HIV Prevention – The DAIDS Perspective

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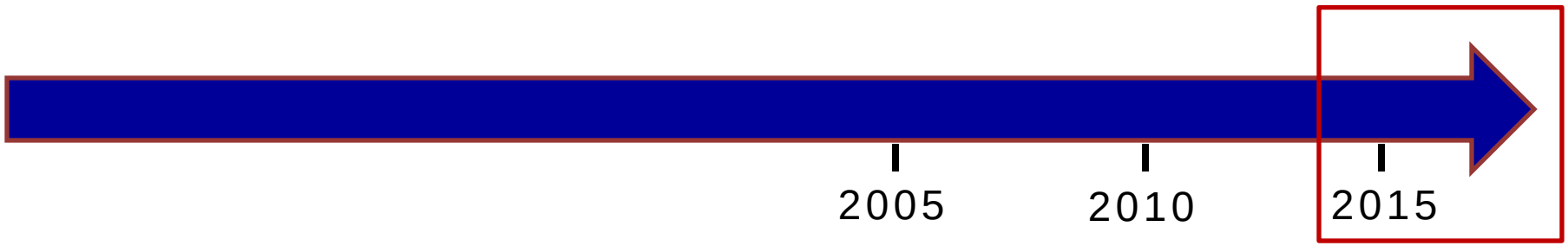
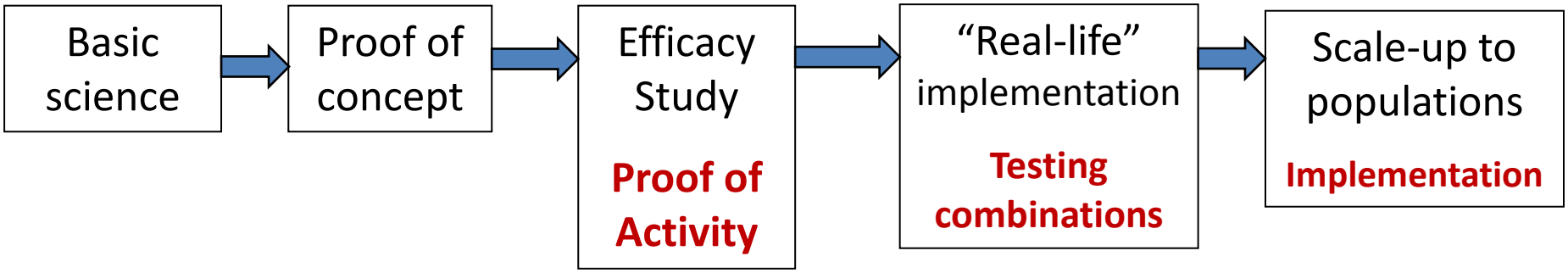
October 29, 2013

The New Era of AIDS Research -- Time of Great Opportunity and Significant Resource Constraints

- **Prevent HIV Infections**
- **Cure HIV infection**
- **Prevent and treat HIV co-morbidities**
- **Assist in taking interventions to scale**

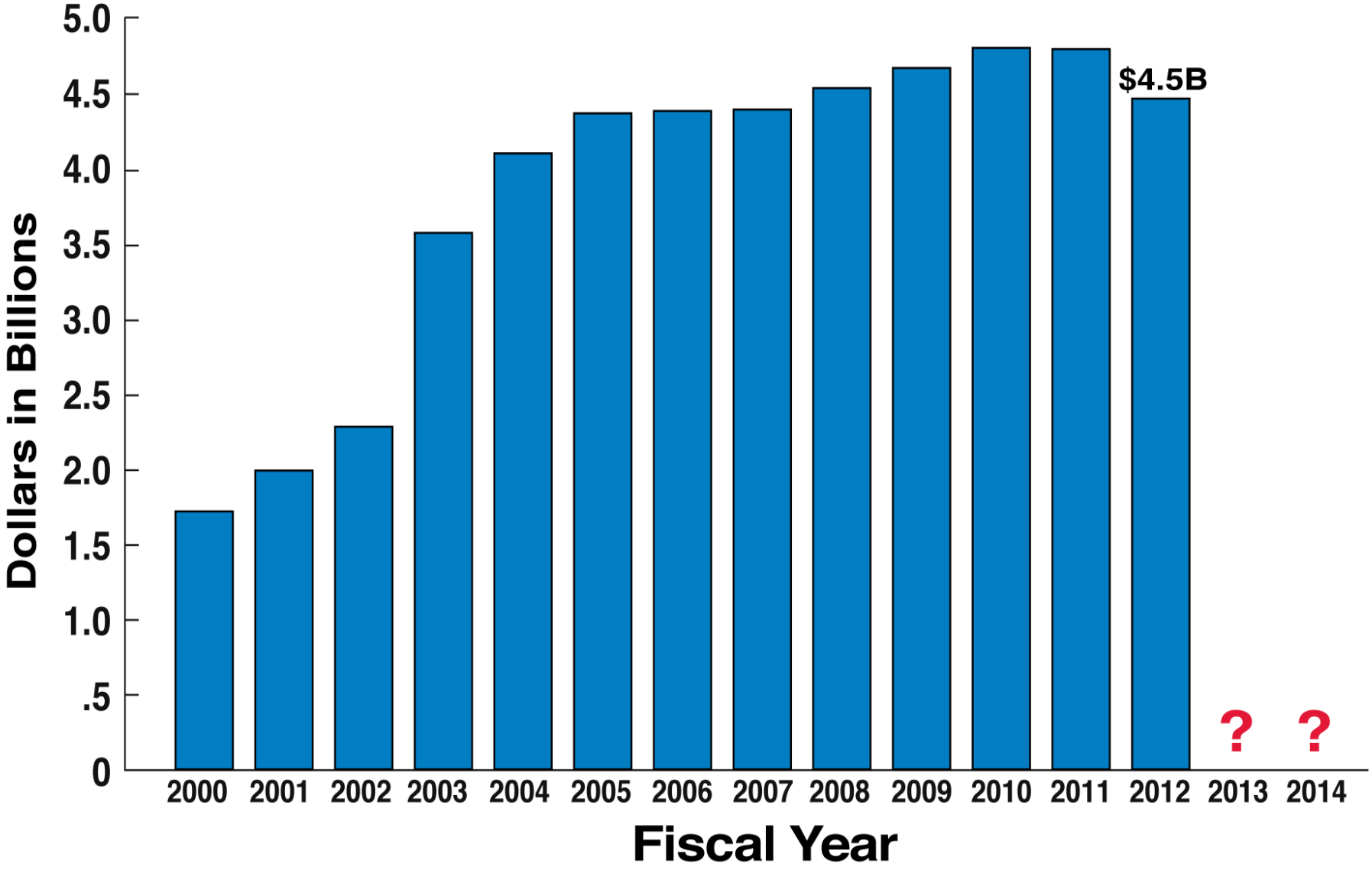


Discovery→Delivery: The Path to Combination Prevention



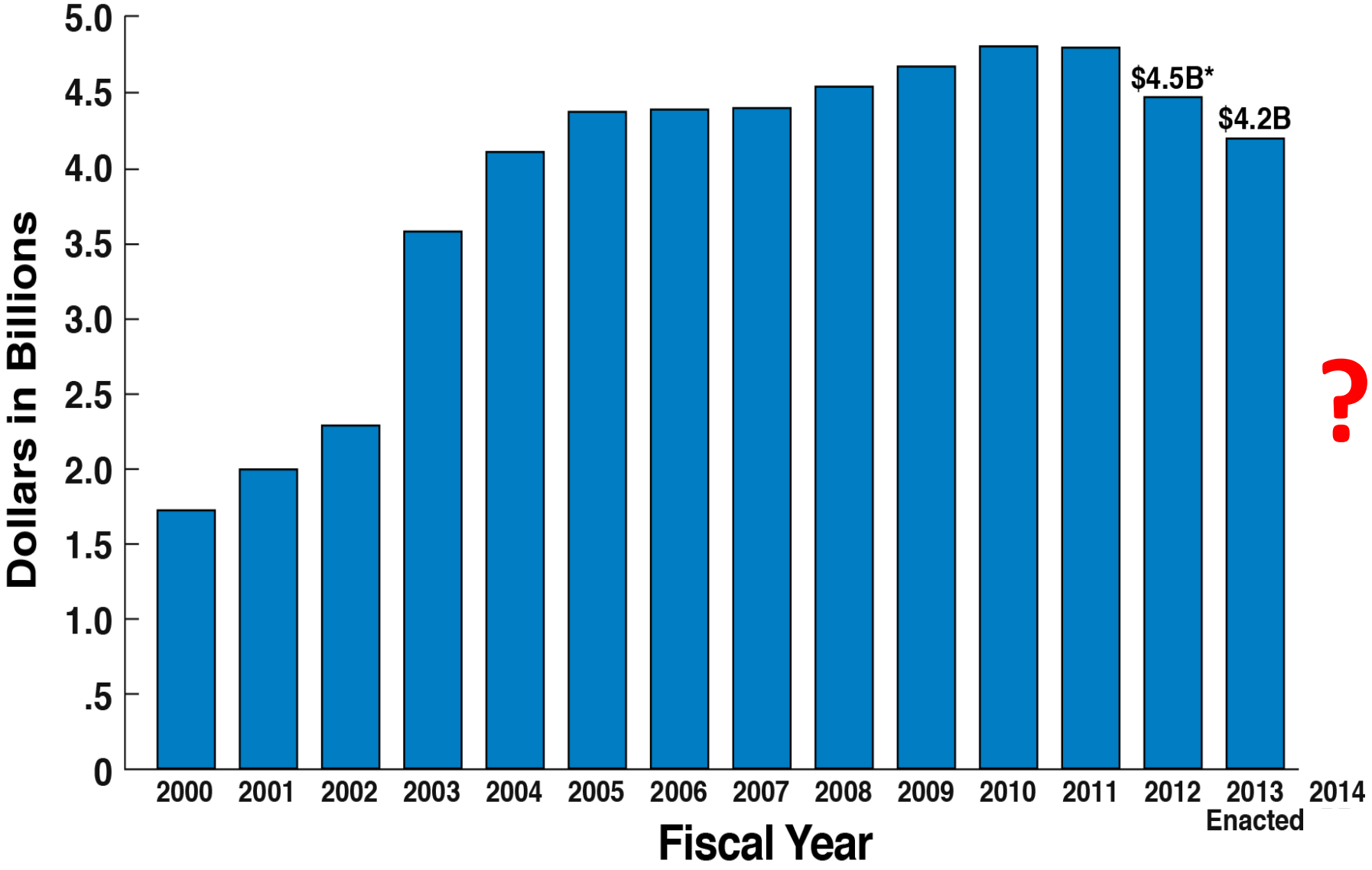
The art of combination prevention is the integration of an essential set of focused, single approaches into an integrated combination prevention program

NIAID Funding History, 2000-2014



*Beginning in FY 2012, budget no longer passes through funds to the Global Fund.

NIAID Funding History, 2000-2014



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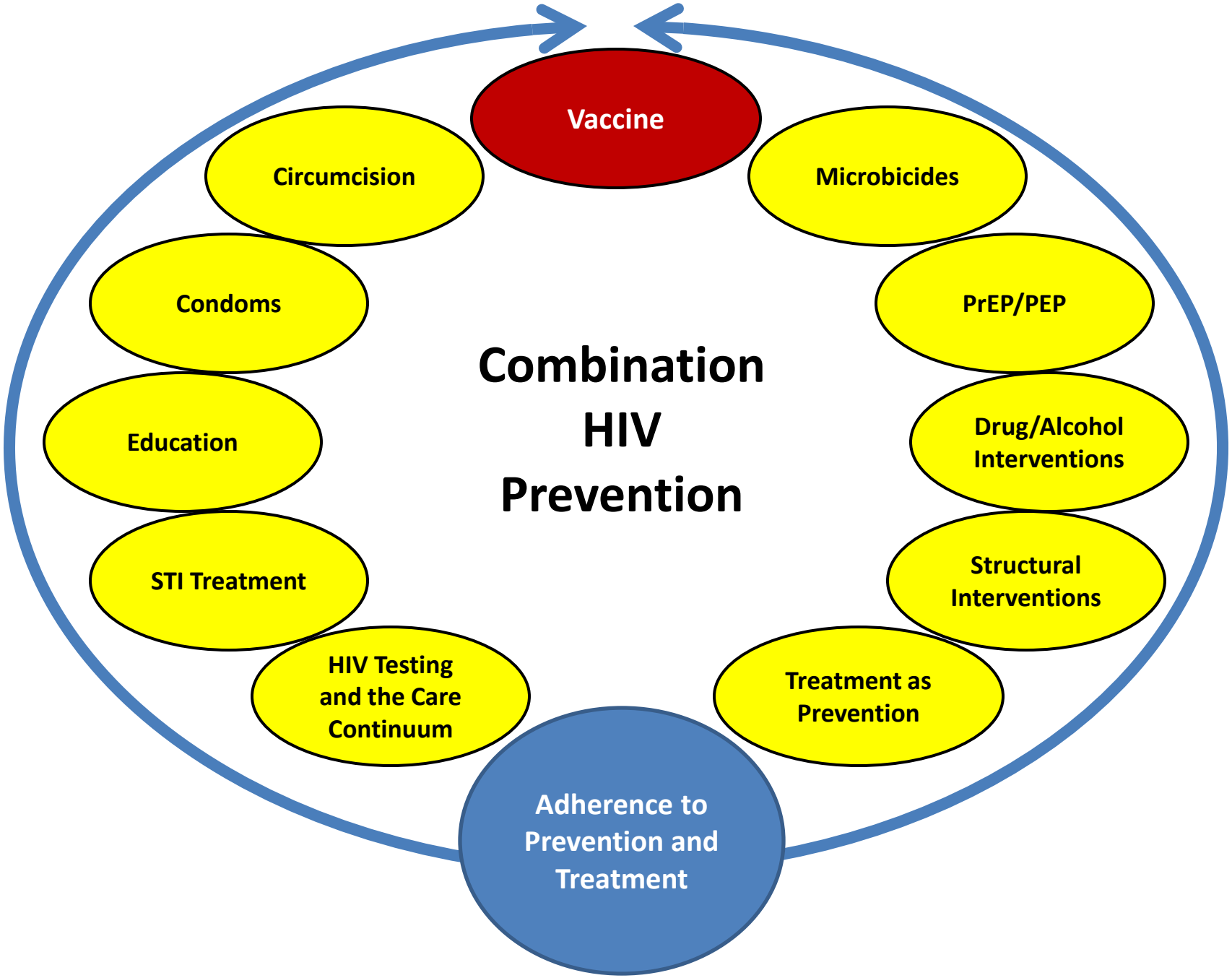
What Data Has Accumulated?

- **Adult Male Circumcision—3 studies**
- **RV 144**
- **HVTN 505**
- **CAPRISA 004**
- **VOICE**
- **IPrEX**
- **Partners PrEP**
- **Fem-PrEP**
- **CDC TDF2**
- **Bangkok Tenofovir Study**
- **Project Accept**
- **HPTN 052**

Biomedical Interventions

Human Behavior


Vaccine
Microbicides
PrEP/PEP
Drug/Alcohol Interventions
Structural Interventions
Treatment as Prevention
Adherence to Prevention and Treatment
HIV Testing and the Care Continuum
STI Treatment
Education
Condoms
Circumcision
Combination HIV Prevention

HIV Prevention Research: Guiding Principles

- No single prevention strategy is enough
- HIV testing is the entry point for individually-focused prevention interventions
- HIV treatment is a critical component of prevention
- Know your epidemic and select interventions based upon effectiveness and cost
- Develop strategies to create interest and demand for HIV prevention
- Evolve prevention strategies with changes in the epidemic

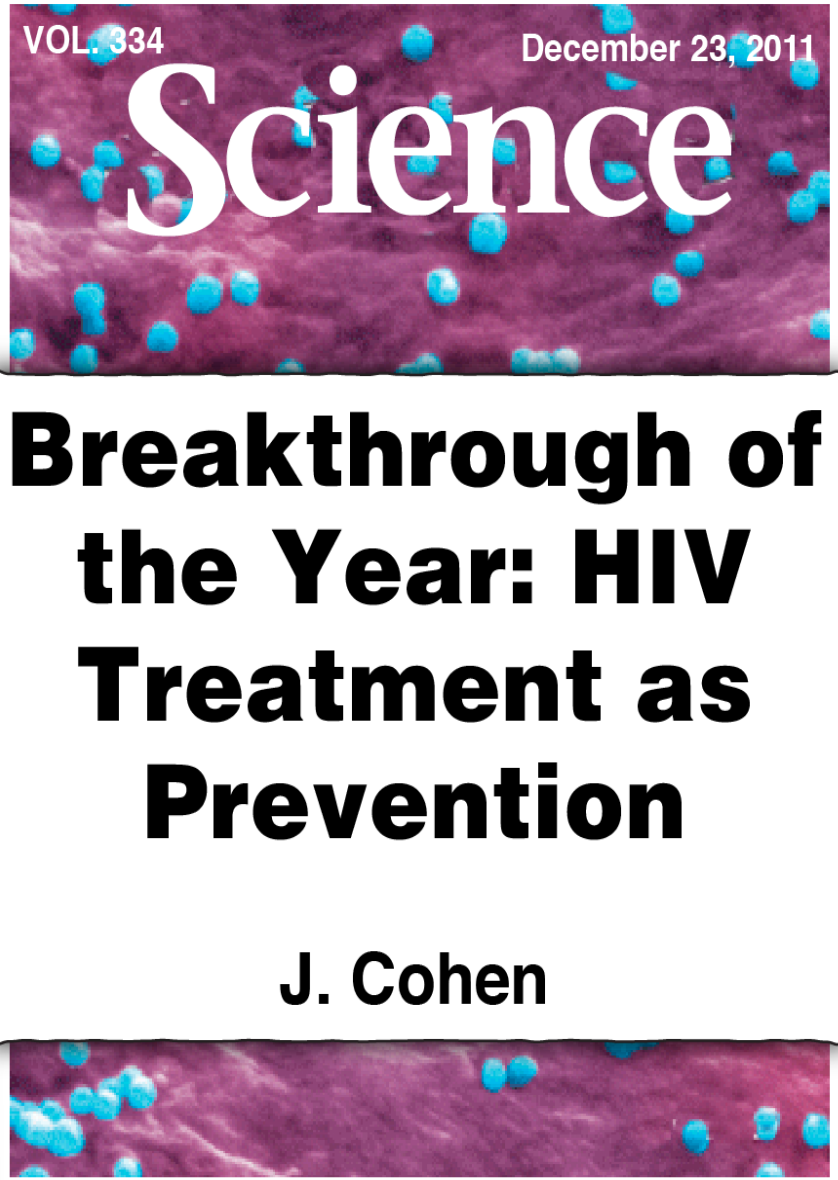
The New England Journal of Medicine

Established in 1812 as THE NEW ENGLAND JOURNAL OF MEDICINE AND SURGERY

Volume 365 August 11, 2011 Number 6

Prevention of HIV-1 Infection with Early Antiretroviral Therapy

HPTN 052 Study Team



Breakthrough of the Year: HIV Treatment as Prevention

J. Cohen

U.S. Department of Health and Human Services

NIH News

National Institutes of Health

National Institute of Allergy and Infectious Diseases (NIAID)

http://www.niaid.nih.gov/

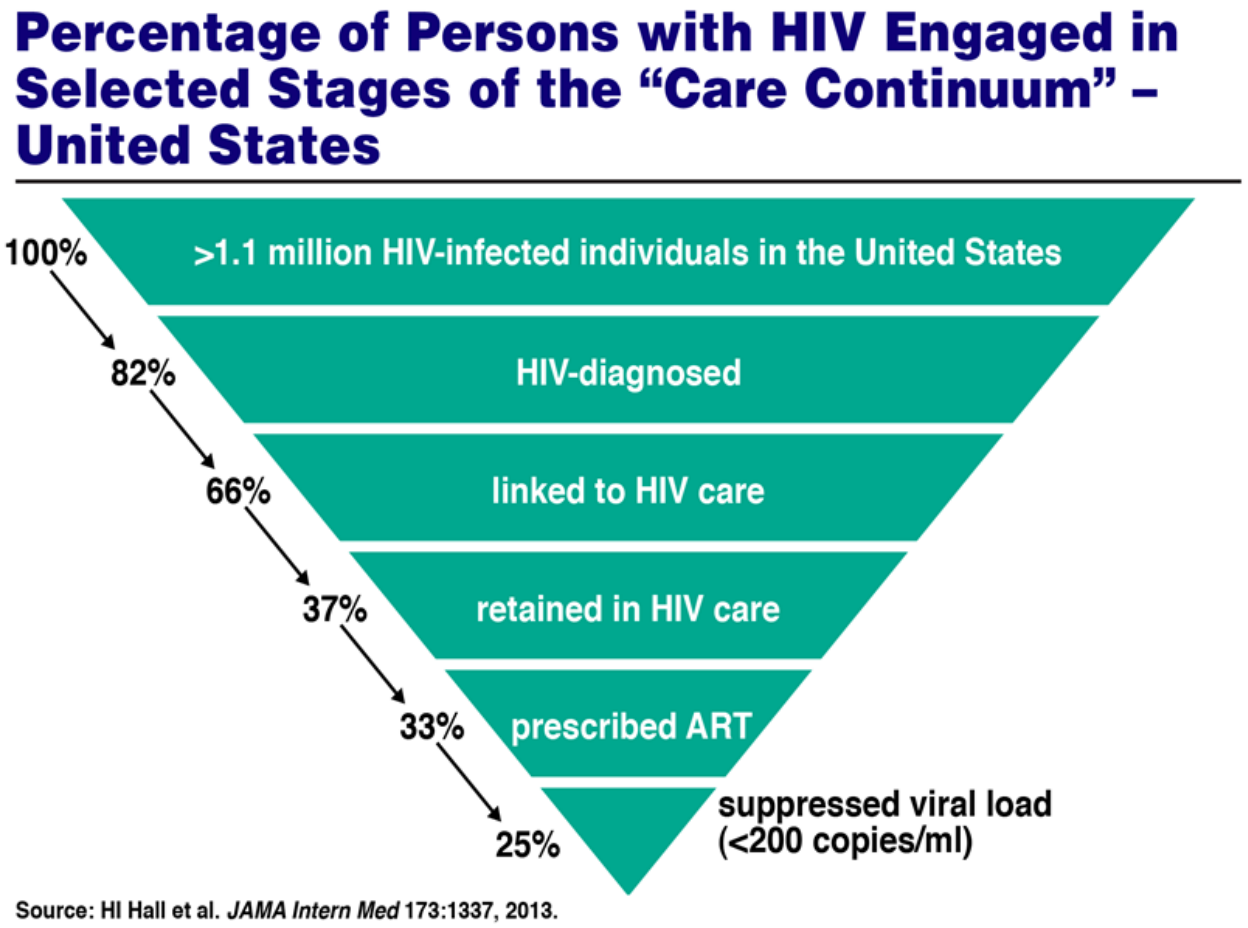
FOR IMMEDIATE RELEASE
Thursday, May 12, 2011

Treating HIV-infected People with Antiretrovirals Significantly Reduces Transmission to Partners

Achieved Complete and Sustained Virological Suppression

- 96% reduction in HIV transmission when ART started in HIV-infected partner at CD4 count of 350-550 compared to <250

Treatment as Prevention—Role of Care Continuum



Ongoing Challenges

Source of infections within a community arise from outside the community

Abstract # 489, CROI 2013

Frequent HIV Introductions into Communities Sustain Local Epidemics in Rural Rakai, Uganda

Mary Grabowski, J Lessler, A Redd, O Laeyendecker, J Kagaayi, T Lutalo, M Wawer, D Serwadda, T Quinn, R Gray, and Rakai Health Sciences Program

The New England Journal of Medicine

Established in 1812 as THE NEW ENGLAND JOURNAL OF MEDICINE AND SURGERY

Published online November 23, 2010

Preexposure Chemoprophylaxis for HIV Prevention in Men Who Have Sex with Men

RM Grant et al. and the iPrEx Study Team

- n= 2,499 HIV-seronegative men or transgender women who have sex with men in Brazil, Ecuador, Peru, South Africa, Thailand and the United States
- Randomized to receive emtricitabine and tenofovir disoproxil fumarate (FTC-TDF, Truvada) or placebo once daily
- 44% reduction in HIV incidence overall in FTC-TDF group; 73% reduction with high adherence (>90% of days)

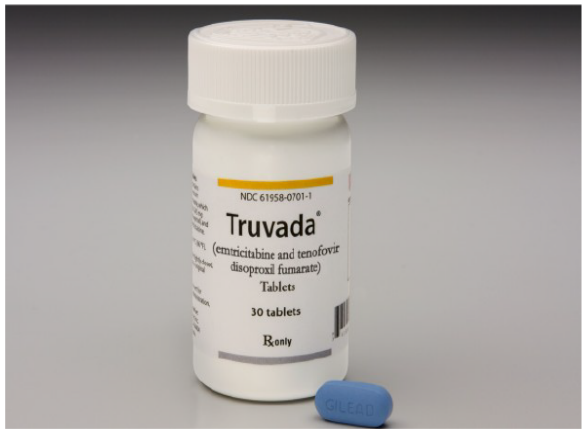
The Washington Post

May 10, 2012

FDA Panel Recommends Approval of Drug to Prevent HIV Infection

By Brian Vastag

For the first time in the 30-year battle against the HIV epidemic, a panel of experts has recommended that the Food and Drug Administration approve a drug to give to healthy people to protect against the infection.

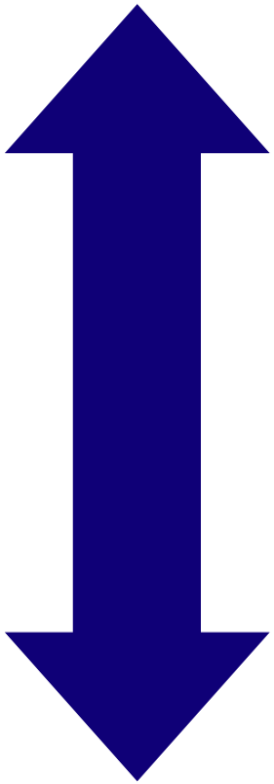


Science NOW March 7, 2013

Human Nature Sinks HIV Prevention Trial

- VOICE Study: >5,000 women in South Africa, Zimbabwe, Uganda
- Once-daily dosing of oral tenofovir, oral Truvada (tenofovir+emtricitabine) or tenofovir gel was not effective
- Poor adherence: study drug detected in <30% of plasma samples from participants

Biomedical Interventions



Behavior and Adherence

The State of the ARV-based Prevention Field

- **Given the efficacy of treatment as prevention, what is the future niche for PrEP and microbicides in comprehensive prevention?**
  - ✓ **Yes**
- **Do we seek to optimize what we have shown to be effective or do we seek a better next generation?**
  - Explore ring and additional longer acting delivery technologies
- **Will coitus-dependent gels be part of the armamentarium?**
  - **Rectal use**
- **Role of multipurpose prevention technologies**
  - Rings as a delivery technology

Vaccine Approaches

First Signal of Efficacy in an HIV Vaccine Clinical Trial

The New England Journal of Medicine

Established in 1812 as THE NEW ENGLAND JOURNAL OF MEDICINE AND SURGERY

Volume 361 December 3, 2009 Number 23

Vaccination with ALVAC and AIDSVAX to Prevent HIV-1 Infection in Thailand

S Rerks-Ngarm, JH Kim, NL Michael et al. for the MOPH–TAVEG Investigators

Summary of Analyses

	ITT	mITT	PP
N (# subjects)	16,402	**16,395**	12,542
Person years	52,985	**52,985**	36,720
Vaccine/Placebo (event #)	56 / 76	**51 / 74**	36 / 50
Vaccine efficacy	26.4%	**31.2%**	26.2%
2-sided p value	0.08	**0.04**	0.16
95% confidence interval	**-4.0, 47.9**	**1.1, 51.2**	**-13.3, 51.9**

Includes 5 vaccine and 2 placebo recipients who were HIV positive at baseline

Decreased event numbers, lower precision

Modest (31%) Efficacy in RV144 Trial Correlates with Non-Neutralizing Antibodies to Epitopes in the V1-V2 Region of HIV Envelope

Immune-Correlates Analysis of an HIV-1 Vaccine Efficacy Trial

BF Haynes et al.

Increased HIV-1 Vaccine Efficacy Against Viruses with Genetic Signatures in Env V2

M Rolland, JH Kim et al.

Vaccine Induction of Antibodies Against a Structurally Heterogeneous Site of Immune Pressure Within HIV-1 Envelope Protein Variable Regions 1 and 2

HX Liao, BF Haynes et al.

VOL. 333 16 September 2011
Science

Sequence and Structural Convergence of Broad and Potent HIV Antibodies That Mimic CD4 Binding

JF Scheid, MC Nussenzweig et al.

Focused Evolution of HIV-1 Neutralizing Antibodies Revealed by Structures and Deep Sequencing

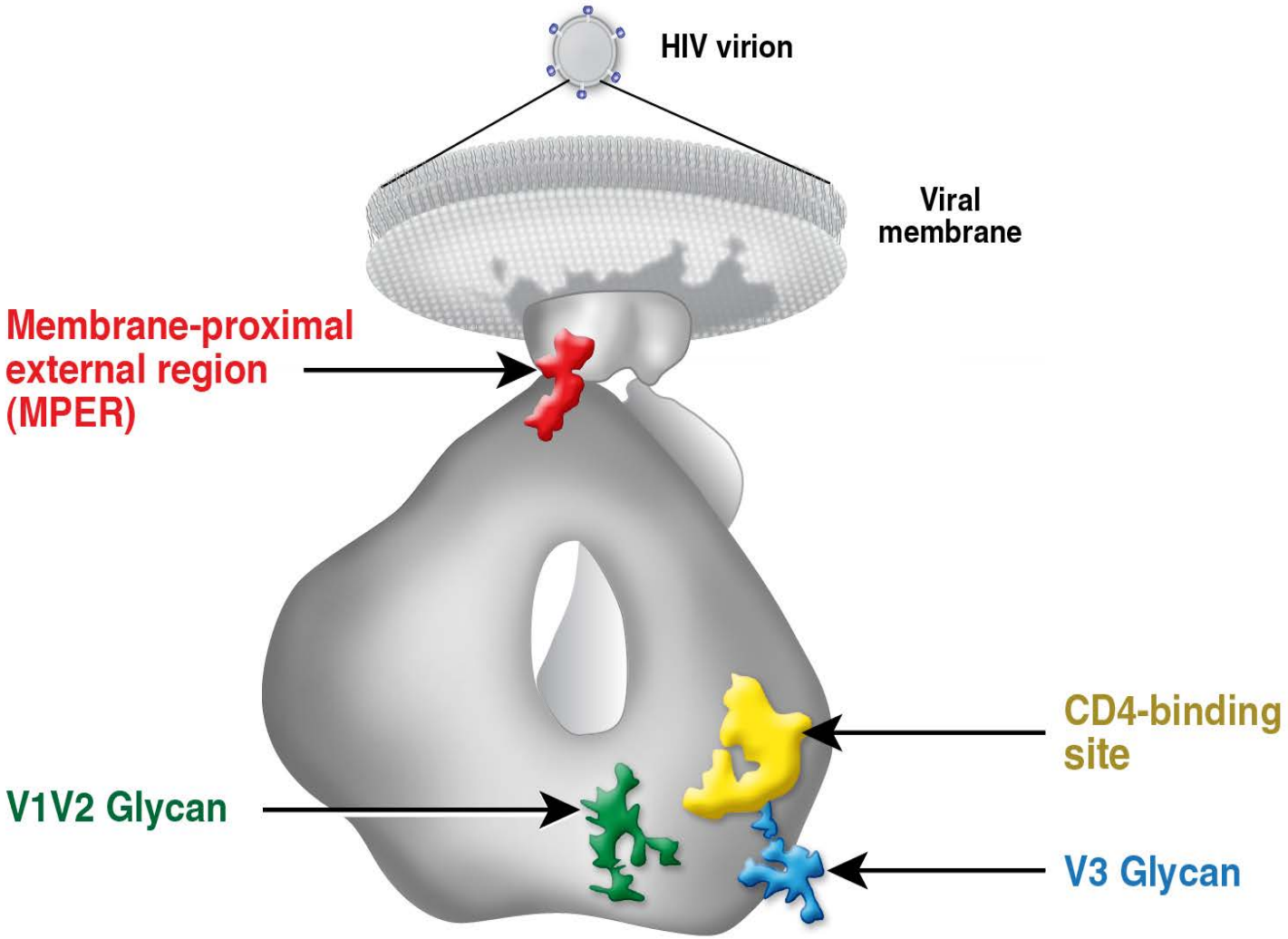
X Wu, JR Mascola et al.

VOL. 477 22 September 2011
nature

Broad Neutralization Coverage of HIV by Multiple Highly Potent Antibodies

LM Walker, P Poignard et al.

HIV Epitopes Targeted by Broadly Neutralizing Human Antibodies



Adapted from Kwong and Mascola, *Immunity* 37:412, 2012.

Critical Challenge in the Development of an HIV Vaccine

Neutralizing Epitope

Immunogen

Published online September 11, 2013

nature

Immune Clearance of Highly Pathogenic SIV Infection

SG Hansen, LJ Picker et al.

- Live CMV vector vaccine induces potent CD8+ T cell response in monkeys that results in profound early control and progressive immune clearance of highly pathogenic SIV
- Implications for preventive and therapeutic HIV vaccines

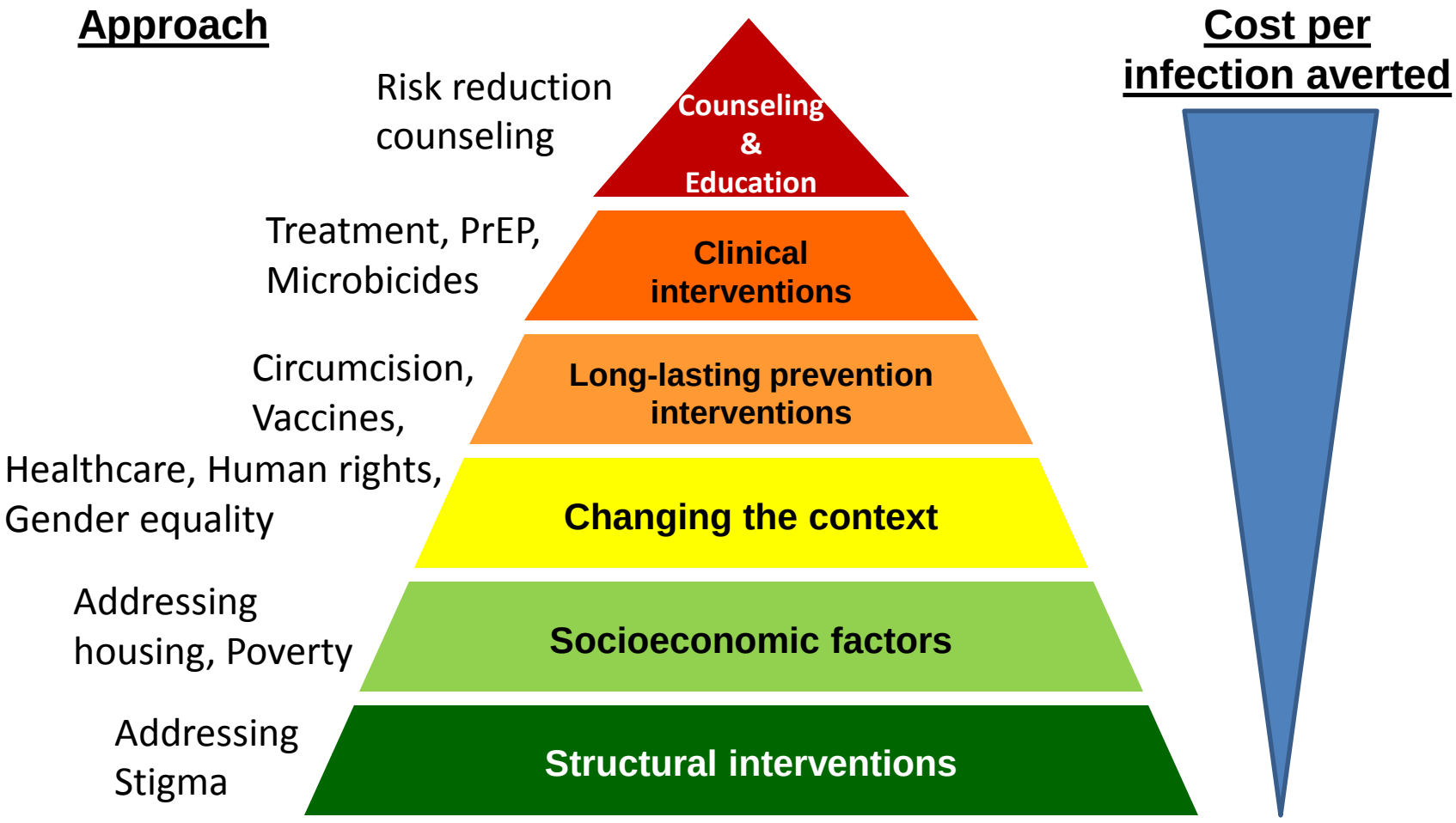
Lessons Learned From Prevention Research

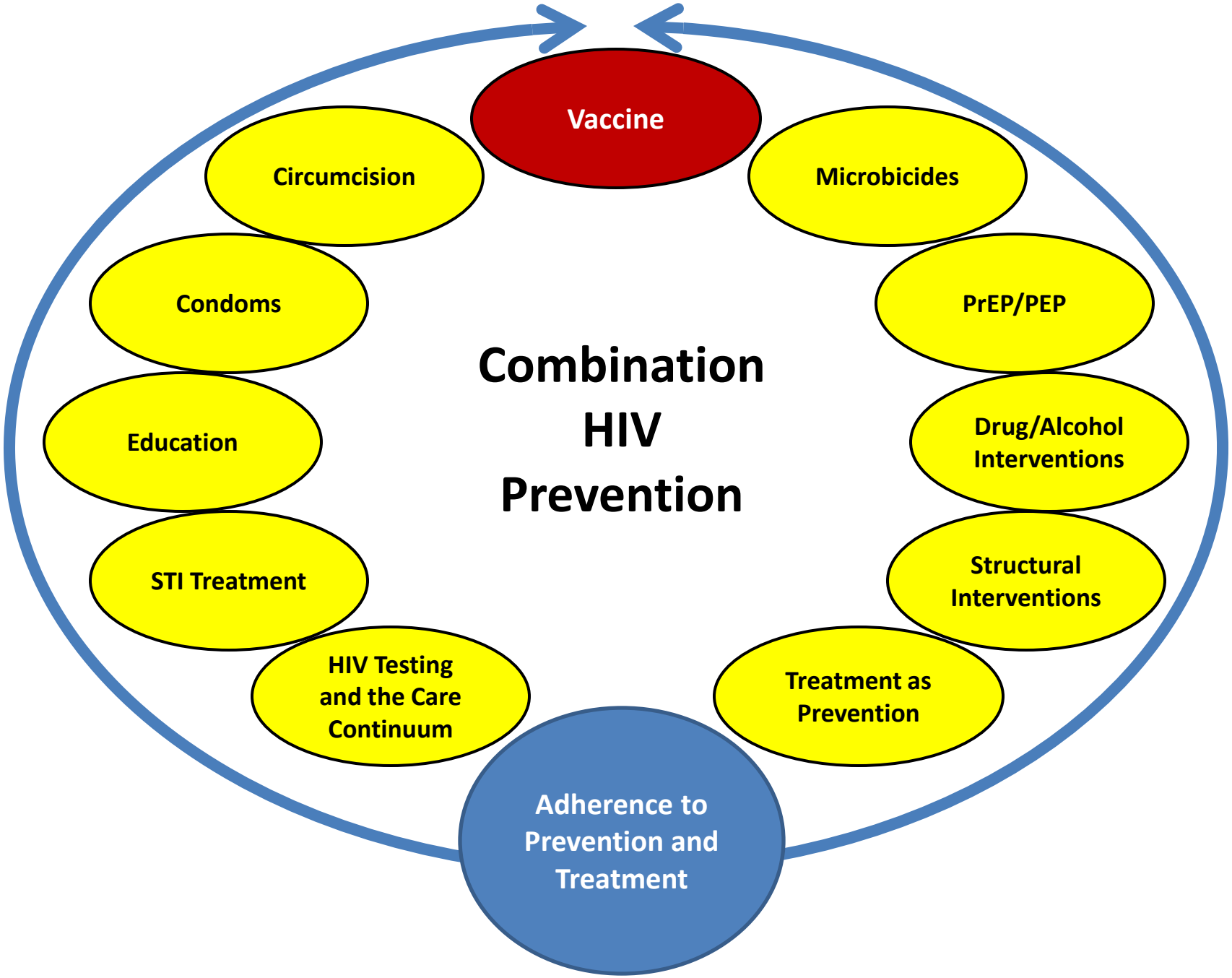
- **The active agent must be at the site of exposure in sufficient concentration for ample duration to abrogate infection**
- **New agents**
  - Does it work for all routes of exposure?
  - How is it administered?
  - Is it behaviorally dependent?

Essential Linkage of Social, Behavioral and Biomedical Research

- **Creation of interest and demand for HIV prevention requires an integrated approach, need to harness social marketing and behavioral economics**
- **Social science research must inform product development in an iterative way**
-

Combination Prevention is More than Biomedical Interventions

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AIDS-Free Generation