

Combination HIV Prevention Research

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HIV Prevention Research: Guiding Principles

- **Multiple strategies needed to assemble a well-rounded “prevention toolkit”**
- **Know the epidemics within the community you are targeting**
- **Individual-focused HIV prevention strategies all begin with HIV testing**
- **No single prevention strategy will be 100% effective, appropriate to or accepted by everyone**

Proven Interventions

- **Screening of blood supply**
- **Condoms**
- **Education/behavior modification**
- **HIV testing/counseling**
- **Treatment/prevention of drug/alcohol abuse**
- **Clean syringes**
- **ARVs to prevent MTCT**
- **ARV therapy of HIV+ individuals**
- **Post-exposure prophylaxis with ARV**
- **Male circumcision**
- **Structural interventions**

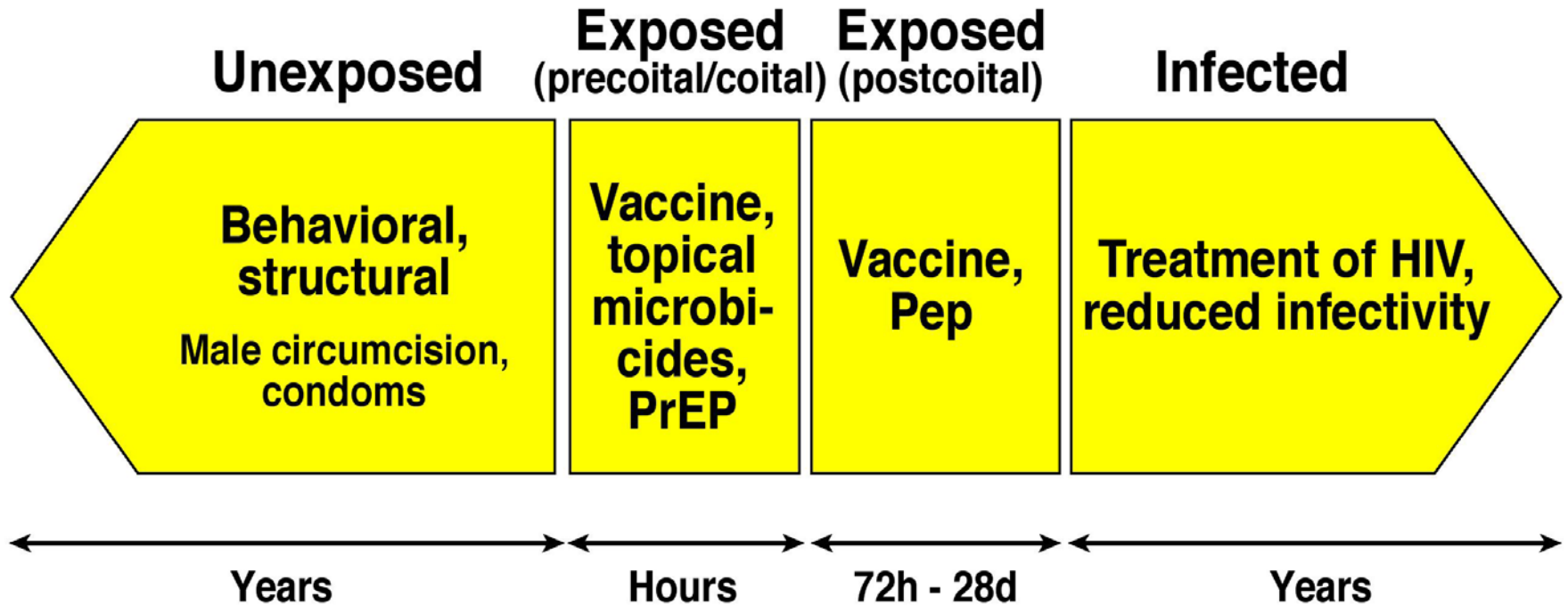
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Interventions Under Development

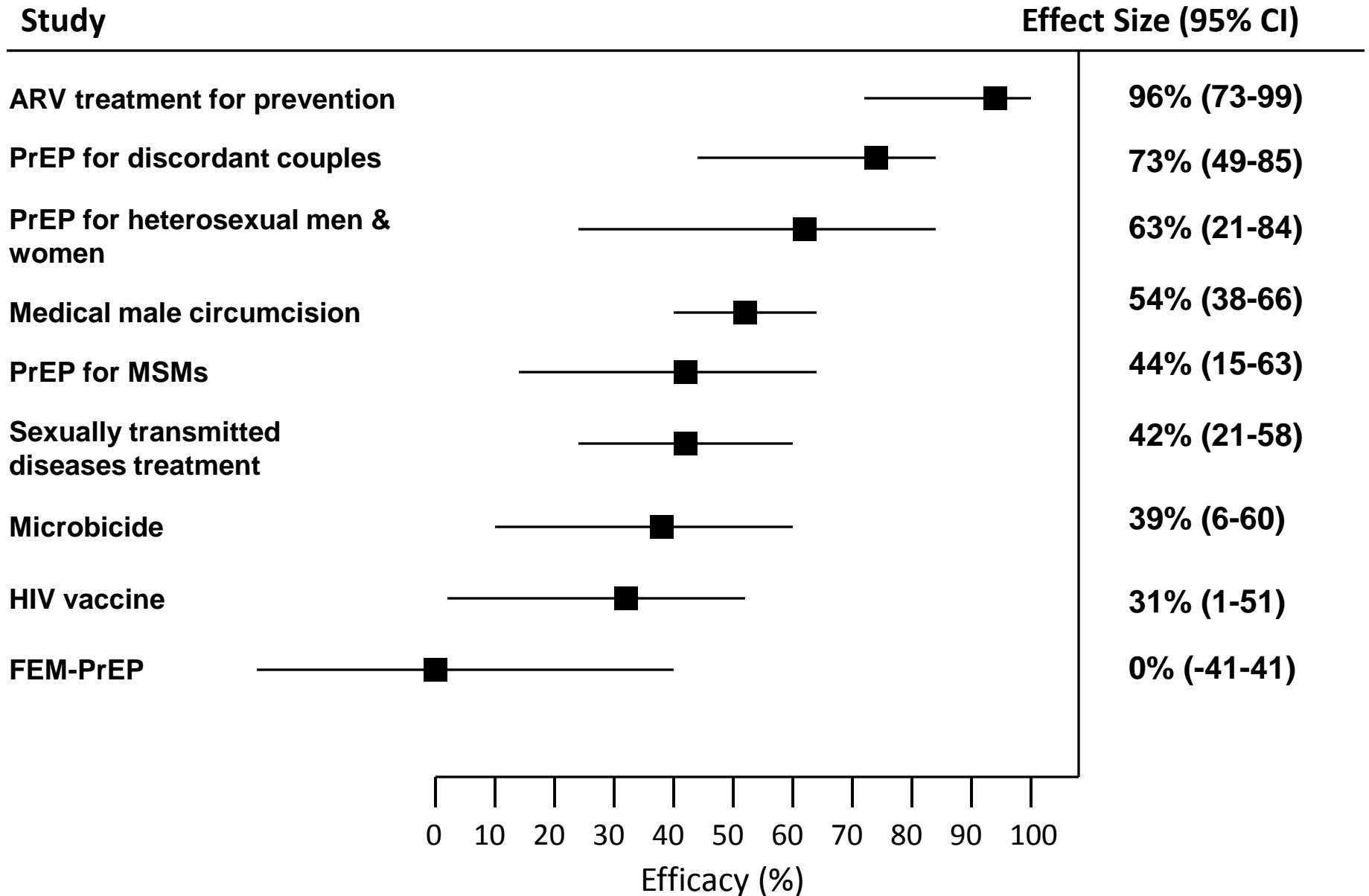
- **Vaccine**
- **Microbicides for vaginal and rectal use**
- **Pre-exposure prophylaxis with ARVs**
- **Seek, test, link-to-care, treat strategy**

← Adherence →

Opportunities for Preventing HIV Infection



HIV Incidence Reduction by Prevention Technologies





U.S. Department of Health and Human Services

NIH News

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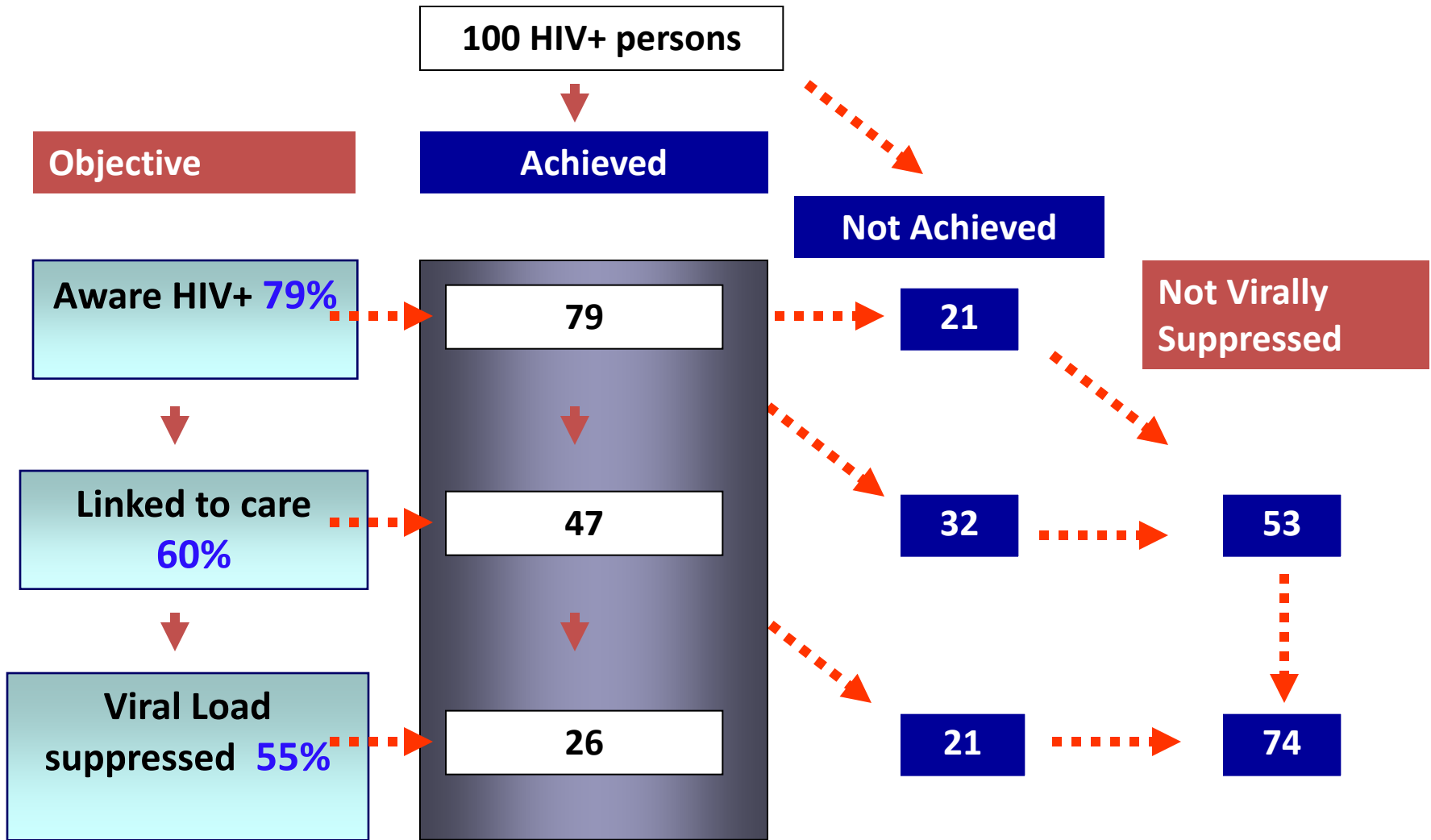
Thursday, May 12, 2011

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

Achieved Complete and Sustained Virological Suppression

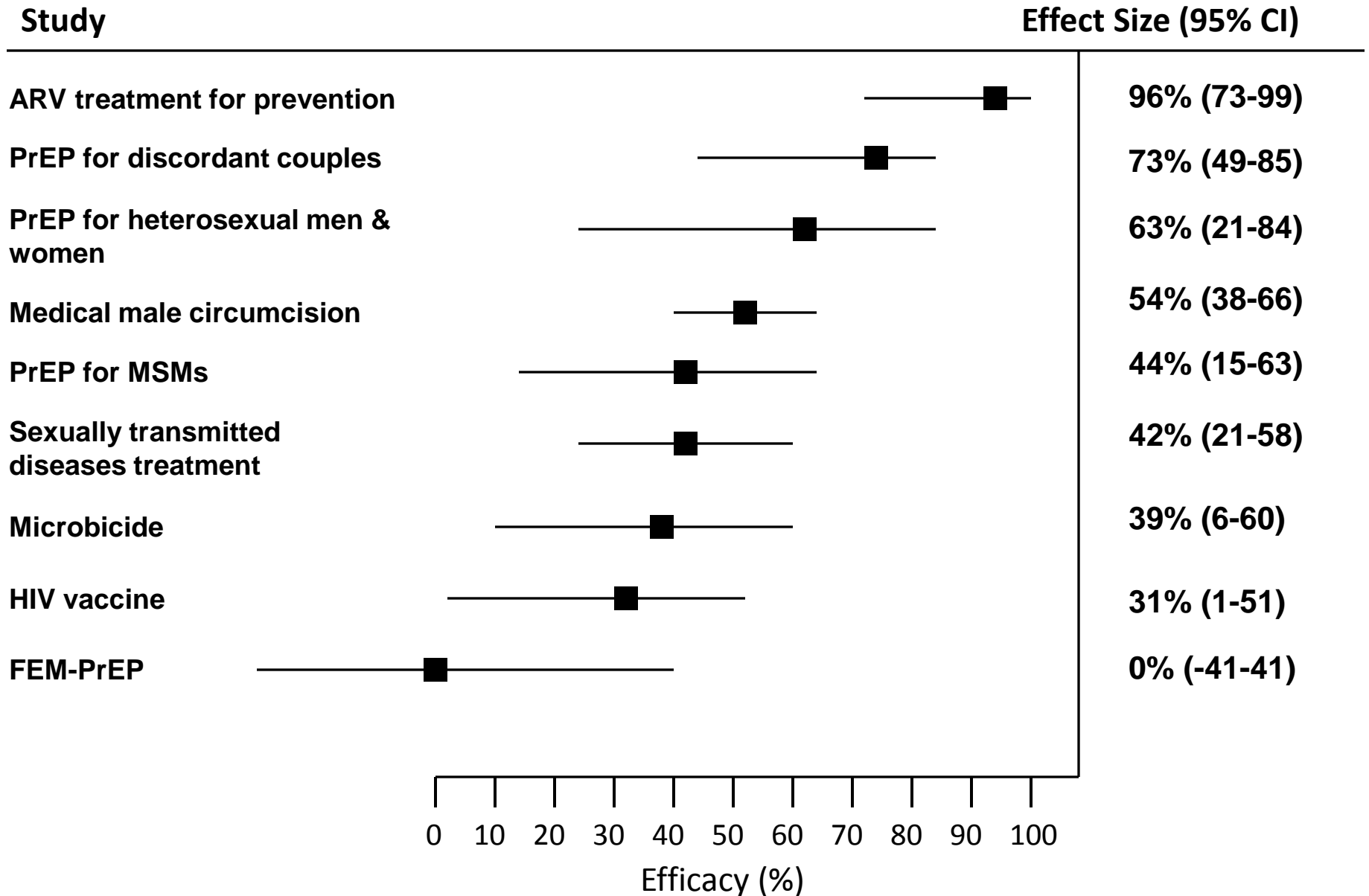
- **96% reduction in HIV transmission when ART started in HIV-infected partner at CD4 count of 350-550 compared to <250**

Cascade Effect: Diminishing Returns



Overall: ~26% of HIV+ persons were in care and estimated to have a viral load <500 copies/ml

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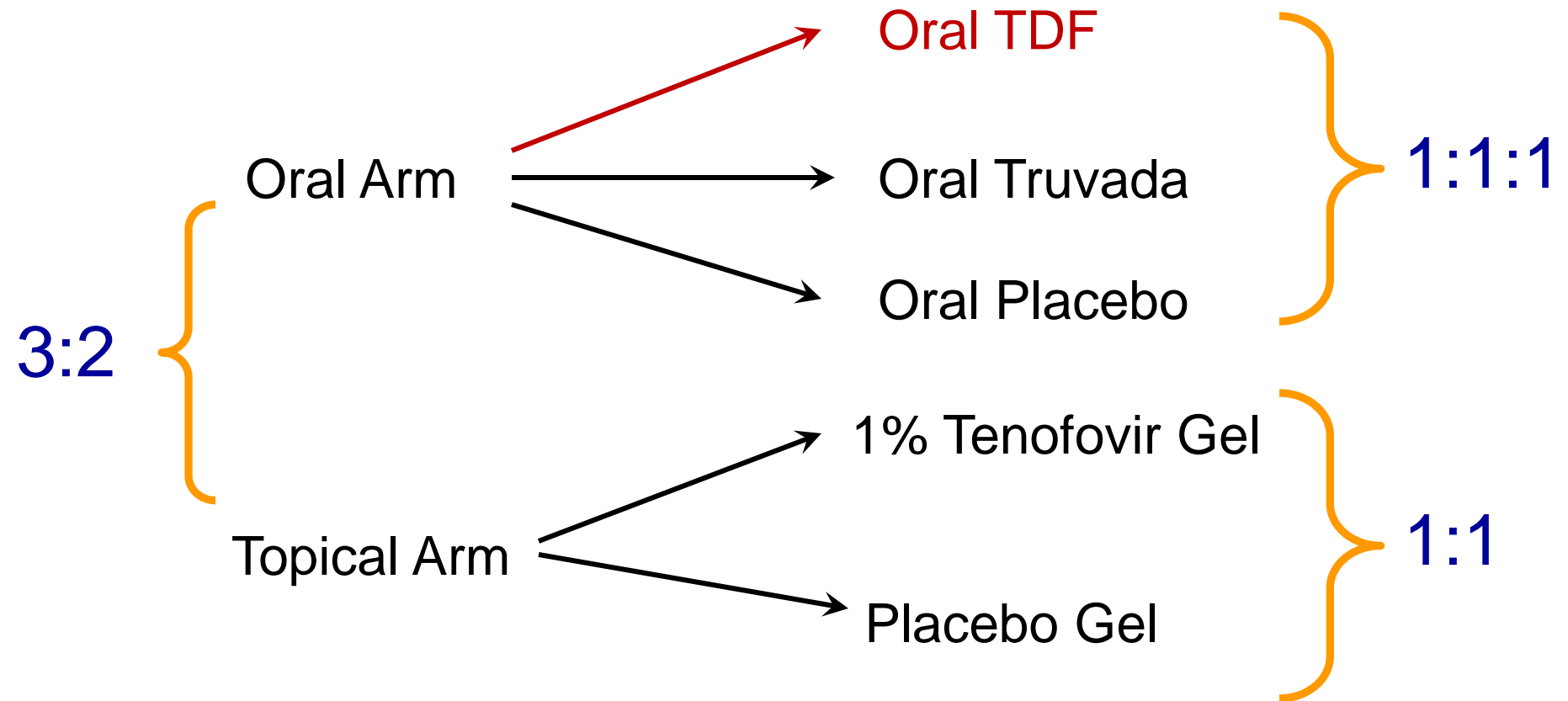
Thursday, September 29, 2011

NIH Modifies 'VOICE' HIV Prevention Study in Women

- **Oral tenofovir discontinued in trial**
- **No safety concerns with oral tenofovir**
- **The remaining arms of the study will continue**

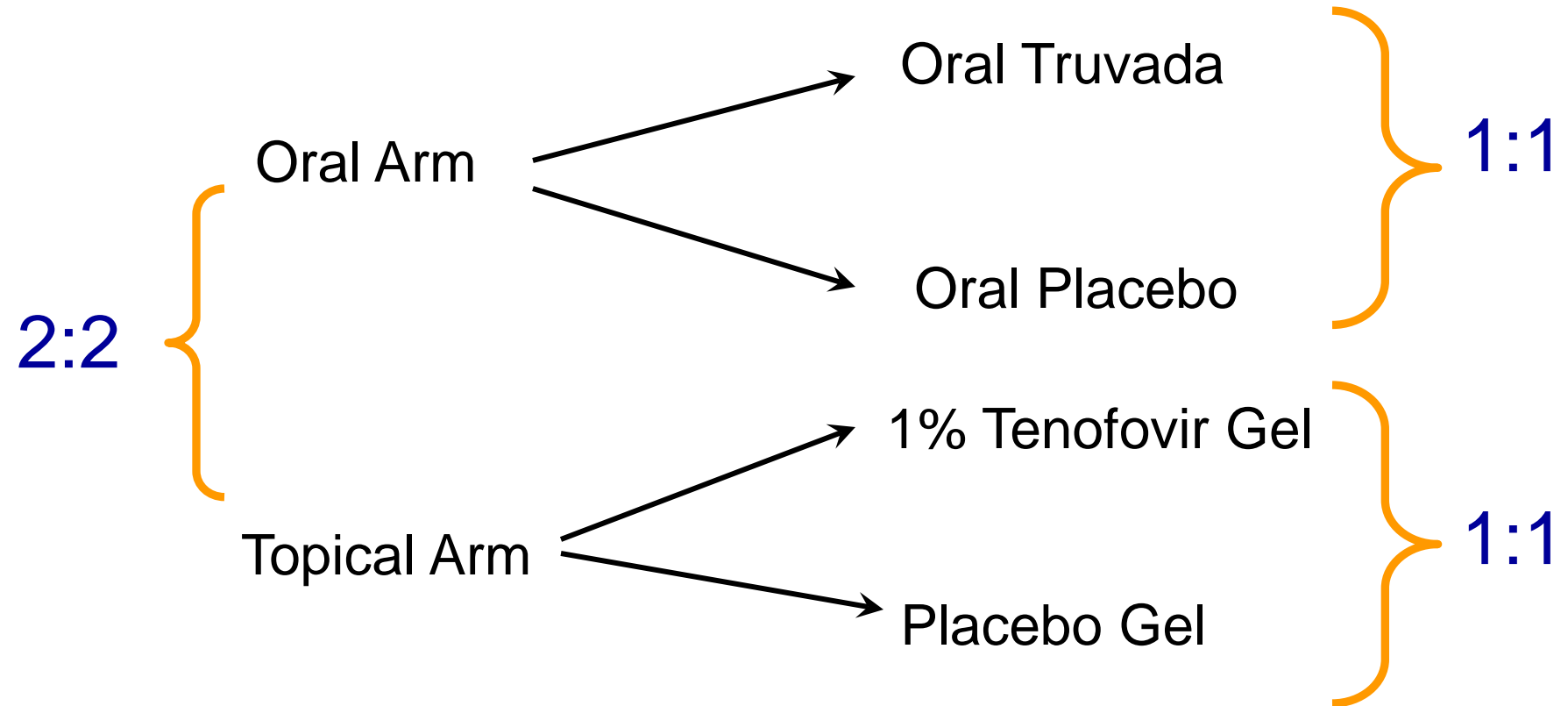
VOICE Study Design

5000 women, 1000 in each group



VOICE Study Design

4000 women, 1000 in each group



iPrEX OLE and San Francisco PrEP Demonstration Project

- **iPrEX Open Label Extension Study:** Assessing adherence, drug levels and risk taking in a well-characterized cohort of trial participants after they are informed regarding the safety and efficacy of FTC/TDF PrEP and offered free open-label dosing
- **San Francisco PrEP Demonstration Project:** Evaluating acceptability, uptake and adherence to daily PrEP among high-risk MSM in non-research settings and assessing risk behaviors before and after access to PrEP

Additional PrEP Trials

- **HPTN 066:** Phase I, randomized, open label, pharmacokinetic study to describe the dose-proportionality and intra-individual variability of tenofovir diphosphate and emtricitabine triphosphate at steady-state in healthy volunteers taking Truvada
- **HPTN 067:** Phase II, randomized, open label, pharmacokinetic and behavioral study of the use of intermittent oral emtricitabine/tenofovir disoproxil fumarate PrEP
- **HPTN 069:** Phase II, randomized, double-blind, controlled four arm study of the safety, tolerability and adherence of maraviroc, maraviroc + emtricitabine, maraviroc + tenofovir, or tenofovir/emtricitabine for PrEP to prevent HIV in at-risk MSM (co-sponsored with the AIDS Clinical Trials Group)

PrEP Future Directions

- **Get an answer about TDF + FTC in VOICE**
- **Define adherence strategies and approaches to social marketing**
- **Perform demonstration projects in relevant populations**
- **Develop and test new agents**
- **Devise means of incorporation of ARVs as prevention into combination packages**

Additional Microbicide Trials

- **CHOICE – Emerging from VOICE**
- **FACTS 001 – Phase III trial assessing the safety and effectiveness of intravaginal 1% tenofovir gel**
- **Dapivirine ring studies**
- **MTN-013 – Phase I safety and pharmacokinetics of dapivirine/maraviroc intravaginal ring**
- **Tenofovir safety studies in special populations**
- **As part of dual use products, clarify impact of hormonal contraception on HIV acquisition**

Topical Microbicides: Future Directions

- **Move 1% Tenofovir gel to licensure?**
- **Expand efforts to develop rectal microbicides**
- **Devise more acceptable, less behaviorally sensitive delivery methods**
- **Evaluate novel clinical trial methodologies**
- **Move licensed product into combination prevention platforms**

The Dynamic Tension in the Prevention Field

- **Given the efficacy of treatment as prevention, what is the future niche for PrEP and microbicides in comprehensive prevention?**
- **Do we seek to optimize what we have shown to be effective or do we seek a better next generation?**
 - Current products are strikingly behaviorally dependent—adherence is a significant issue
- **Can long acting formulations be devised—improving both treatment outcomes as well as prevention**
 - Rings, implants, injectibles, long acting oral formulations

Optimistic, Long Range Vision

- **The therapeutic armamentarium will continue to improve with development and roll out of ART requiring 4-12 doses per year**
- **PrEP and microbicides could then be delivered through 4-12 doses a year**
- **These would be tools that can control and start ending the HIV pandemic**

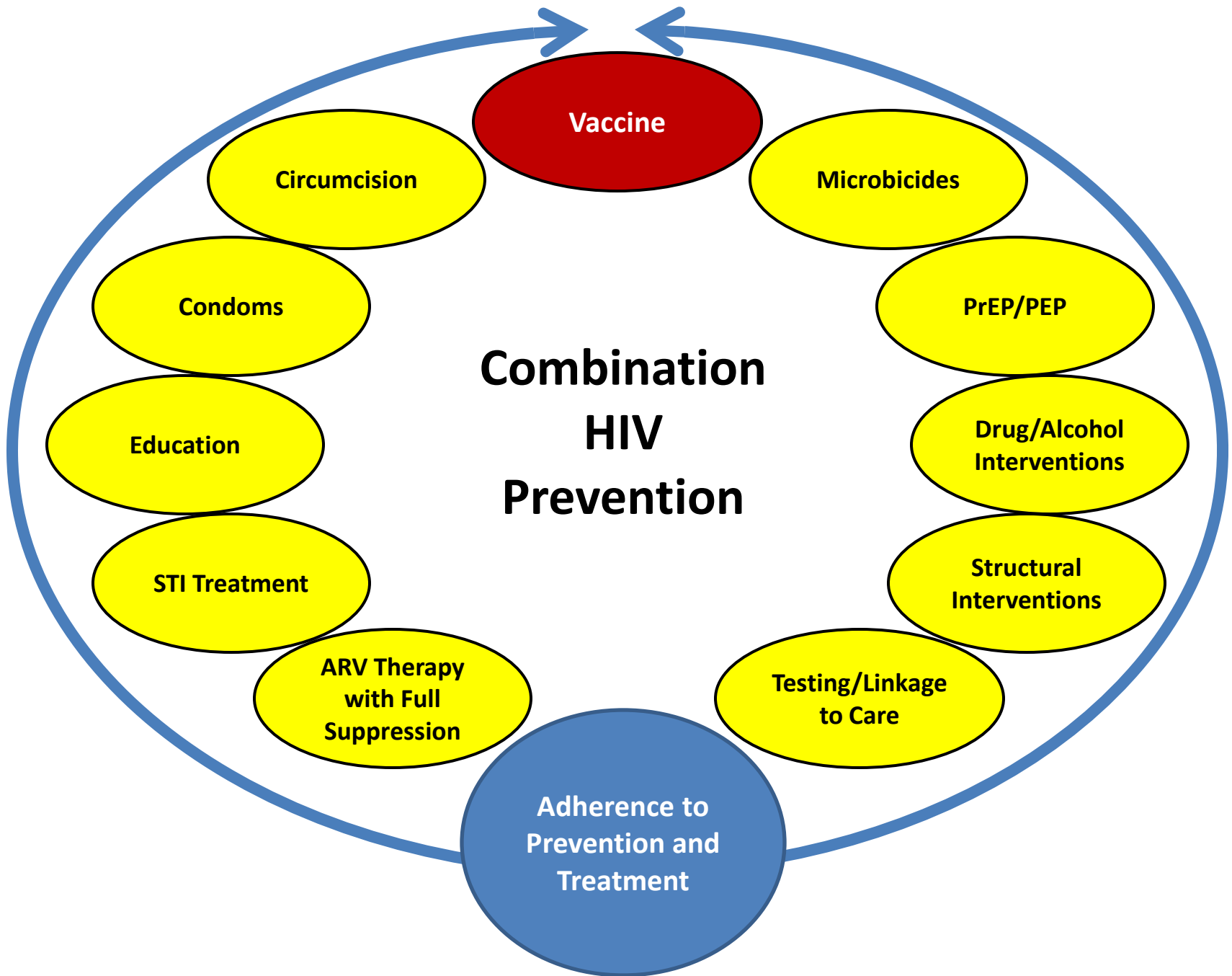
Integrated Prevention Strategies (Combination Prevention)

- **In partnership develop and test integrated biomedical and behavioral prevention strategies to reduce incidence on a population level**
 - Efficacy
 - Importance of community mobilization and structural interventions
 - Locally/culturally appropriate
 - Feasible for scale up
 - Sustainable

Scientific Advances

Implementation





**Our Common Goal:
Controlling and Ultimately
Ending the HIV/AIDS
Pandemic**



Questions?
