

When Paradigms Shift: Challenges of a World in Which Combination Prevention is Our Standard, Most Everyone is Eligible for Lifetime ART and Treatment is Prevention

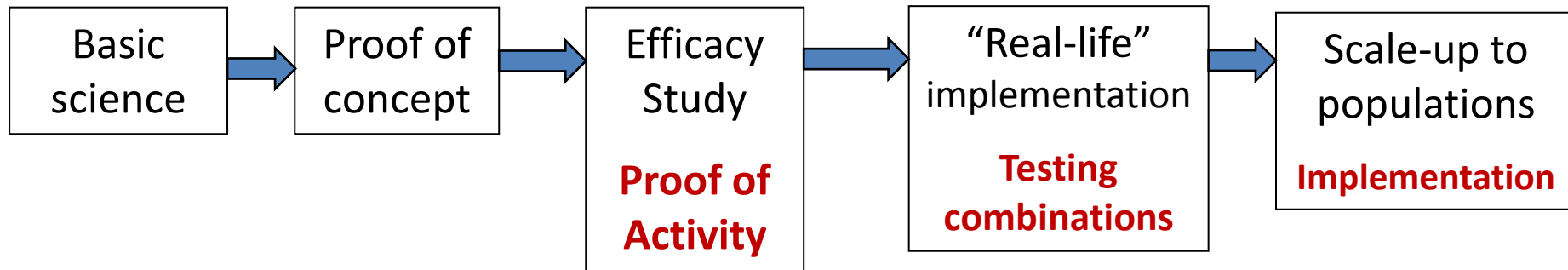
Carl W. Dieffenbach, Ph.D.

Director, Division of AIDS, NIAID, NIH

June 5, 2012



Discovery→Delivery: The Path to Combination Prevention



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

**Combination
HIV
Prevention**

The diagram consists of a central text block surrounded by nine yellow oval shapes, each containing a different HIV prevention method. The ovals are arranged in a circular pattern, with three on each side of the center. The central text is in a larger, bold, blue font, while the text in the ovals is in a bold, black font.

Education

Condoms

STI treatment

**Testing/
counseling**

**Treatment as
Prevention**

**Drug/alcohol
treatment**

Circumcision

Microbicides

PrEP

Harm reduction

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**

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 behavior/adherence be changed?**
- **Coitus-dependent gels will be part of the armamentarium**
- **Develop long-acting formulations—improving both treatment outcomes and prevention**
 - Rings, implants, injectables,

Essential Linkage of Social, Behavioral and Biomedical Research

- **Social science research must inform product development in an iterative way**
- **Develop strategies and messages to promote social acceptance of knowledge of HIV status and social responsibility for treatment for HIV infection**
- **Creation of interest and demand for HIV prevention requires an integrated approach**

Combination HIV Prevention

Education

Condoms

STI treatment

**Testing/
counseling**

**Treatment as
prevention**

PMTCT

**Drug/alcohol
treatment**

**Male
circumcision**

Microbicides

PrEP

Harm reduction

JAMA

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Universal Voluntary Testing and Treatment for Prevention of HIV Transmission

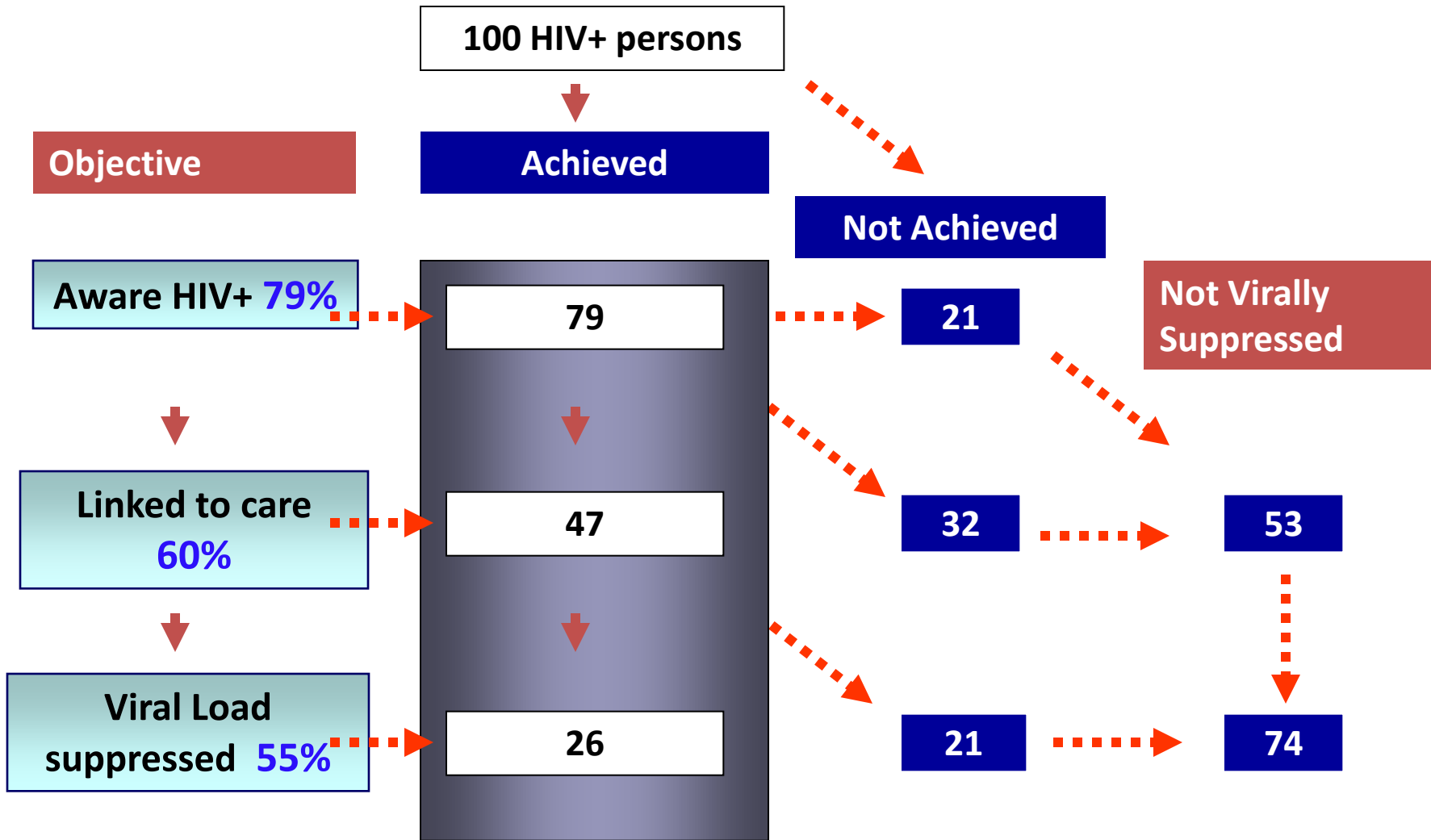
CW Dieffenbach and AS Fauci

"As with all mathematical models, the voluntary test and treat model is based on a number of assumptions that require validation with research."

Selected Research Issues Related to the Voluntary “Test and Treat” Approach

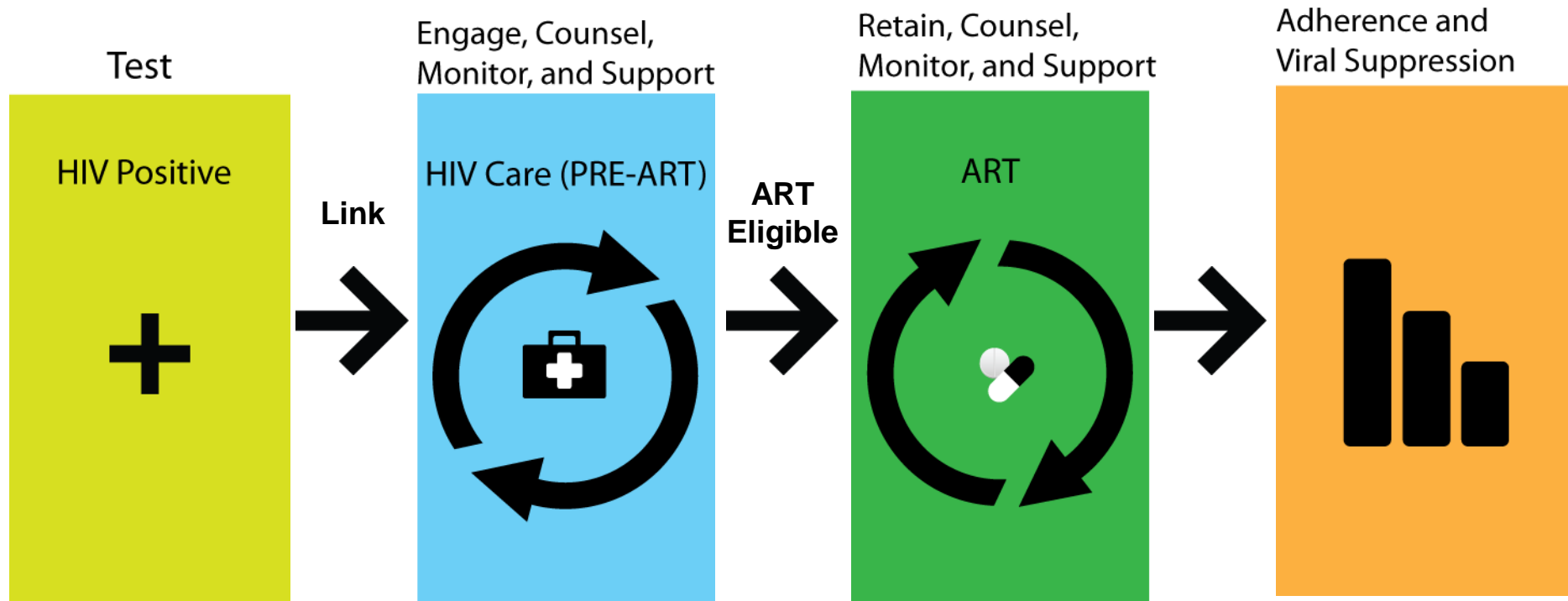
- **Universal testing**
- **Relationship of the stage of HIV infection to efficiency of transmission**
- **Efficacy of ART in preventing HIV transmission**
- **Drug resistance**
- **Behavioral “disinhibition”**
- **Benefit to the individual**
- **Cost-effectiveness for society**

Cascade Effect: Diminishing Returns



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

HIV Care/Prevention Continuum



Coverage, acceptability, effectiveness, quality

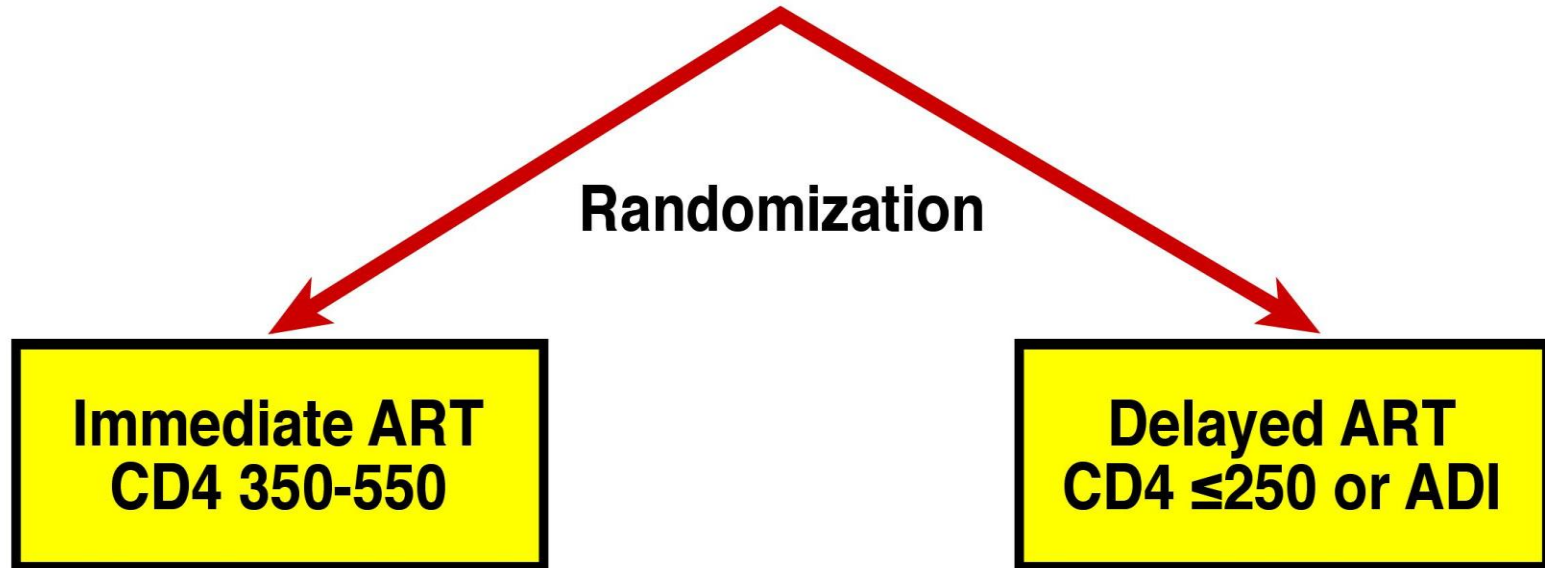
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HPTN 052 Study Design

**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**





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Prevention of HIV-1 Infection with Early Antiretroviral Therapy

HPTN 052 Study Team

VOL. 334

December 23, 2011

Science

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**

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U.S. Department of Health and Human Services

NIH News

National Institutes of Health

June 8, 2009

National Institute of Allergy and Infectious
Diseases (NIAID)

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

Starting Antiretroviral Therapy Earlier Yields Better Clinical Outcomes

*Interim Review Leads to Early End of Clinical
Trial in Haiti*

- ~4-fold increased risk of death for patients deferring ART until CD4 count dropped below 200 vs. initiating ART at CD4 count between 200-350 (n=816)

Additional Evidence for Clinical Benefit of Early Treatment

- CHER neurological benefit of treatment lost by delaying initiation of therapy in infants
- HPTN 052 completing analysis of all clinical events by treatment arm--anticipated this summer
 - 20 cases of extra pulmonary TB
 - 17 in the delayed arm
 - 3 in immediate arm ($p=0.0013$)

START

**HIV-infected individuals who are ART-naïve
with CD4⁺ count > 500 cells/mm³**

Early ART Group

**Initiate ART immediately
following randomization**

Deferred ART Group

**Defer ART until the CD4⁺ count
declines to < 350 cells/mm³ or
AIDS develops**