

CLOSING KEYNOTE: MOBILIZING FOR GLOBAL PREVENTION AND EARLY DETECTION OF CERVICAL CANCER

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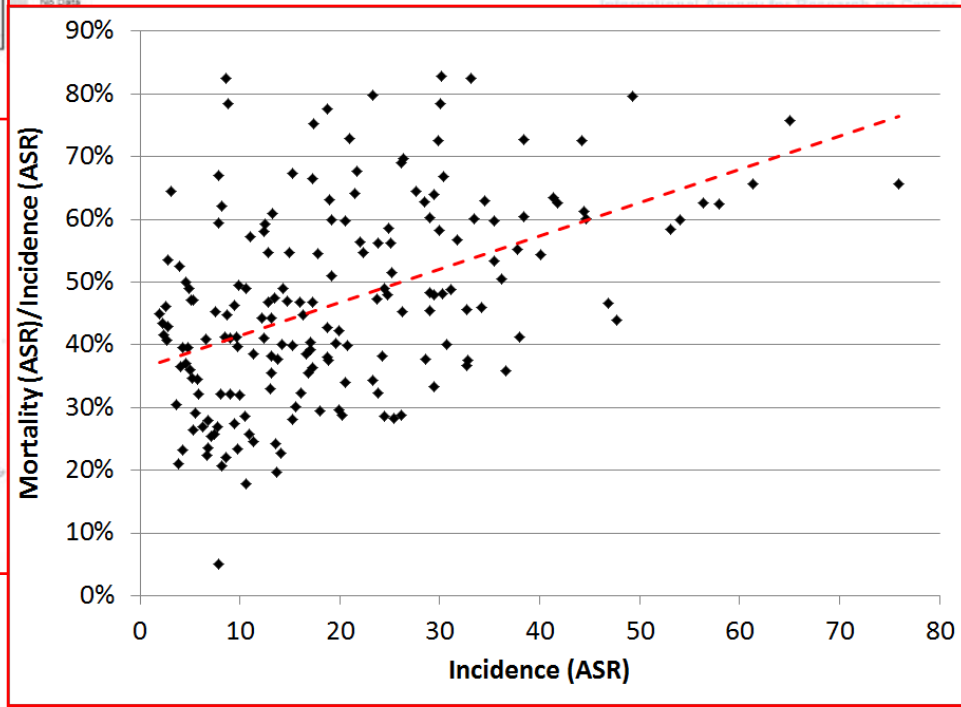
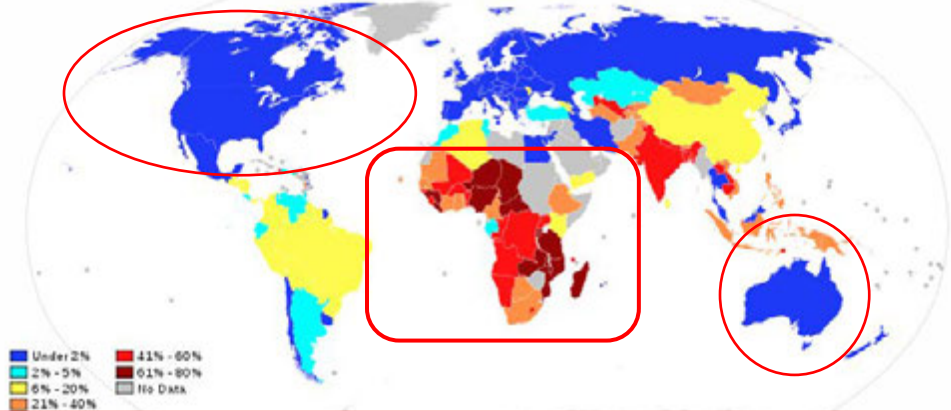
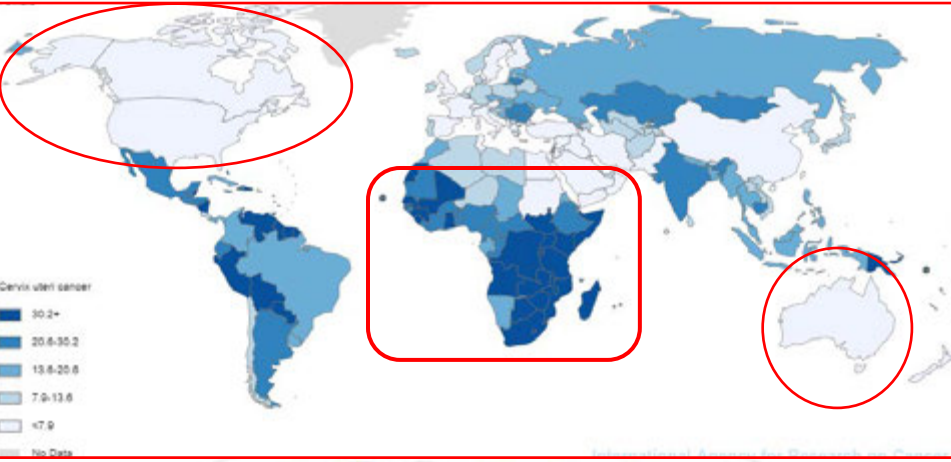
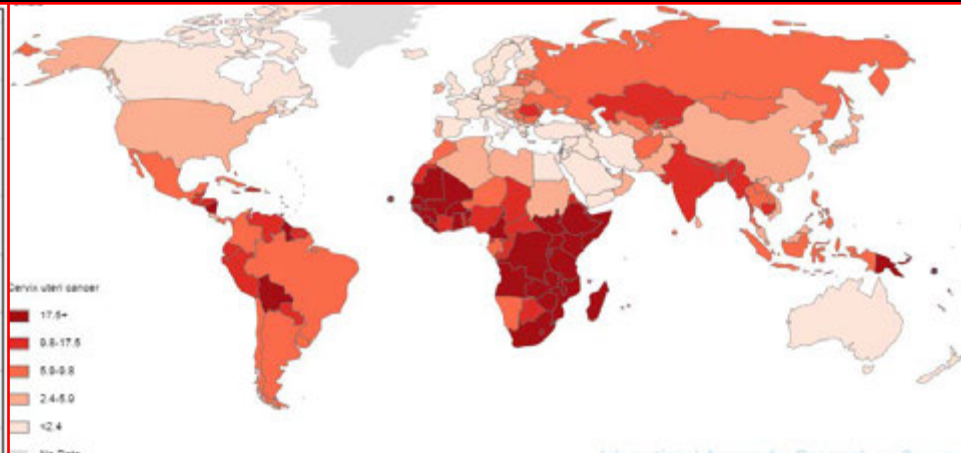
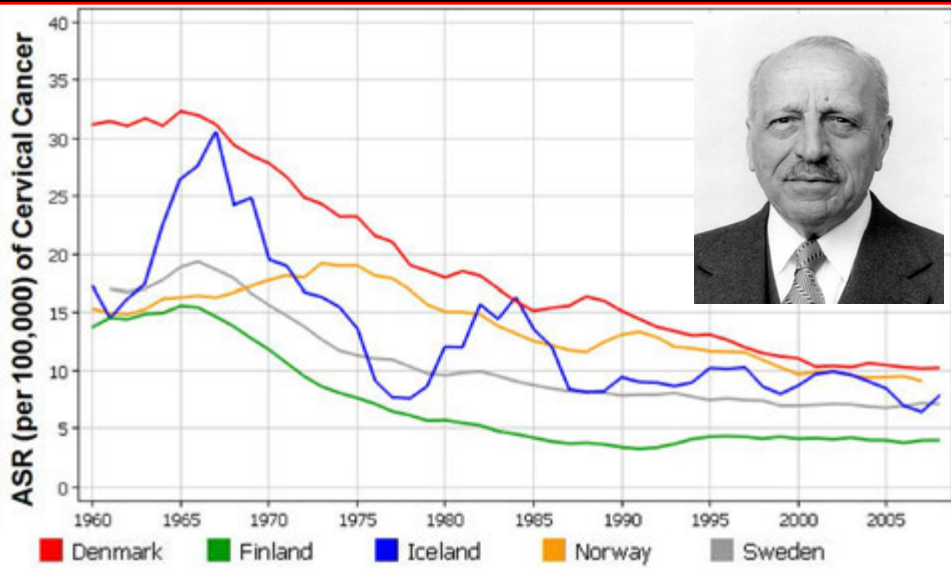
April 21, 2017

Cancer has gotten personal



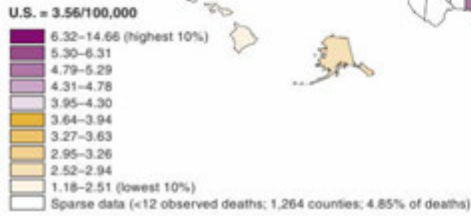
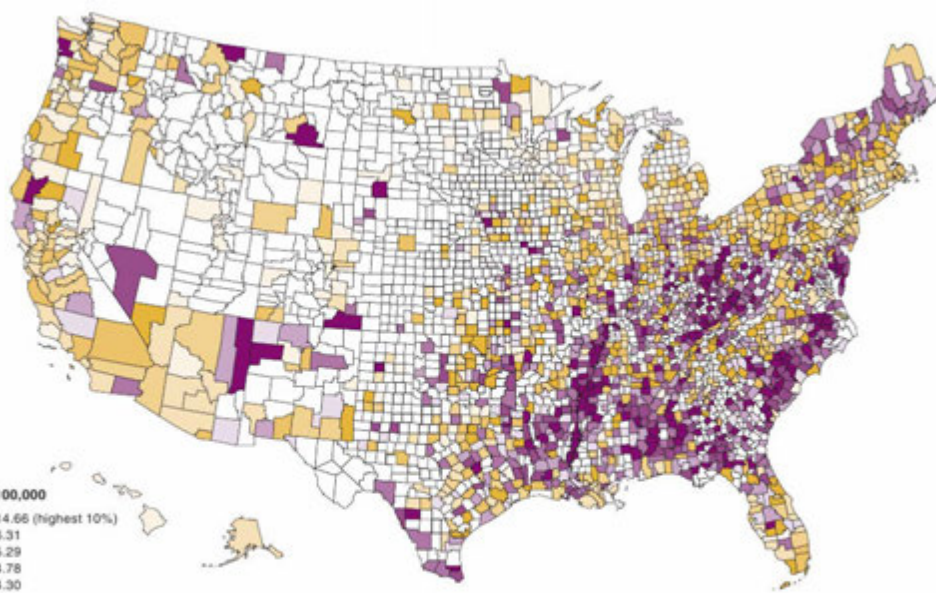
Disclosure

The following talk is for mature audiences only. It may contain adult language and provocative statements, some (or many) with which you may disagree. It is intended to instigate open discussion and even disagreement in the hopes that we can accelerate progress and start saving (more) lives. This will NOT be a data-driven talk. This is a call to arms.

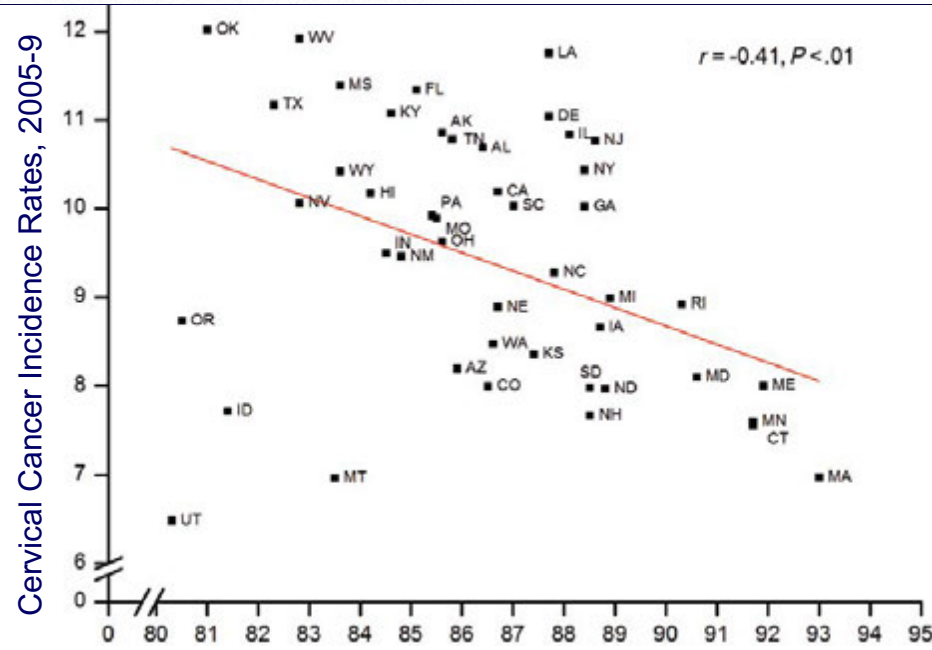


Global Cervical Cancer

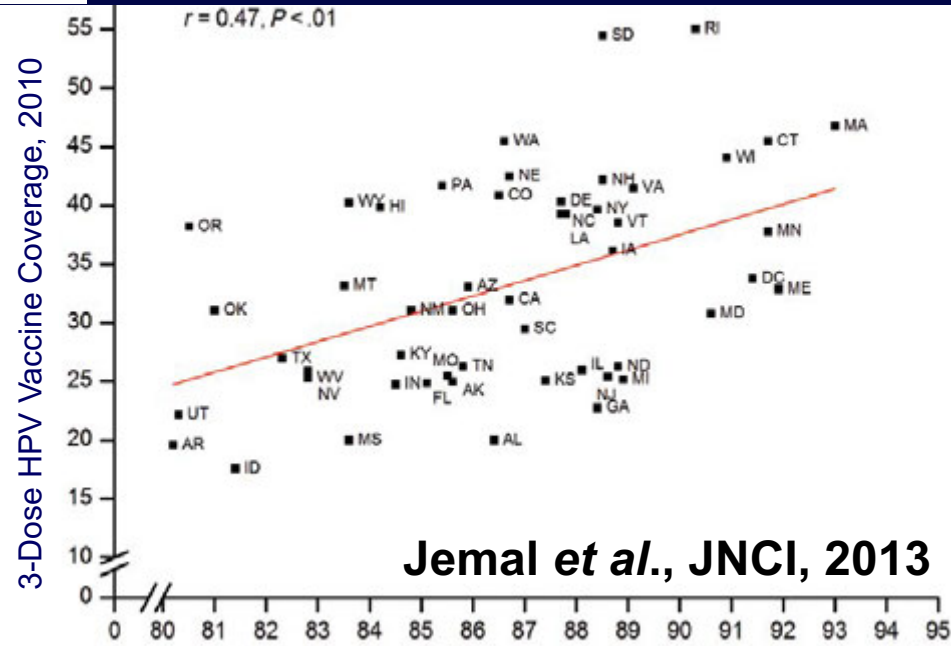
U.S. Cervical Cancer Health Disparities



NIH Pub. No. 05-5282



Pap Testing Prevalence (2010)



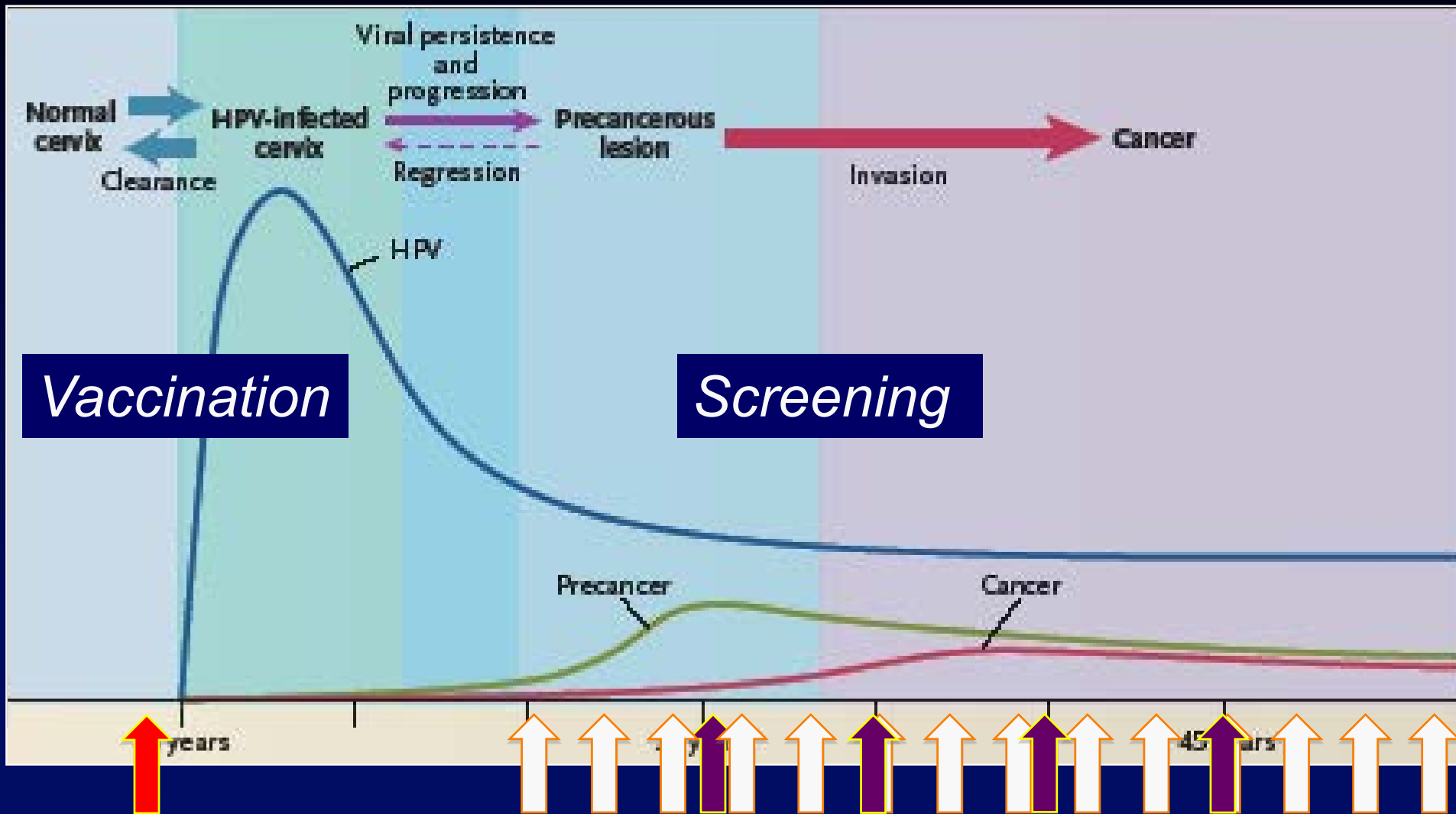
Pap Testing Prevalence (2010)

Jemal et al., JNCI, 2013



"I'll have an ounce of prevention."

The Promise of Cervical Cancer Prevention



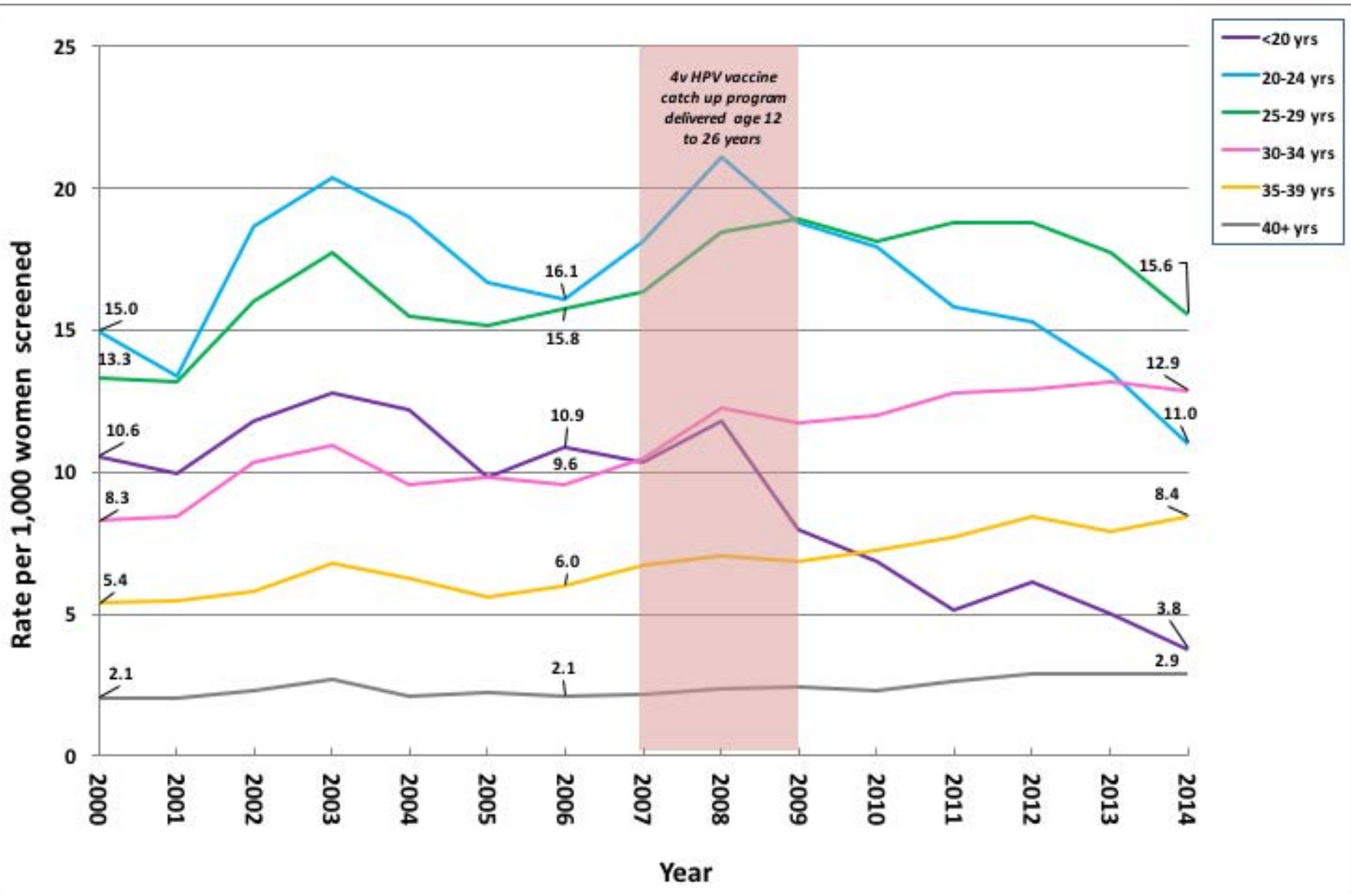
Outline

1. Barriers to Vaccination: The Curious Case of Japan
2. Barriers to Screening: Don't Let Perfection Be the Enemy of Good
3. The Big Picture

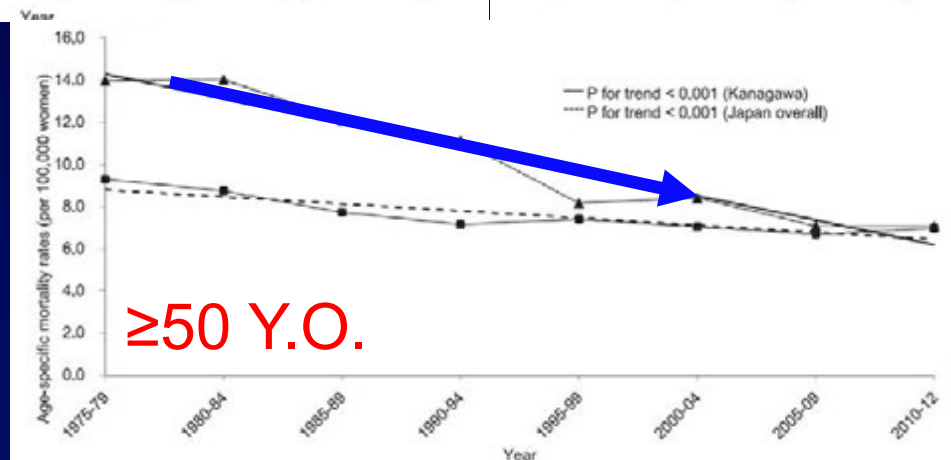
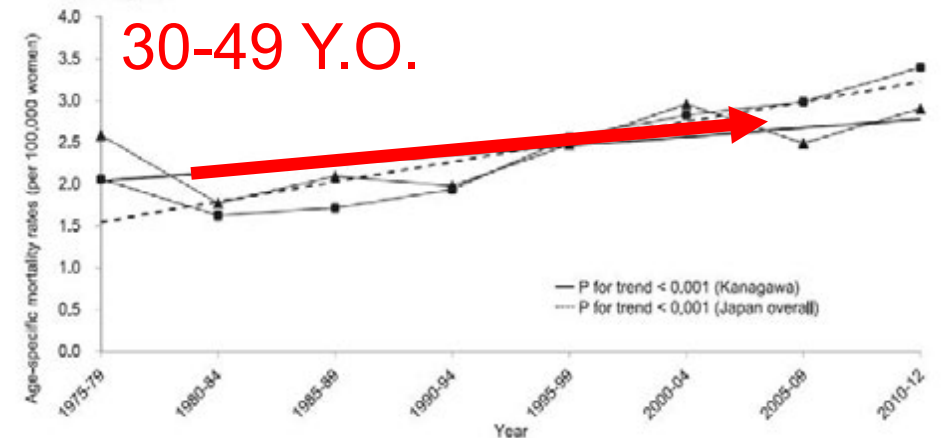
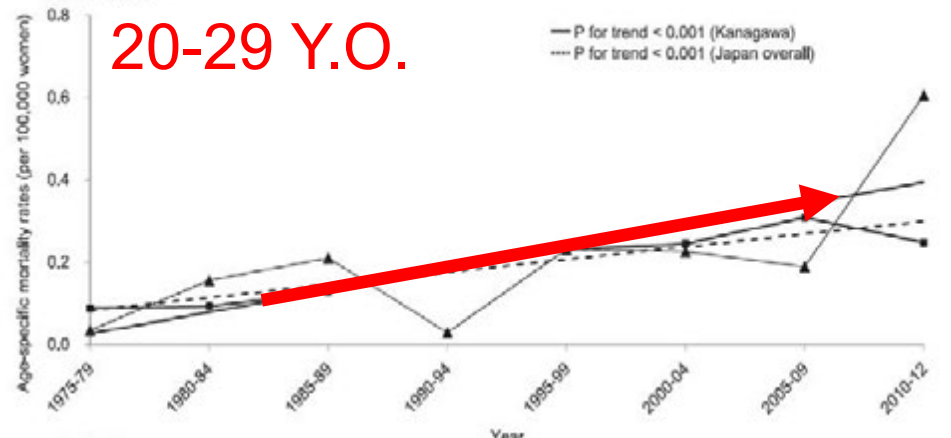
Current HPV Vaccines

	HPV Types	Manufacturer	FDA Approval	Expected Preventive Effect
Gardasil	HPV16, HPV18, HPV6, HPV11	Merck	2007	70% Cervical Cancer 90% Genital Warts
Cervarix	HPV16, HPV18	GSK	2009	70-80% Cervical Cancer
Gardasil 9	HPV16, HPV18, HPV6, HPV11, HPV31, HPV33, HPV45, HPV52, HPV58	Merck	2015	90% Cervical Cancer 90% Genital Warts

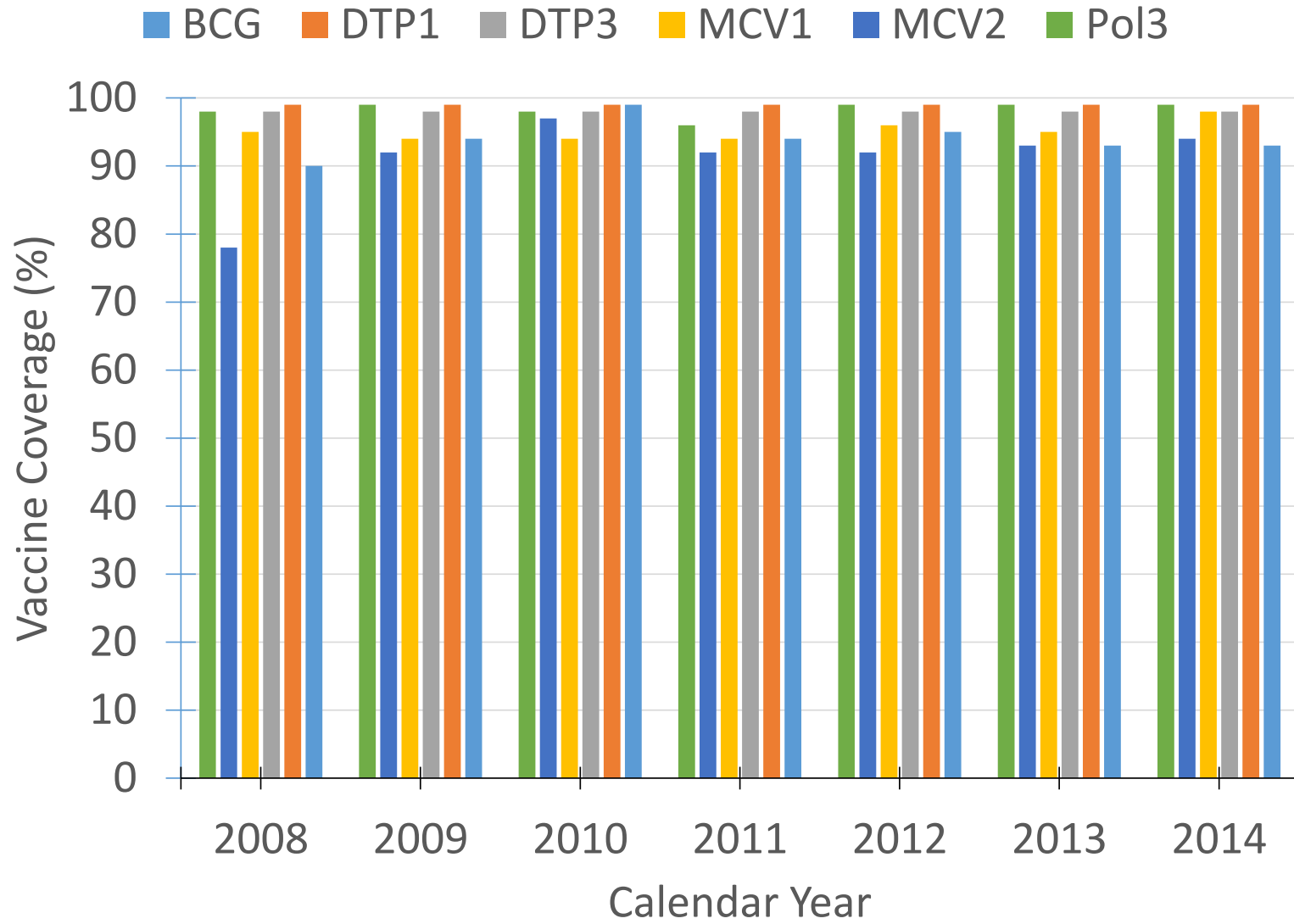
Decline In Precancer Now Up To Age Of 30 Years



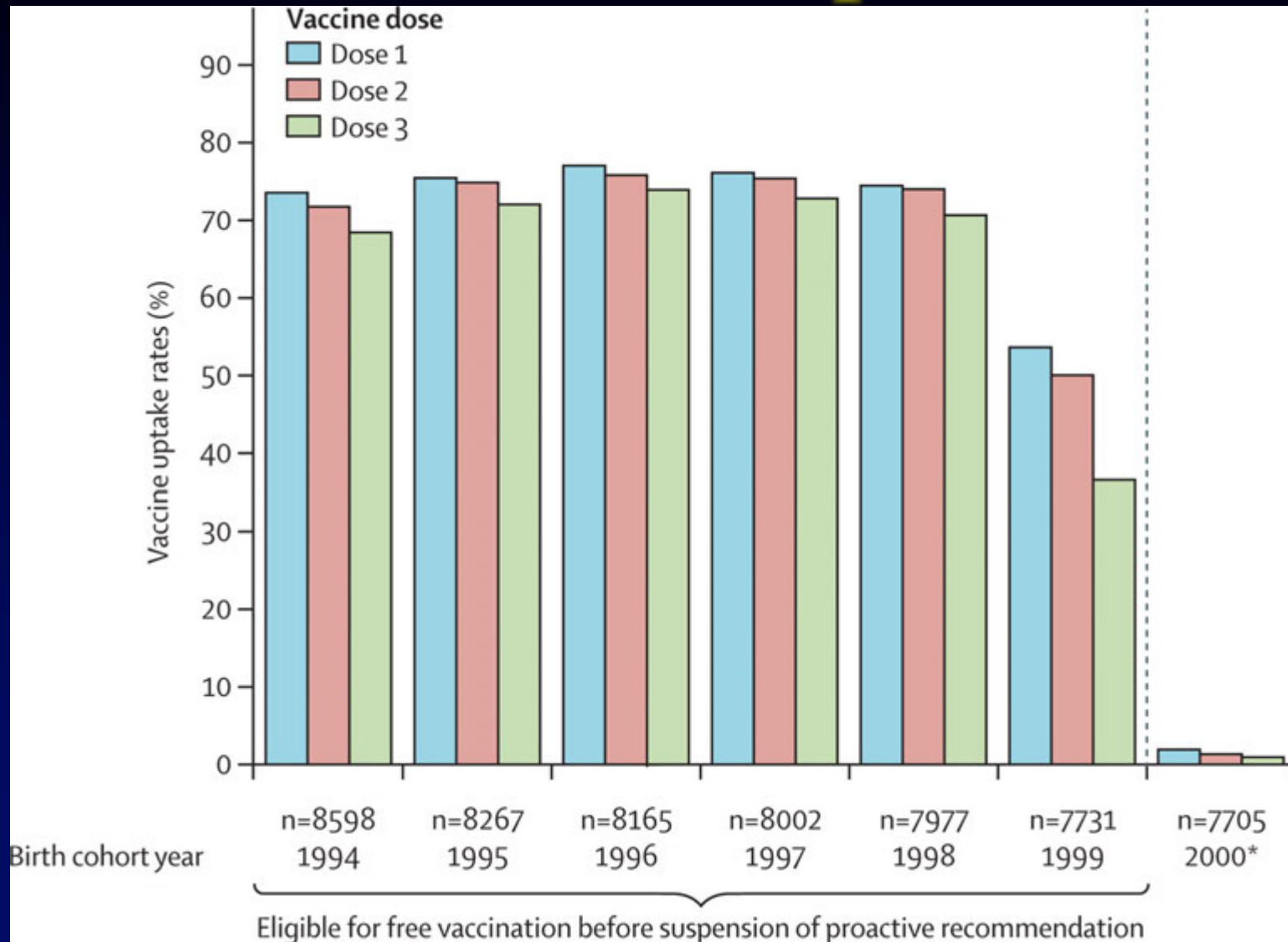
Rise in Cervical Cancer Incidence in Japanese Women under 50 Years Old



Vaccination Coverage in Japan



HPV Vaccination Coverage By Birth Cohort in Japan



Safety

World Health Organization's Global Advisory Committee on Vaccine Safety (03/14/2014):

“...continue to affirm that its benefit-risk profile remains favorable...”

The European Medicines Agency's Pharmacovigilance Risk Assessment Committee (05/11/2015):

“...the evidence does not support a causal link between the [HPV] vaccines and development of complex regional pain syndrome and postural orthostatic tachycardia syndrome...”

Organizations That Have Approved the Use of HPV Vaccination

- ✓ Food and Drug Administration (USA)
- ✓ World Health Organization/Pan-American Health Organization (List of Essential Medicines)
- ✓ Center for Disease Control and Prevention (USA)
- ✓ National Advisory Committee on Immunisation (Canada)
- ✓ Australian Technical Advisory Group on Immunisation
- ✓ National Health Service (UK)
- ✓ European Medicines Agency (European Union)

Comparing Adverse Events

HPV Vaccination

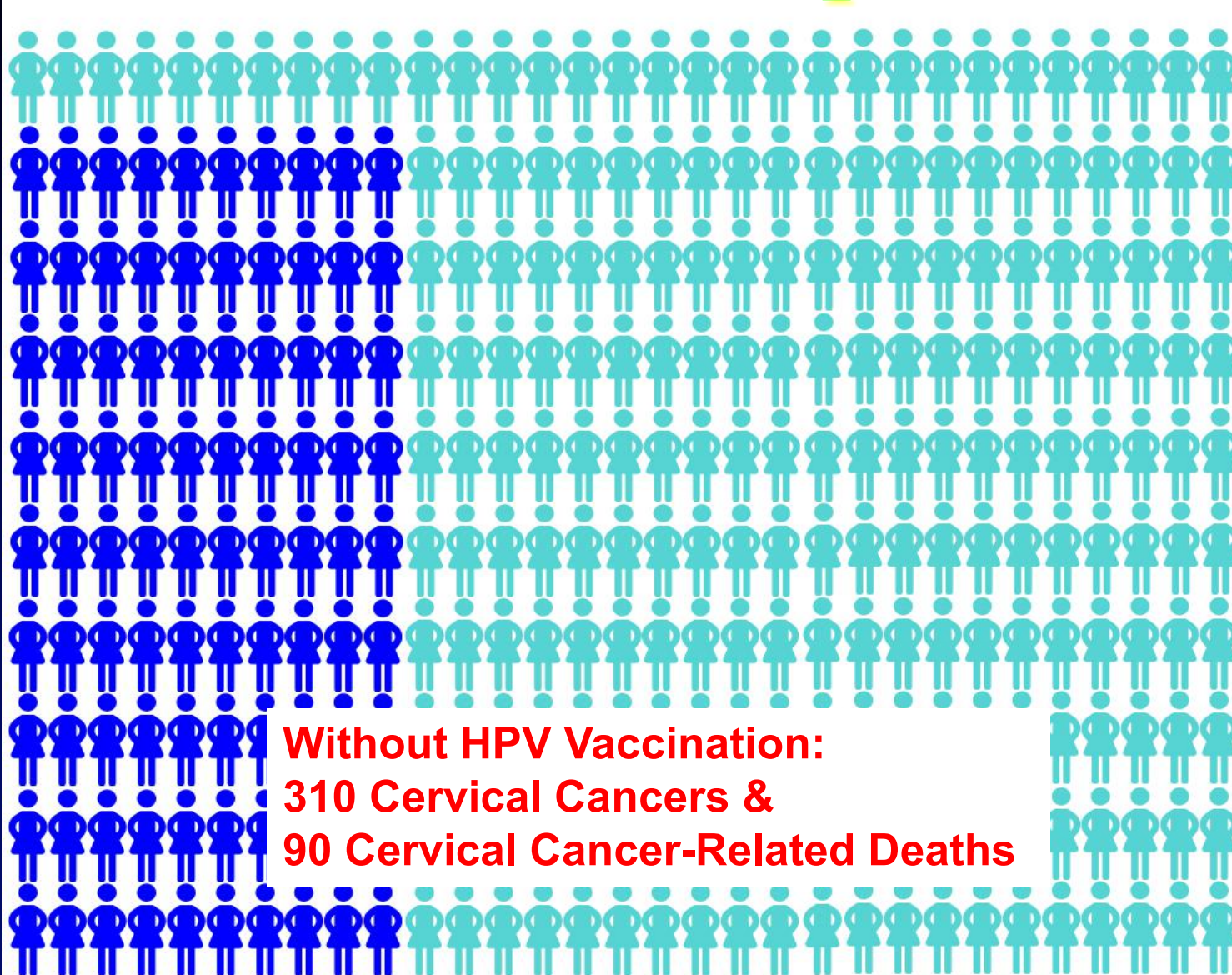
Adverse Event	Comment
Syncope (Fainting)	Rare
Anaphylaxis	Very rare
Neurogenic disease	Unproven
Immunological disease	Unproven
Chronic Pain	Unproven/ Extremely rare

VS.

Cervical Cancer

Adverse Event	Comment
DEATH	Proven
Loss of Fertility	Proven
Surgically Induced Menopause	Proven
Bladder & Bowel Complications	Proven
Radiation-Induced Cancer	Proven

Benefits:Harms of HPV Vaccination in Japan



**Without HPV Vaccination:
310 Cervical Cancers &
90 Cervical Cancer-Related Deaths**

**With HPV
Vaccination:
1 SAE?**

vs. 

A Little Perspective

Chronic Fatigue Syndrome	1 in 400
Suicide (10-24 y.o.)	1 in 3,900
Self-Inflicted Injuries (10-24 y.o.)	1 in 115
Fatal Accidental Injury (10-19 y.o.)	1 in 25,000
Teen Births (15-19 y.o.)*	1 in 250
HPV Vaccination SAE	1 in $\geq 50,000$

History of Polio

- 1 in 200 infections leads to irreversible paralysis. Among those paralyzed, 5% to 10% die when their breathing muscles become immobilized.
- Polio cases have decreased by over 99% since 1988, from an estimated 350 000 cases then, to 74 reported cases in 2015. The reduction is the result of the global effort to eradicate the disease through vaccination.
- Poor sanitation led to early exposure in children and natural immunity. Improved sanitation increased the proportion of children and adults at risk of paralytic polio infection, by reducing childhood exposure and immunity to the disease (no protection from maternal antibodies and more severe immune responses).

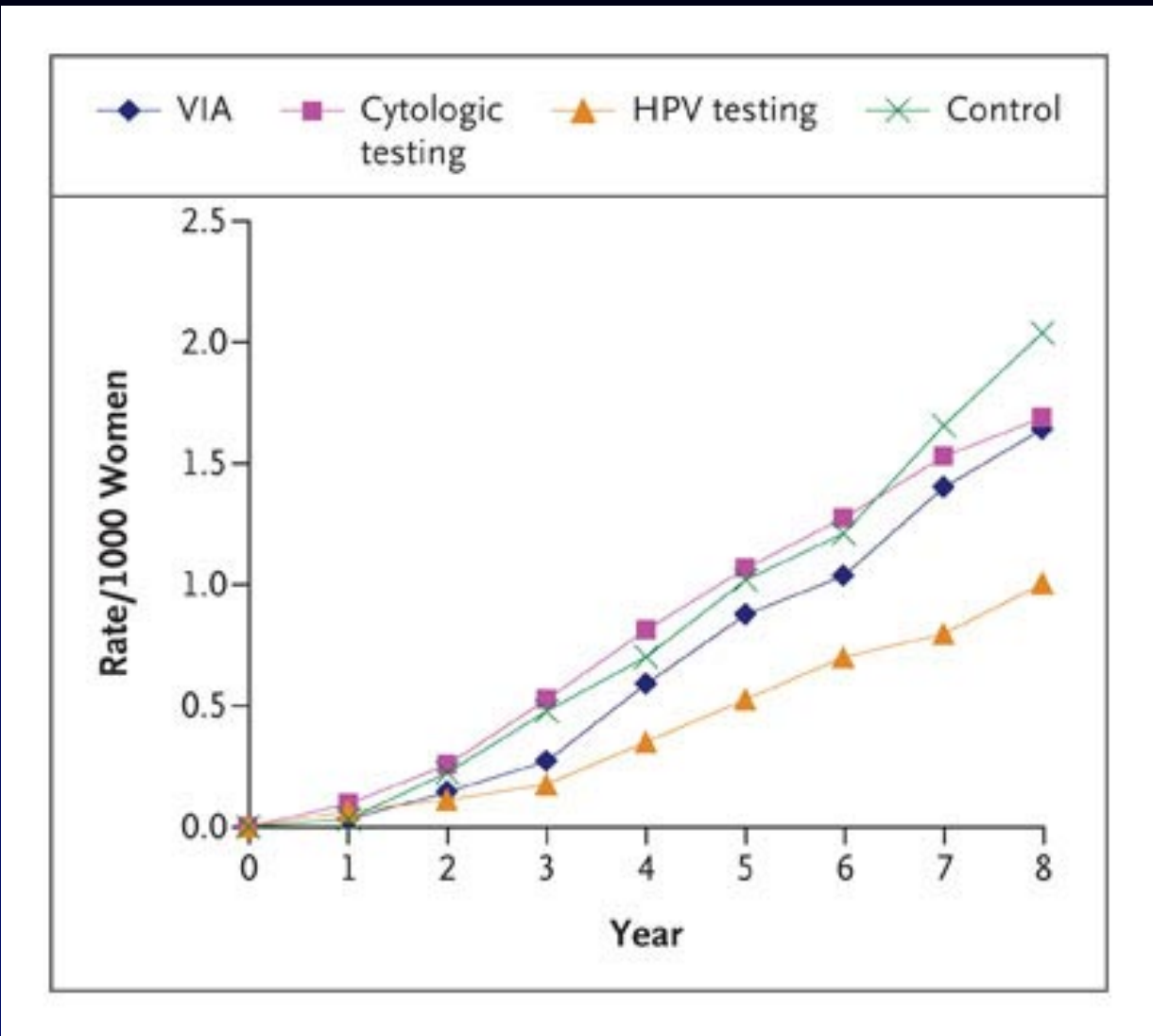
The Anti-HPV Vaccine Lobby

Claims Against HPV Vaccinations	True or False	Comment
HPV vaccines have not been shown to prevent cervical cancer	True	<p>HOWEVER, HPV vaccines have been shown to prevent Pap-detected precancers, the same precancers that if detected and treated are supposedly the reason for Pap screening reduced cervical cancer incidence.</p> <p>Therefore, either both HPV vaccines and Paps work to prevent cervical cancer or they do not?</p>
HPV vaccines cause serious adverse events	False	There is no epidemiological evidence or biological rationale for this to be true.
HPV vaccines encourage adolescents to have more and/or riskier sex	False	Many epidemiological studies have not been able to find a link between HPV vaccination and sexual behaviors

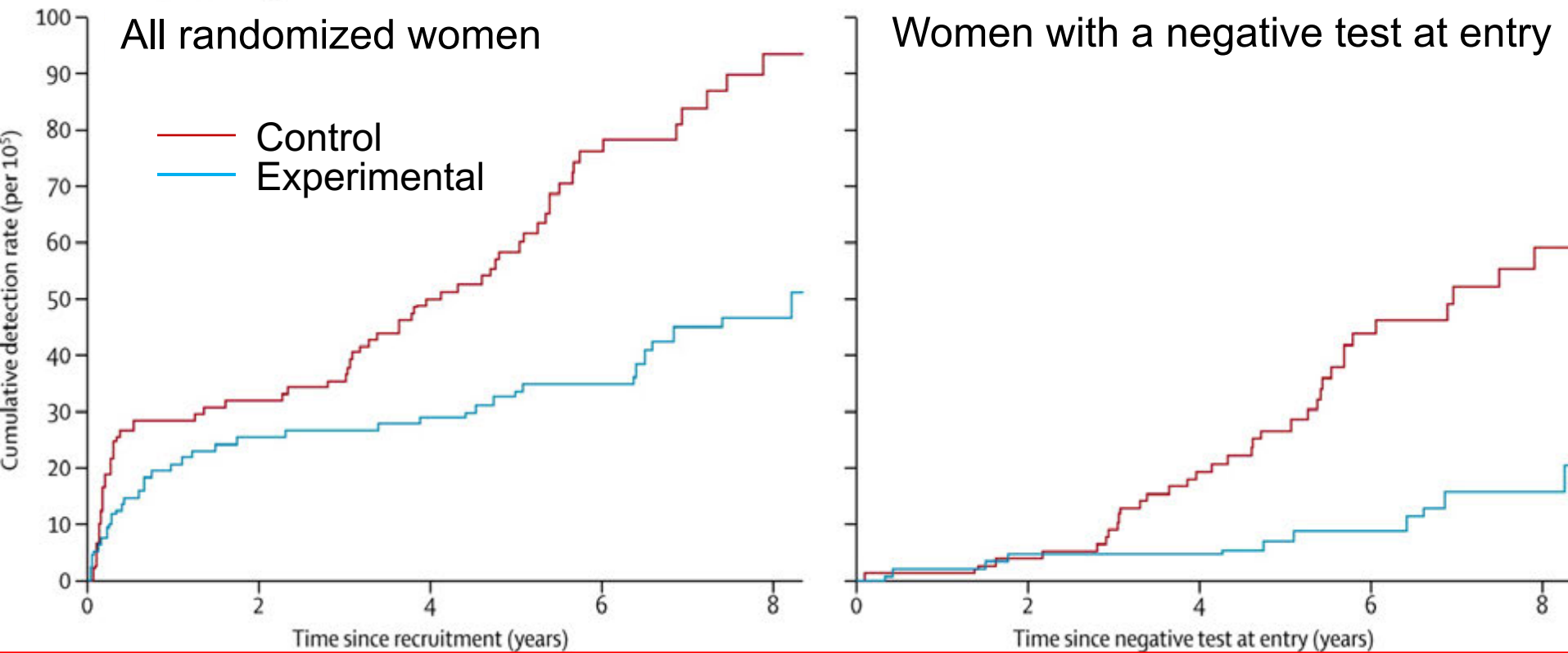
Outline

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HPV Testing Reduces the Risk of Cervical Cancer Related Death (India)

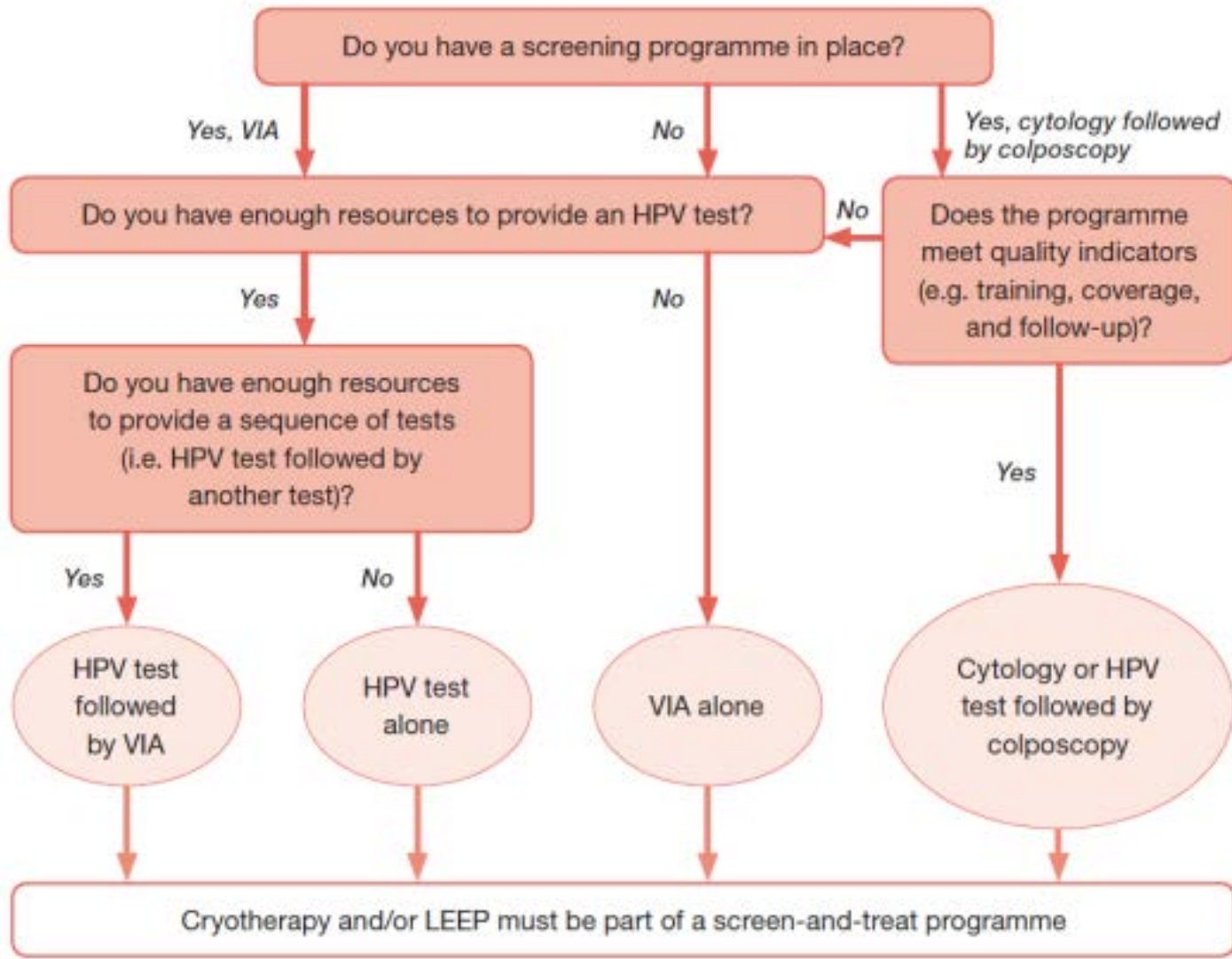


HPV vs. Pap: Pooled RCT Data on Cumulative Incidence of Cervical Cancer

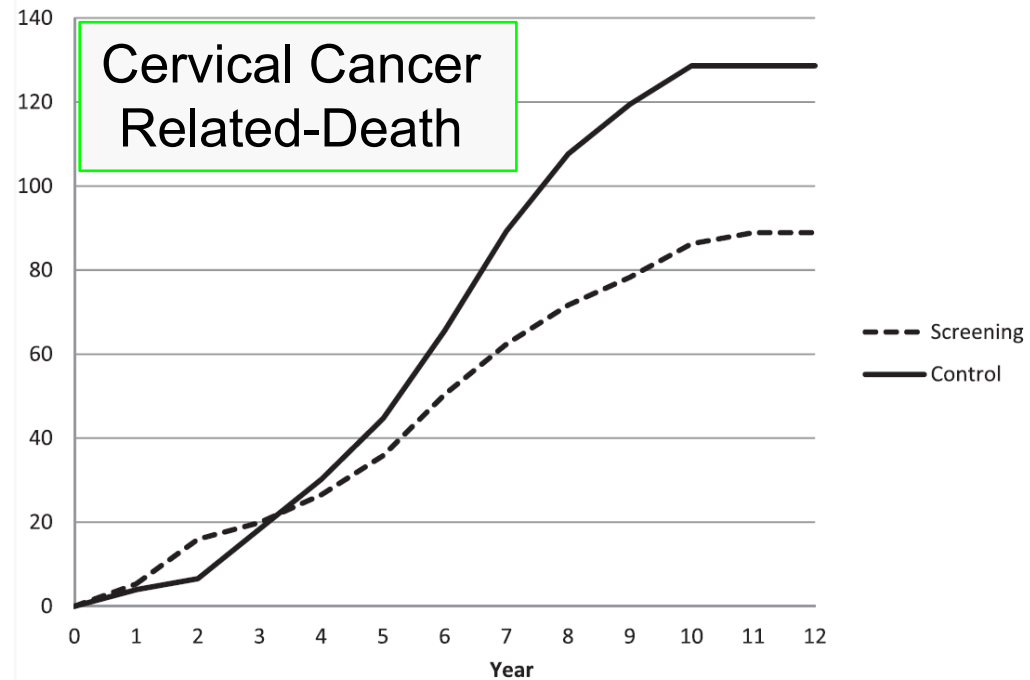
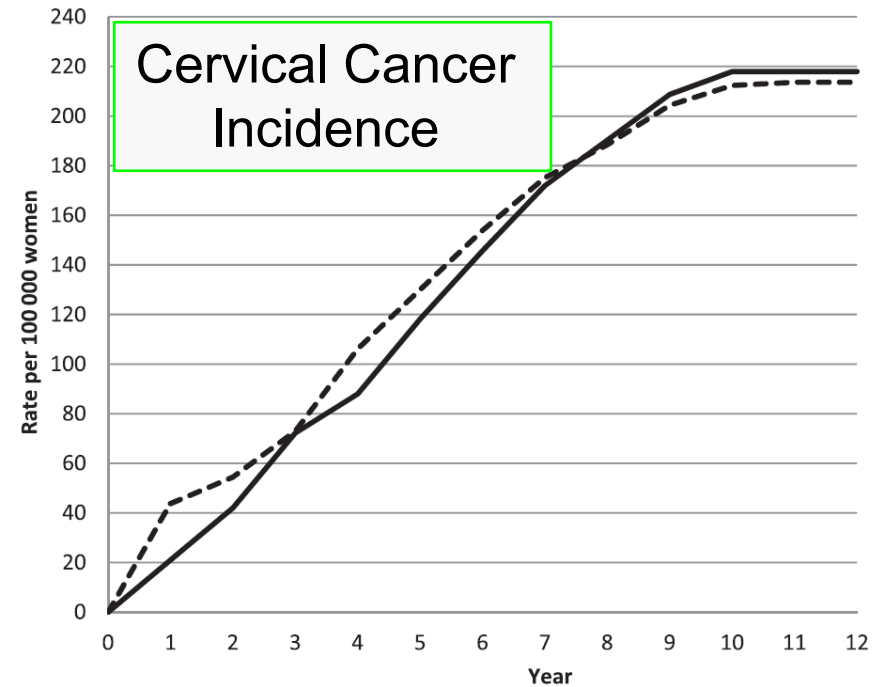


New WHO Guidelines

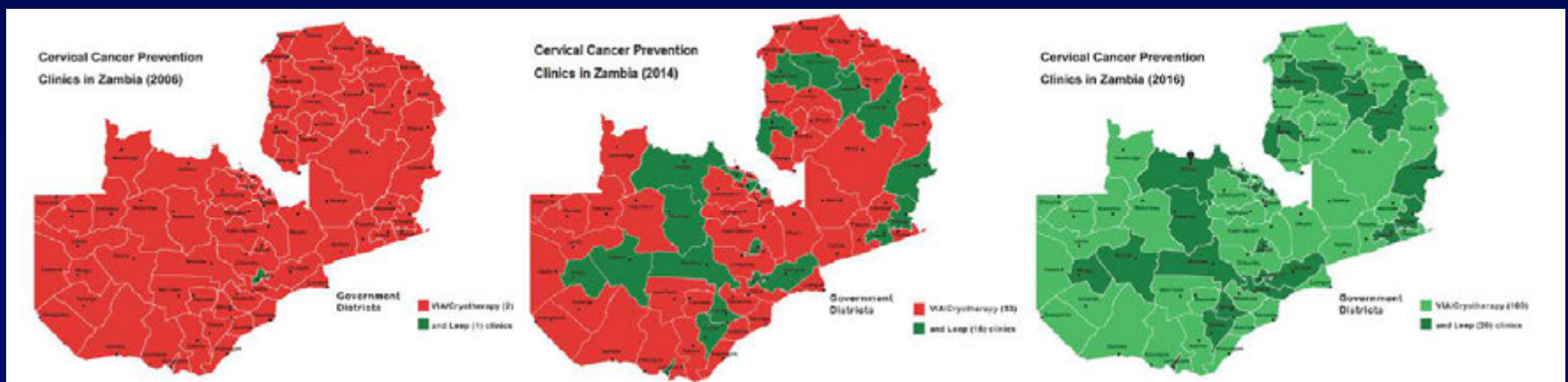
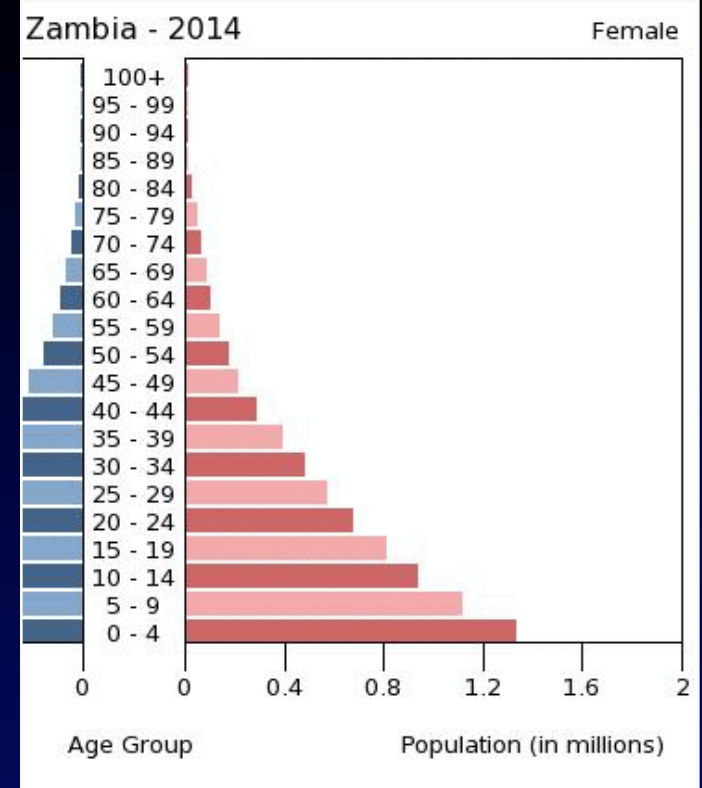
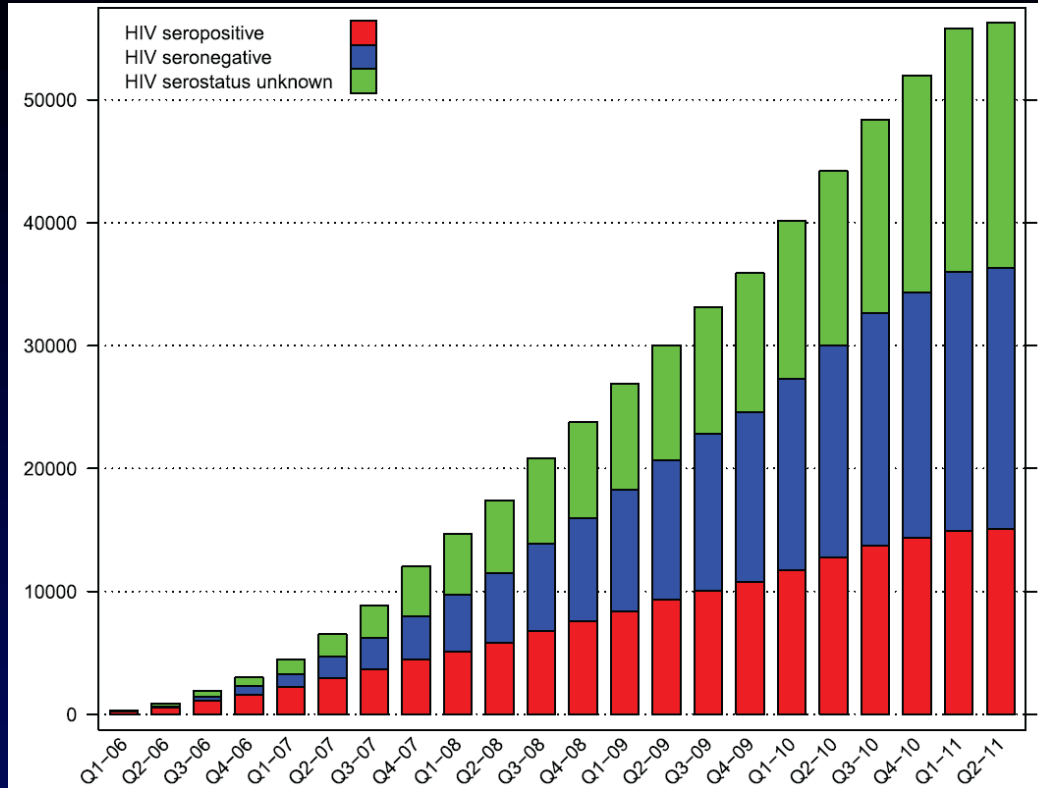
Decision-making flowchart for programme managers



VIA: Success or Failure?



Zambia

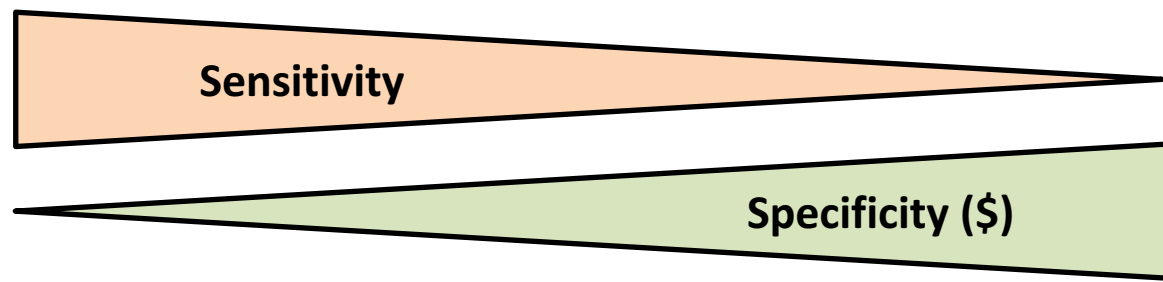
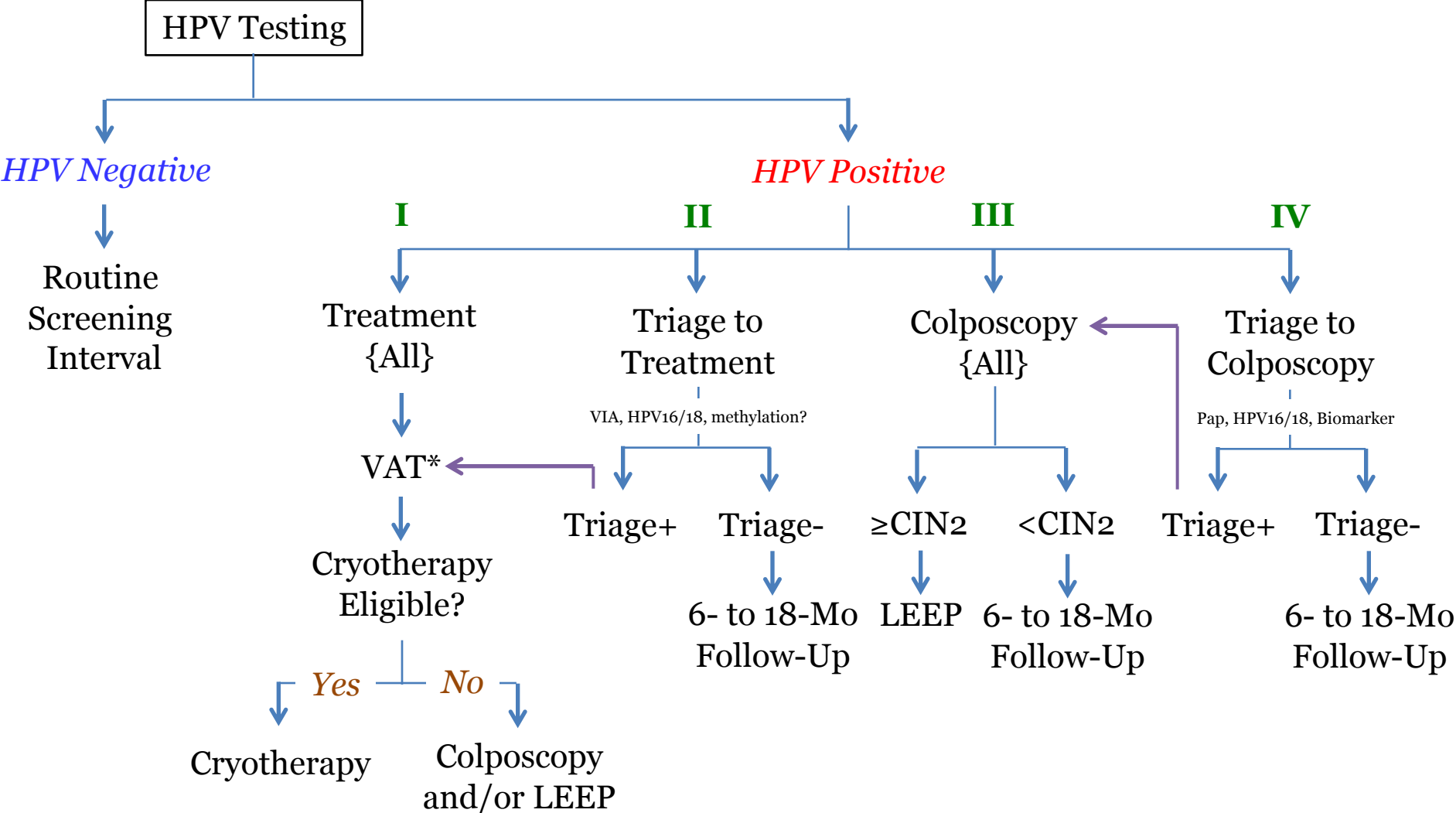


The Challenge of Screening Women Aged 30-49 Years

1. Screening women age 30-49 years represents ~20% of the female population and 10% of the total population. Therefore, for a small country of 10 million people (e.g., Rwanda), that is 1 million to be screened in a place that has never screened even 10% of the population. Plus, every year, another 0.5% reaches screening age.
2. Women aged 40-49 years are at the peak of cervical cancer incidence. Most LMICs do not have the capacity to manage all those screen-detected cancers.
3. Screening tests probably work best in younger women, whose cervical transformation zone is more visible and easier to sample.
4. Scaling up to screen 10% of the population will require a large but temporary workforce that later will be looking for jobs.

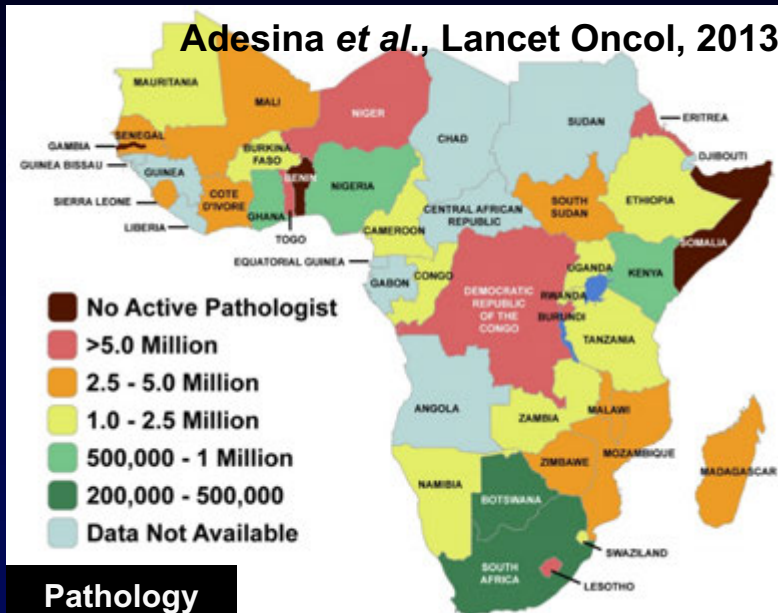
Answer: Further Age Restriction

1. Restrict to 30-39, 30-34, 35-39 or even just 30 or 35 years of age.
2. Get good at screening these women who are the mostly likely to be benefit.
3. Try to get at least one high-quality screen in them and every subsequent 1-year age cohort. The first screen is the most effective and therefore cost effective.
4. Then if the resources are available, consider catch-up screening in the older age groups and/or more than once in a lifetime.

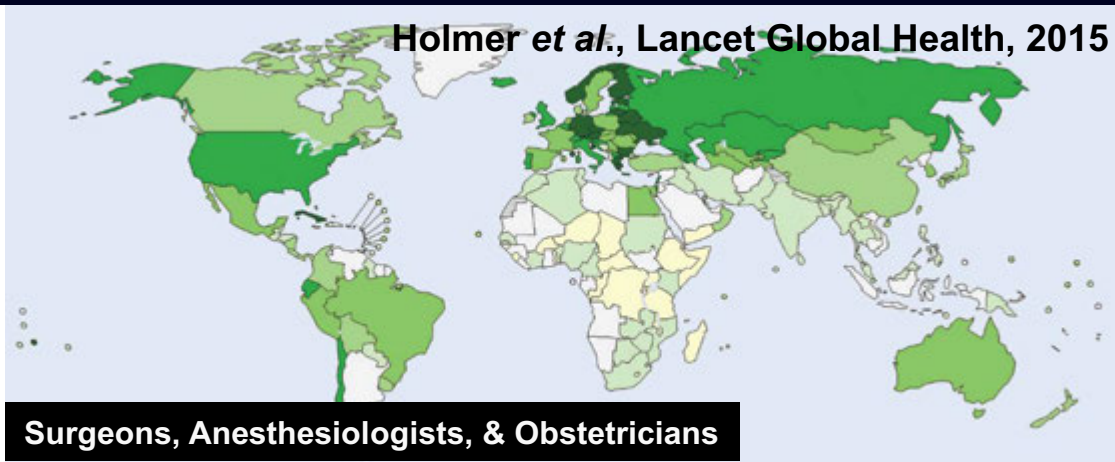


Barriers to Care

Adesina et al., Lancet Oncol, 2013



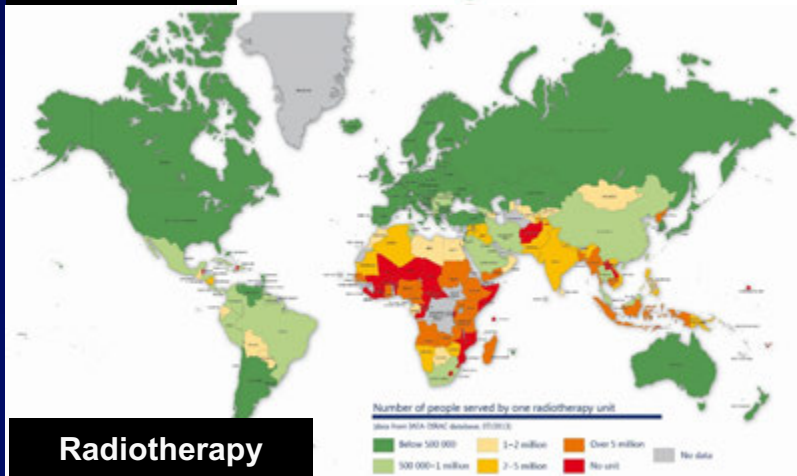
Holmer et al., Lancet Global Health, 2015



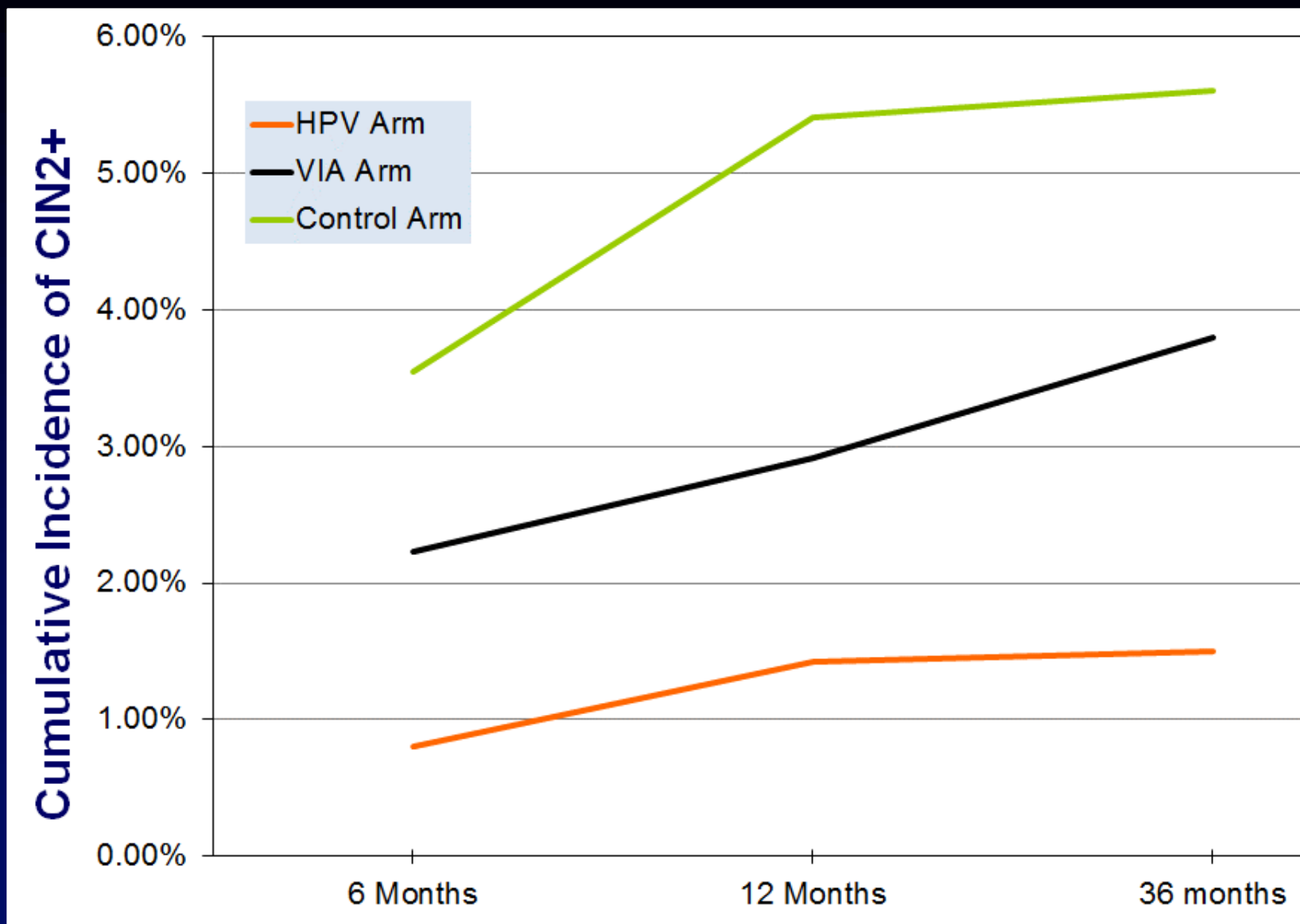
Access to Morphine Around the World



Radiotherapy



Screen and Treat in South Africa



Outline

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What Are the Barriers to Global Adoption of HPV-Targeted Cervical Cancer Prevention?

1. Misinformation/Vested Interests
2. Coordinated Procurement & Investment
3. Human Capital and Capacity
4. Health System Infrastructure & Logistics
5. Inertia

(to name a few)

{BE PRACTICAL}

2008: Gardasil "is a good vaccine and ... is generally safe,"

2009: "Gardasil has been associated with at least as many serious adverse events as there are deaths from cervical cancer developing each year."

2009: Harper stated to the Guardian "I fully support the HPV vaccines," she says. "I believe that in general they are safe in most women."^[17]

In the December 2009 issue of *Current Opinion in Obstetrics and Gynecology*, Harper published an opinion piece regarding the potential risks of both Gardasil and Cervarix, and concluded that, given the various limitations and risks of the vaccines, the benefits and risks of HPV vaccination must be weighed with the benefits and risks of HPV screening (Pap smears) to reduce cervical cancer in a cost-effective manner

2013: "Population health models show that if the HPV vaccine does not last for at least 15 years, no cancers will ever be prevented; women will just get the cancers at a later time in life after the vaccine has worn off"

2012: "[I]t's critical to note that more than 70 healthy young girls have died from a neurological reaction that occurred soon after getting Gardasil

2013: stated that newly developed pap screenings that combine HPV testing and cytology have a nearly 100% ability to detect pre-cancers and cancers; she noted that Gardasil doesn't last long enough to prevent cervical cancer and that there are some harms associated with it.

[http://www.ncbi.nlm.nih.gov/pubmed/?term=HPV+Vaccine+Harper
_D](http://www.ncbi.nlm.nih.gov/pubmed/?term=HPV+Vaccine+Harper_D)

= 63 Citations

MNCH vs. Cervical Cancer

Local cervical cancer prevention and control

**PREGNANCY-RELATED COMPLICATIONS
(MATERNAL MORTALITY)**

CERVICAL CANCER

ANNUAL DEATHS

273,500
women
DIE ANNUALLY

275,000
women
DIE ANNUALLY

MORTALITY TRENDS

↓34%
DECREASE IN MORTALITY
1990-2008

↑45%
INCREASE IN MORTALITY
1990-2008

PRIORITIZATION IN MILLENIUM
DEVELOPMENT GOAL (MDG)?

YES
(MDG 5—IMPROVING MATERNAL HEALTH
FROM PREGNANCY-RELATED
COMPLICATIONS)

NO

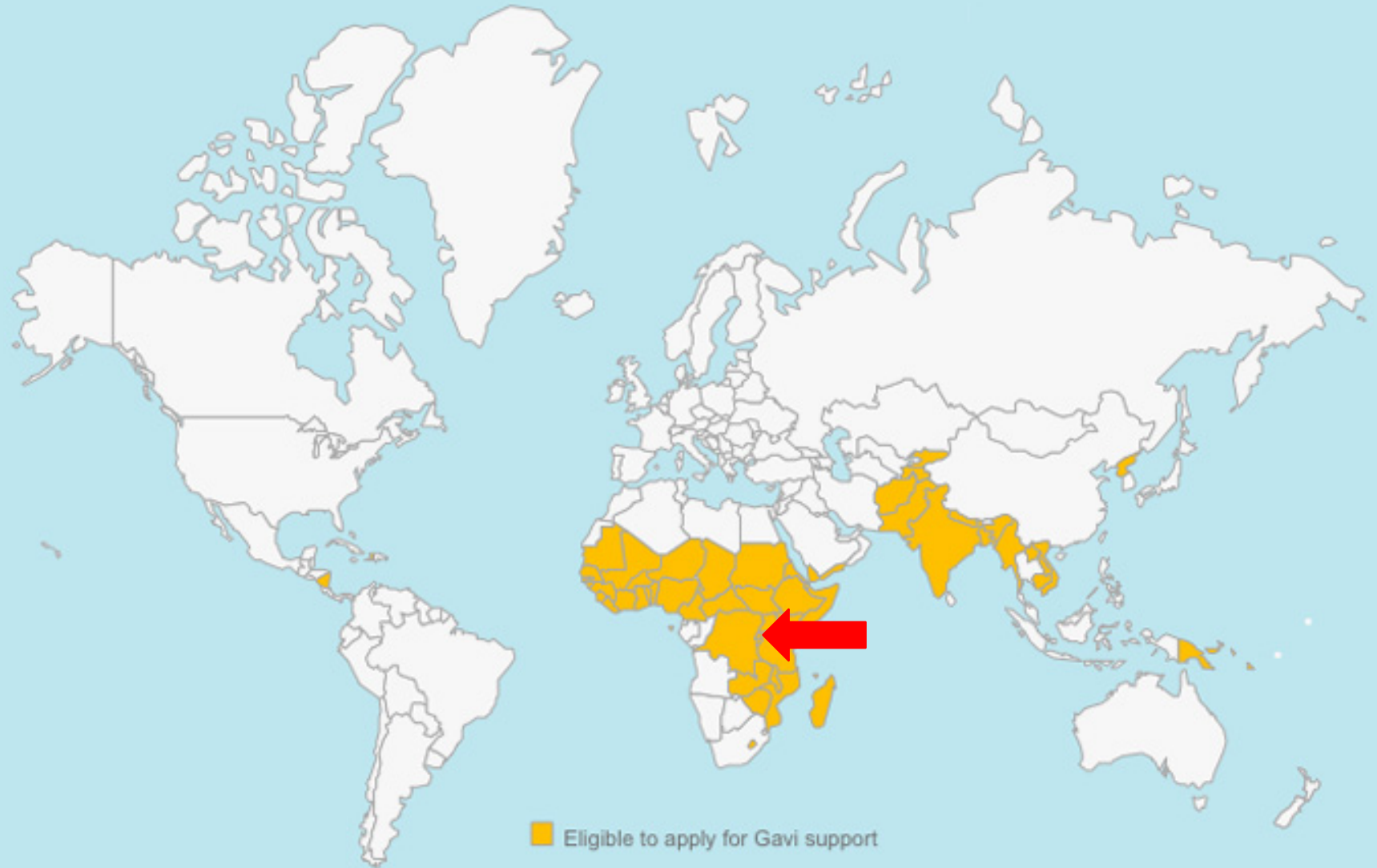
CURRENT ANNUAL INVESTMENT IN
DEVELOPING WORLD

USD 12 billion

???

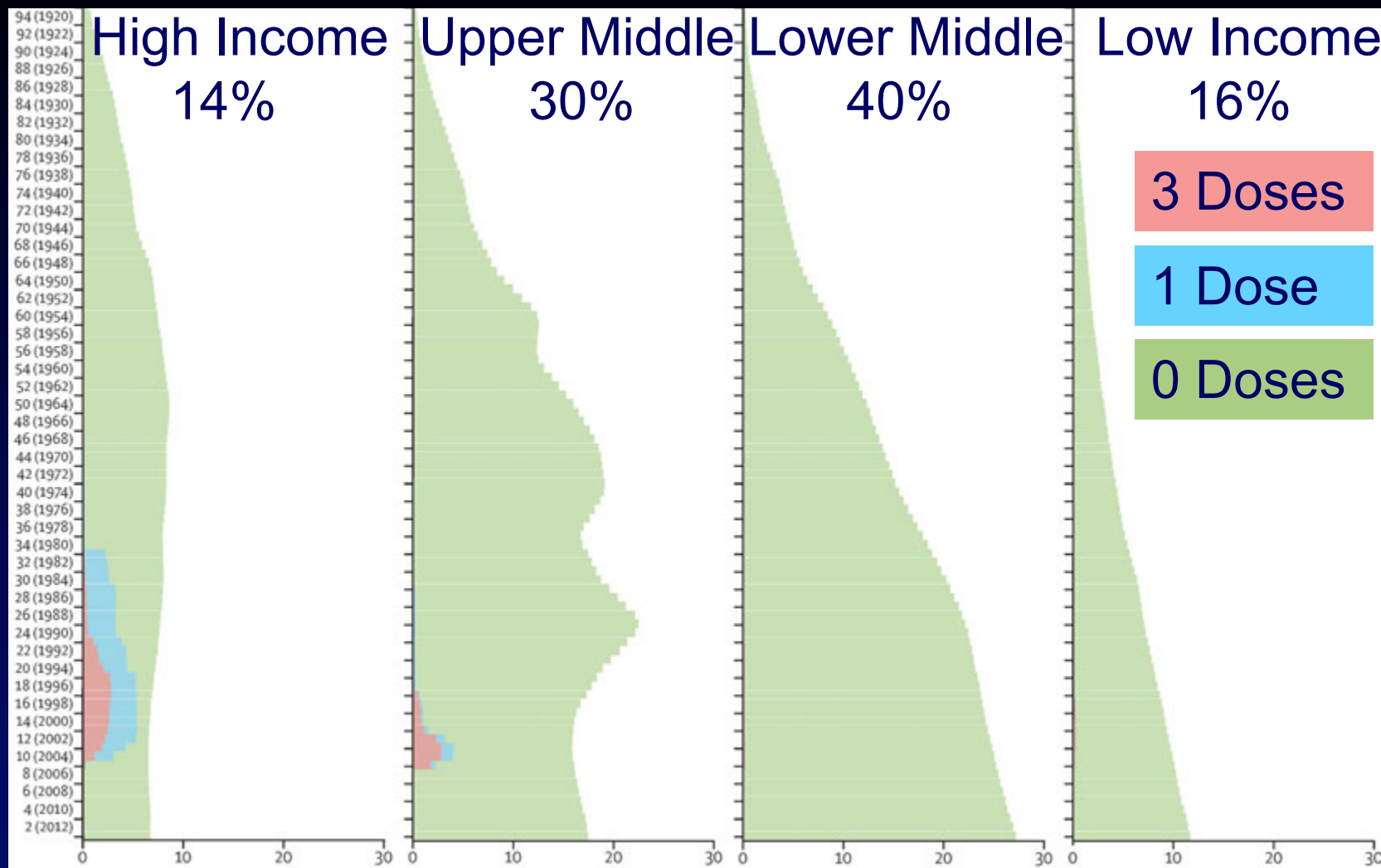
EXACT FIGURE UNKNOWN

Global Alliance for Vaccination and Immunization (GAVI)



Roll-Out (?) of HPV Vaccination

Age in Years (Birth Year)

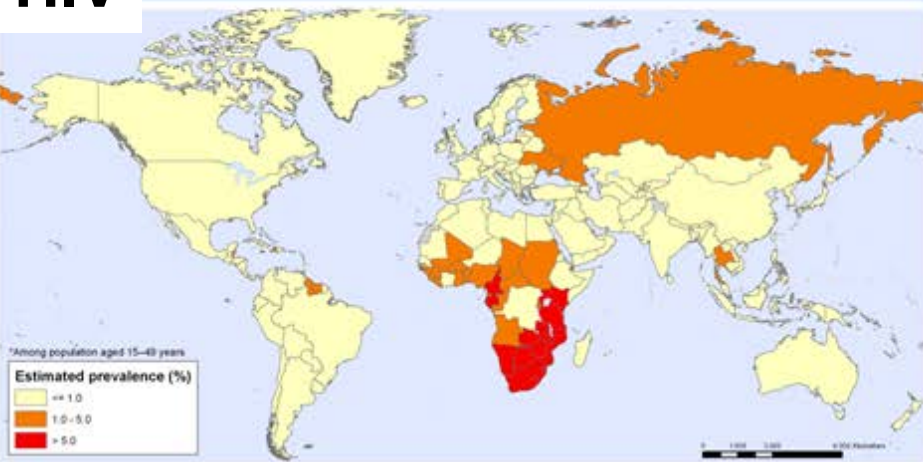


Number of Women (Millions)

Integrated Healthcare Delivery

HIV

HIV, estimated prevalence*, 2009

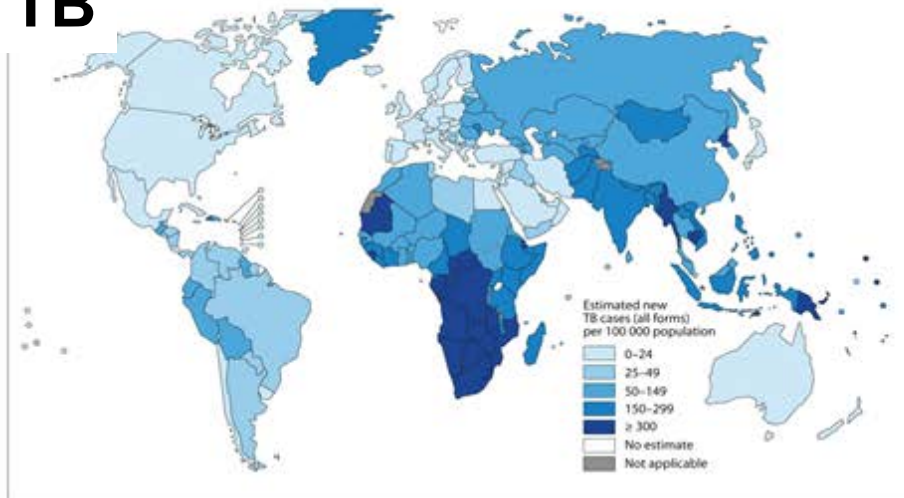


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Data Source: WHO/AIDS Map Production: Public Health Information and Geographic Information Systems (GIS) World Health Organization © WHO 2011. All rights reserved.

TB

Estimated tuberculosis (TB) incidence rates, 2011

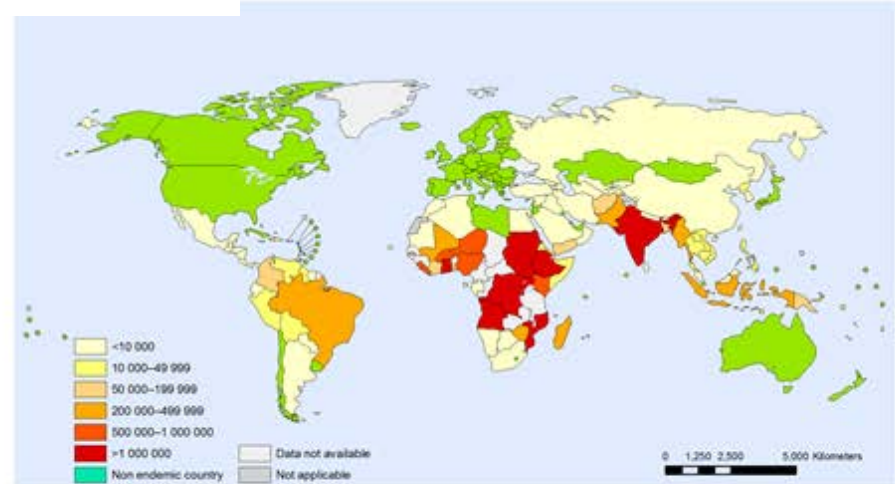


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Source: Global Tuberculosis Report 2012, WHO, 2012. © WHO 2012. All rights reserved.

Malaria

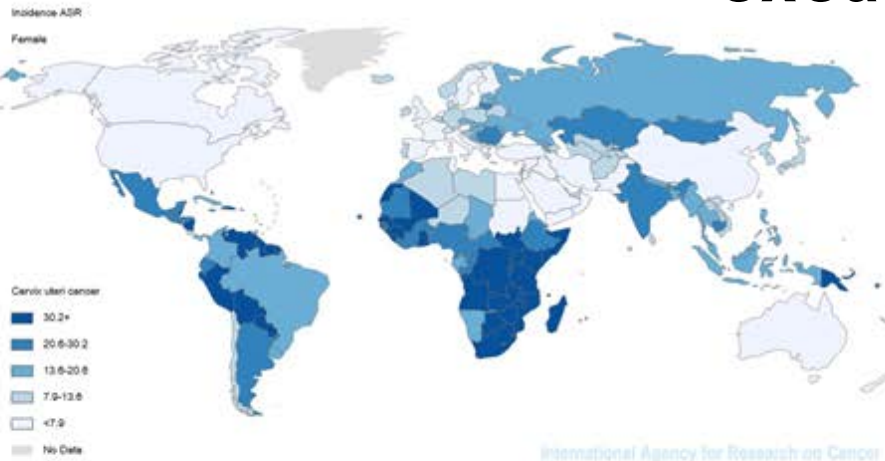
Number of malaria reported confirmed cases, 2010



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Data Source: World Health Organization Map Production: Public Health Information and Geographic Information Systems (GIS) World Health Organization © WHO 2012. All rights reserved.

CxCa



Source: GLOBOCAN 2012 (IARC) International Agency for Research on Cancer World Health Organization

“Knowing is not enough, we must apply.
Willing is not enough, we must do”
-Goethe

GC3's ONE Campaign:

All women deserve at least one high-quality preventive or curative service against cervical cancer in their lifetime.

