

Dissecting the “Know-Do” Gap

Implementation Science for HIV/STIs

August 2, 2013

Judith N. Wasserheit, MD, MPH
Professor of Global Health & Medicine
Vice Chair Department of Global Health
University of Washington

Dissecting the “Know-Do” Gap

- How do we **know** that we “know” something?
 - What kind of evidence is good enough?
 - When is an intervention/program ready for “prime time”?
- How do we **do** more of what we “know”
... and do it better?

Challenge: Design a multi-component HIV prevention package for sub-Saharan Africa using evidence-based interventions

Question: What goes into the package?

Randomized Controlled Trials



Results of 44 RCTs of 48 interventions to prevent sexual transmission of HIV

Type of Intervention	HIV prevention efficacy			Total
	Positive effect	Adverse effect	No effect	
<i>Behavioral & Microfinance</i>	---	---	8	8
<i>Diaphragm</i>	---	---	1	1
<i>Vaginal Microbicides</i>	1	1	12	14
<i>Male Circumcision</i>	3	---	1	4
<i>HIV Treatment</i>	1	---	---	1
<i>Pre-Exposure Prophylaxis (PrEP)</i>	4	---	3	7
<i>STI Treatment</i>	1	---	8	9
<i>Vaccine</i>	1	---	3	4
Total	11	1	36	48

Sources: Padian, et al. *AIDS* 2010;24:621-635. Abdool Karim, et al. *Science* 2010;329:1168-74. Grant, et al. *NEJM* 2010;363:2587-2599. Cohen, et al. *Lancet* 2011;377:1719. Thigpen, et al. *NEJM* 2012;367:423-434. Baeten et al. *NEJM* 2012; 367:399-410. Hillier, S. *CROI* 2012, Session 1, Paper 2. Marrazzo JM. *CROI* 2013, Session 8, Paper 26LB.

3 Reasons for Flat RCT Results



Wrong Concept



Inert Intervention



Design/conduct gone awry

Frequency of flat results varies by intervention type across STI/HIV RCTs

Intervention	Adherence, changing epidemic phase &/or intervention provision to controls in dilute form	Frequency of flat RCTs
Behavioral Diaphragm M&F condoms Microbicides STI treatment	Often important	44/65 (68%)
Male circumcision Vaccines	Rarely required	5/19 (26%)

Our Inconvenient Truth



Control Group



Out of Control Group

Criteria to Support Causality in Observational Epidemiological Studies

1. Strength of the association
2. Consistency of the association
3. Temporal relationship of the association
4. Dose-response relationship
5. Specificity of the association (not essential)
6. Biological plausibility of the association

Source: Advisory Committee to Surgeon General of PHS, 1964; Hill. AB
Proc. R. Soc. Med. 1965; 58:295-300.

Evidence-based Recommendations: An Approach to Rating Evidence Quality

<u>Category</u>	<u>Type of Evidence</u>
I.	≥ 1 well-designed RCT
II.	≥ 1 well-designed non-randomized CT; cohort, case-control, or multiple time series studies; or dramatic results from uncontrolled experiments
III.	Opinions of respected authorities based on clinical experience, descriptive studies or reports of expert committee

Source: UNAIDS/WHO Consultation on STD interventions for preventing HIV; what is the evidence? 2000, p. 42; US Preventive Services Task Force Guidelines for prevention of OIs.

Dissecting the “Know-Do” Gap

- How do we *know* that we “know” something?
- How do we *do* more of what we “know”
... and do it better?
 - How do we increase speed, fidelity, efficiency & relevant coverage in implementation & scale-up?
 - How do we monitor & iteratively refine interventions & programs?

US STD prevention program development cycles

Gonorrhea

- **1964:** Thayer-Martin culture medium developed
- **1964-1968:** 48 % jump in reported rates (159 to 236 per 100,000)
- **1968:** 6 demonstration projects established to screen asymptomatic women & treat partners of symptomatic men
- **1972:** National gonorrhea control program initiated (\$16 million)
- **1975:** Reported rates began sustained decline
- **1980s:** Declining interest in face of other STD epidemics

Chlamydia

- **1965:** Development of tissue culture
- **1984:** Non-culture tests introduced
- **1984-1988:** 26-fold jump in reported rates (3 to 82 per 100,000)
- **1985:** First national chlamydia prevention guidelines published
- **1985-1986:** 8 demonstration projects established to screen asymptomatic women & treat partners of asymptomatic men
- **1988:** Region X demonstration project established to screen asymptomatic women in family planning clinics in 4 states
- **1994:** National chlamydia prevention program initiated (\$8.3 million)
- **2000:** Chlamydia reporting nationwide

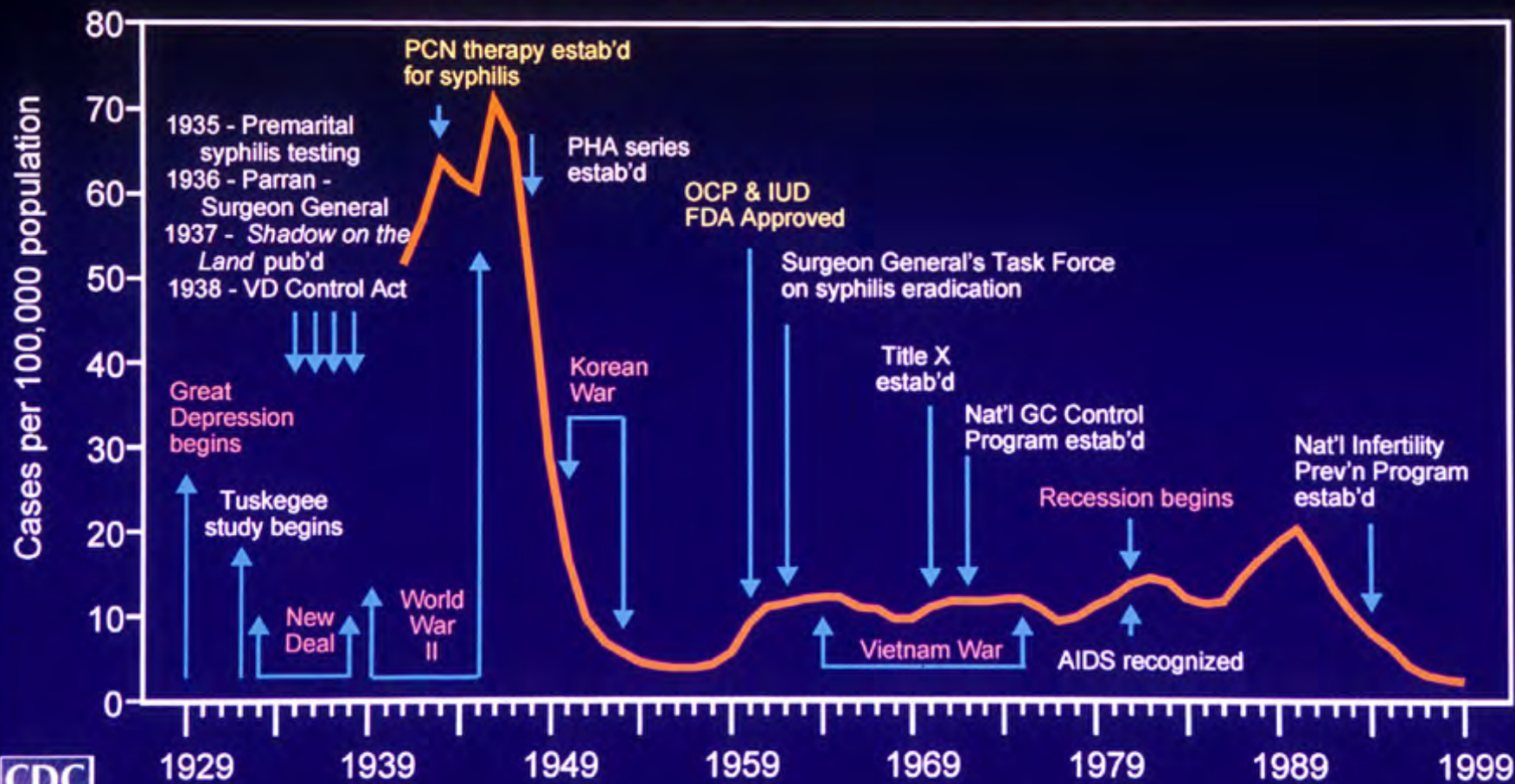


Syphilis: Complications & Costs

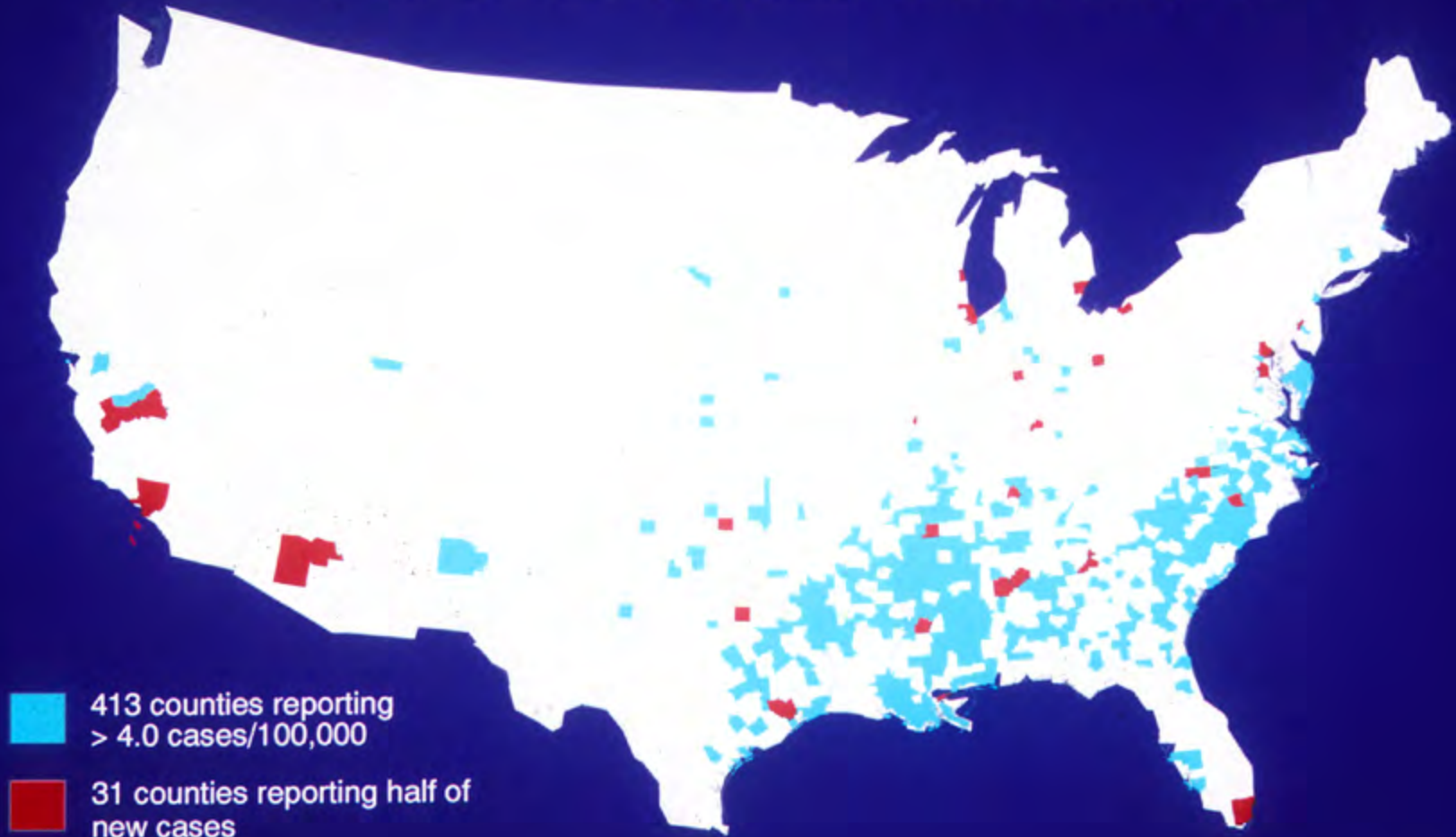
- Congenital infection in over 70% of exposed fetuses or perinatal death in up to 40% of cases, depending on timing of infection in mother
- 3 to 5 fold increased risk of HIV transmission
- Neurological, cardiac, bone & soft tissue disease
- Annual cost almost \$1 billion



U.S. Primary and Secondary Syphilis Rates Fell 95% from 1946 to 1956




Primary and secondary syphilis, United States, 1997*



*Note: 1997 P&S rate for the U.S. is 3.2 per 100,000 (HP2000 target = 4.0)

Source: CDC STD Surveillance System



The National Plan to Eliminate Syphilis from the United States



October 1999

Division of STD Prevention
National Center for HIV, STD, and TB Prevention
Centers for Disease Control and Prevention

Syphilis Elimination: Public Health Importance

(Stakeholder, policy & economic analyses – Steve Gloyd)

- Persistence of syphilis is a sentinel public health event
 - Identification & repair of breakdown in basic public health capacity
 - Rebuilding of trust in public health system
- Reduction of glaring health disparity
- Prevention of HIV transmission
- Improved infant health
- Annual cost-saving of almost \$1 billion

National Syphilis Elimination Plan

Five Key Strategies

- **Cross-Cutting Strategies**

1. Enhanced surveillance (Surveillance – Sarah Gimbel)
2. Strengthened community involvement and partnerships (Dissemination research)

- **Intervention Strategies** (OR, QI, qualitative HSR – Archis Ghate, Pam Kohler, James Pfeiffer)

3. Rapid outbreak response
4. Expanded clinical and laboratory services
5. Enhanced health promotion

Progress on Syphilis Elimination

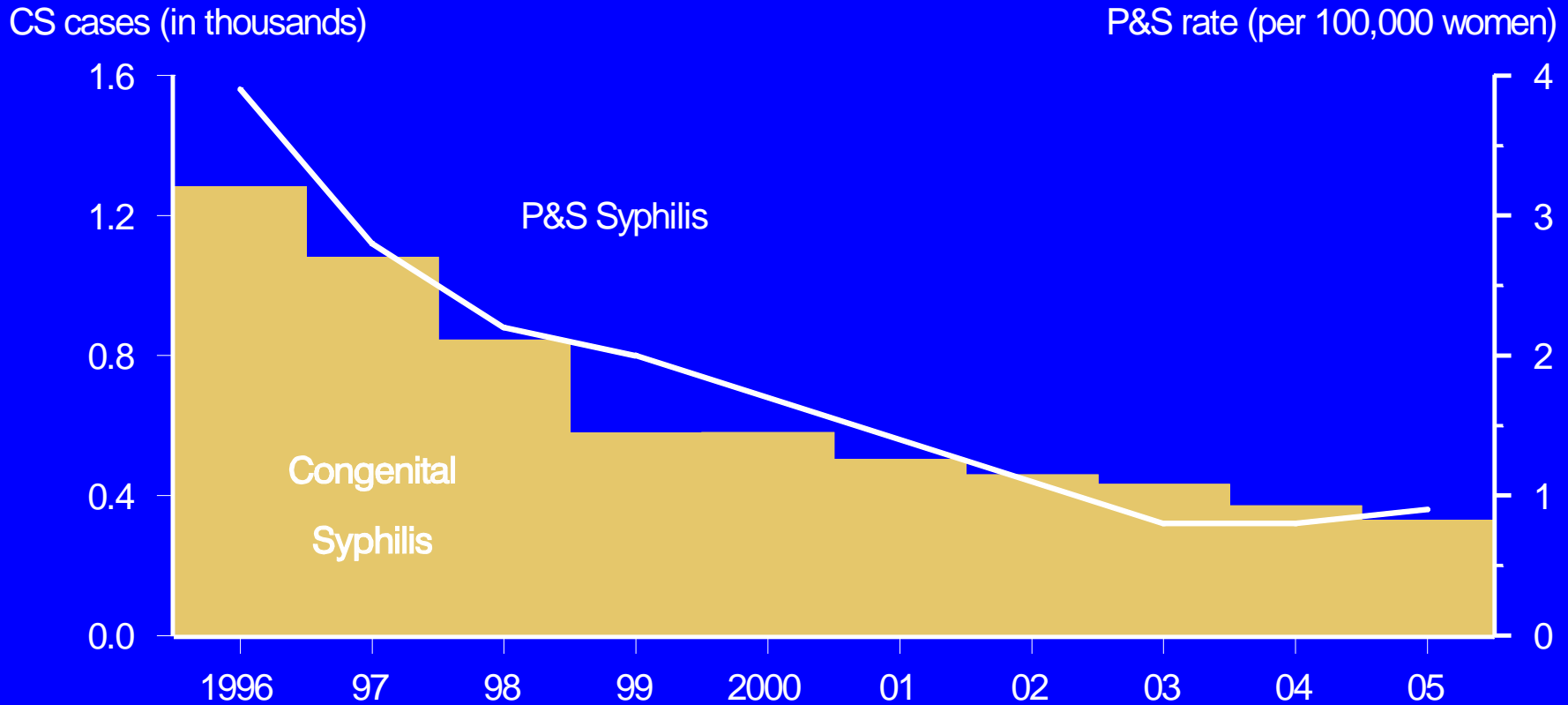
(Impact evaluation & measuring effectiveness – Marie Ng, Jim Hughes)

	2011	2010	2005	2000	1999	1998	1997
P&S syphilis rate (per 100,000 population)*	4.5	4.5	3.0	2.2	2.5	2.6	3.2
% syphilis-free counties	68.5%	69%	78%	80%	79%	78%	75%
Number of counties responsible for 50% of new cases	26 (& 2 cities)	27	19	22	25	28	31
Black:White rate ratio	7:1	8:1	5:1	21:1	30:1	34:1	43:1
Male:Female rate ratio	8.2:1	7.2:1	5.7:1	1.5:1	1.5:1	1.3:1	1.2:1

*US P&S syphilis rates fell 89.7% 1990-2000 and rose >100% 2000-2010

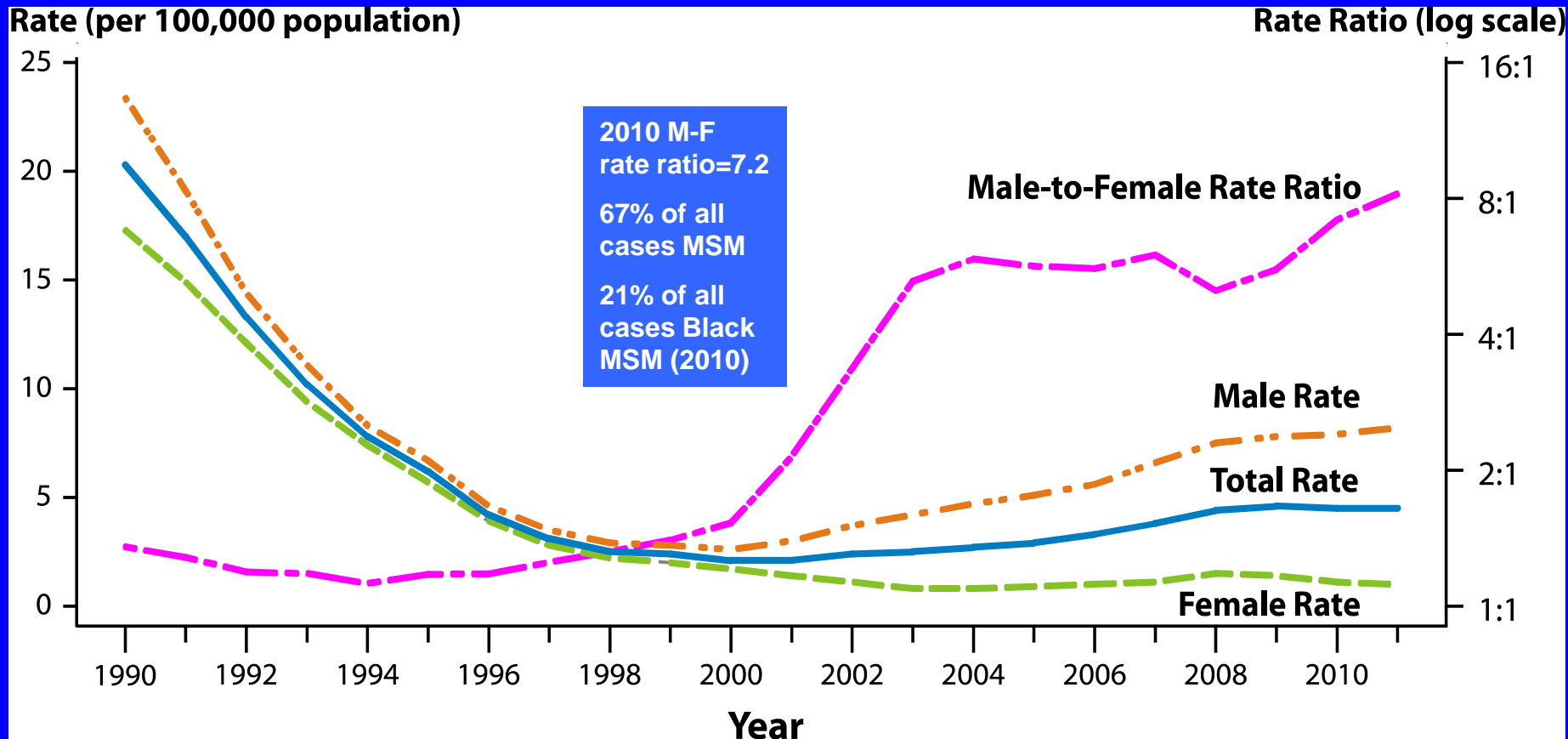
Source: CDC STD surveillance

75% drop in US congenital syphilis rates* 1996–2005 paralleling declines in P&S syphilis rates in women

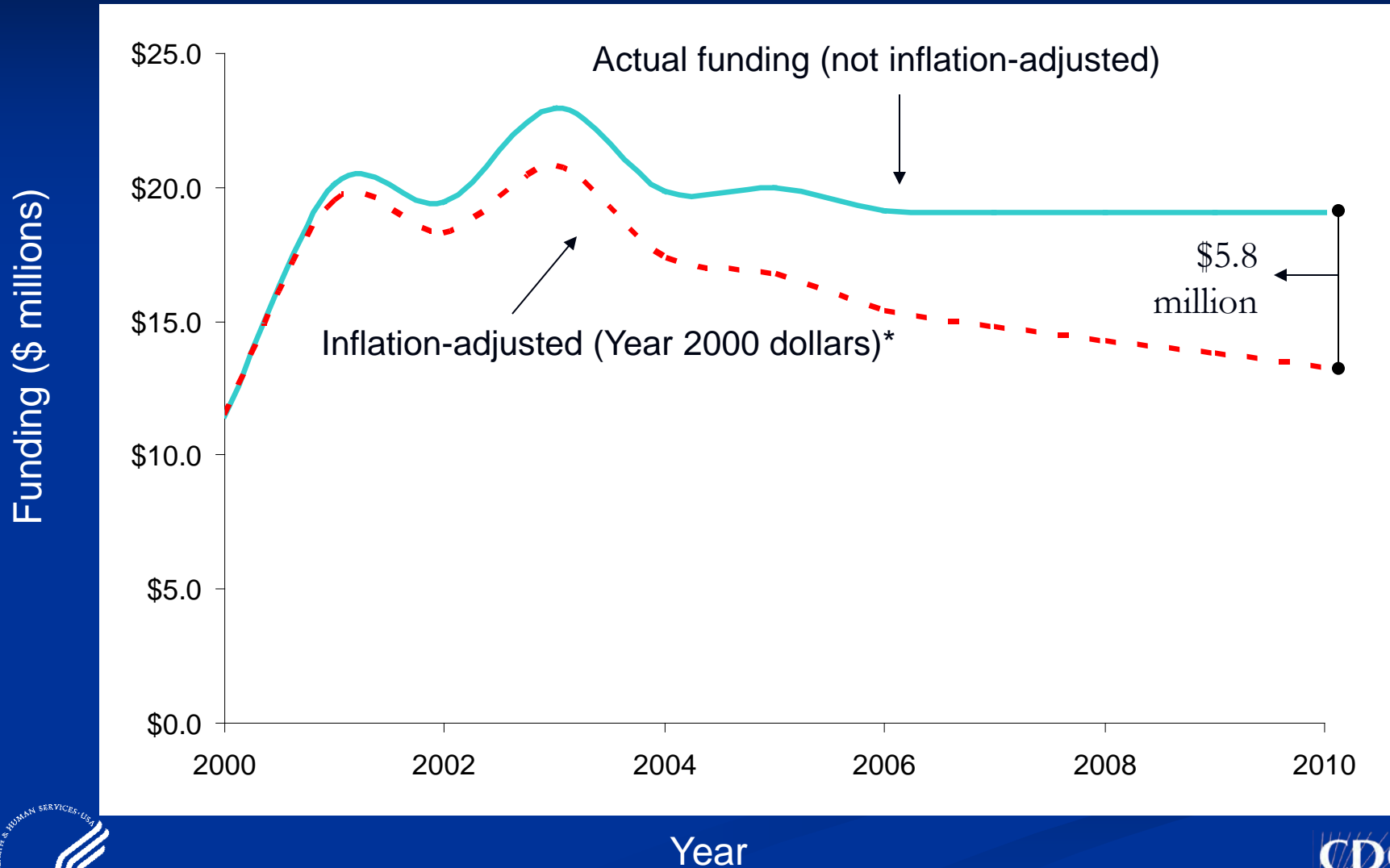


*CS rates fell from 32.9 to 8.2 cases/100,000 live births (1996 - 2005); then rose 25% to 10.3 cases/100,000 LB by 2008. CS rates fell 19% to 8.5/100,000 LB by 2011 w/ a 33% drop in P&S rates in women. (Source: CDC STD Surveillance)

U.S. Male:Female P&S Syphilis rate ratio rose ~7-fold (1.2 to 8.2) from 1996 to 2011



Actual & inflation-adjusted Syphilis Elimination funding, 2000-2010



*Adjusted to 2000 US dollars using biomedical research and development price index (BRDPI). Predicted values applied for BRDPI in years 2007-2010.



Challenges for the SE Effort

- Level Funding
 - Responding to new epidemics while
 - Maintaining gains among groups first targeted
- Ensuring quality surveillance & epi analysis
- Ensuring availability of quality clinical, lab, & partner services in public & private sectors
- Multi-level factors associated with risk for syphilis & other STDs
 - Tailoring Interventions to different populations
 - Evaluating & adapting efforts (2006 revised SEE Plan)



A dark blue world map is visible in the background of the top portion of the slide, showing the continents of North America, South America, Africa, Europe, Asia, and Australia.

The ***science*** of implementation & scale
up is critical to global health
(including HIV/STI prevention & control)

This is the scientific frontier that
will define what we can achieve in
eliminating health disparities