

MTN Annual Meeting

The HIV Prevention Landscape

Carl W. Dieffenbach, Ph.D.

Director, Division of AIDS

April 22, 2009



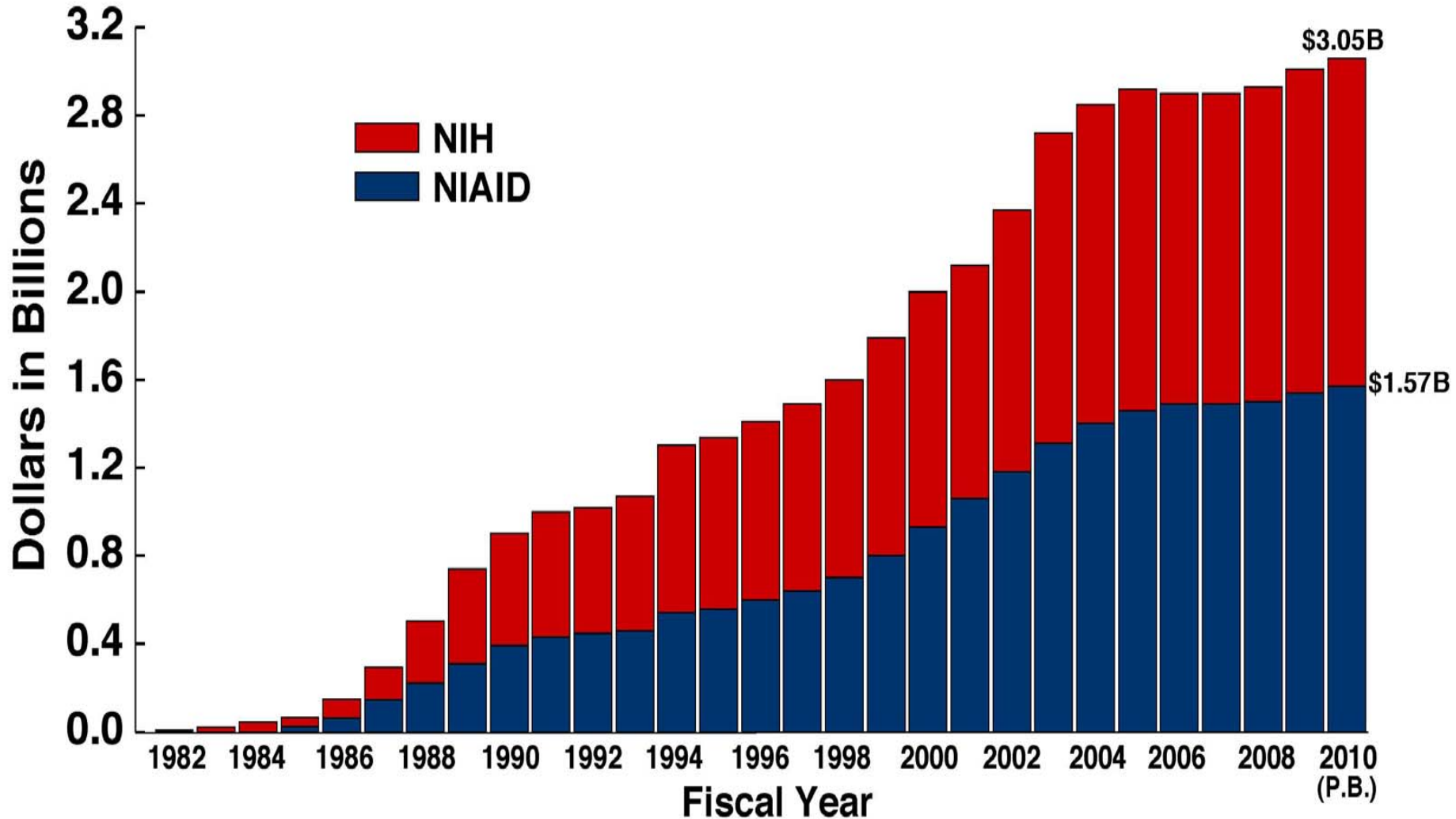
Vision for HIV Research

- **Foster research that unravels the fundamental processes governing host/virus interactions**
- **Based upon these findings, identify and test ways to:**
 - prevent HIV infection
 - treat HIV disease
 - cure HIV infection

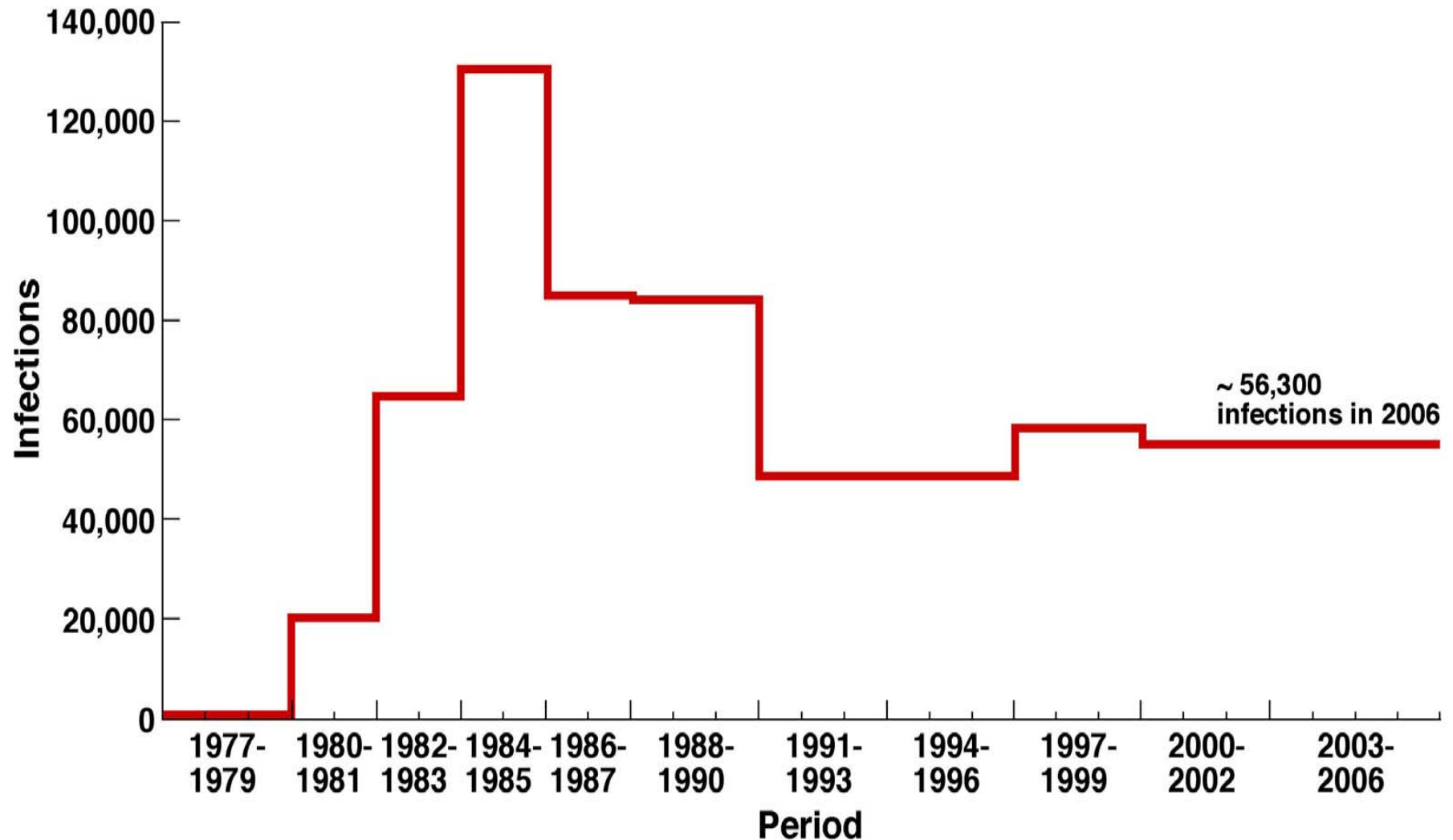
Current State of HIV Research

- **Shifting focus of vaccine research from development to discovery**
- **Several important prevention studies underway or planned (i.e., PrEP, VOICE, HPTN 052, HPTN 061, HPTN 064, HVTN 906)**
- **Treatment regimens continue to evolve with fewer side effects**
- **Untreated HIV infection appears linked to underlying pathology, premature aging, and increased morbidity**
- **Challenges remain due to significant budgetary constraints**

NIH and NIAID AIDS Research Funding FY 1982-2010 (PB)



Estimated Number of New HIV Infections Among Adults/Adolescents, USA, 1977-2006



Source: CDC/JAMA 300:520, 2008. Extended-back-calculation model, 50 US states and the District of Columbia.

Health Care Costs of HIV Infection

- **Each new HIV infection ultimately costs \$300,000 in health care expenses**
- **At 56,300 new HIV infections a year in the U.S., \$17B in health care costs added annually**

HIV Prevention Research: Guiding Principles

- **Multiple strategies needed to assemble a well-rounded “prevention toolkit.”**
- **No one prevention strategy will be 100% effective, appropriate to or accepted by everyone.**
- **Multiple prevention strategies must be evaluated in different populations, domestically and globally, to determine the best combinations for a given population.**

Approaches to HIV Prevention

- Education and behavior modification
- Condoms, and other barrier methods
- Treatment/prevention of drug/alcohol abuse
- Clean syringes (i.e. needle exchange programs)
- Interruption of mother-to-child transmission
- Circumcision
- HIV/STI Testing
- Antiretroviral treatment as prevention
- Pre-exposure prophylaxis (PrEP)
- Topical microbicides
- Vaccination

Integration of Treatment & Prevention

- **Use of antiretrovirals as microbicides**
- **Pre-exposure prophylaxis**
- **Universal voluntary testing and treatment**

Promising Results from HPTN 035

- **Results of phase II/IIb study of PRO 2000 (0.5%) & BufferGel announced in February**
- **Both products safe**
- **PRO 2000: 30% effective (33% effectiveness would have been considered statistically significant)**
- **BufferGel: no effect on HIV transmission**
- **First human clinical study suggesting that a microbicide --a gel, foam or cream -- may prevent male-to-female sexual transmission of HIV infection when applied topically inside the vagina**

Topical Microbicides: Future Directions

■ PRO 2000

- Ongoing study of PRO 2000 (0.5%) conducted by Microbicides Development Programme; results expected by end of this year
- Rectal safety study of PRO 2000 planned

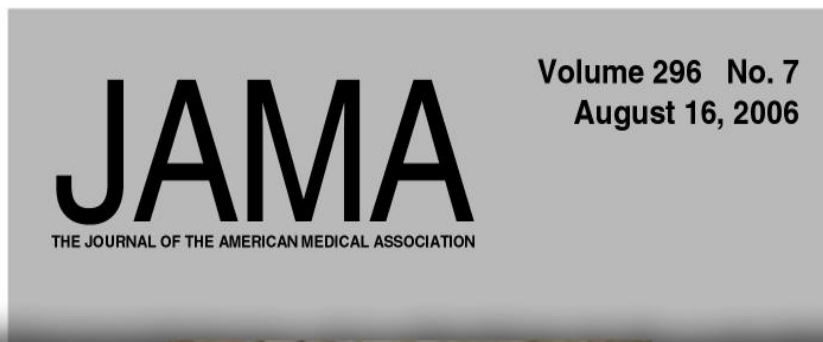
■ Tenofovir

- CAPRISA 004: phase IIB trial, 1% Tenofovir gel vs. placebo in South Africa; results will be available next year

■ Other Research Plans

- Devise more acceptable delivery methods
- Expand efforts to develop rectal microbicides
- Develop products with outstanding safety and resistance profiles
 - Explore combinations
 - Alternative microbicide strategies e.g., modulation of female reproductive tract (FRT) homeostasis
 - Vaccines and microbicides
- Evaluate novel clinical trial methodologies

A Role for Pre-Exposure Chemoprophylaxis of HIV Infection?



Preexposure Prophylaxis for HIV: Unproven Promise and Potential Pitfalls

AY Liu, RM Grant & SP Buchbinder

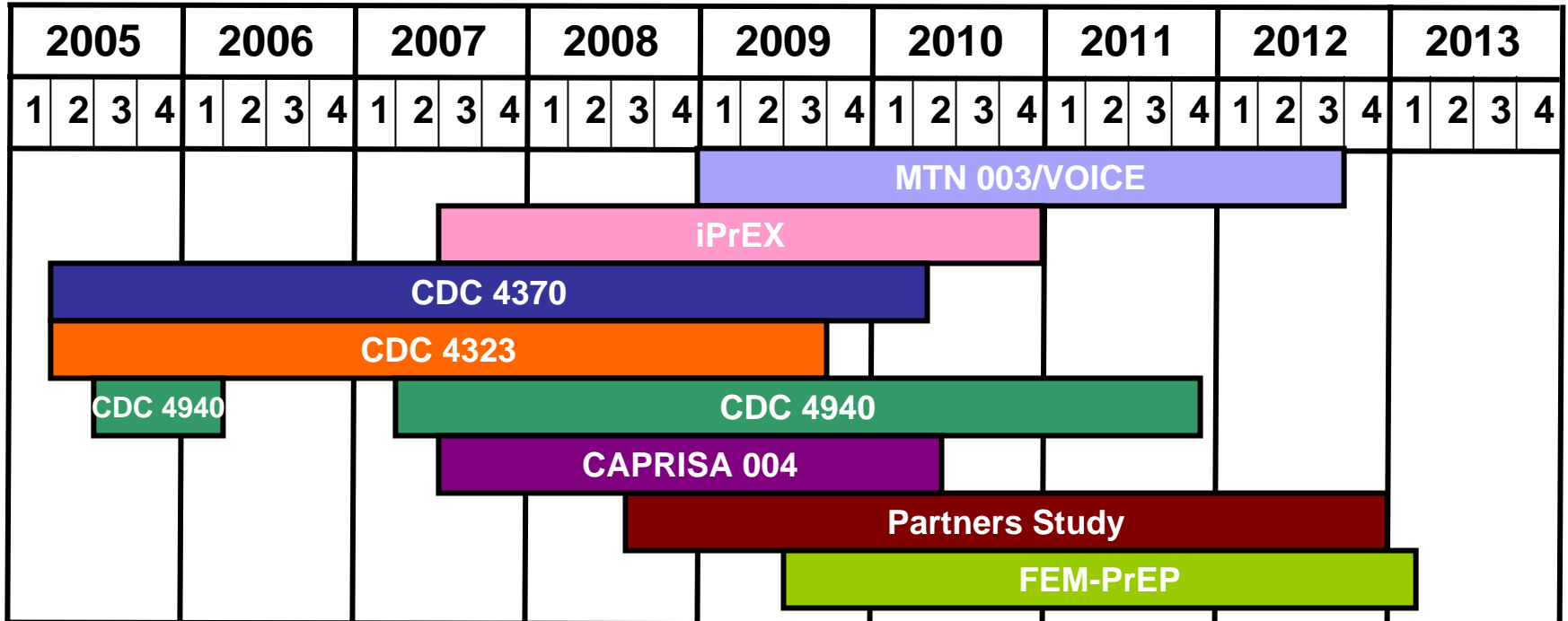


Chemoprophylaxis of HIV Infection: Moving Forward with Caution

RM Grant & MA Wainberg

Will people at risk adhere? The importance of understanding behavior!

Timeframe for Ongoing & Planned PrEP Trials



MTN 003/VOICE – Phase IIb, topical Tenofovir, oral Tenofovir, oral Truvada vs. placebo (multi-country)

iPrEX – Phase III, Truvada among MSMs in Peru, Ecuador, South Africa, Brazil, Thailand, US

CDC 4370 –Phase II/III, daily Tenofovir or placebo among IDUs in Thailand

CDC 4323 – Phase II safety study, daily Tenofovir or placebo among MSMs in US

CDC 4940 – Phase III, daily Truvada or placebo in Botswana

CAPRISA 004 – Phase III, 1% Tenofovir gel or placebo in South Africa

Partners Study – Phase III, daily Tenofovir, Truvada, or placebo in discordant heterosexual couples (Kenya and Uganda)

FEM-PrEP – Phase III, daily Truvada or placebo in high risk women (multi-country)

PrEP Future Directions

- **First, prove the concept**
- **Establish improved dosing schedules to maximize adherence**
- **Engage partners in operations research social marketing**
- **Develop and test new agents, combinations and delivery systems**
 - Safe, potent, longer half-lives
 - Non-overlapping resistance profiles with existing ART
 - Improved animal models

Voluntary “Test and Treat” Concept

THE LANCET

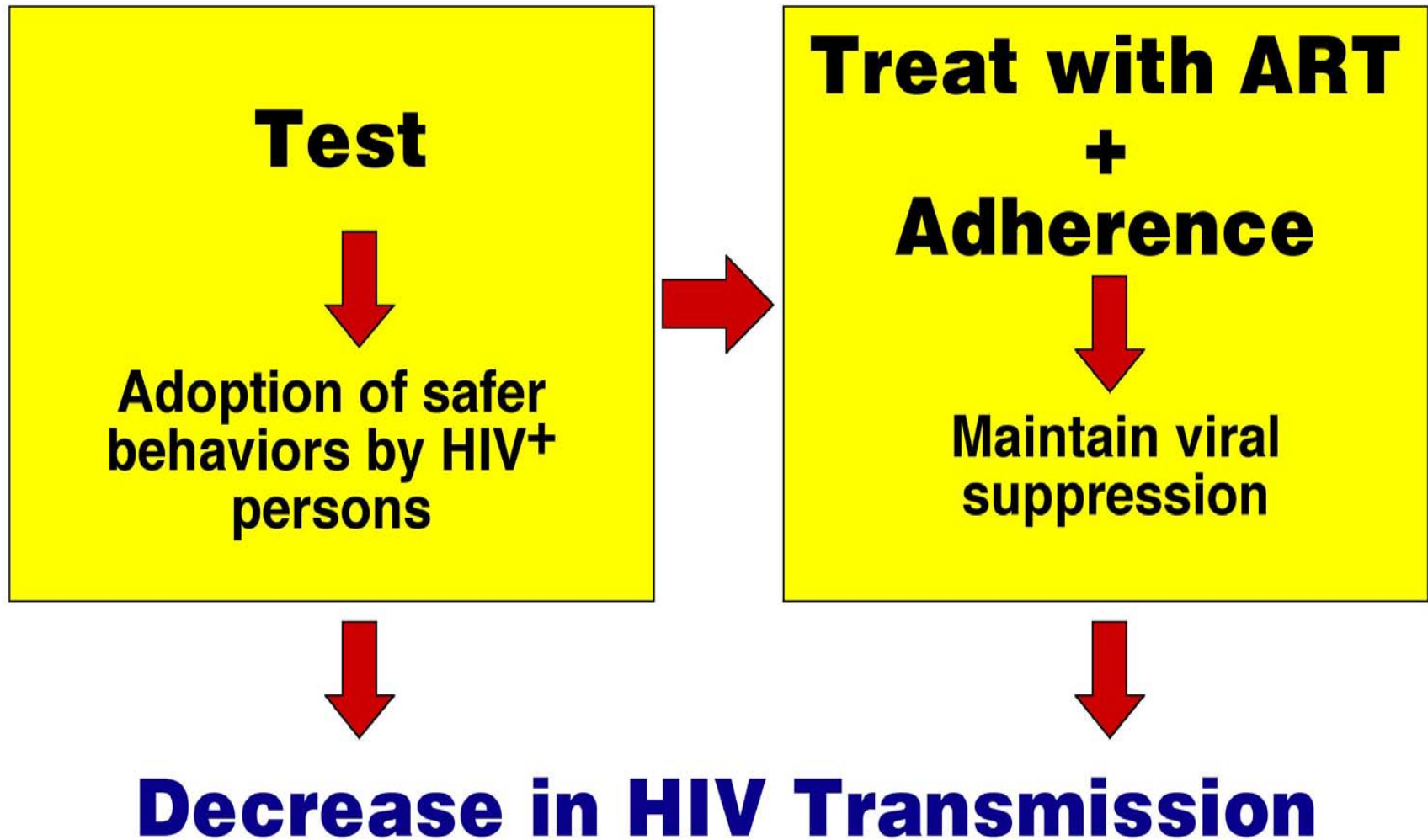
Available online November 27, 2008

Universal Voluntary HIV Testing with Immediate Antiretroviral Therapy as a Strategy for Elimination of HIV Transmission: a Mathematical Model

RM Granich et al.

- **Model indicates that universal and annual voluntary HIV testing followed by immediate antiretroviral therapy treatment (irrespective of clinical stage or CD4 count) could reduce new HIV cases by 95% within 10 years**
- **Concerns: feasibility, protection of individual rights, drug resistance, toxicity, financing**

Test and Treat Hypothesis



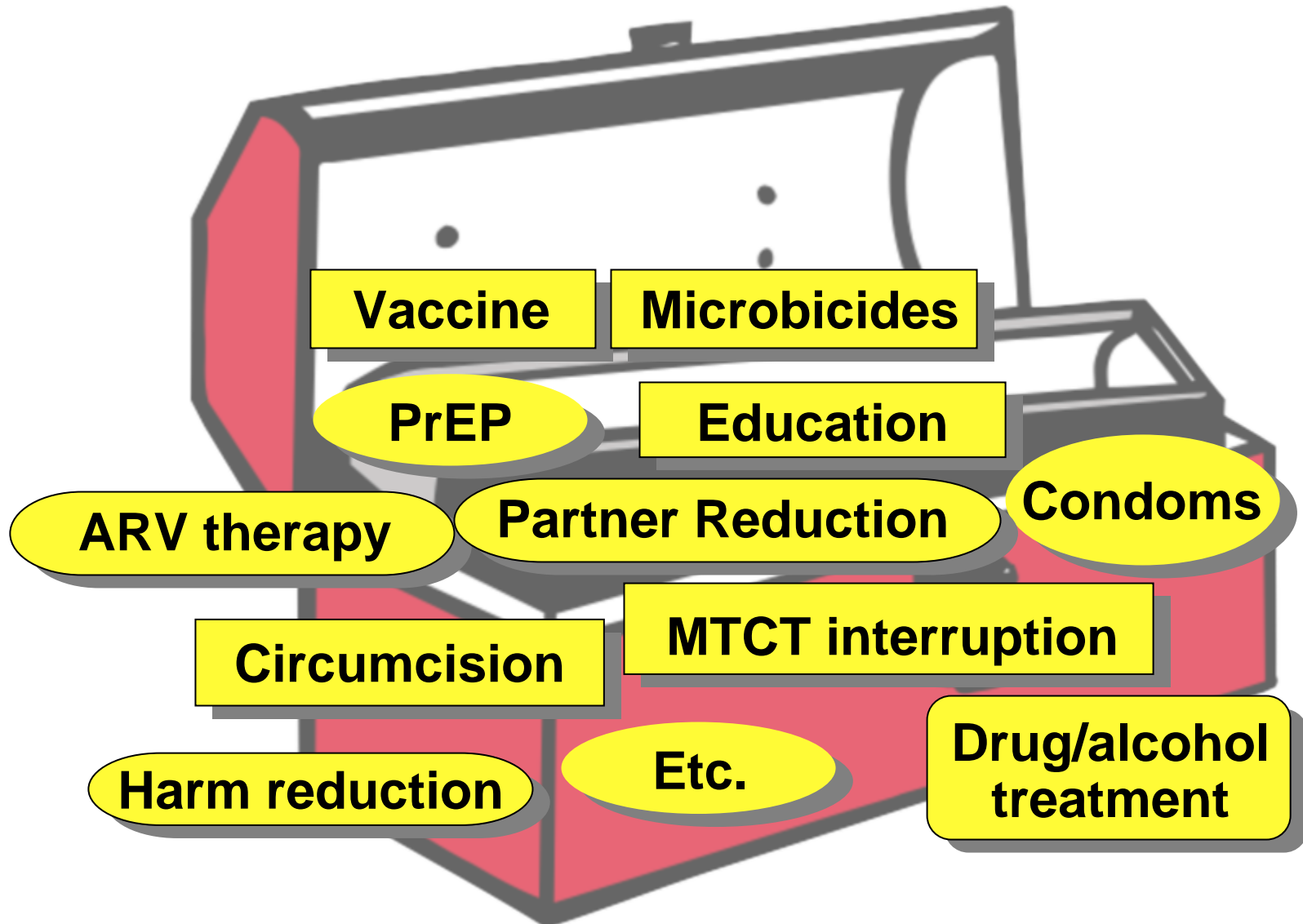
Pilot the Voluntary Test and Treat Concept

- **Design in progress**
 - NIH working with CDC
- **Goals**
 - To compare current community standards for testing and treating to protocol-enhanced programs
 - Opt-out testing
 - Linkage of HIV+ people to care
 - Antiretroviral therapy
- **Will assess critical research questions, including cost effectiveness**
- **Cost for three-year pilot in 2 cities**
 - \$10 million per year

Population-Specific Prevention Research Activities in the U.S.

- **HIV Prevention Trials Network Domestic Research Agenda**
- **Three new pilot studies:**
 - Two observational studies of women in defined geographic areas at high risk of HIV
 - Multi-faceted intervention in Black MSM
- **Goal: To determine how we can best reach at-risk populations in the U.S. and tailor interventions to more effectively prevent HIV**

A Comprehensive HIV Prevention “Toolbox”



Questions?
