Prevention of HPV-Associated Cancers

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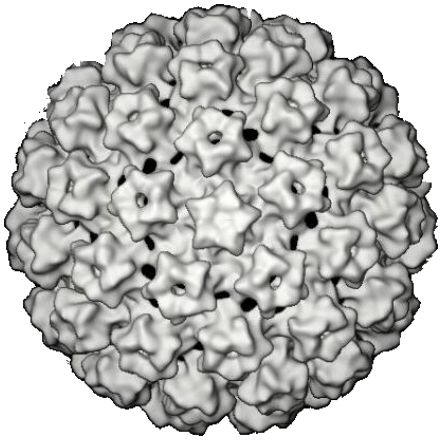
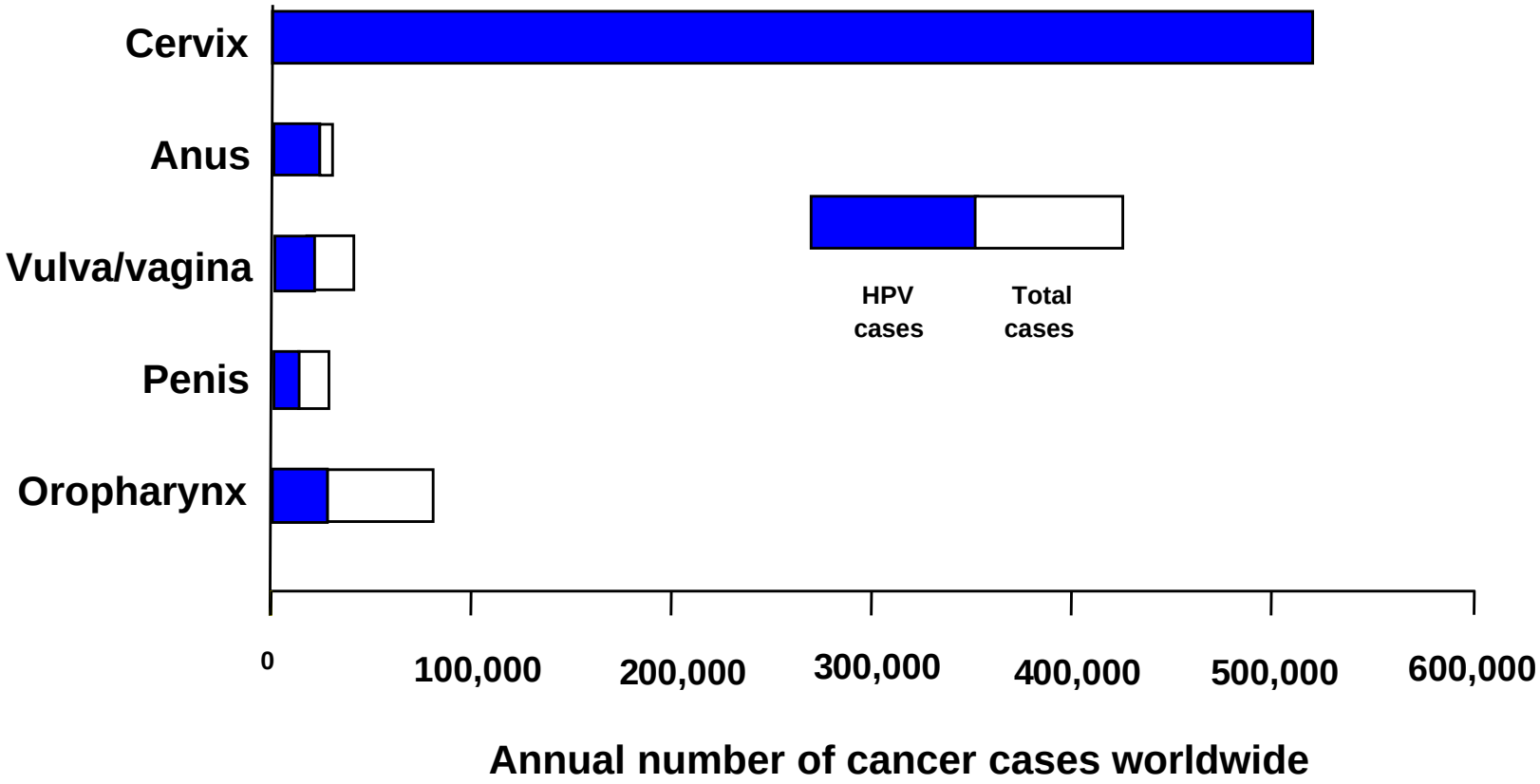


Promise and Problems

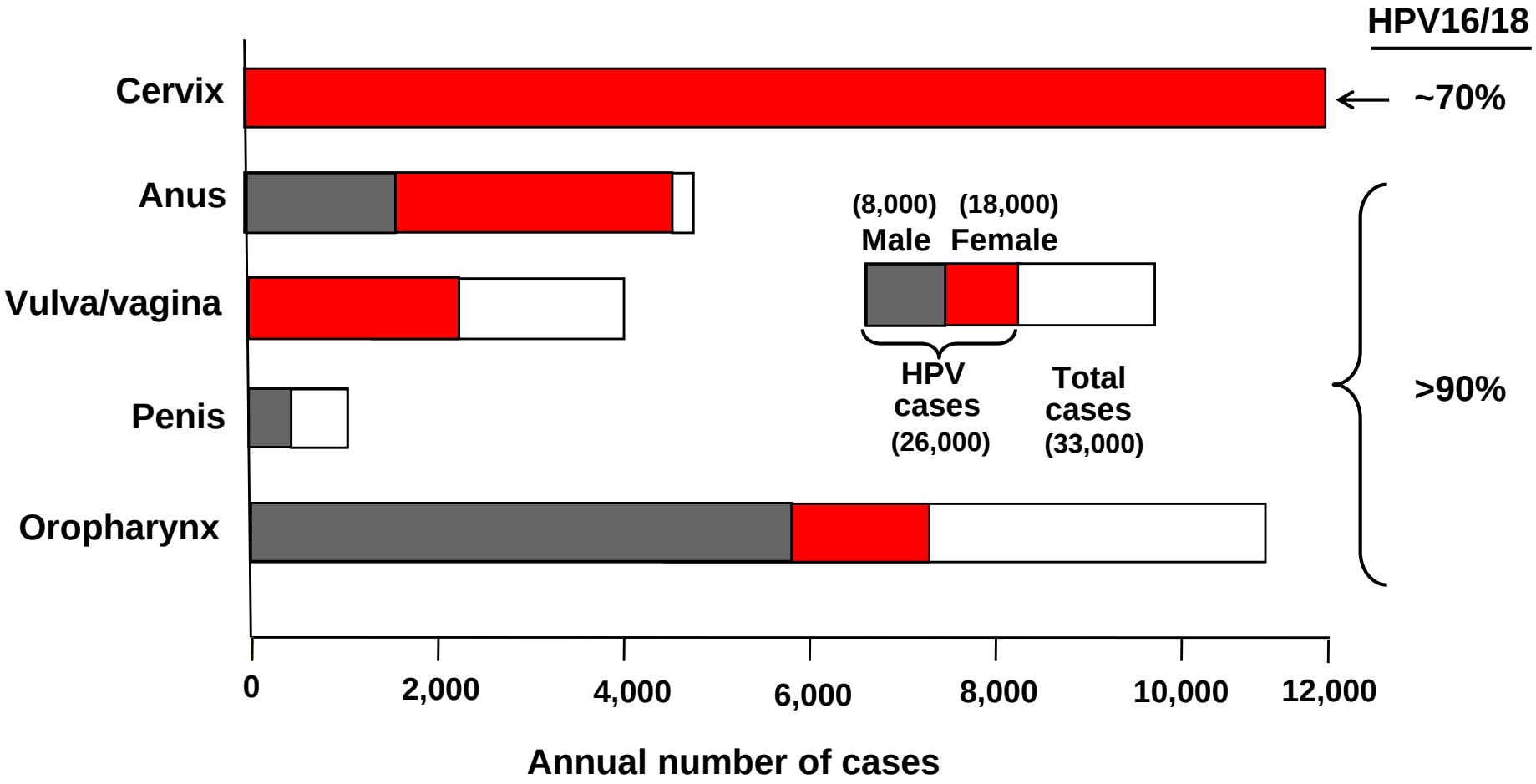
Worldwide Incidence and Distribution of Cancers Attributable to HPV



HPVs cause 5% of all cancers

de Martel, Lancet Onc, 13: 607-15, 2012

United States: Annual Incidence and Distribution of Cancers Attributable to HPV

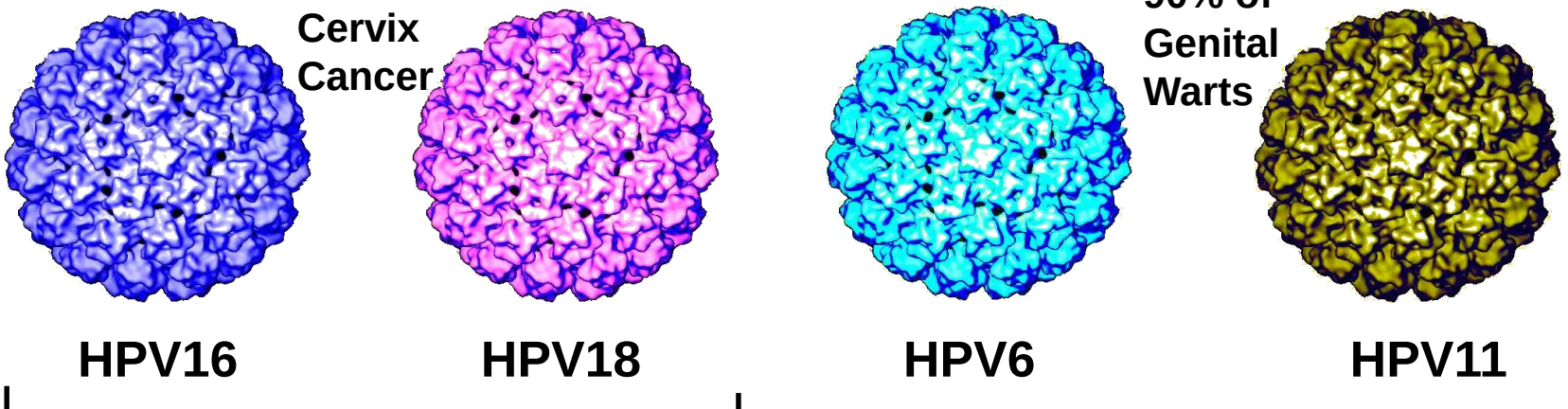


- Pap screening has reduced the incidence of cervical cancer by ~ 80%
- Incidence of HPV-positive oropharynx cancer 1988-2004 increased 225%

MMWR Weekly 61:253-80, 2012

The Commercial Vaccines Are Composed of Multiple Types of HPV L1 VLPs

Gardasil (Merck)



Cervarix (GlaxoSmithKline)

Three intramuscular injections over 6 months

Merck's Gardasil-9 has nine types of VLPs

Performance of HPV Vaccines in Clinical Trials

Safety

- Low grade transient injection site reactions common.
- Systemic reactions mild and self-limiting.
- No pattern of serious adverse events, in trials or post -licensure that would suggest a causal relationship.

Efficacy

- Virtually 100% protection from precancer caused by post-vaccination HPV16/18 infections.
- 95% protection from HPV16/11 genital warts by Gardasil.
- Limited protection against infections by other types.
- No effect on preexisting infections or lesions.

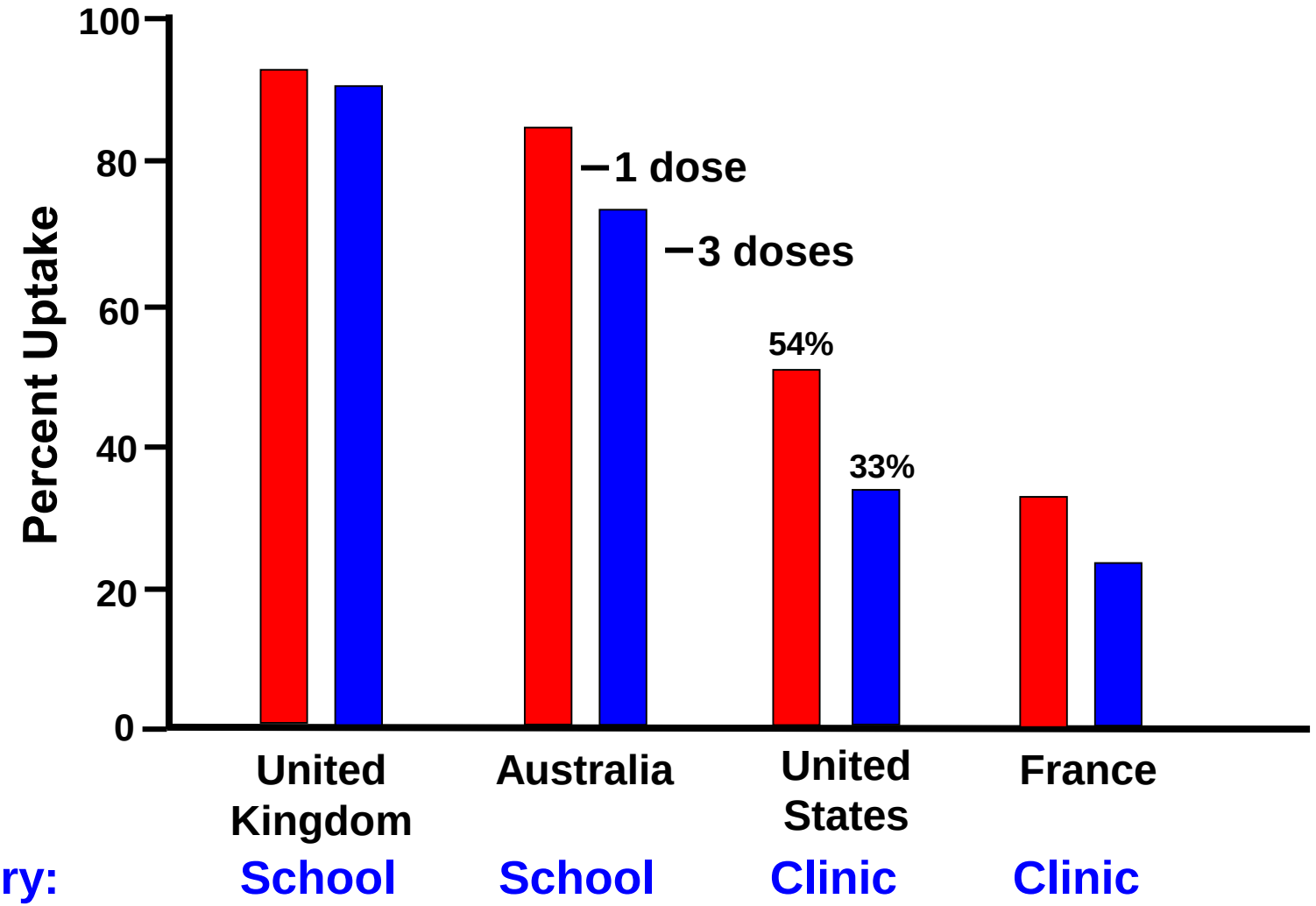
HPV Vaccine Development: A Poster Child for Public/Private Partnership

- **Public Sector Contributions:**
  - **basic knowledge that HPV causes cervical cancer**
  - **development of vaccine technology**
  - **vaccine validation in preclinical animal models**

- **Corporate Contributions:**
  - **industrial scale vaccine production**
  - **clinical trials leading to FDA approval**
  - **marketing and distribution**

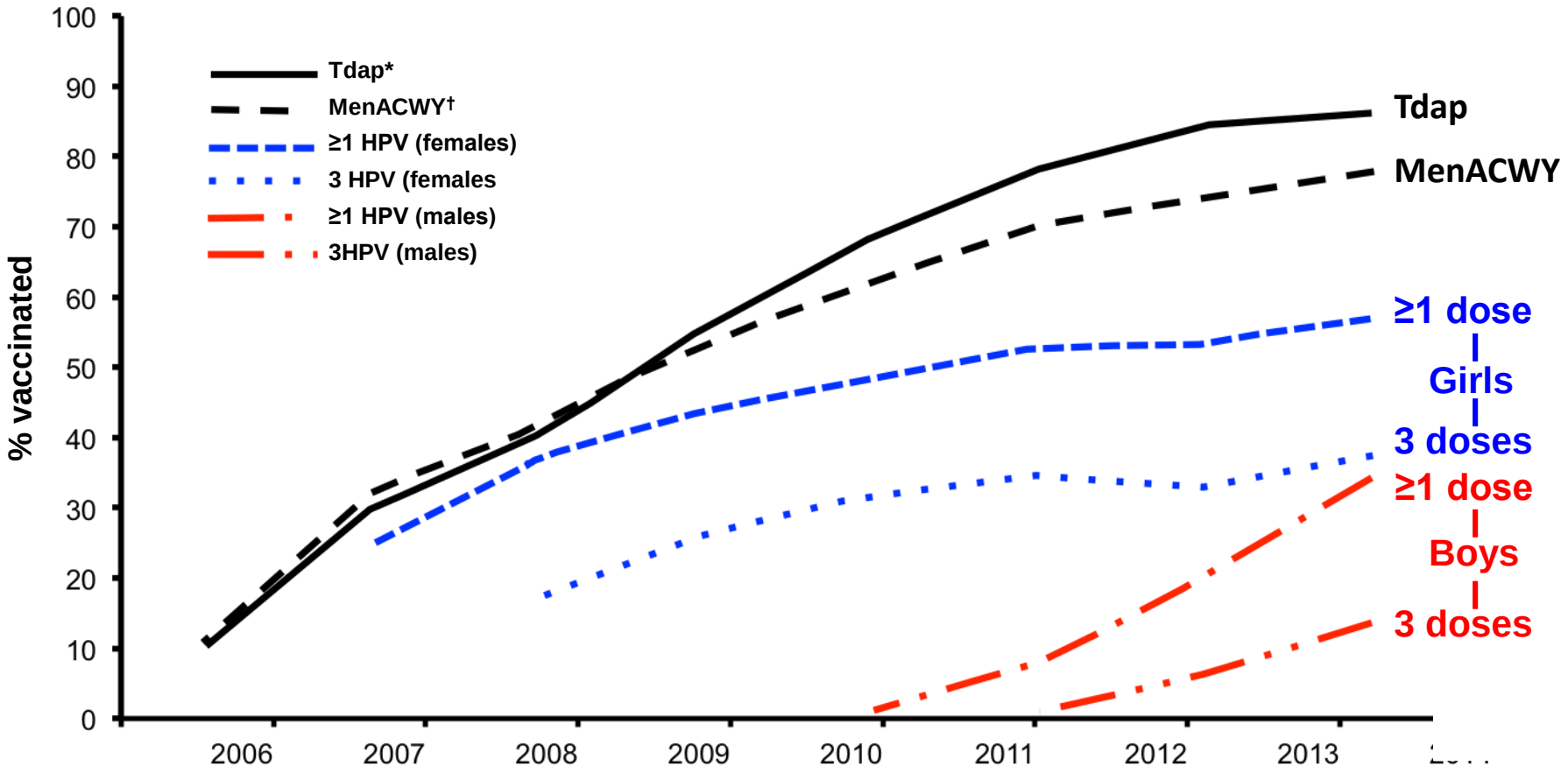
- **Outcomes:**
  - **an intervention to prevent several major cancers**
  - **jobs in the American pharmaceutical industry**

Variable Uptake of HPV Vaccine
(2012 data for girls)



Trends in U.S. Vaccination Rates: Ages 13-17 Yrs

MMWR Vol 63, #29, July 25, 2014

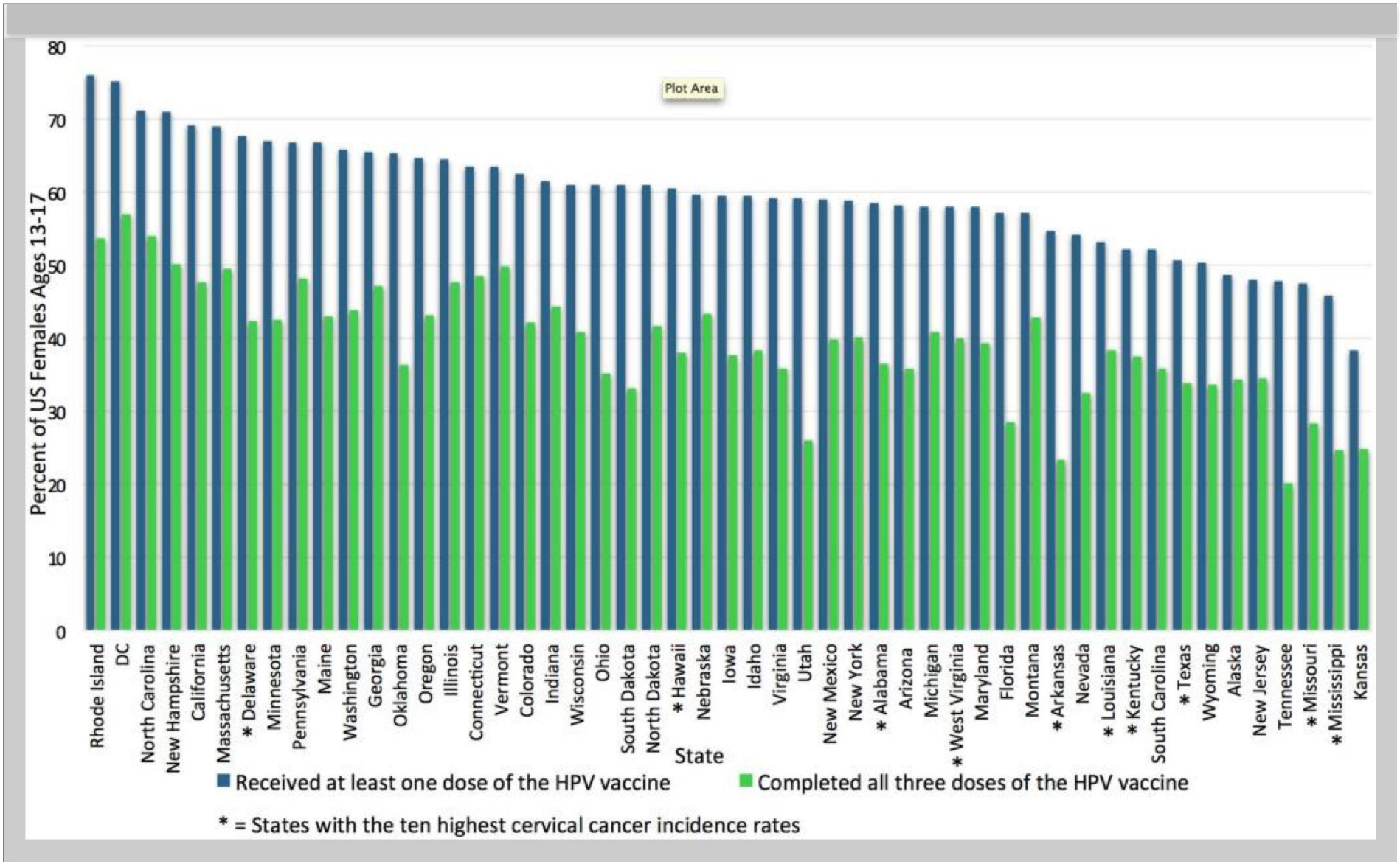


Abbreviations: Tdap = tetanus, diphtheria, acellular pertussis vaccine; MenACWY = meningococcal conjugate vaccine; HPV-1 = human papillomavirus vaccine, ≥1 dose; HPV-3 = human papillomavirus, ≥3 doses.

*** Tdap and MenACWY vaccination recommendations were published in March and October 2006, respectively.**

† HPV vaccination recommendations were published in March 2007.

Uptake of HPV Vaccines By State in 2014



Reduction in HPV6/11/16/18 Prevalence in the USA

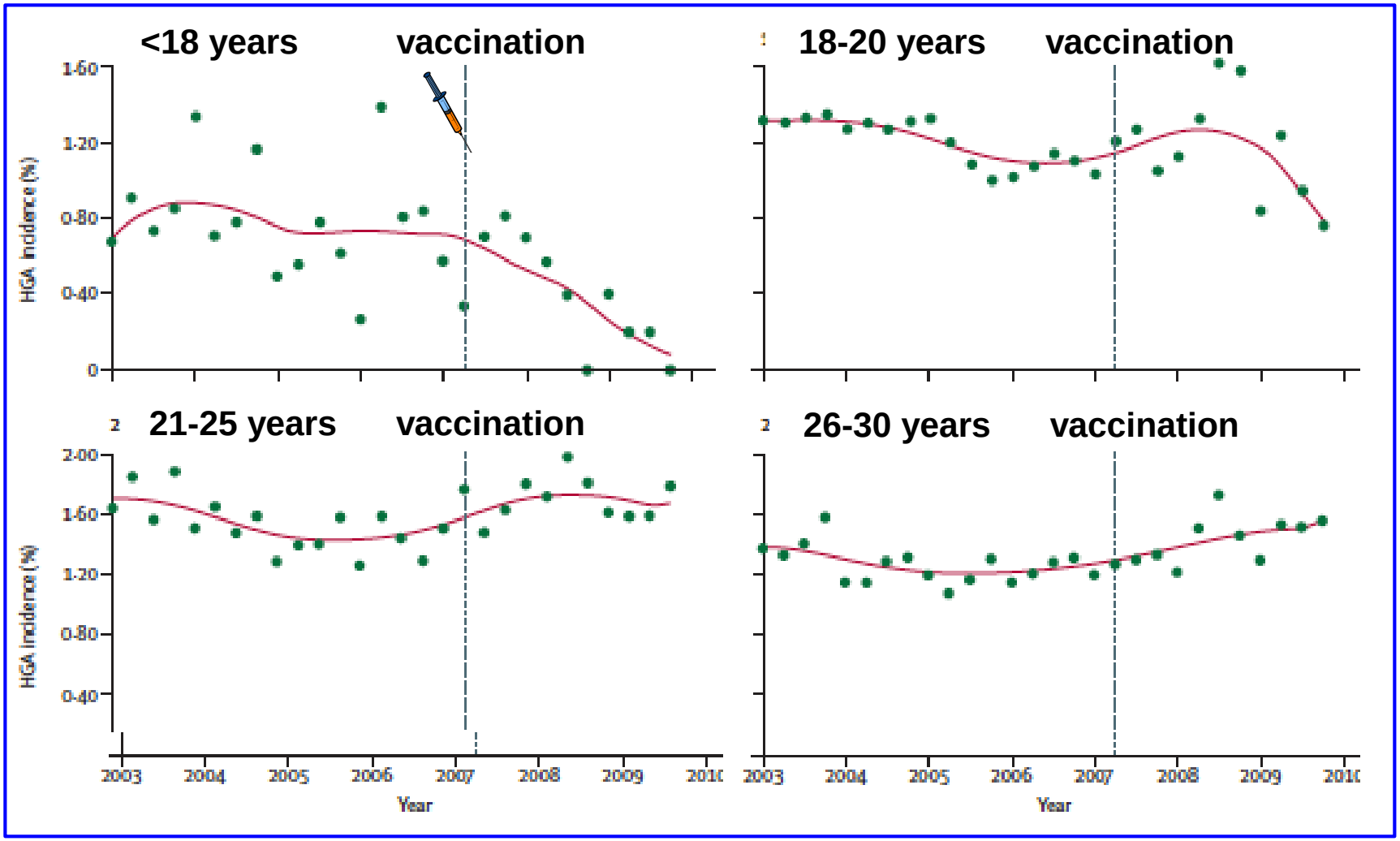
Comparing Post-Vaccination to Pre-vaccination:
(2009-2012) (2003-2006)

Reduction in 14-19 yo: 64%

20-24 yo: 34%

Data from the CDC: L Markowitz et al., Pediatrics, March 2016

Effectiveness: Reduction in Cervical Precancer by Gardasil in Australia

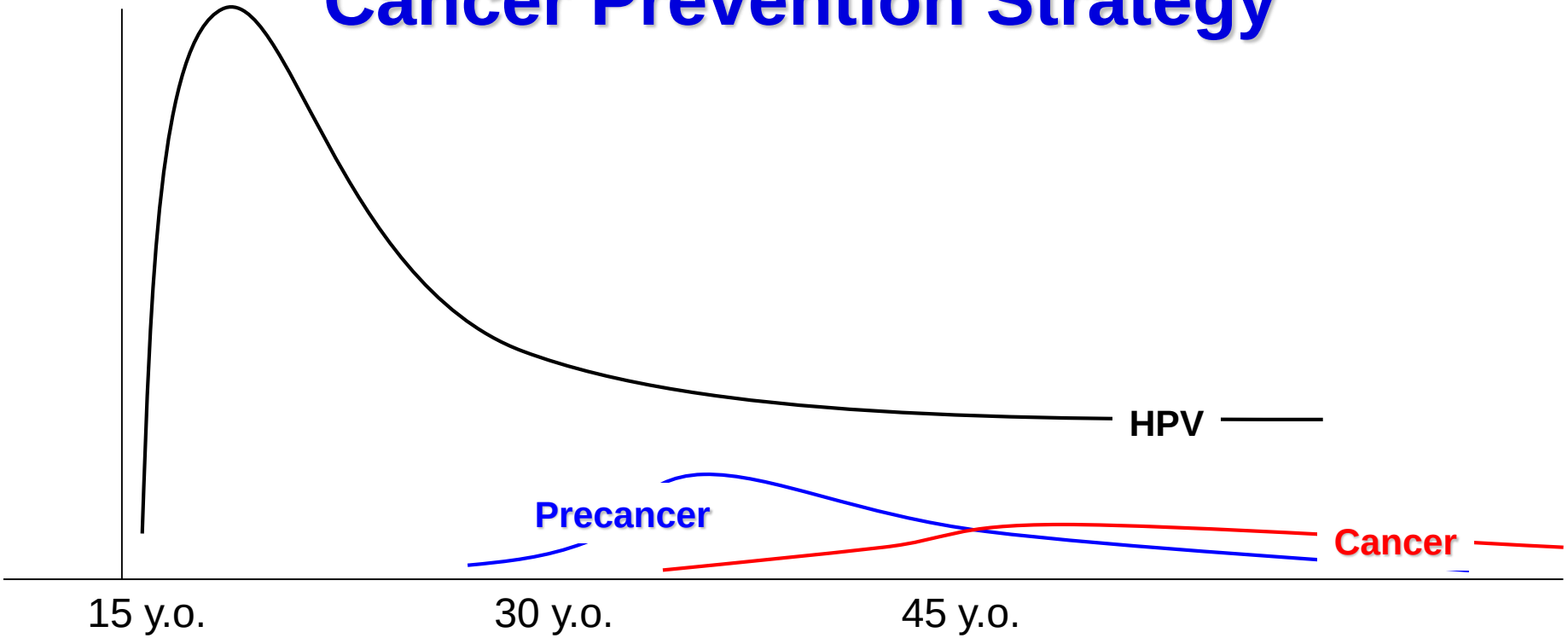


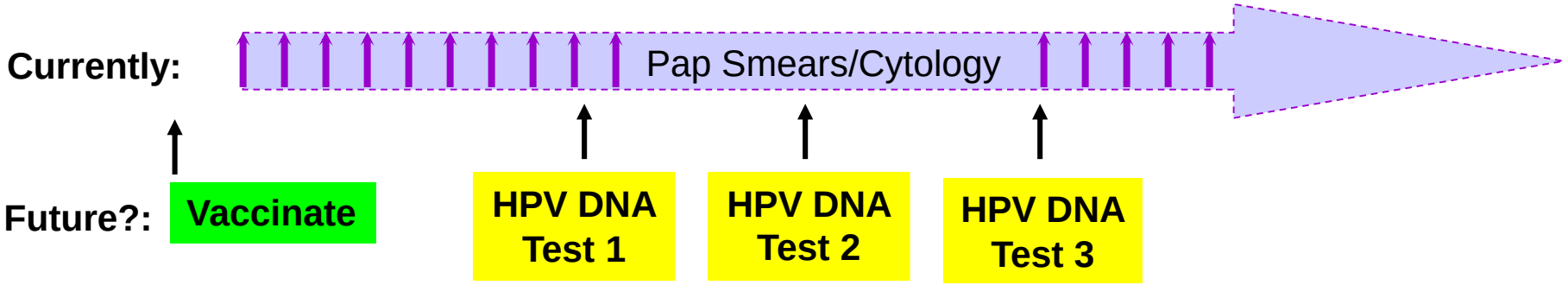
Brotherton et al, Lancet 377: 2085-92, 2011

Increasing Vaccine Uptake

- **Convince GPs and Pediatricians to more strongly recommend the vaccines. Monitor their vaccination rates.**
- **Overcome parental hesitancy. Stress cancer prevention and better response in 9-14 year olds.**
- **Counter misinformation campaigns by anti-vaccine groups.**
- **Promote vaccine distribution in pharmacies and schools.**
- **Support a two dose schedule for <15 year olds.**

A Shift to an HPV-Based Cervical Cancer Prevention Strategy





Thanks to Mark Schiffman and Phil Castle, NCI

Cervical Cancer Screening Issues

Current Options:

- **Pap Smear: 3 yr interval in 21 yo+**
- **Pap/HPV DNA co-testing: 5 yr interval in 30 yo+ (2011)**
- **HPV DNA primary screen: at least 3 yr interval in 25 yo+. FDA approved 2014, U.S. guidance published 2015.**

Current Issues:

- **Educating women about their options.**
- **Convincing vaccinated women to continue screened.**
- **Discouraging over screening.**

Prevention of HPV Cancers: What Next?

- **Will one dose of vaccine be enough for protection?**
- **What is the optimal cervical cancer screen strategy for vaccinated vs unvaccinated women?**
- **How do we manage women diagnosed with oncogenic HPV infection? Can suitable treatments be devised?**
- **Can effective screening and treatment programs be devised for HPV-associated premalignant lesions at other sites, e.g. oral, anal?**

Final Thoughts

Government-sponsored research and investment by the pharmaceutical industry has generated interventions that could essentially prevent cervical and other HPV-associated cancers in the next generation of women and men.

These interventions need to be better utilized for their full potential to be realized.

There is still an unmet need to better diagnose and treat individuals who are already have oncogenic HPV infections.