

Moving the HIV Prevention Agenda Forward: The DAIDS Perspective

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Microbicide Trials Network

Regional Meeting

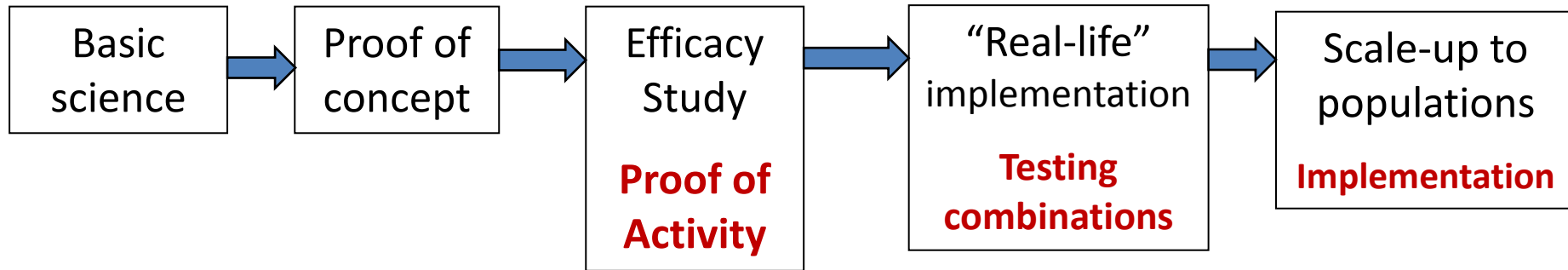
October 2, 2012



How Biomedical Prevention Methods Work

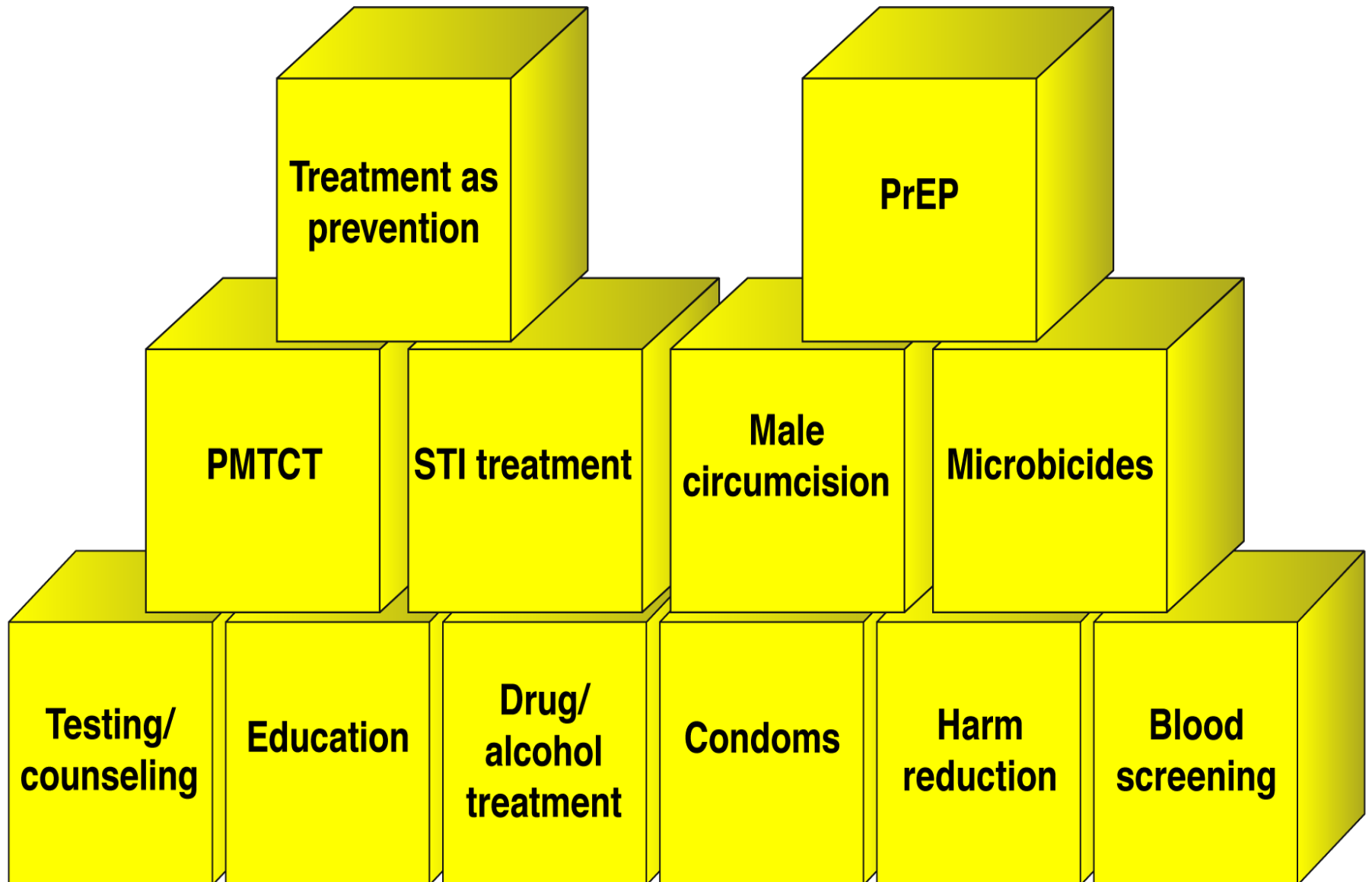
- **All PrEP, microbicides, or a vaccine response--antibodies and CMI-- must be armed, ready and waiting at the site and time of virus exposure**
- **Further, the antiviral activity must remain active until the virus is eliminated**

Efficacy → Effectiveness: The Path to Combination Prevention



How do we move from single products to integrated combination prevention programs?

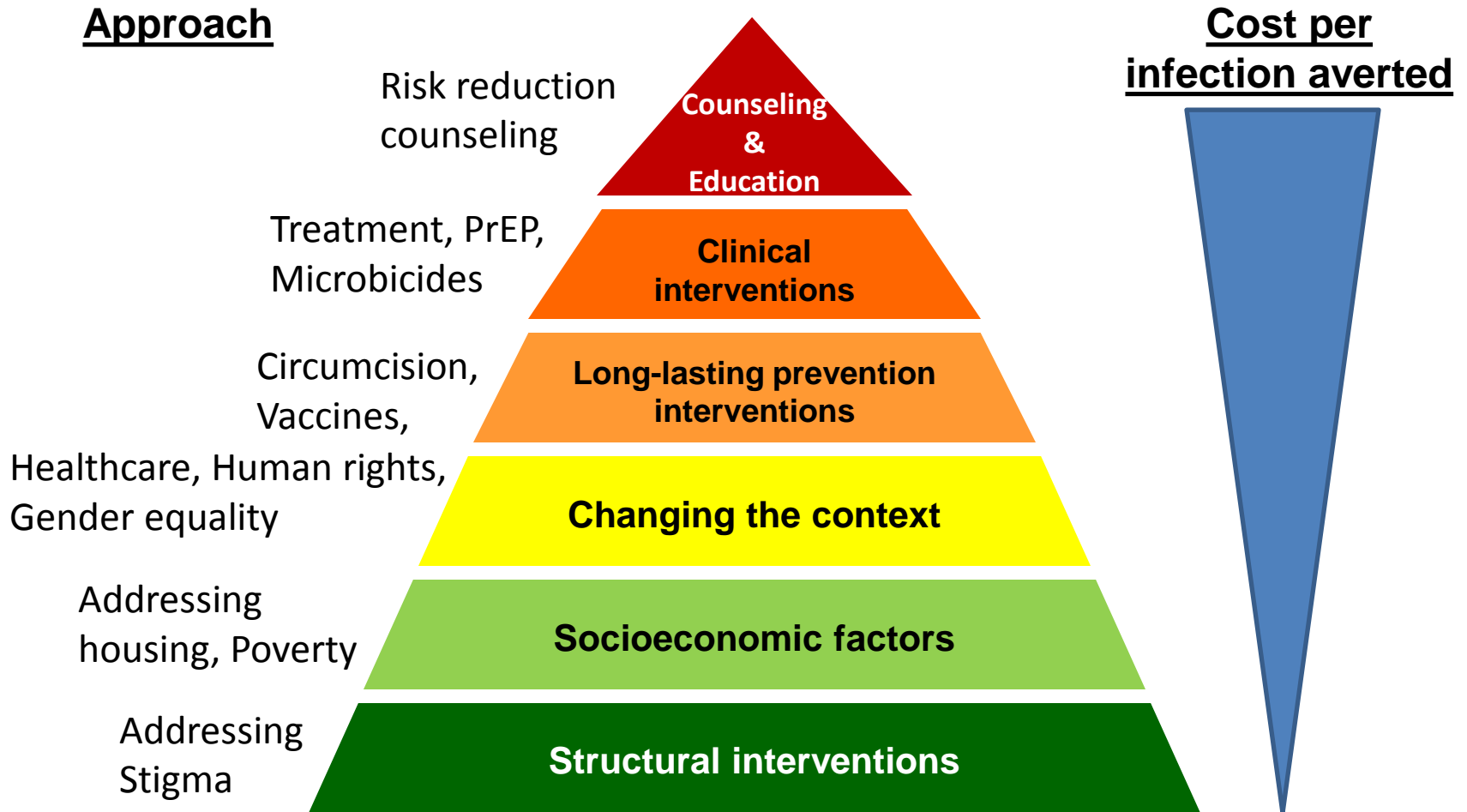
Combination HIV Prevention



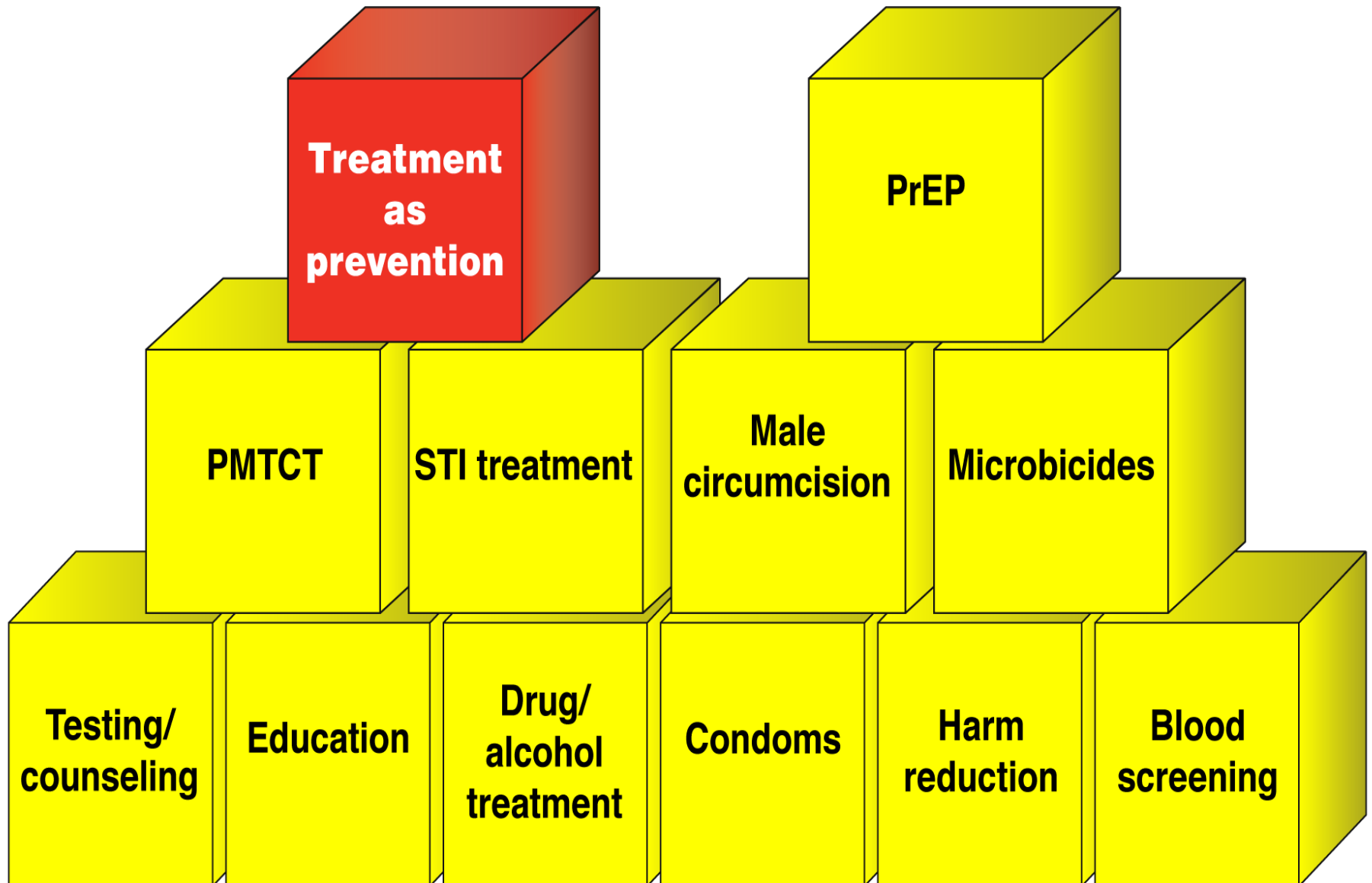
HIV Prevention Research: Guiding Principles

- **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 epidemics within the community and select prevention interventions based upon effectiveness and cost**
- **Evolve prevention strategies with changes in the epidemic**

Combination Prevention is More than Biomedical Interventions



Combination HIV Prevention



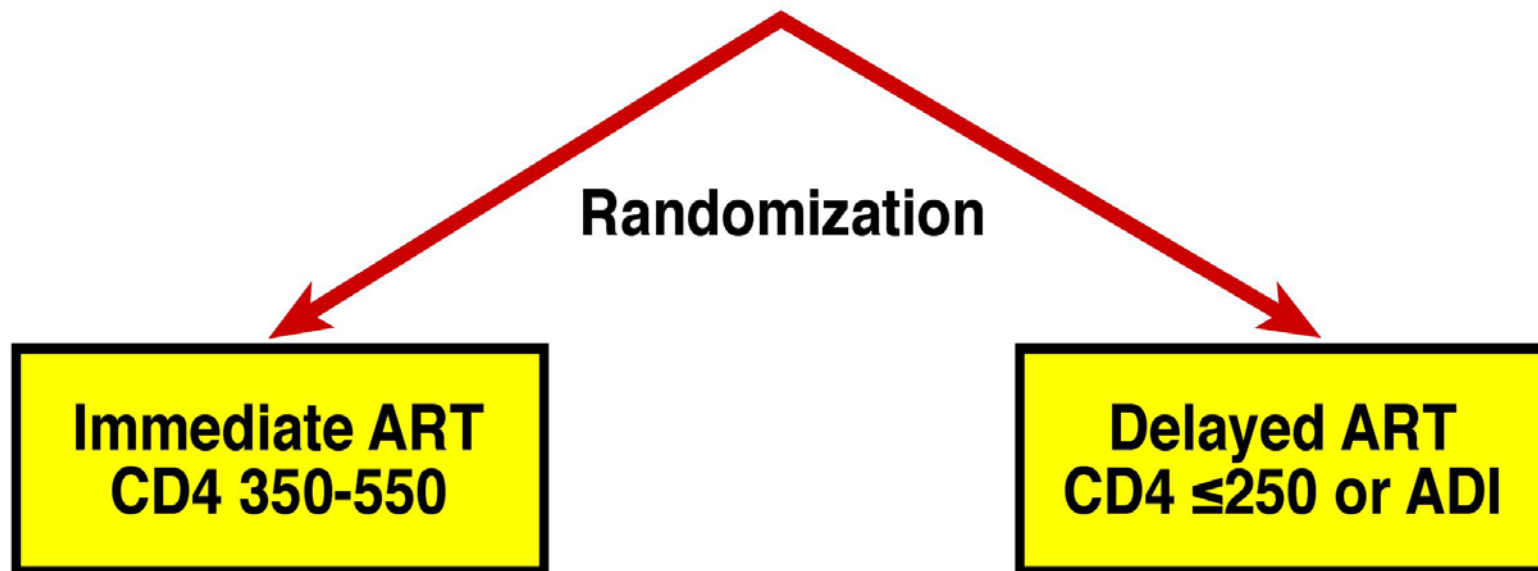
HPTN 052 Study Objectives/Goals

- **To determine: a) whether antiretroviral use by an HIV-infected person could prevent the transmission of the virus to his/her sexual partner and; b) what is the optimal time of initiation of therapy**
- **To evaluate the optimal time for an HIV-infected person to begin taking antiretroviral therapy in order to reduce HIV related illness and death**

HPTN 052 Study Design

Entry criteria: HIV⁺ subjects with CD4⁺ T cell counts
350 to 550 cells/ μ L

1763 serodiscordant couples (97% heterosexual)
Of HIV-infected partners - 890 were men and 873 were women





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

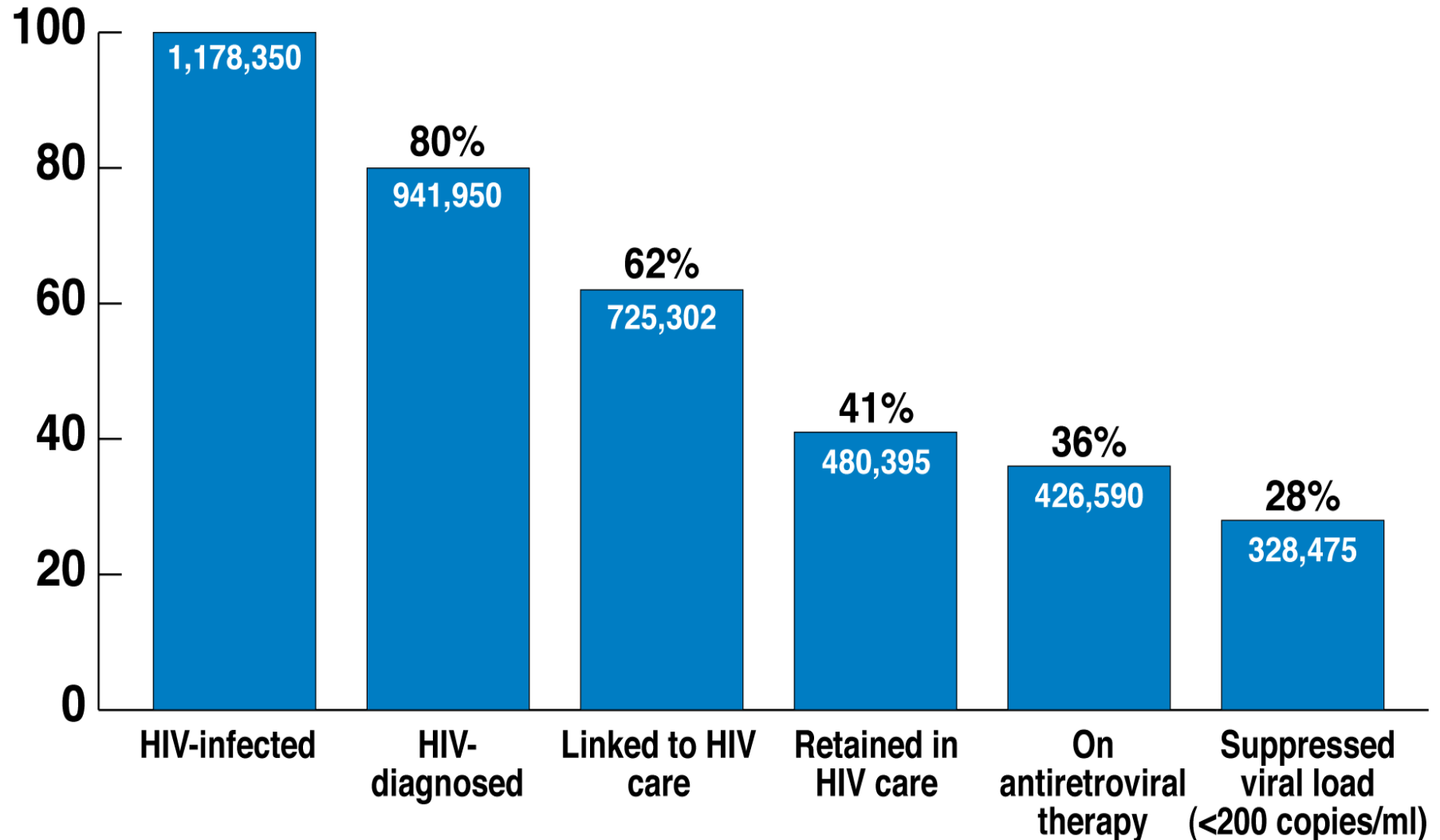
Thursday, May 12, 2011

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

Achieved Complete and Sustained Virological Suppression

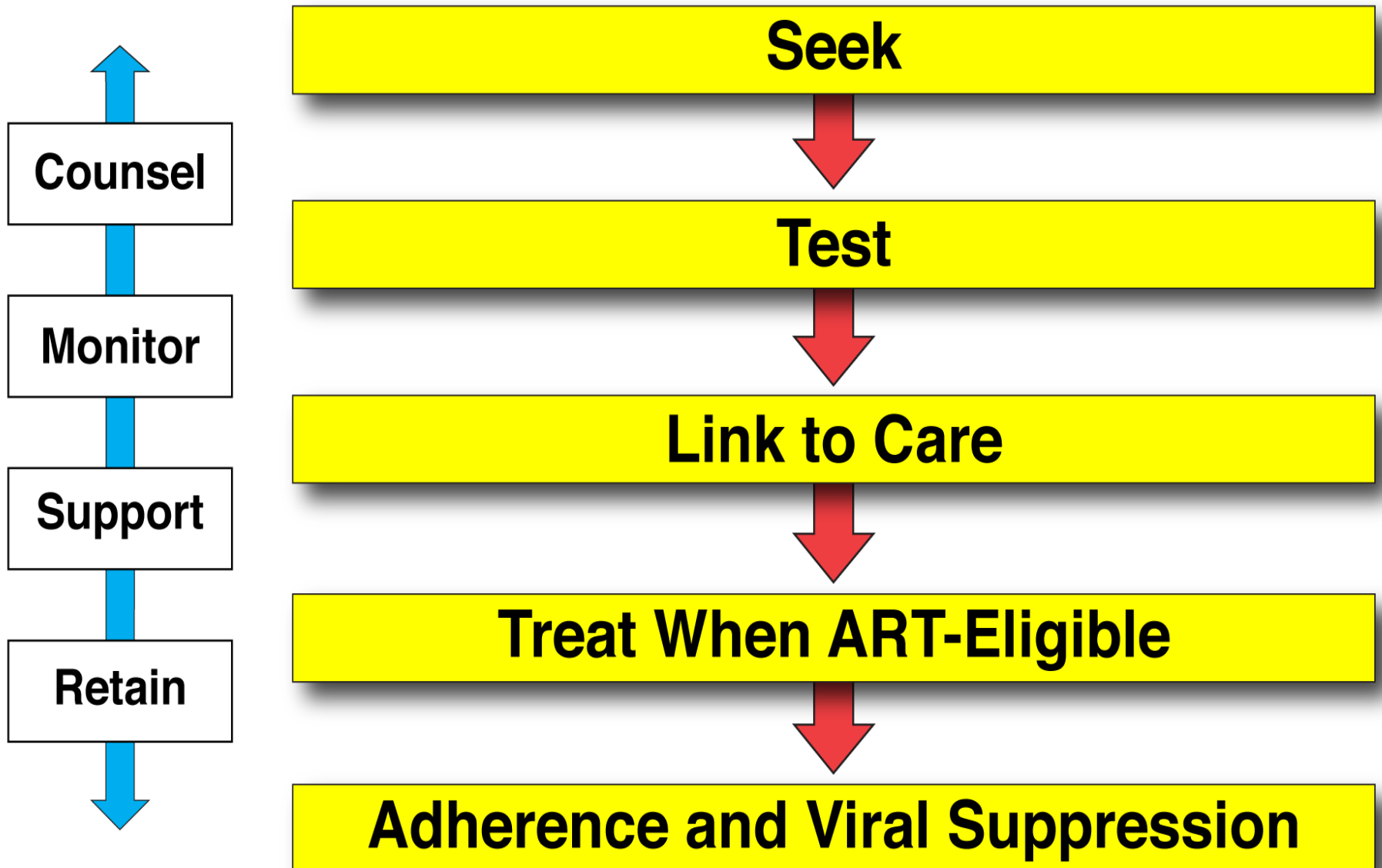
- **96% reduction in HIV transmission when ART started in HIV-infected partner at CD4 count of 350-550 compared to <250**

Proportion of HIV-Infected Individuals in the United States at Each Stage of Care

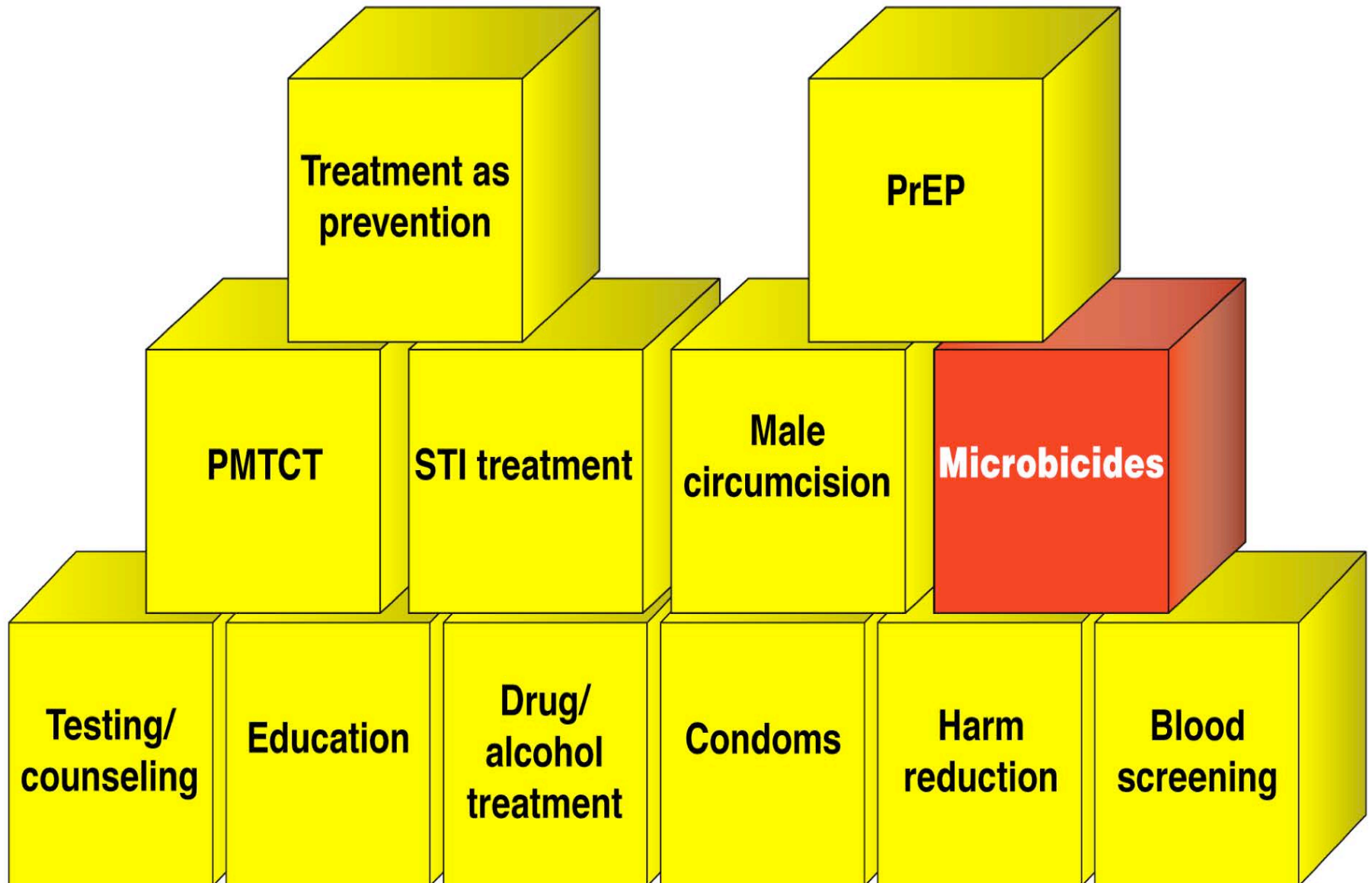


Source: CDC, 11/2011

The HIV Care Continuum



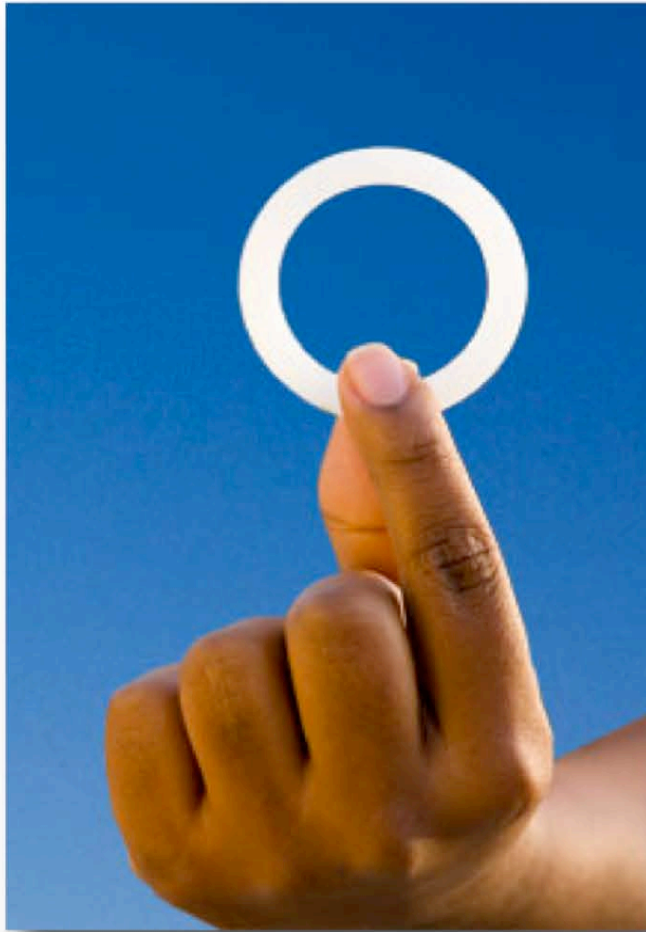
Combination HIV Prevention



Microbicides: Mixed Results

- **CAPRISA 004** – 1% tenofovir gel before and after intercourse reduced incidence by 39%; with adherence > 80%, incidence reduced by 54%
- **VOICE** – 1% tenofovir gel daily. Study arm discontinued due to futility
- **FACTS 001** – Ongoing study in South Africa of 1% tenofovir gel before and after intercourse

Dapivirine Microbicide Rings

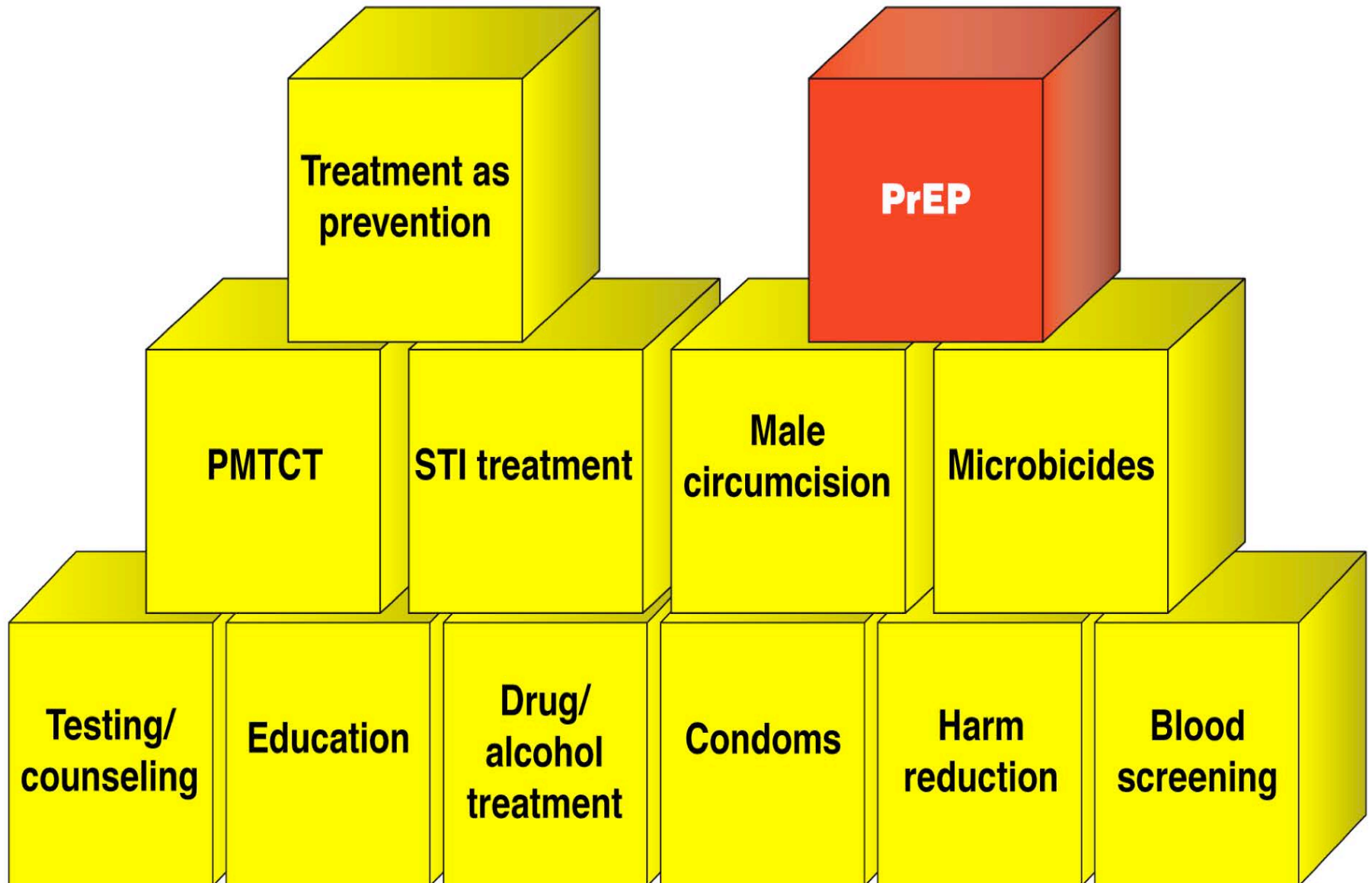


- Monthly use
- Two large-scale trials in 2012
 - **ASPIRE** ~3500 women in Malawi, South Africa, Uganda, Zambia, and Zimbabwe
 - **The Ring Study (IPM 027)** ~1,650 women in South Africa, Rwanda, and Malawi

Rectal Microbicides

- **Completed first clinical trials with vaginally formulated microbicides used rectally**
- **Ongoing program (CHARM) to develop rectal-specific microbicide formulations for Tenofovir and Maraviroc**
- **Completed two Phase I clinical trials of vaginal microbicides used rectally**
- **Phase II trial in development using oral FTC/TDF and rectally-applied tenofovir reduced-glycerin 1% gel**

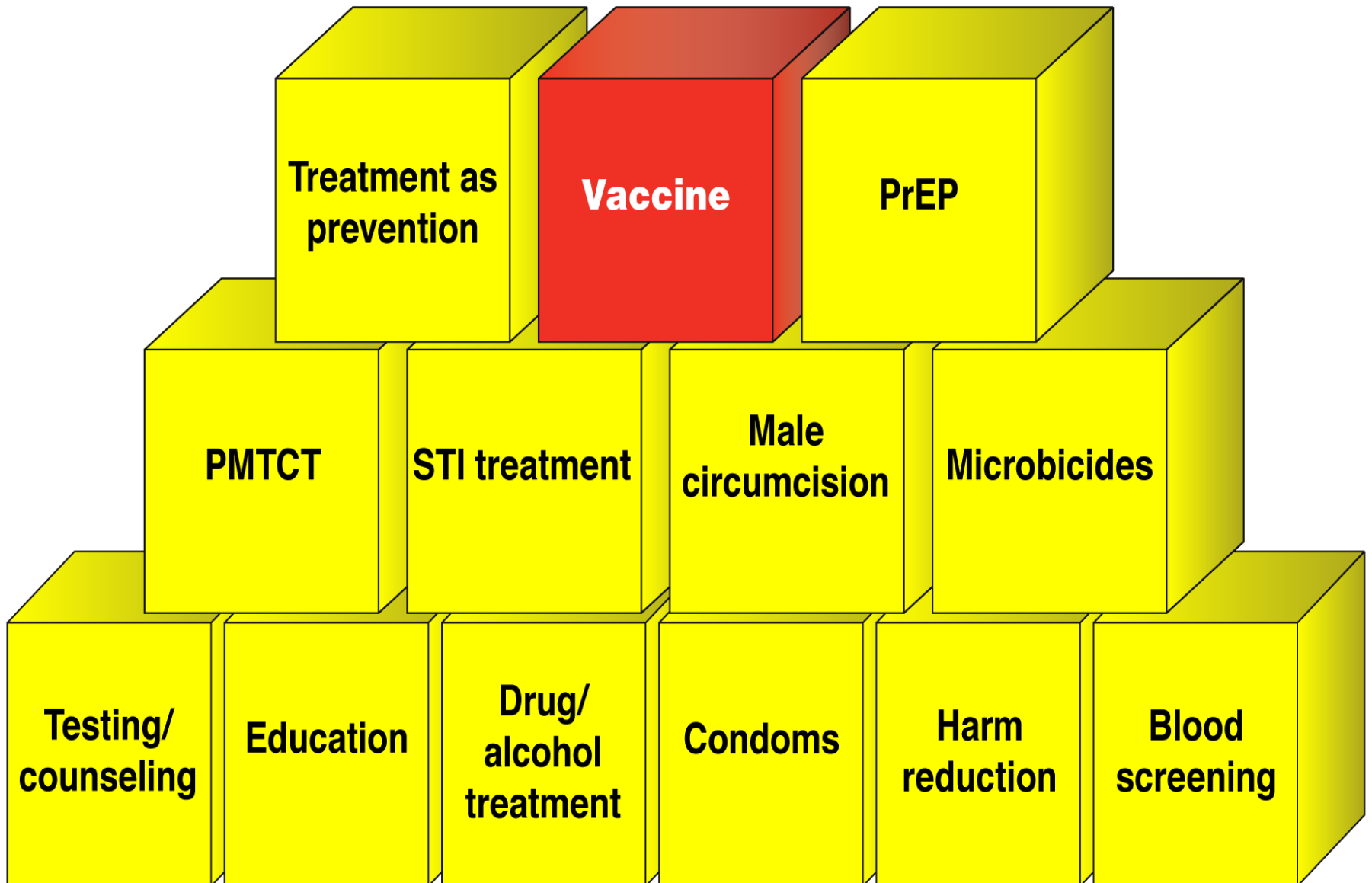
Combination HIV Prevention



Oral PrEP: Mixed Results

	<u>Efficacy</u>
MSM – iPrEx (Americas, Thailand, SA)	42%
Heterosexual discordant couples – Partners PrEP (Kenya, Uganda)	75%
Heterosexual men and women – TDF2 (Botswana)	62%
Women – FEM-PrEP (Kenya, SA, Tanzania)	0%
Women – VOICE (SA, Uganda, Zimbabwe)	0%

Combination HIV Prevention



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

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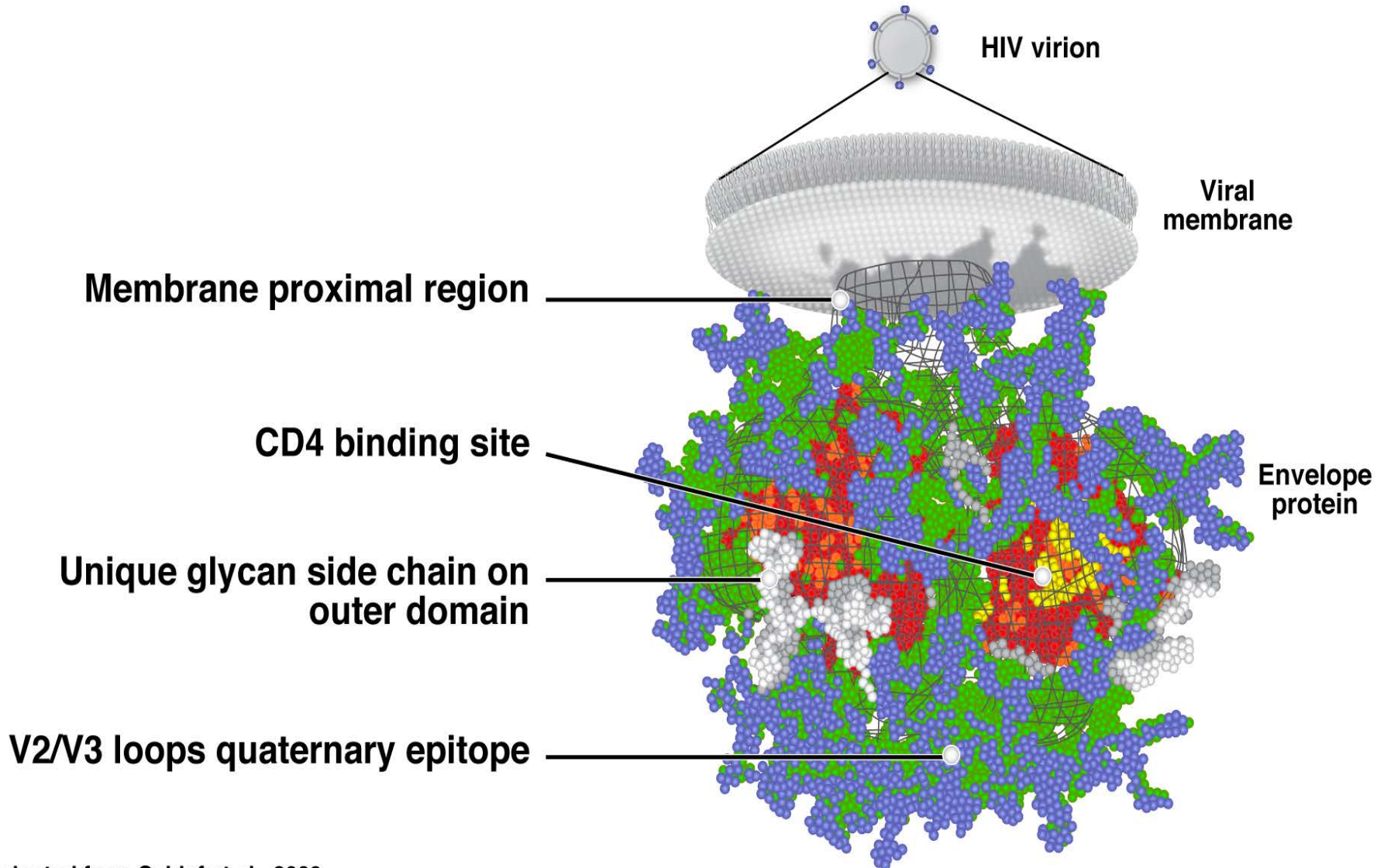
Vaccination with ALVAC and AIDSVAX to Prevent HIV-1 Infection in Thailand

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

HVTN 505

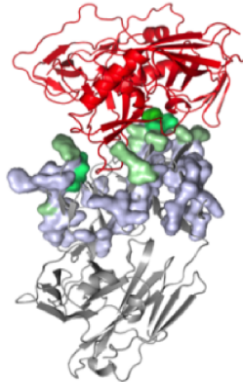
- **Phase IIb study in the U.S.**
- **Vaccine regimen designed by NIAID Vaccine Research Center (VRC)**
- **Study will address two key questions:**
 - Will the vaccine prevent infection?
 - Will the vaccine significantly reduce viral load in individuals who become infected with HIV?
- **Participants: 2500 U.S. men or trans-women who have sex with men**
 - Circumcised
 - No measurable Ad5 antibodies
- **~2100 currently enrolled**

Structure-Based HIV Vaccine Design: Conserved Targets Defined by Neutralizing Antibodies

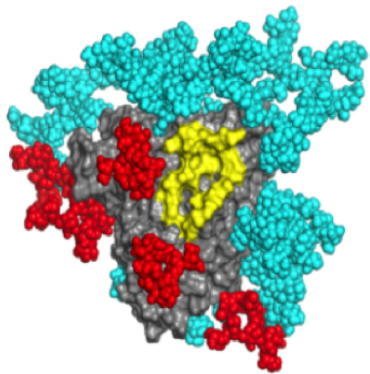


Neutralizing Antibody Approach to HIV Prevention

gp120

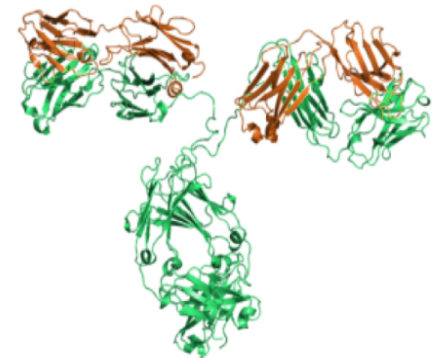


Structure-based
Immunogen
Design



Vaccine

Provision of
Neutralizing
Antibodies



Passive transfer of IgG
Gene-based vectors (AAV)

THOUGHTS ON THE NEAR TERM FUTURE

Next Generation Products

- **How can we develop delivery systems that work well within the lives of people that would benefit most?**
 - Packaging or product design to improve adherence
 - Ring technology adapted to use with squat toilets
- **Must keep the user in mind**

Next Generation Products

- **New agents**
- **Combination products**
 - Antiviral, contraceptive
- **New Formulations**
 - Gels -- rectal and vaginal
 - A provocative thought -- gels that are safe and effective in HIV+ people
- **Long acting formulations and delivery devices**