

Decreasing the Impact of HPV-related Infections and Cancers

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The Burden of HPV

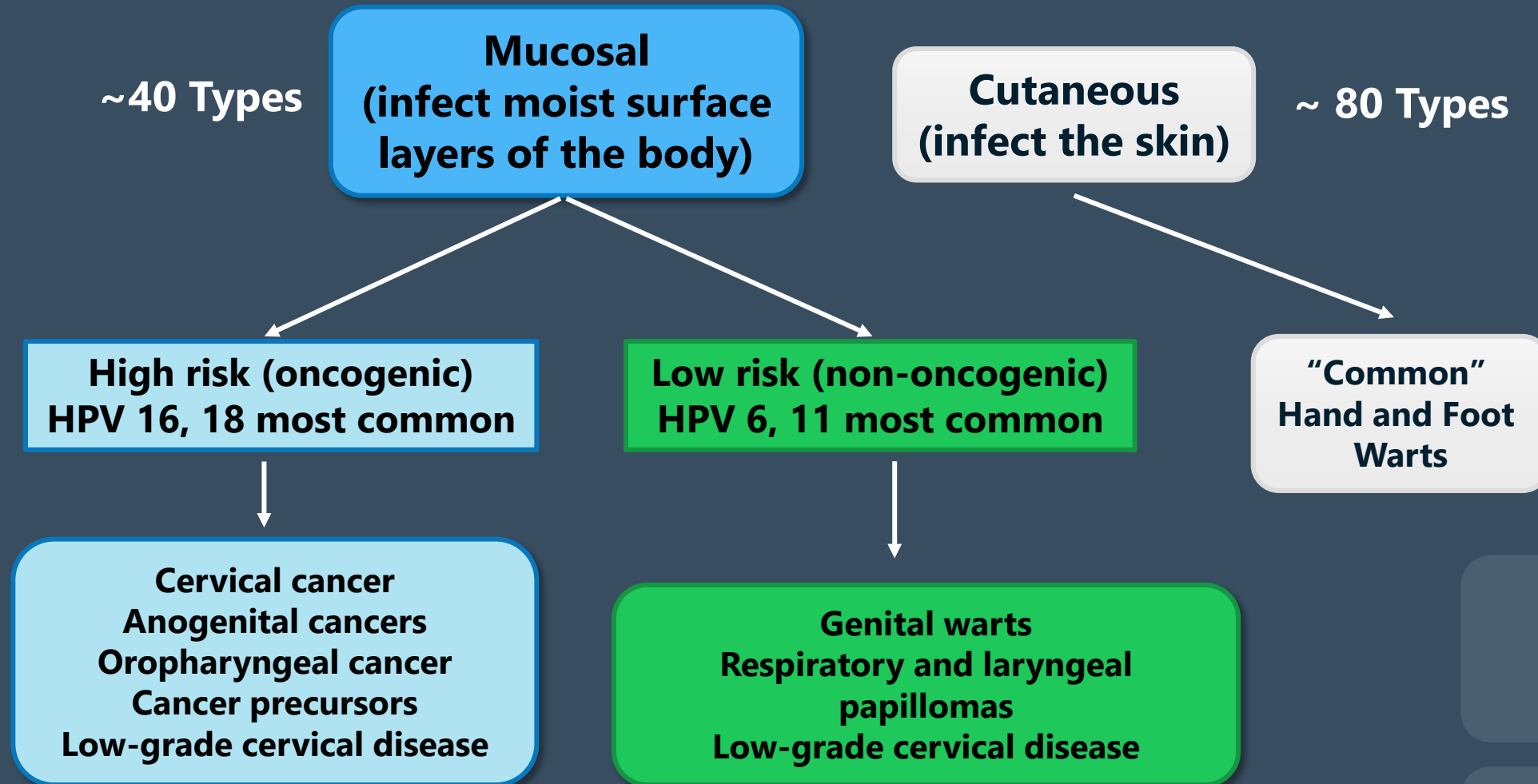
- Most common sexually transmitted infection in the United States and worldwide
- Approximately 31,500 cancers attributed to HPV
 - Classified as a carcinogen
- Easily transmissible and highly ubiquitous
 - Most males and females are exposed during their lifetime
- Peak prevalence within a few years of median age of sexual debut (average age 17 in the US)

Natural History HPV

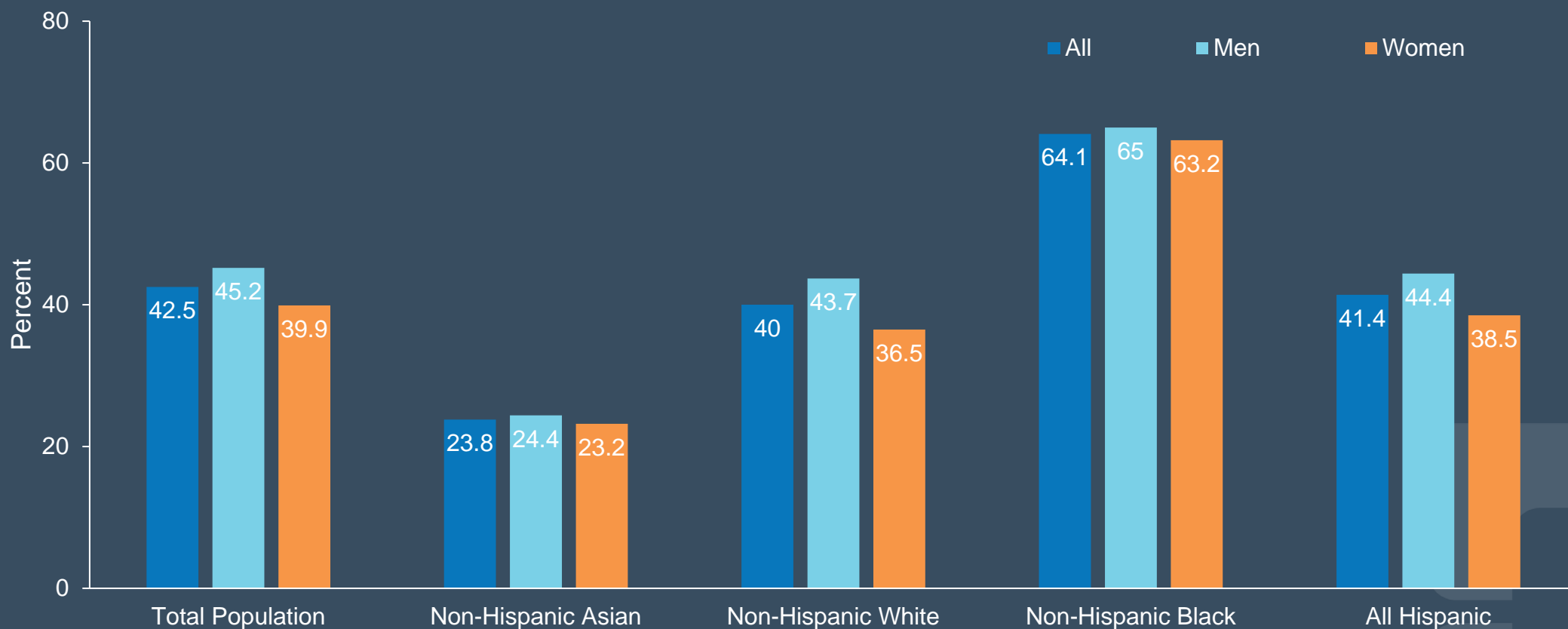
- Genital HPV acquired through sexual and skin-to-skin contact
- Most (> then 90%) genital HPV infections are transient (undetectable within 1-2 years)
 - Remission vs. clearance
- Persistent infection with oncogenic types increases risk of cervical precancerous and cancer



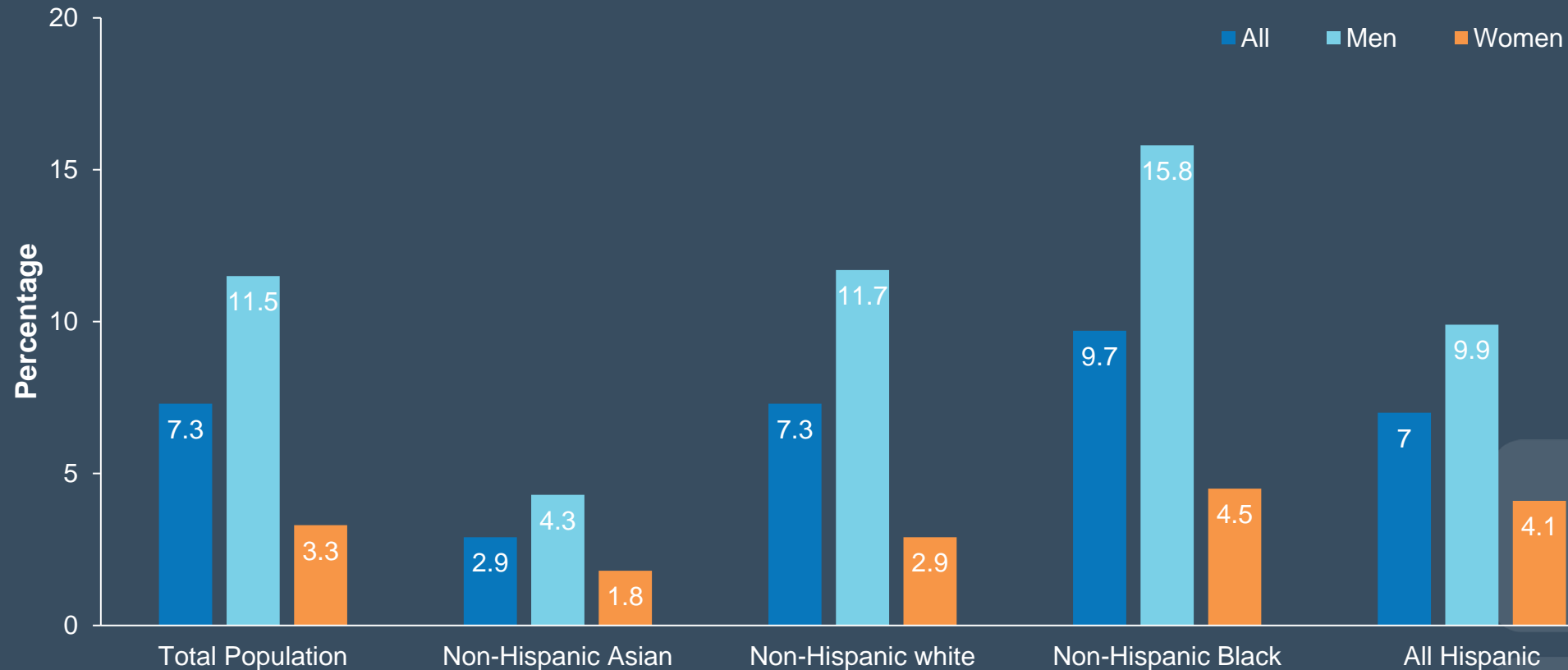
HPV: >150 Types



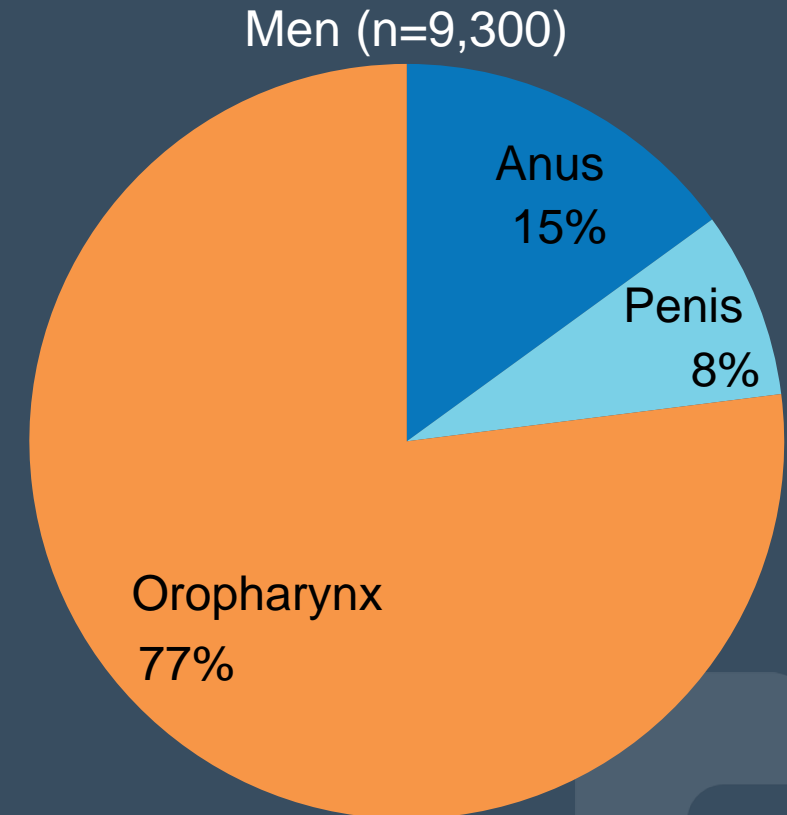
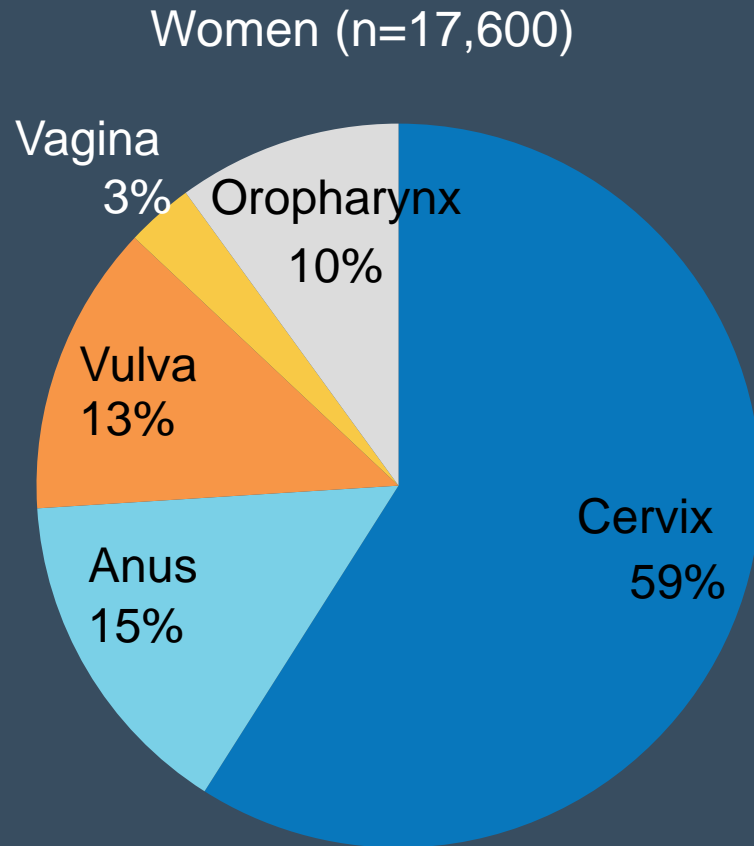
Prevalence of Genital HPV Among Adults Aged 18-59 (2013-2014)



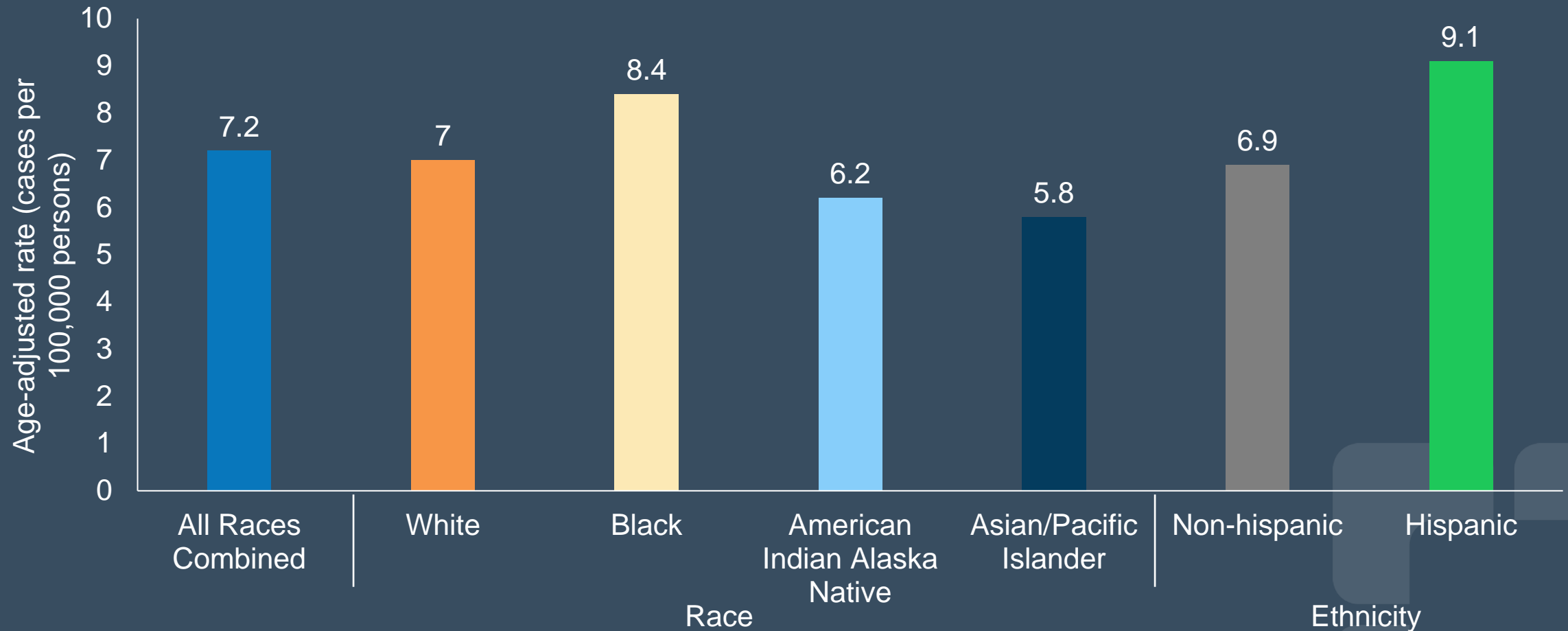
Prevalence of Oral HPV Among Adults Aged 18-69 (2011-2014)



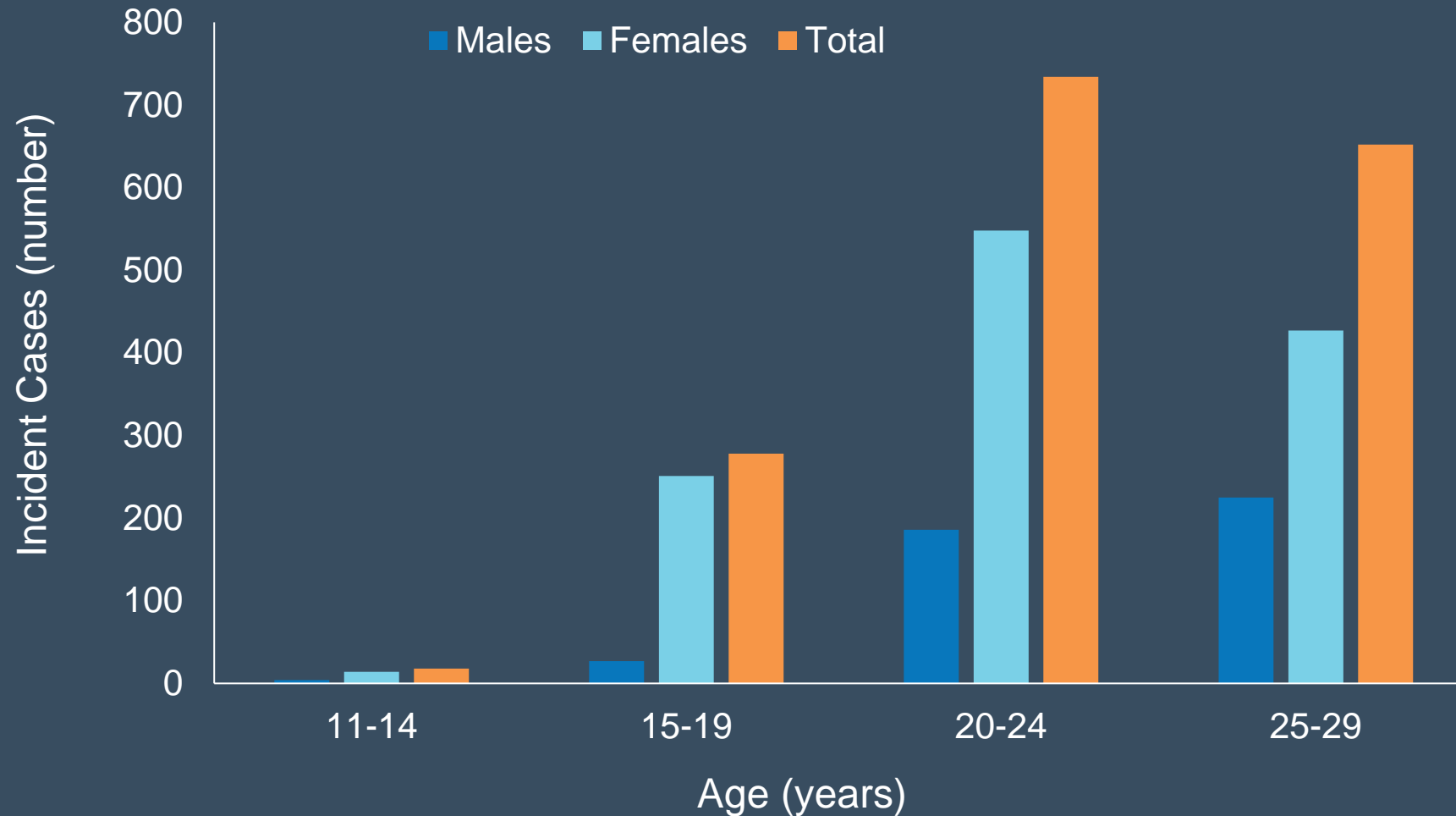
HPV-attributable Cancers



HPV-associated Cervical Cancer Rates By Race and Ethnicity, 2011-2015



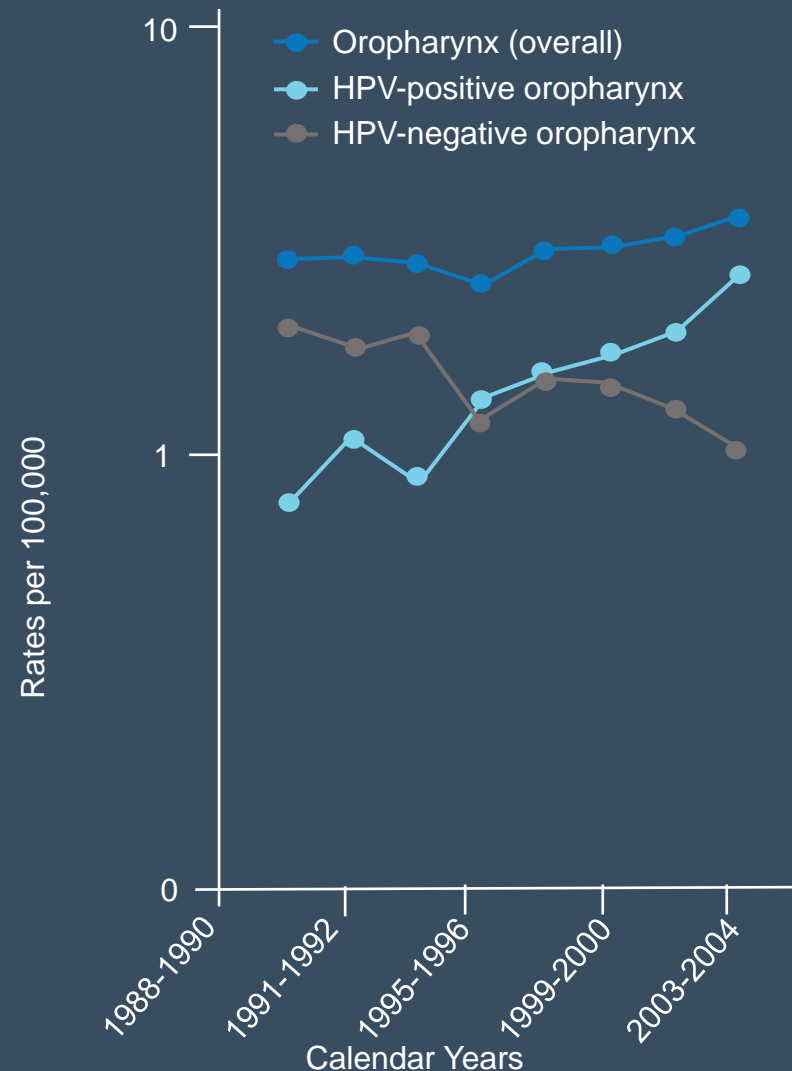
Incidence of Genital Warts, 2000-2005



Incidence rate highest among women (6.3/1000 person-years) and men (2.9/1000 person-years) aged 20 to 24 years old

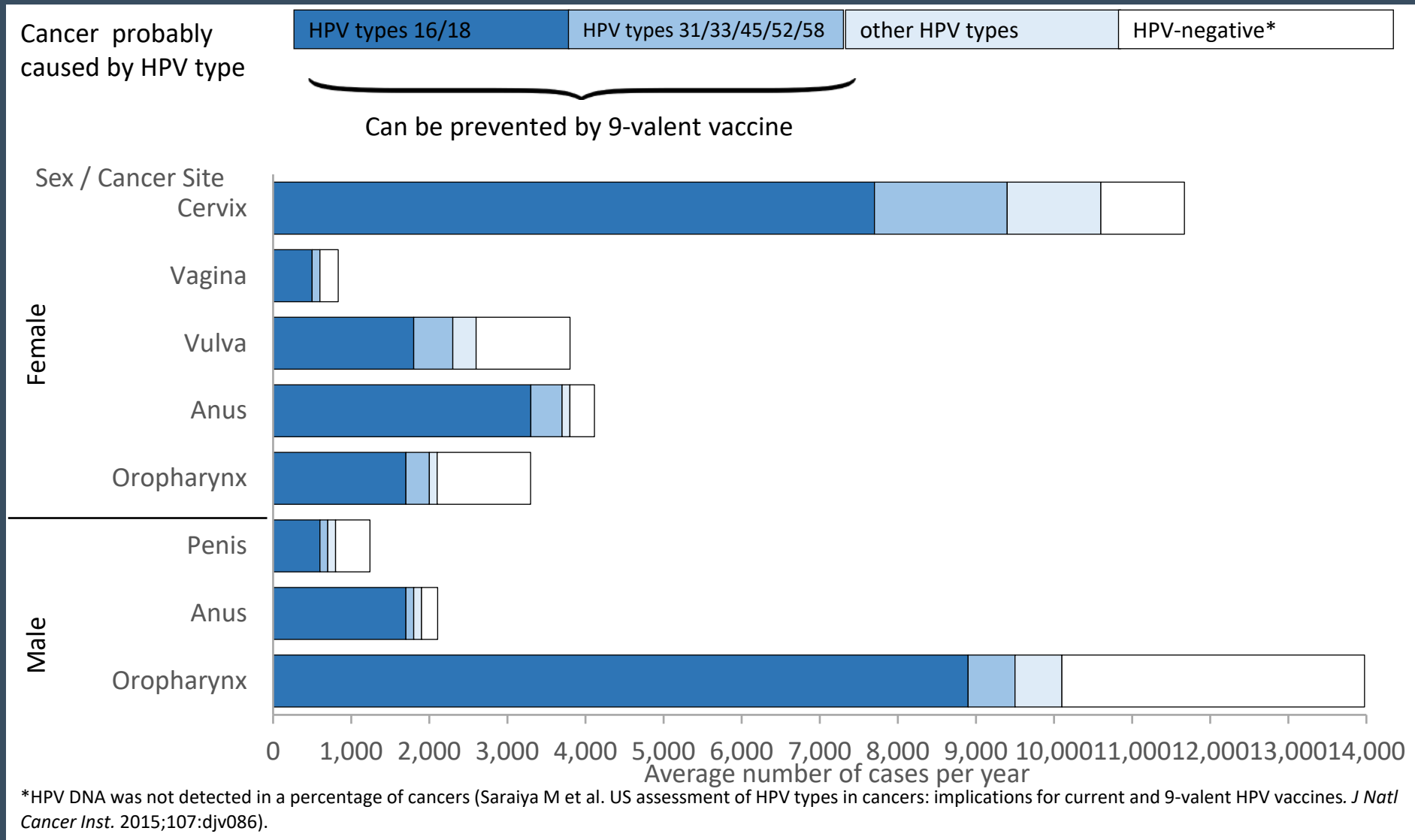
Incidence of Oropharyngeal Cancer

- Increased over past 20 years
 - Smoking- and alcohol-related cancers decreased by 50%
 - HPV-related cancers increased by 225%

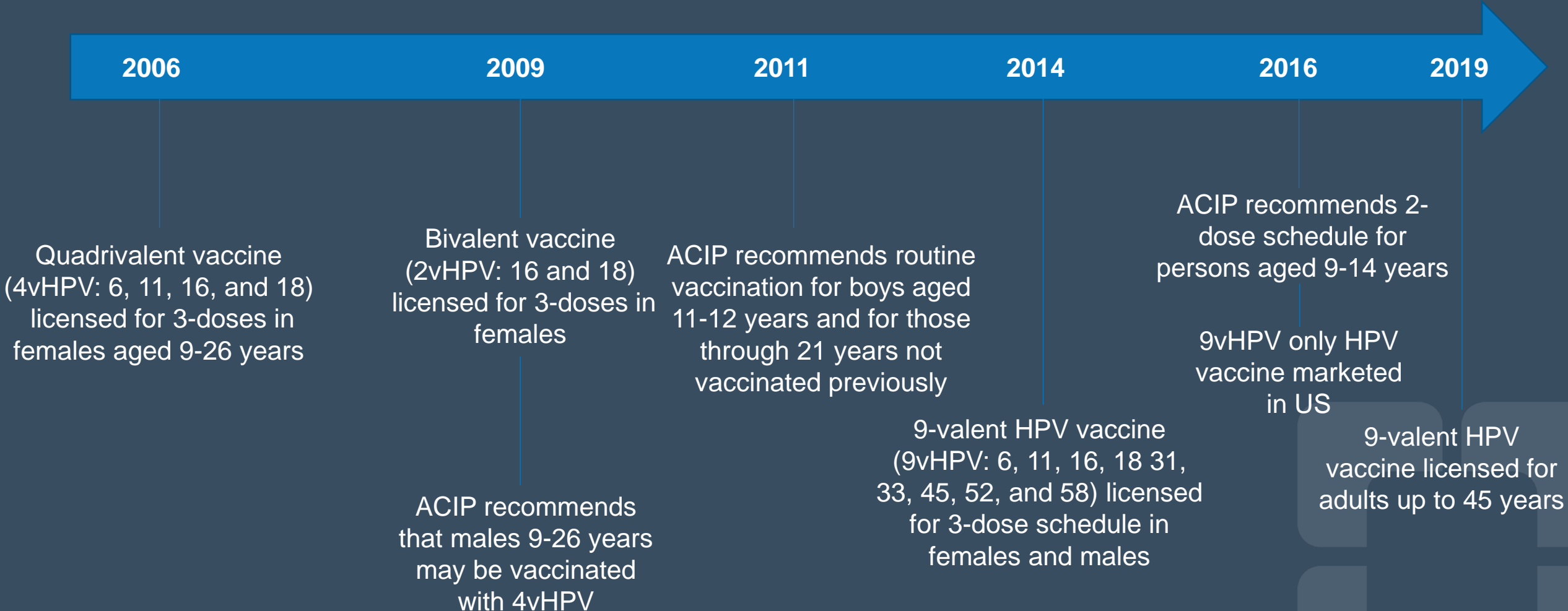


Adapted from Chaturvedi AK et al. *J Clin Oncol.* 2011;29(32):4294-301.

Cancers Attributable to HPV



HPV Vaccines and Recommendations



ACIP Recommendations

Population	Recommended Number of HPV Vaccine Doses	Recommended Interval Between Doses
Persons initiating HPV vaccination between ages 9-14 years (except immunocompromised persons)	2	0, 6-12 months (minimum interval of 5 months)
Persons initiating HPV vaccination between ages 15-26 years Immunocompromised persons initiating HPV vaccination between 9-26 years Catch-up HPV vaccination for persons aged 27-45 years (based on shared clinical-decision making)	3	0, 1-2, 6 months (minimum interval of 4 weeks between dose 1 and 2; 12 weeks between dose 2 and 3; and 5 months between dose 1 and 3)

Contraindications: known allergy to vaccine component or yeast.

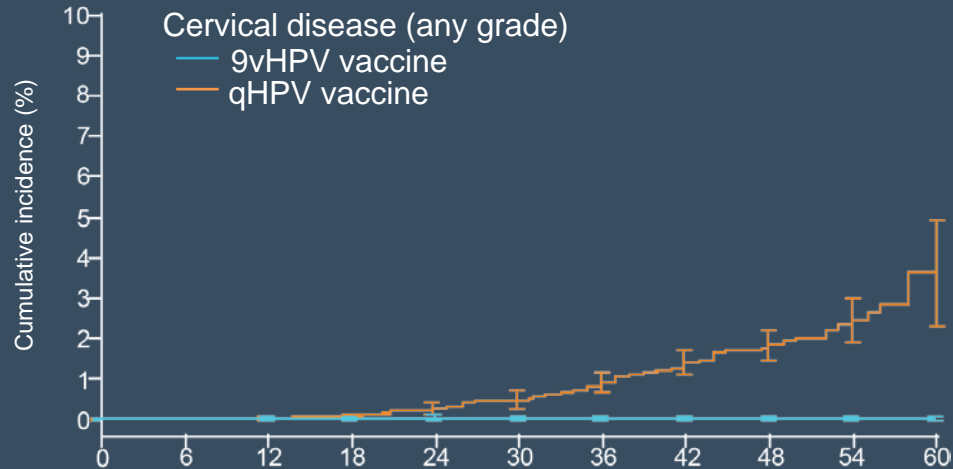
ACIP Recommendations (cont)

- For persons adequately vaccinated with 2vHPV or 4vHPV, there is no recommendation on additional vaccination with 9vHPV
- If vaccination schedule is interrupted, series does not need to be restarted

Efficacy of 9vHPV Vaccine

Phase 3 Trial in Women Aged 16-26 Years

Per Protocol efficacy population



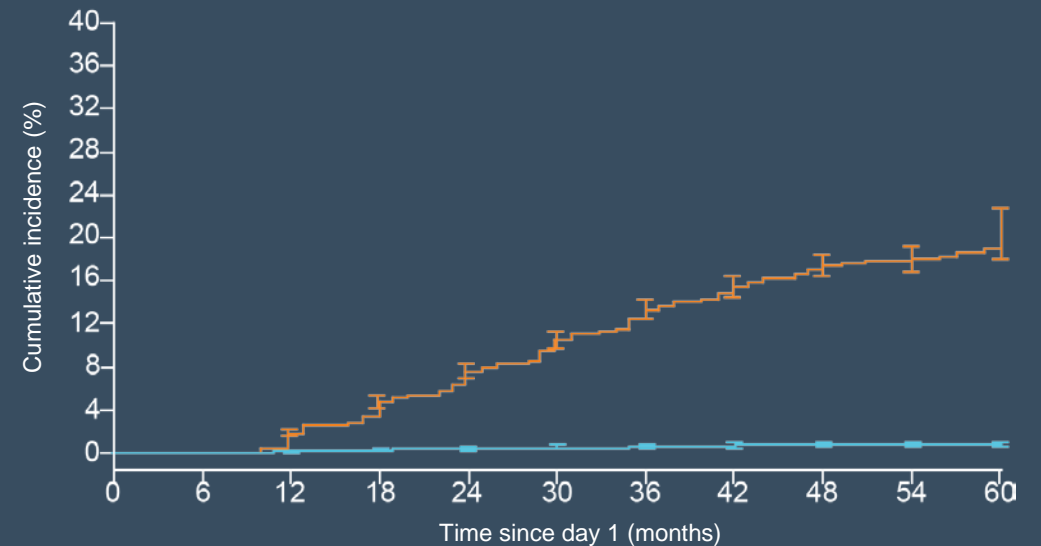
Numbers at risk

9vHPV	5949	5949	5825	5673	5543	5381	5197	4623	2661	608	146
qHPV	5943	5943	5810	5665	5520	5363	5177	4582	2653	587	141

Cumulative cases

9vHPV	0	0	2	2	2	2	2	2	2	2	2
qHPV	0	0	0	4	15	30	51	75	93	104	108

Persistent infection of ≥ 6 months' duration



Numbers at risk

9vHPV	5941	5941	5817	5661	5518	5338	5106	4454	2537	570	135
qHPV	5955	5955	5725	5420	5123	4817	4484	3826	2118	459	113

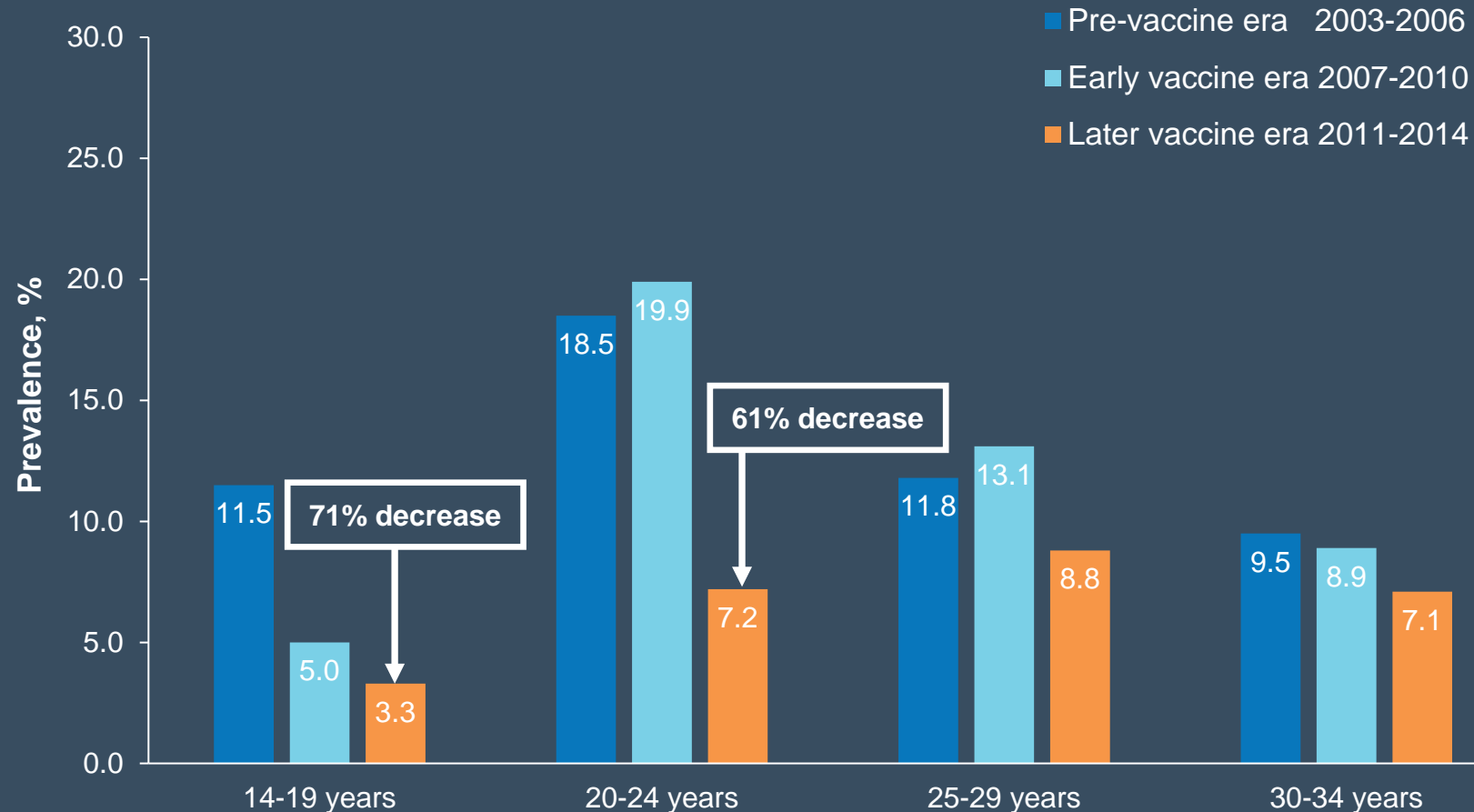
Numbers at risk

9vHPV	0	0	9	14	23	29	33	38	41	41	41
qHPV	0	0	107	276	438	599	742	855	930	940	945

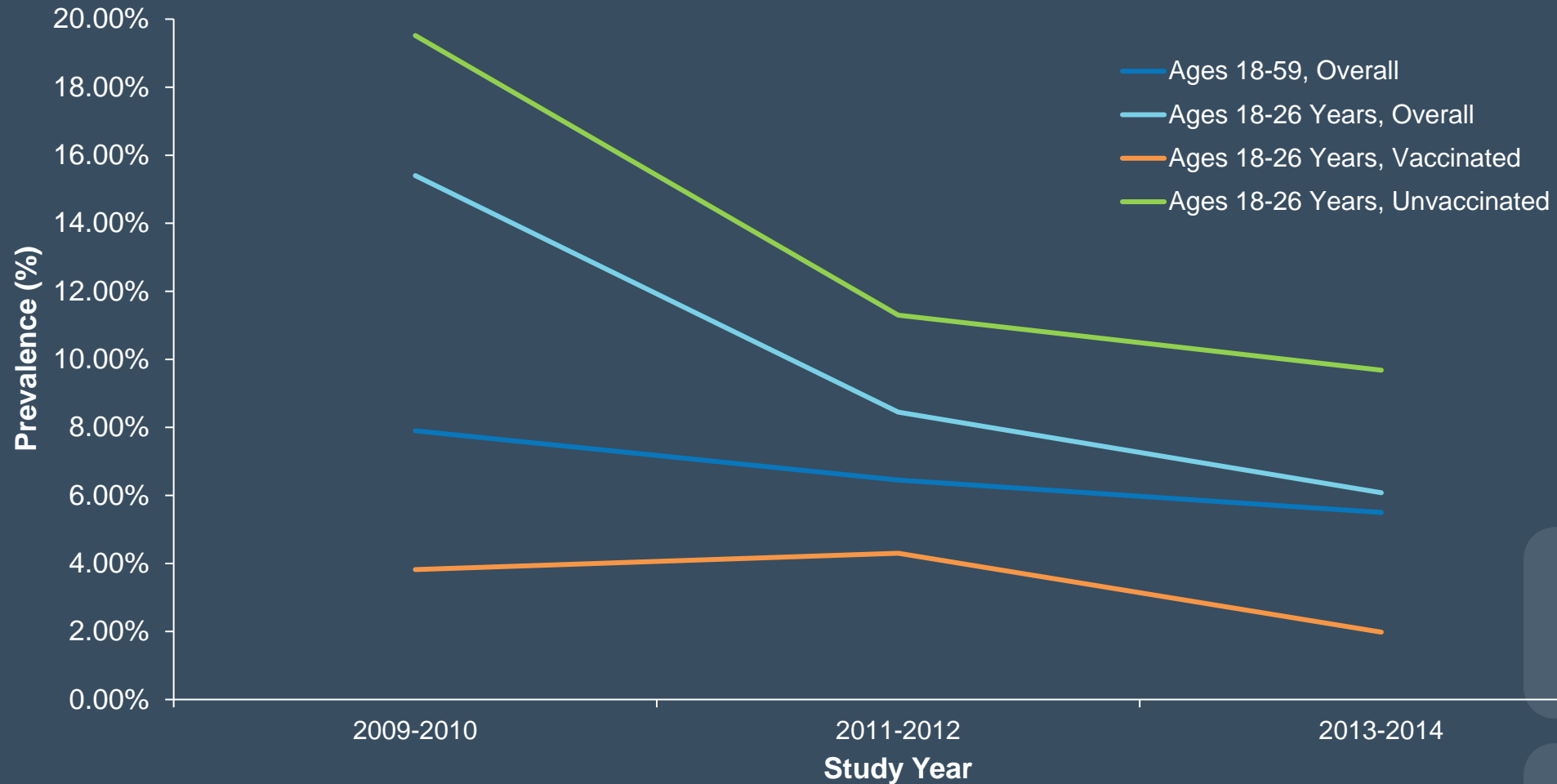
Population-level Effects of HPV Vaccination

- Systematic review and meta-analysis of 20 studies from 9 high-income countries
- In countries with $\geq 50\%$ HPV vaccination:
 - HPV type 16 and 18 infections decreased significantly between pre-vaccination and post-vaccination periods by 68% (RR 0.32, 95% CI 0.19-0.52)
 - Anogenital warts decreased significantly by 61% (0.39, 0.22-0.71) in girls 13-19 years of age
 - HPV types 31, 33, and 45 reduced in girls 13-19 years of age (RR 0.72, 95% CI 0.54-0.96)

Decreased HPV Prevalence After Vaccination



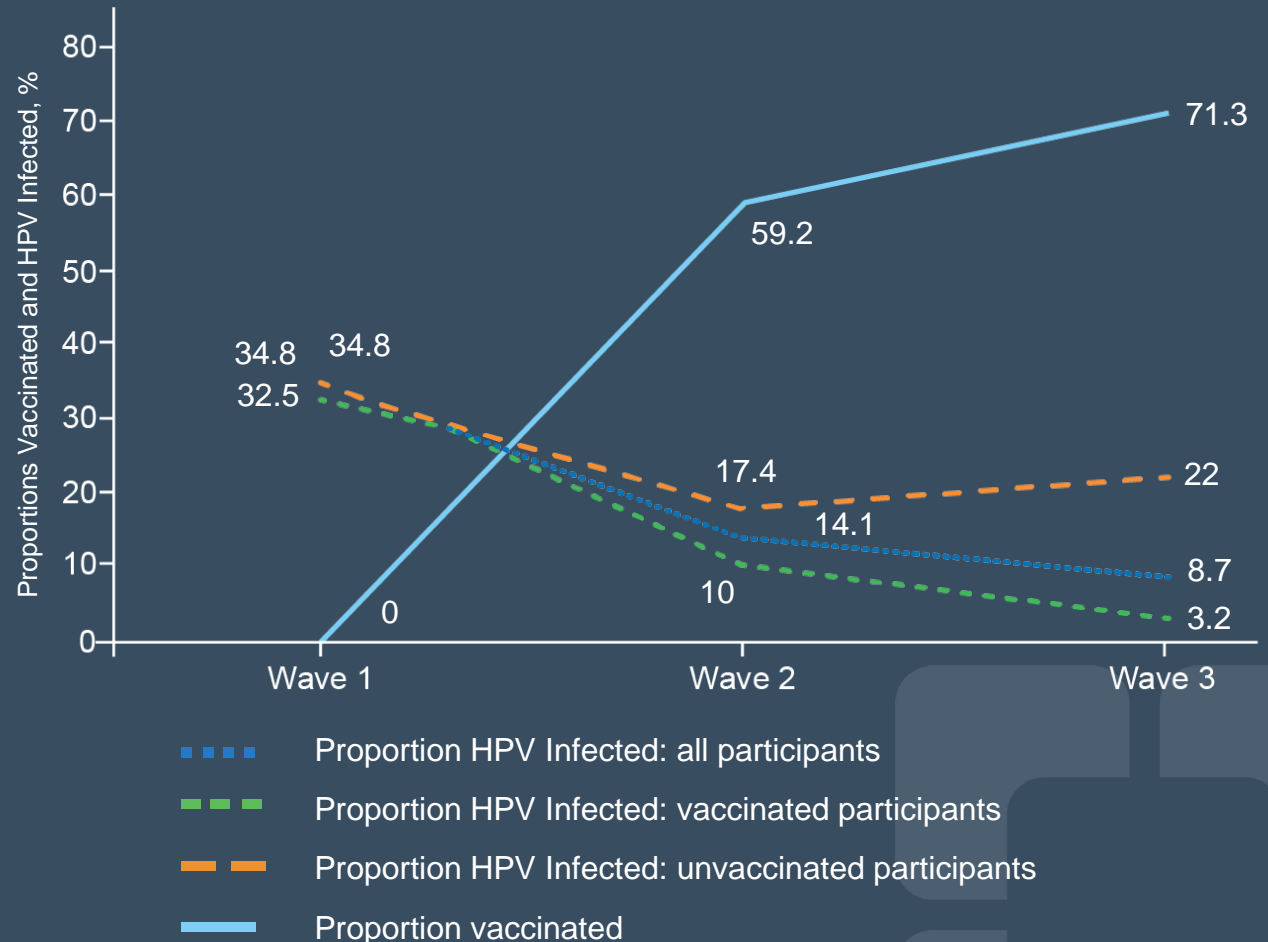
Changes in HPV Prevalence: 2009-2010 and 2013-2014



Adapted from Berenson AB et al. *Obstet Gynecol.* 2017;130(4):693-701.

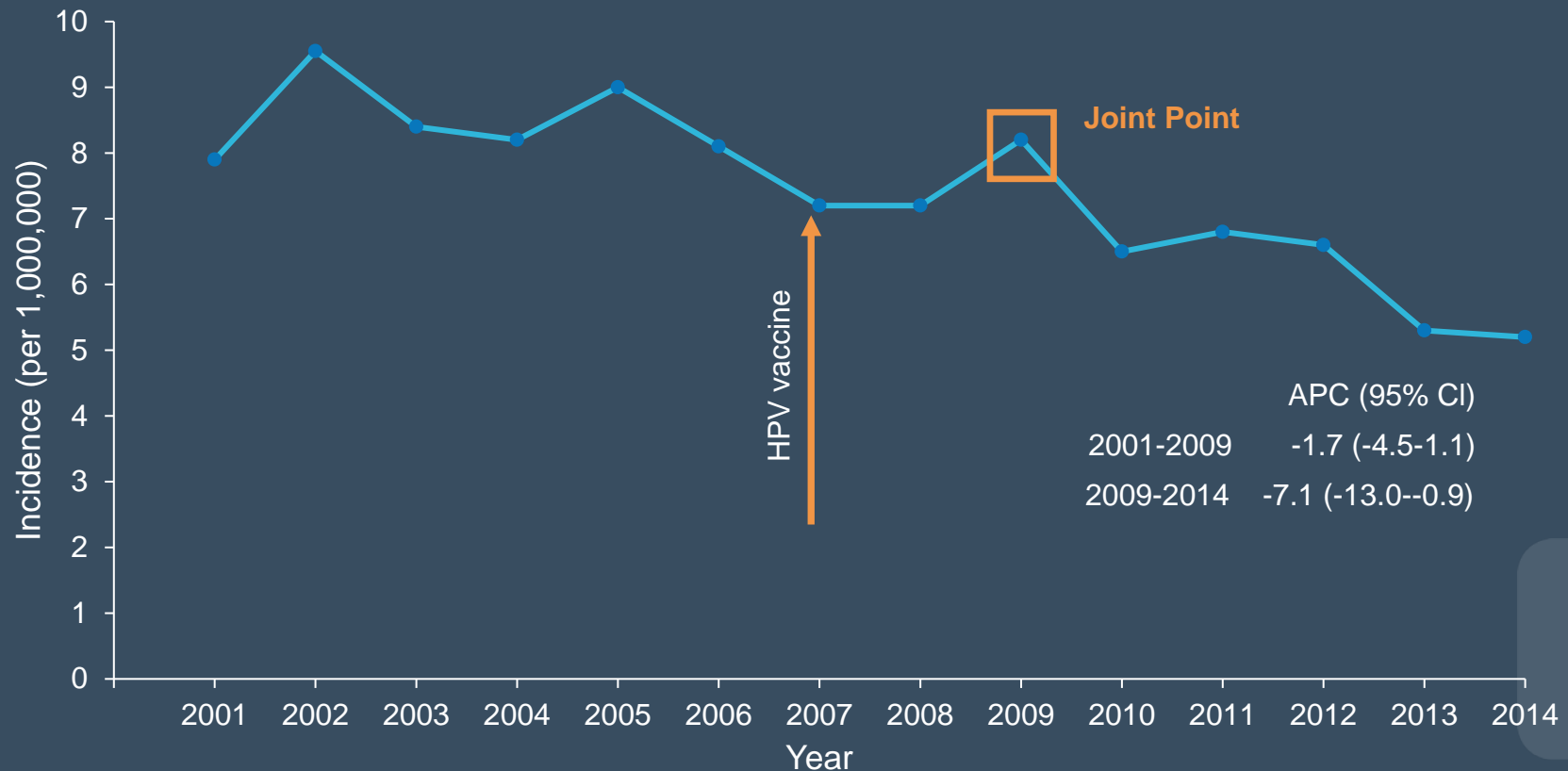
Decreased Vaccine-type HPV After Vaccination in a Community Setting

- 3 samples of sexually experienced, 13-26-year-old adolescent girls and young women:
 - Before widespread vaccine introduction (wave 1)
 - 3 years after vaccine introduction (wave 2)
 - 7 years after vaccine introduction (wave 3)
- Determined prevalence of vaccine-type HPV (HPV-6, -11, -16, and -18) among all, vaccinated, and unvaccinated women at waves 1, 2, and 3
- Vaccine-type HPV prevalence decreased by 75% among all women and by 90.8% among vaccinated women

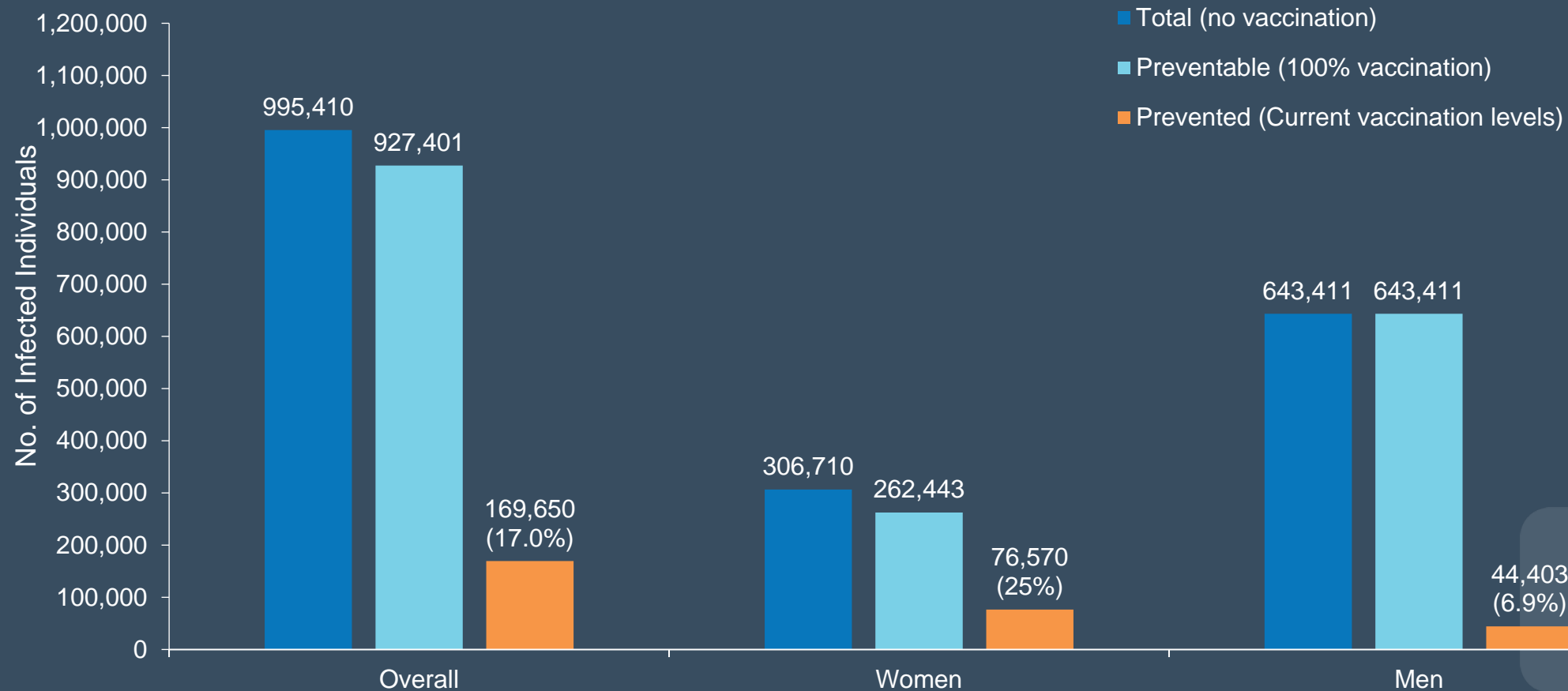


Adapted from Kahn JA et al. *Clin Infect Dis*. 2016;63:1281-1287.

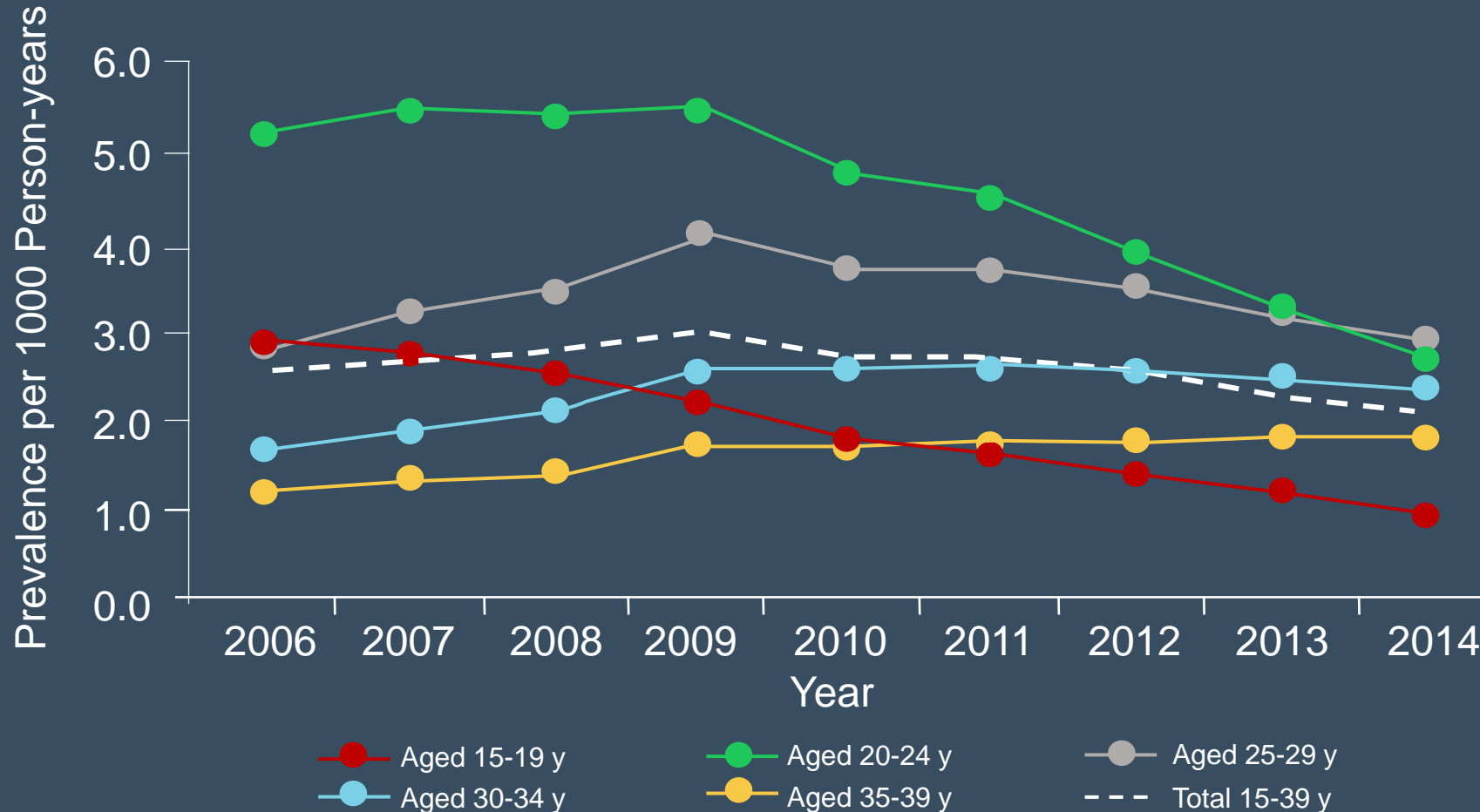
Decreased Incidence of Cervical Cancer After Vaccine Introduction



HPV Vaccination Reduces Vaccine-type Oral HPV Infections



Declines in Anogenital Warts in Women



Safety of HPV Vaccination

- 80 million 4vHPV doses and 0.8 million 2vHPV doses distributed in the US as of September 2015
- Most common adverse events are mild:
 - Syncope, dizziness, nausea, and headache
- Comparisons of those who did or did not receive the vaccine did not reveal increased risks for:
 - Autoimmune disorders, anaphylaxis, VTE, blood clots, neurologic disease
- 9vHPV expected to have similar safety profile
 - Safety will continue to be monitored

Duration of Protection After HPV Vaccination

- HPV vaccination induces memory B cells and neutralizing antibodies
- 5-8.5 years after administration of an experimental monovalent HPV (type 16) vaccine, an antigen challenge resulted in anamnestic response characterized by rapid and robust antibody production
 - Probable mechanism is immune memory
 - Evidence that vaccination remains effective through 8.5 years after administration

Cost Effectiveness of HPV Vaccination

- Usually measured in quality-adjusted years (QALY) with $< \$50,000$ considered to be cost effective
- 9vHP vaccination of females aged 12-26 years and males aged 12-21 years with cost an estimated \$16,600 (in 2016 U.S. dollars) per QALY gained

Conclusions

HPV...

- Exposure is ubiquitous
- Causes many cancers
- Vaccines are safe
- Vaccination is effective

Why aren't more people vaccinated?





Every life deserves world class care.