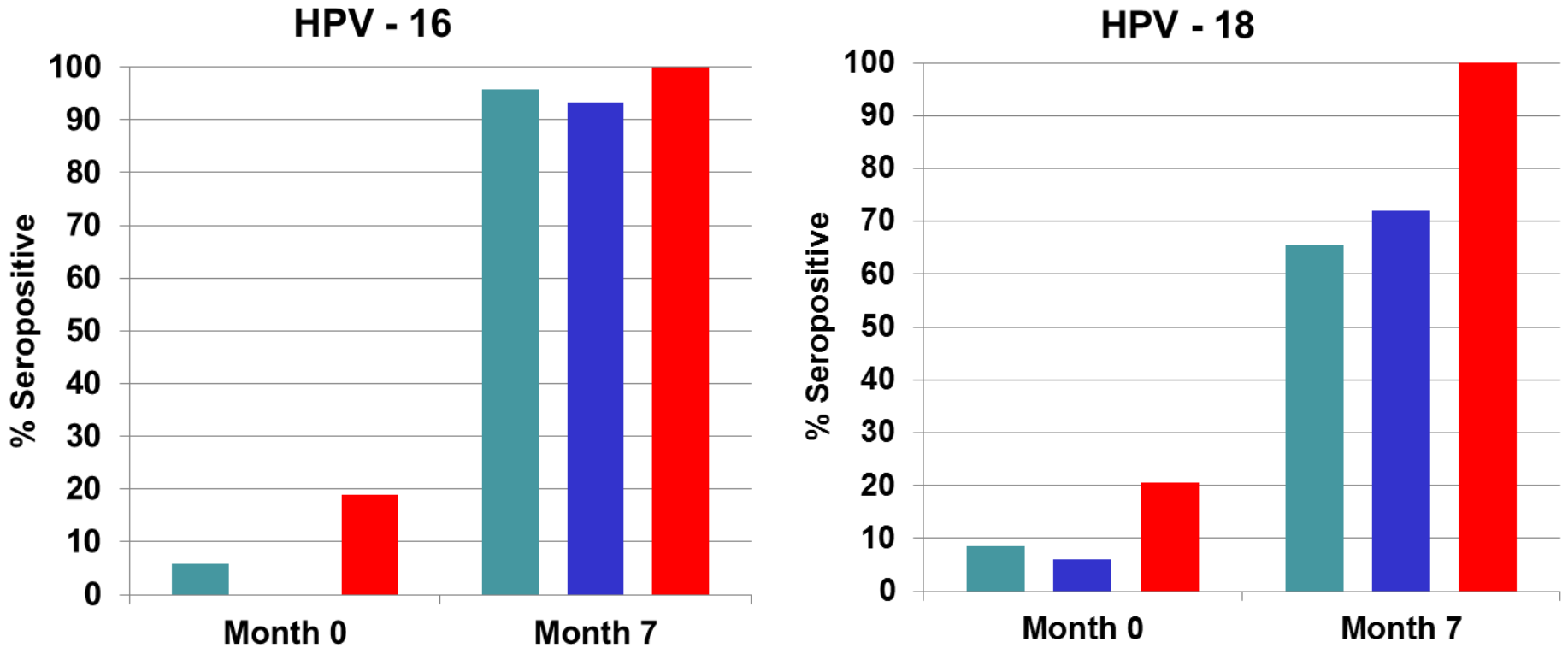
Outcome	4vHPV (n)	Placebo (n)	HR (95.1% CI)
Persistent oral HPV, or single detection at last visit	7	10	0.68 (0.26, 1.80)
Persistent oral HPV	1	8	0.12 (0.02, 0.98), *P* =.019

Wilkin T et al, *CROI* 2016

qHPV Vaccine Induces Oral HPV-16 and HPV-18 Antibodies in Mid-Adult Aged Men

Percent seroconversion following 3 doses of qHPV vaccine

Cutoff: HPV-16 L1 ELISA: 19 EU/ml HPV-18 L1 ELISA: 18 EU/ml

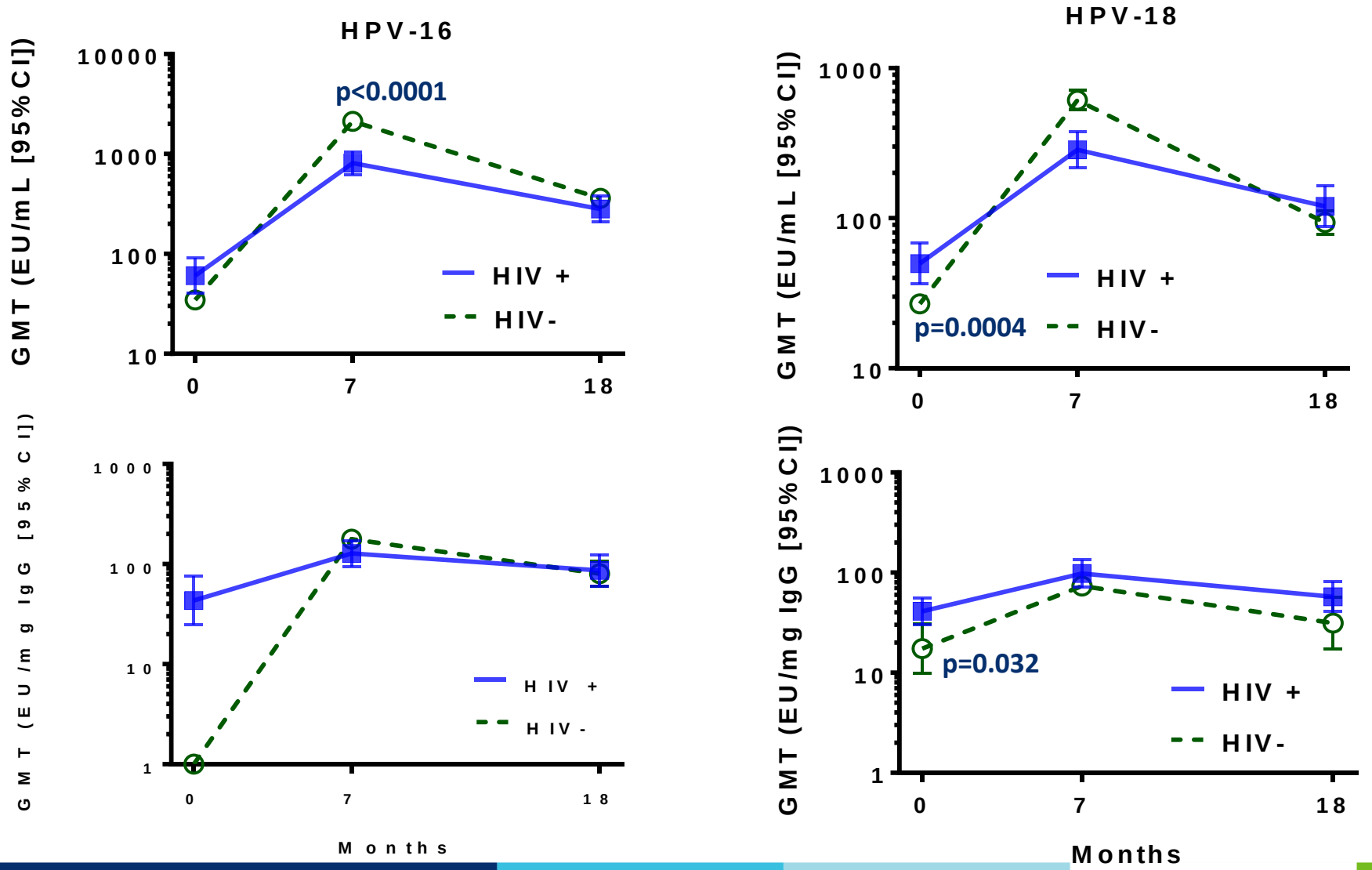


Pinto LA ..... Giuliano AR, *JID* 2016

Serum and oral HPV-16 and HPV-18 antibody levels in HIV+ and HIV- individuals

SERUM

ORAL GARGLES



Pinto L et al, *Vaccine*, 2019

Conclusions

- The qHPV vaccine provides durable protection from vaccine type-related anogenital disease and persistent infection through at least 10 years post-vaccination in males aged 9–26 years
- Durable protection was also observed through at least 10 years post-vaccination with the 9vHPV vaccine in boys 9–15 years
- Persistent HPV antibody responses were observed through at least 10 years after vaccination is all study populations
- Results support implementing gender-neutral vaccination and catch-up vaccination programs

IPVS2025

37TH ANNUAL CONFERENCE OF THE INTERNATIONAL PAPILLOMAVIRUS SOCIETY

Research toward the global elimination of HPV-related diseases and cancers

OCTOBER 23-26, 2025 | BANGKOK, THAILAND

SAVE THE DATE

ipvconference.org | #IPVS2025

IPVS International Papillomavirus Society

Thank you!

Anna R Giuliano, PhD
Center for Immunization and Infection Research in Cancer
Moffitt Cancer Center

Anna.giuliano@moffitt.org
813.745.6820