How to get all women involved: communication and outreach

Diane M Harper, MD, MPH, MS

Director, Gynecologic Cancer Prevention Research Group

Professor, Obstetrics and Gynecology, Community and Family Medicine, Biomedical and Health Informatics

University of Missouri Kansas City School of Medicine

Disclosure

- I was a founding member of the expert panels to design and implement the phase II and phase III vaccine trials for both companies.
- My institution has not received money from either GSK or Merck for HPV vaccine research since 2006.

Avoiding the Disaster in Andhra Pradesh and Gujarat, India

- April 2010 Gardasil dissemination programs were suspended
- The Objection to the program
  - voiced by over 70 civil society groups, public health organizations, medical professionals, human rights organizations, women's groups and others was

THE **LACK OF INFORMATION** PROVIDED TO THE PUBLIC SO THAT EACH PARTICIPANT COULD BE AFFORDED THE **OPPORTUNITY FOR INFORMED DECISION MAKING** ABOUT THEIR OWN CERVICAL CANCER PROTECTION.

Community Engagement in International Research: Considerations for Ethics Review

- **Meaningful engagement to reduce risks of harm –** active discussion
- New strategies for engaging host communities during international research studies could improve the protection of both individual research participants and their communities.

US Presidential Commission for the Study of Bioethical Issues
http://www.primr.org/Conferences.aspx?id=15818

Components of Informed Decision Making: Basic Information

- Cervical cancer rate in the region

Current Rates of Cervical Cancer

Age-standardized Incidence and Mortality Rates for Cervix Uteri Cancer,

- Globocan 2008
- WHO/ICO Information Centre on HPV

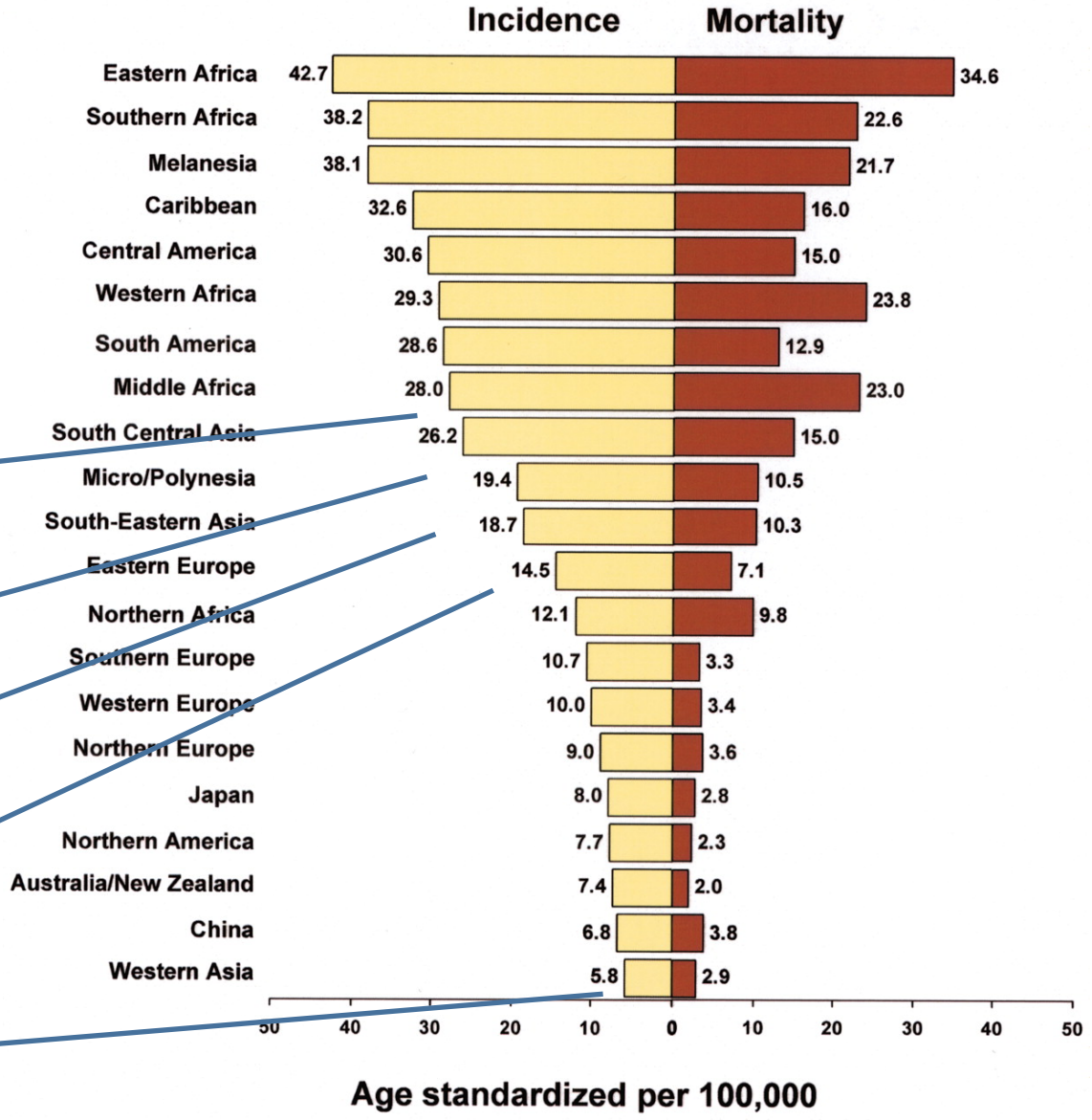
India: 28/100,000

Central America: 22/100,000

Costa Rica: 18/100,000

Mexico: 13/100,000

Finland: 4/100,000

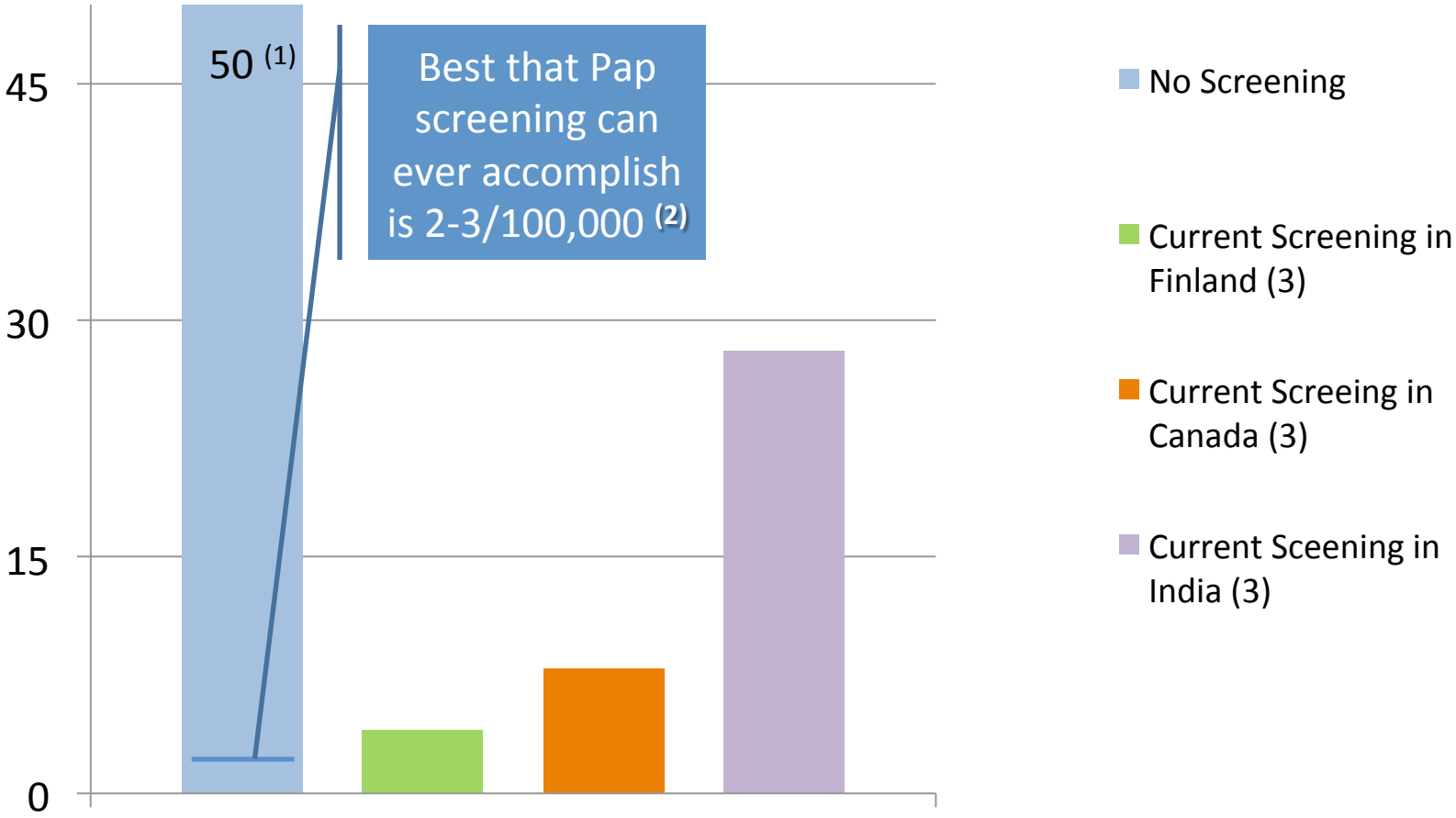


WHO/ICO HPV information centre

Parkin, DM et al. CA Cancer J Clin 2005;55:74-108.

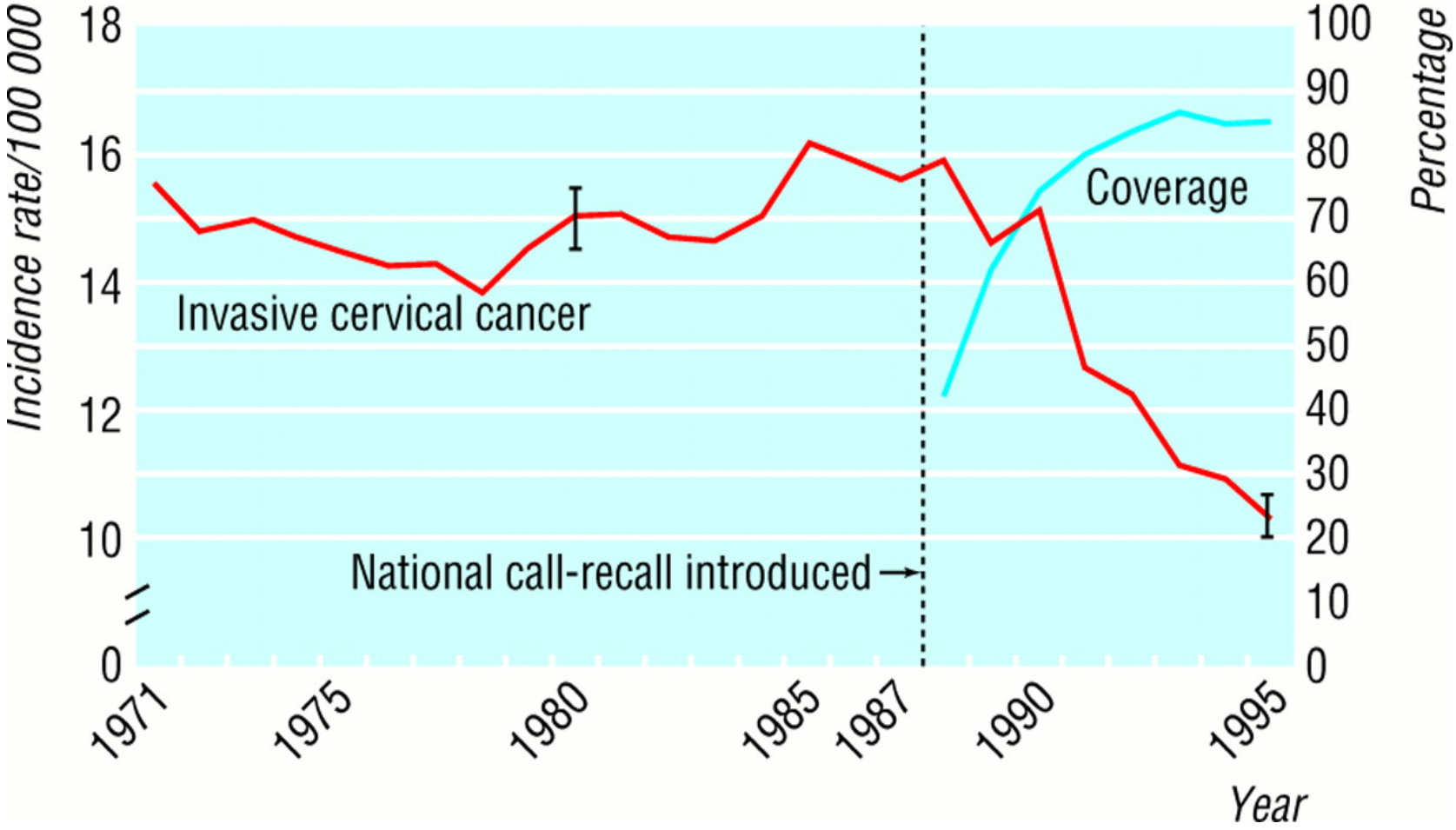
Lowest Incidence Rates of Cx Ca Achievable per 100,000 women:

Are there screening facilities in the region?



1. Parkin, DM. CA Cancer J Clin 2005;55:74-108.
2. Sawaya GF. Obstet Gynecol 1999;94:307-310.
3. WHO/ICO HPV information centre

Age standardised incidence of invasive cervical cancer and coverage of screening (UK, 1971-95)



Quinn, M. et al. BMJ 1999;318:904

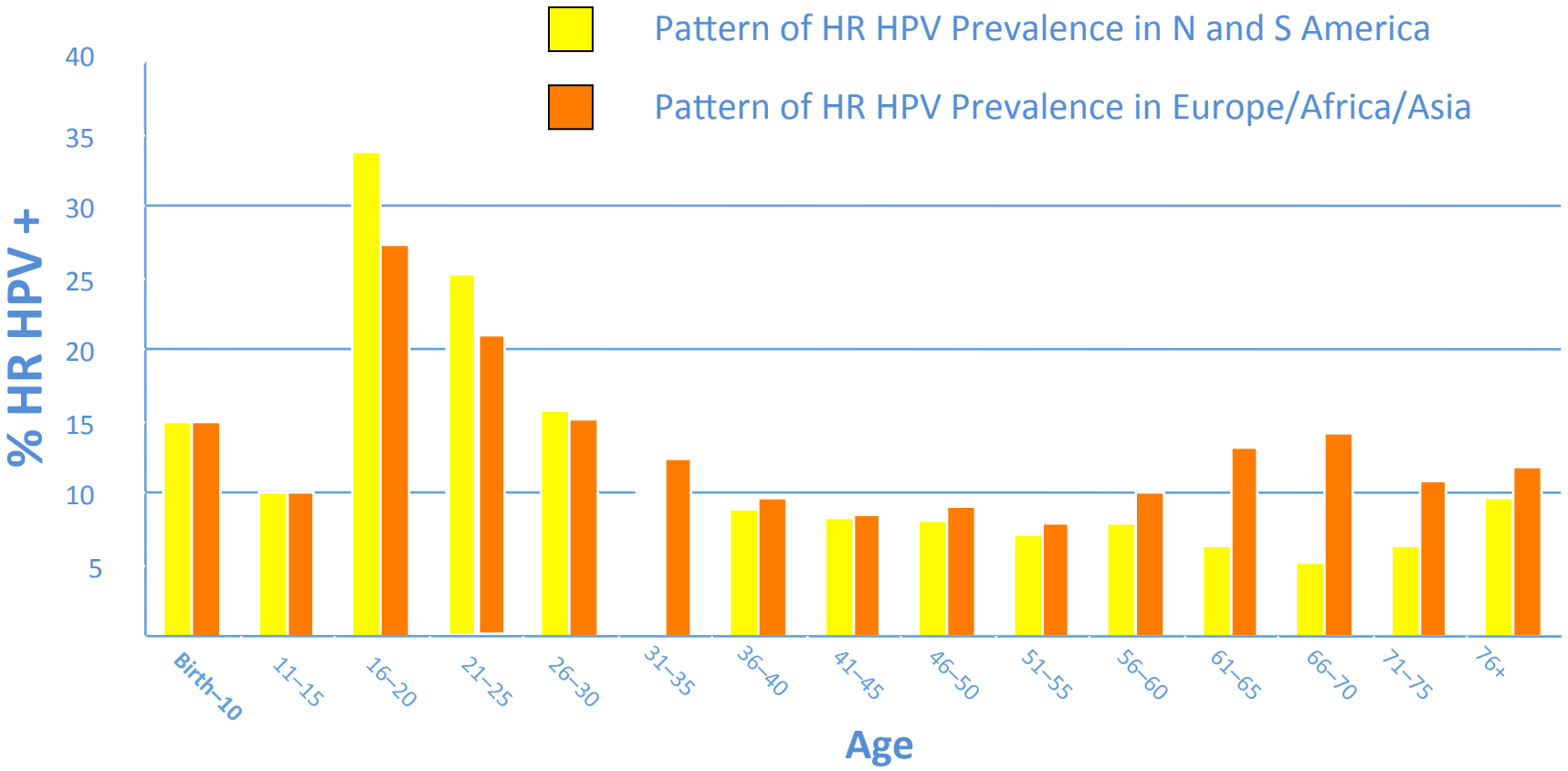
Basic Information

- Cancer rate in the region
- Current cervical cancer screening tests available in the region
  - The benefits and limits of Pap screening
- Regional practices for treatment of detected CIN necessary for cancer prevention
  - VIA with cryosurgery
  - Referral for LEEP/conization

Basic Information about HPV

- HPV Infections
  - Occur in ALL ages from birth to death
  - Skin to skin infection
    - Mostly, but not always sexually transmitted

HPV Prevalence by Age



Cubie HA. *J Med Virol.* 1998;56:210-216.
Rintala MA, et al. *Clin Infect Dis*. 2005;41:1728-1733.
Smith EM, et al. *Int J Cancer.* 2004;108:766-772.
Stone KM, et al. *J Infect Dis.* 2002;186:1396-1402.

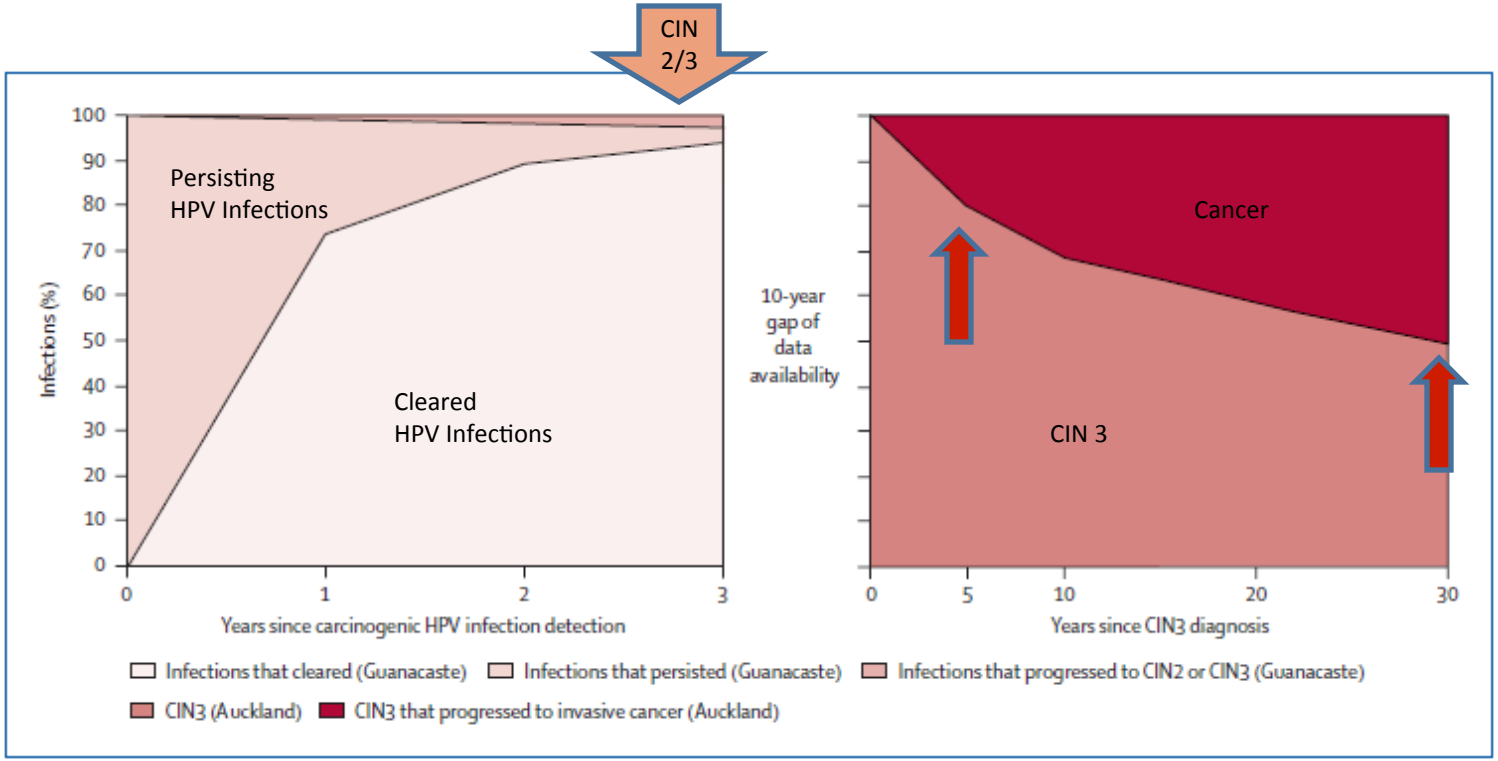
Schiffman and Krüger Kjaer. *J National Canc Institute*. 2003;
Smith EM, et al. *Sex Transm Dis.* 2004;31:57-62.
Bandyopadhyay S, et al. *Asian Pac J Cancer Prev*. 2003;4:179-184.
Dunne EF, et al. *J Infect Dis.* 2005;191:1817-1819.

Basic Information about HPV

- HPV Infections
  - Skin to skin infection
    - Mostly, but not always sexually transmitted
  - Occur in ALL ages from birth to death
  - **15 different types** of HPV cause cervical cancer
  - 90% of HPV infections **go away** by themselves
  - 5% of HPV infections progress to a **pre-**cancer

HPV Clearance and Progression

Within 3 years, **5% of HPV infections progress to CIN 2/3**



20% of CIN 3 progresses to cancer within 5 years

40% of CIN 3 progresses to cancer within 30 years

Schiffman M et al. Lancet Oncol 2008;9:404-6
McCredie MRE et al. Lancet Oncol 2008; 9: 425–34

Basic Information about HPV Vaccines

- Cervarix

  HPV 16/18 VLPs with AS04

  Efficacy against 7 oncogenic types: 16/18/31/33/45/51/52

  Efficacy against CIN 3 from all HPV types: 93%

- Gardasil

  HPV 6/11/16/18 with AAAP

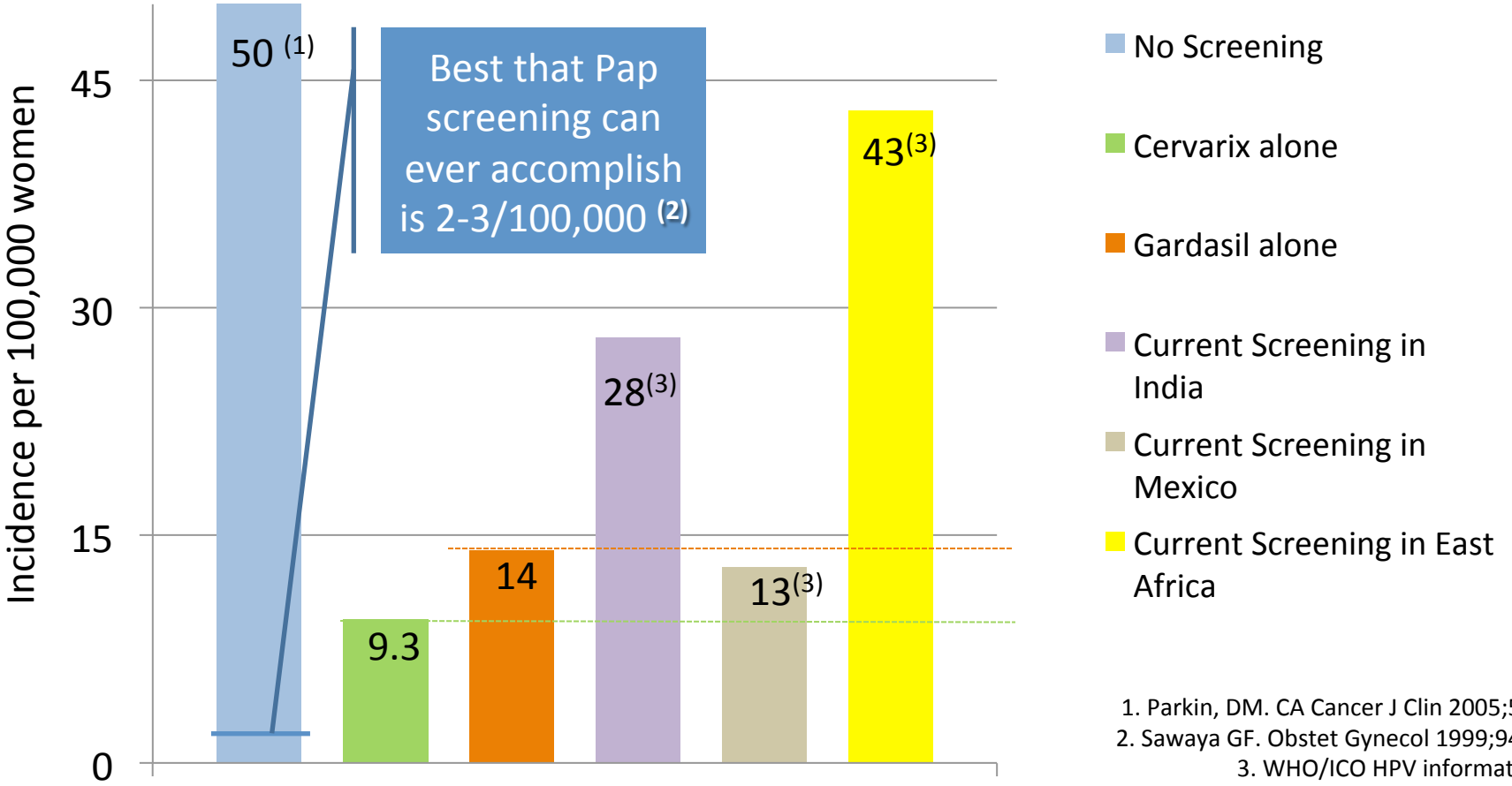
  Efficacy against 2 oncogenic types: 16/18

  Efficacy against CIN 3 from all HPV types: 43%

Heitmann ER et al. Curr Obstet Gynecol Rep 13 July 2012

Lowest Population Incidence Rates of Cervix Cancer Achievable after 60 years: Screening, Vaccination, Neither

Vaccine assumptions: 100% coverage, 3 doses received, lifetime efficacy



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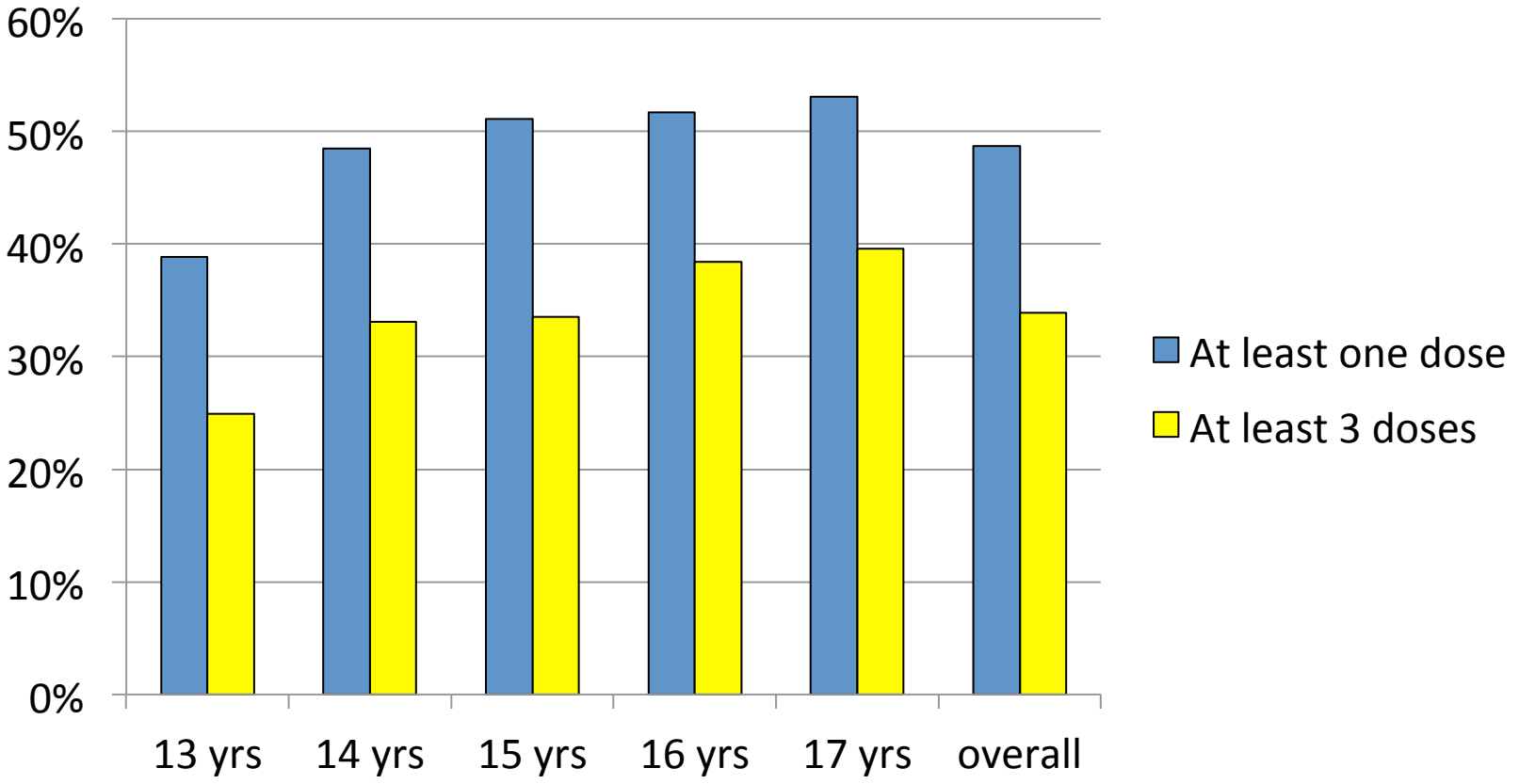
Gardasil Dosing Schedule Adherence in US by age:

66% of doses are wasted



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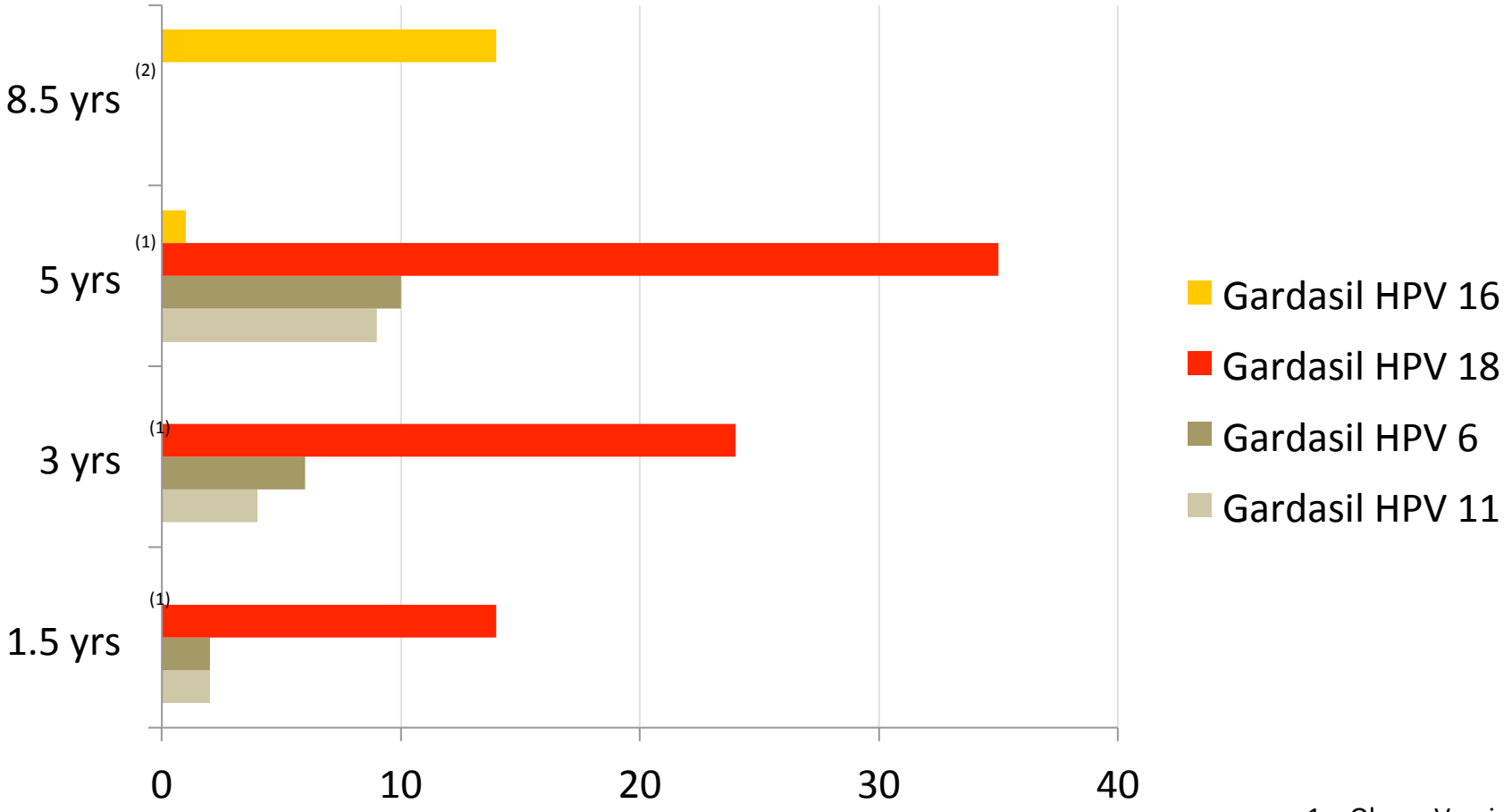
  Immune titer loss in women:

  - HPV 16: 15% lose all antibodies after 8.4 yrs
  - HPV 18: 35% lose all antibodies after 5 yrs
  - HPV 6: 10% lose all antibodies after 5 yrs
  - HPV 11: 9% lose all antibodies after 5 yrs

Heitmann ER et al. Curr Obstet Gynecol Rep 13 July 2012

Percentage loss of Gardasil antibody titers over time

Cervarix HPV 16 and HPV 18 has no antibody loss at 9.4 yrs (PBNA) [3]



1. Olsson Vaccine 2007
2. Rowhani-Rahbar Vaccine 2009
3. Roteli-Martins CM, Hum Vacc 2012.

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  Duration of efficacy: at least 9.4 yrs

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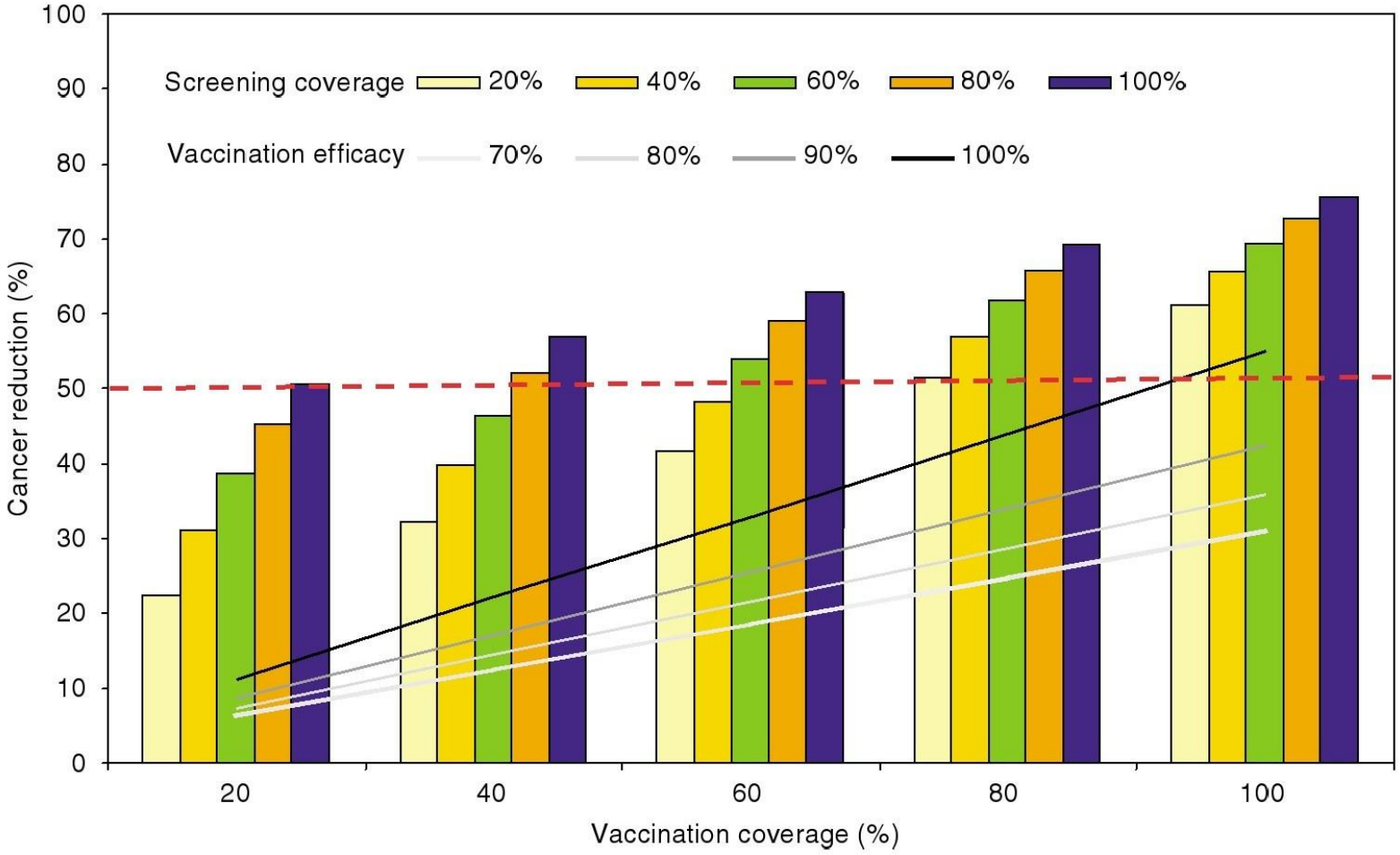
Heitmann ER et al. Curr Obstet Gynecol Rep 13 July 2012

Booster Shots Needed?

- zur Hausen (Nobel laureate) stated that booster shots are likely, especially with Gardasil
- If vaccine duration is less than 15 years, cervical cancers are only postponed, if no boosters are given

JNCI J Natl Cancer Inst (2010) doi: 10.1093/jnci/djq229
Barnabas 2006 PLoS Med

Options that consider vaccine coverage and efficacy vs. screening



Diaz M et al. Br J Cancer. 2008 July 22; 99(2): 230–238.

Side Effects

Everything in medicine has side effects!

>25% population: pain

10-25% population: redness, induration, mild fever (100°-102°F)

1-10% population: itchiness, dizziness, moderate fever (>102°F)

<1% population: severe allergic reactions, life threatening

Risk/benefit balance

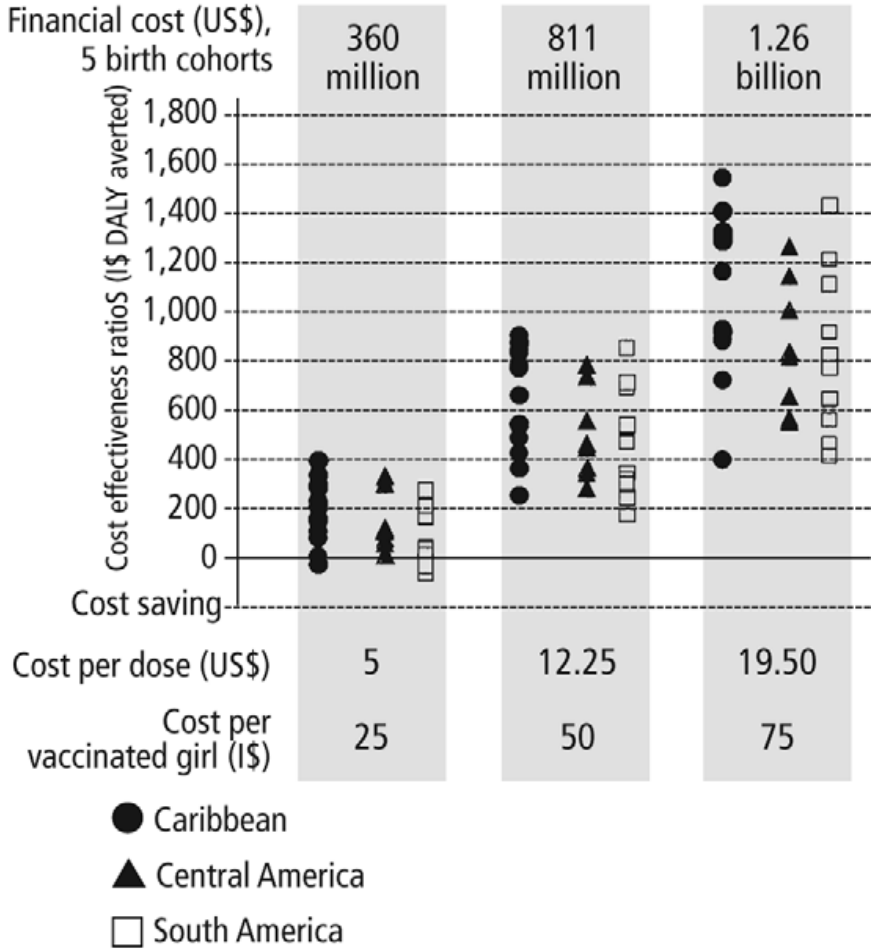
Merck consent form for Gardasil: IRB #: PRO10070407

Conclusions:
How to Get All Women Involved?
Informed Decision Making

- Full ethical disclosure of all options
- Culturally appropriate language
- Respect the personal value attributed to each option
- Personal health decisions may not always immediately align with public or population health goals
  - Opportunity for discussion must remain open

Cost effectiveness may not mean **affordability**

- Cost for only **5 years** of vaccine programs to cover **70%** of **12 year** old girls ranges from **$360M - $1.26B** when costs to vaccinate one girl range from **$25-$75**.



Goldie SJ et al. Reprod Health Matters 2008;16:86-96.