

# **Clinical and Public Health Policy Implications of Findings that:**

▲ Adherence to HIV Medications and Emotional/Physiological Coping with Stress are Independently Associated with Specific Five-Year Outcome Indicators

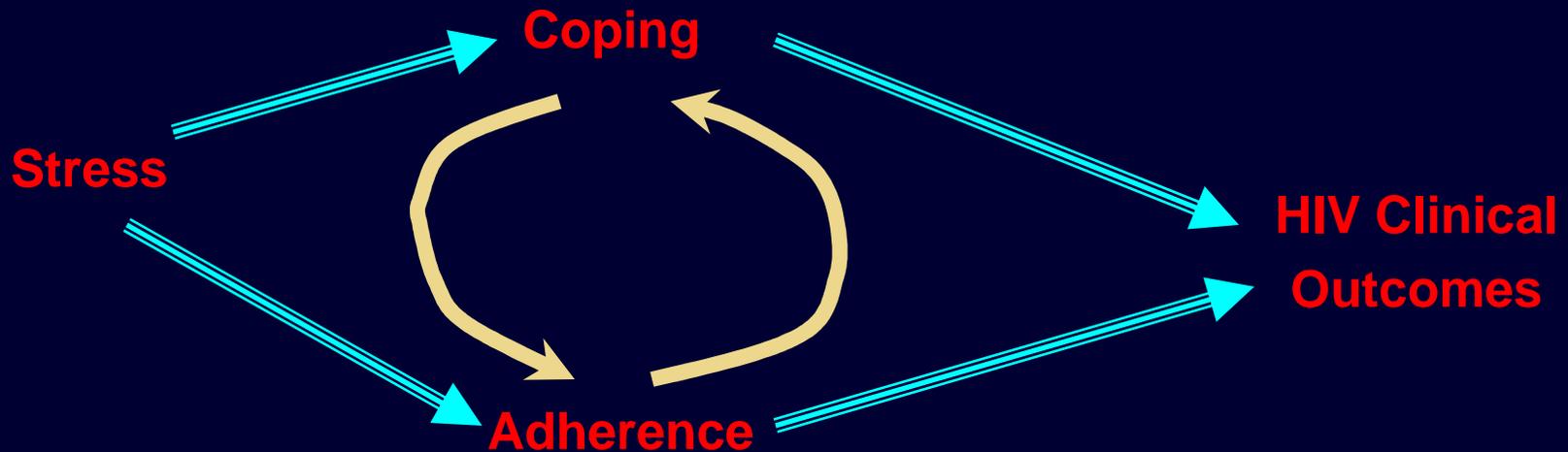
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# Longitudinal Study Overview

- 5-year NIH R01 study to identify the complex mechanisms by which coping, psychosocial, and behavioral variables may interact with immunological factors and physiological response patterns to influence HIV progression.
- 200 HIV+ participants (49% men, 92% African American in HIV primary care clinic in inner city Baltimore.
- 69% currently prescribed Antiretroviral Therapy-ART
- 25% on cardiovascular meds-- high blood pressure
- 34% on psychiatric medications-- antidepressants
- 17% on methadone maintenance

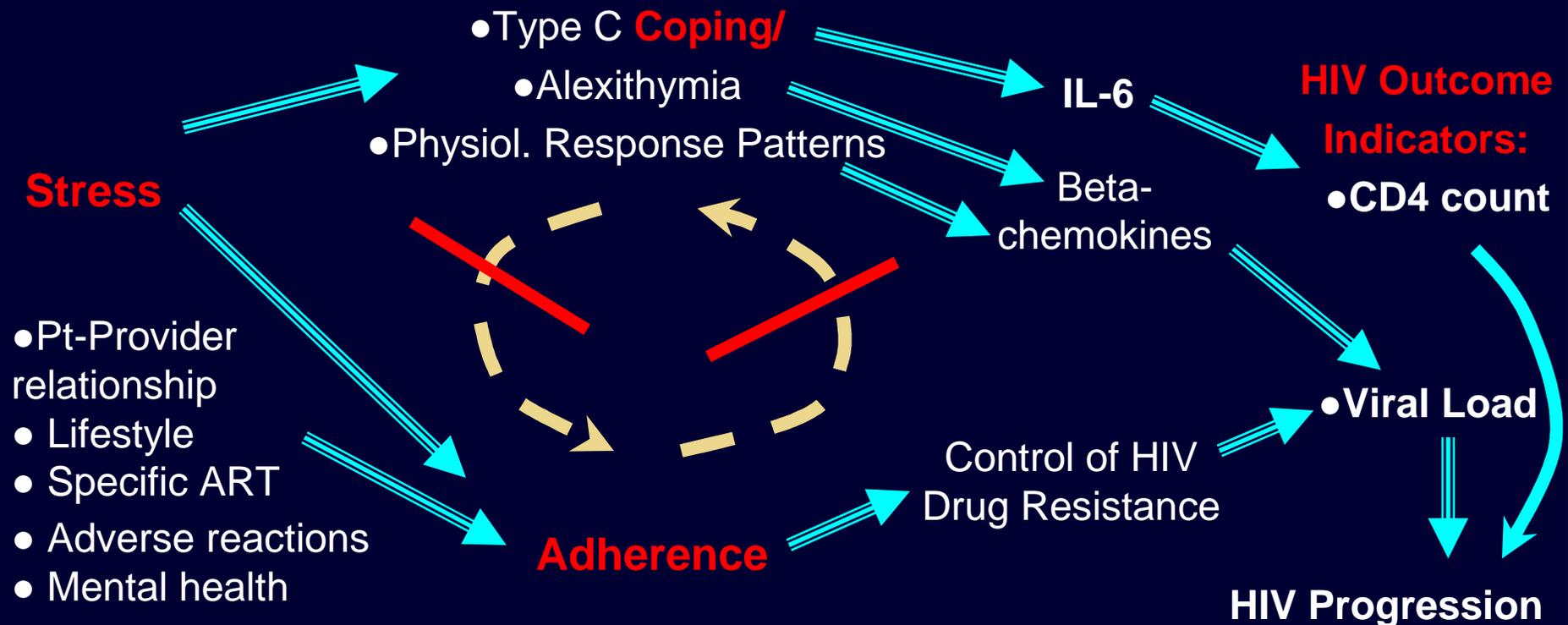
# Hypothetically. Adherence and Coping Factors Interact to Influence HIV Clinical Outcomes

**Psychoneuroimmunology (PNI) Route**



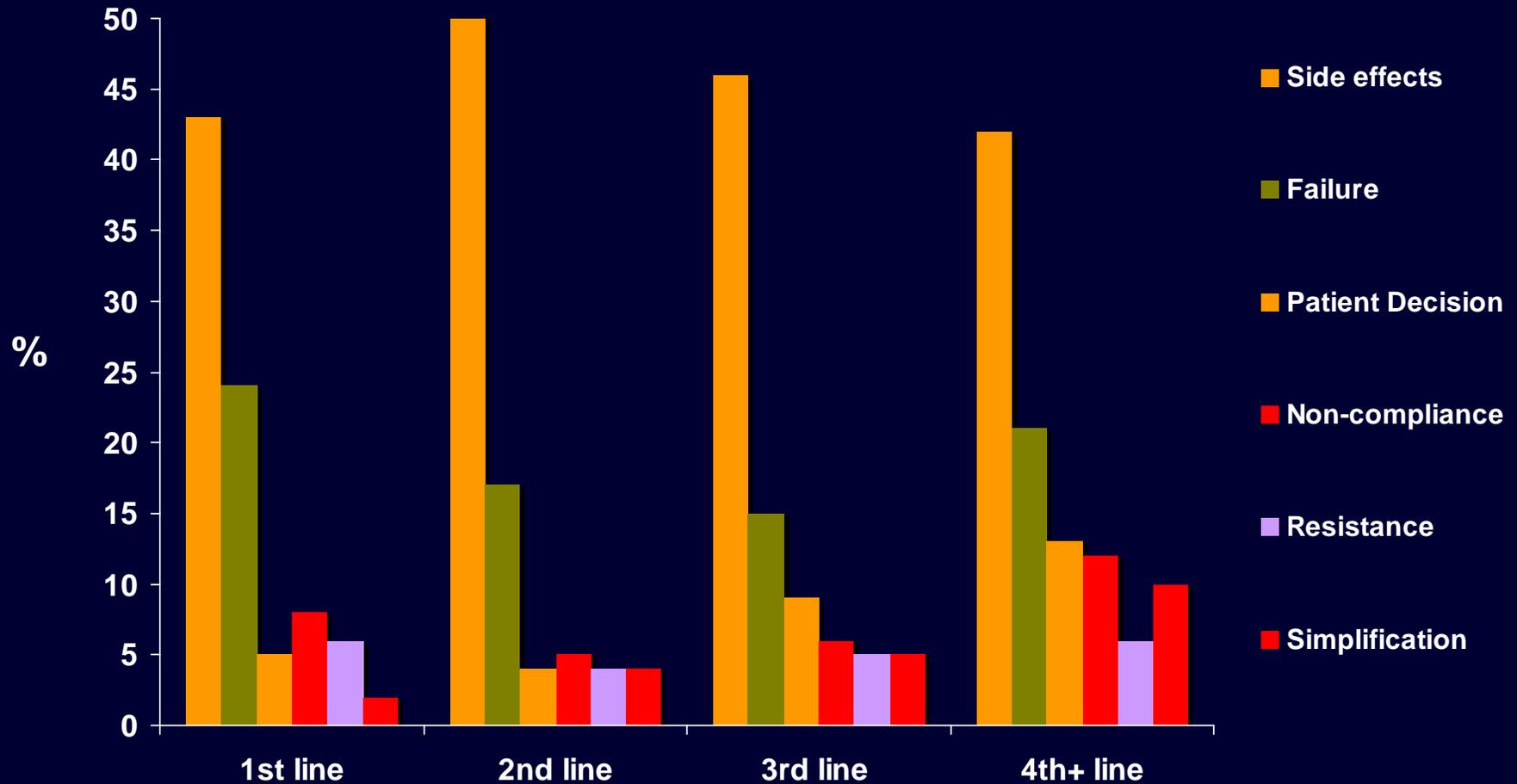
**Behavioral Route**

# However, Results Show that Coping and Adherence Affect Specific Outcome Indicators By Different Mediators of Progression



# ART Success is Dependent on Adherence

*Reasons for ART Failure*



ISIS 2003b Source: HIV in the USA Therapy Monitor

**“It’s much more important to know what sort of patient has a disease than what sort of disease a patient has.”** -William Osler

**“Drugs don’t work if people don’t take them.”**  
- C. Everett Koop

**“...adherence is still the most important predictor of a successful response to ART (anti-retroviral treatment).”** -Andrew Kambugu, *Lancet* April 2012

## Evaluating Assumptions about “Pill Burden”

Although HIV medical and behavioral medicine practitioners generally agree that social and mental instability and other factors such as relationship with one’s provider are the most important factors predicting suboptimal adherence, the pharmaceutical industry has proposed pill burden as a main factor, and in response, has developed pills combining 2 or 3 medications (Truvada—most commonly prescribed, Combivir, Trizivir, Epzicon, and Atripla).

# Design and Methods

- We evaluated how this “reduced pill burden” ART strategy contributed to ART adherence and clinical outcomes in 395 largely African-American (96%) HIV+ men (204) and women (186) in a Baltimore primary care outpatient clinic or hospital inpatient ward, *who were currently on a ART regimen.*
- Because inpatients tended not to return for outpatient treatment, 6 and 12 mo. clinical outcomes were generally only available for outpatients.
- Adherence was assessed with a structured interview validated for this population; HIV-1 RNA (viral load, VL) and CD4+ cell count were obtained from electronic medical records.

# Results

- There was no difference in adherence defined as number of missed doses between patients taking one pill containing 2-3 medications and their counterparts who took more pills, each with a single medication; however, those taking pills with 2-3 combined drugs (Truvada, Combivir, Trizivir, Epzicon) missed more medications in total (Atripla was not prescribed at the time of data collection).
- For all patients with available follow-up, the number of missed doses was negatively associated with log CD4+ cell count ( $p = .05$ ).
- Assessing adherence as total number of missed medications (vs. the # missed doses) was the most significant and predictive measure of both log VL ( $p = .05$ ) and log CD4+ cell count ( $p = .004$ ;  $N = 177$ ).

## Defining HIV Medicine Adherence as Number of Prescribed Medications vs. Doses Taken is the Best Predictor of Clinical Outcomes

- These findings call into question the notion that pill burden is one of the primary causes of suboptimal adherence and treatment failure. Instead, the findings suggest that HIV+ patients who have trouble taking 3 pills with 3 individual medications are just as likely to have trouble taking one pill containing 3 medications.
- Results suggest that missing one pill containing 2-3 medications, particularly Truvada, will result more quickly in treatment failure (detectable VL) and lower CD4+ cell count. These findings have important implications for medical and public health practices of prescribing ART, promoting adherence, as well as for the current CDC emphasis on “treatment as prevention.”

# “Treatment as Prevention” Unequivocally Successful for Secondary Prevention

- Key driver of HIV transmission is plasma HIV-1 RNA (viral load--VL).
- Reducing VL through appropriate and optimally adhered-to antiretroviral treatment (ART) reduces VL to undetectable levels.
- Greatly reduced VL decreases HIV transmission from HIV-infected to uninfected persons, as shown in studies of vertical transmission, serodiscordant heterosexual couples, and injecting drug users.
- HPTN 052, a randomized trial of HIV serodiscordant couple, was halted by the data safety and monitoring board because of compelling results.
- Not only did treatment significantly reduce morbidity and mortality, as well as tuberculosis, but there was a dramatic 96% reduction in HIV transmission to serodiscordant (HIV-uninfected) partners with immediate treatment of the HIV+ partner.

# “Treatment as Prevention” Applied to “At Risk” but Healthy People (PrEP)

- PrEP = Pre (before) Exposure (coming into contact with HIV) Prophylaxis (taking medication to prevent becoming HIV-infected).
- Previous examples: travelers who take medication to prevent malaria; HIV+ mothers who take HIV medications to prevent passing HIV to their babies before and during birth.
- If medications are in the bloodstream when someone is exposed to HIV, then the virus will not be able to establish itself and infect the person.
- FEM-PrEP study (oral tenofovir emtricitabine) in sub-Saharan Africa was prematurely terminated because the intervention did not appear to be efficacious, although the CAPRISA 004 2010 study of vaginal tenofovir (i.e., used as a microbicide) was successful.
- Poor adherence to oral medication was hypothesized to be responsible for this “surprising” result.

# Premature Exaltation in the Press (PrEP) for PrEP Study in Serodiscordant Partners

- Press Release 7-13-11 (Seattle) : “In a result that will fundamentally change approaches to HIV prevention in Africa, an international study has demonstrated that individuals at high risk for HIV infection who took a daily tablet containing an HIV medication—either the antiretroviral medication tenofovir or tenofovir in combination with emtricitabine—experienced significantly fewer HIV infections than those who received a placebo pill. These findings are clear evidence that this new HIV prevention strategy, called pre-exposure prophylaxis (or PrEP) substantially reduces HIV infection risk.”

# Premature Exaltation in the Press (PrEP) for PrEP Study in Serodiscordant Partners

- "This study demonstrates that antiretrovirals are a highly potent and fundamental cornerstone for HIV prevention and should become an integral part of global efforts for HIV prevention."

# Adherence and HIV Drug Resistance

- HIV+ individuals who continue to practice transmission risk behaviors place their negative partners at high risk of infection. Such behaviors also expose HIV+ partners to secondary infections (e.g., hepatitis, STDs) which may accelerate disease progression or complicate treatment, as well as the risk of superinfection with drug-resistant HIV strains.
- The co-occurrence of suboptimal adherence and transmission risk behaviors results in the transmission of drug-resistant strains of HIV to newly infected individuals, as well as superinfection with resistant strains among HIV+ individuals.
- To the extent that both suboptimal adherence and transmission risk behaviors are more common in disadvantaged and/or ethnic/racial/sexual minorities, there is the potential for biological entrenchment of social, economic, and healthcare access disparities, creating ***HIV biodisparity***.

# Biodisparity Model

