Prevention for Positives: Past, Present, and Possible Future Directions

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A Global Prevention “Cocktail”

• Until about 2000, HIV prevention approaches focused almost exclusively on seronegatives, and relatively little attention was devoted to “prevention for positives” (CDC, 2003; Global HIV Prevention Working Group, 2004; Janssen et al., 2001; NIH, 1997; WHO, 2004)

• For an effective global HIV prevention portfolio, we need to consider the implementation of “prevention cocktails” that involve potent HIV prevention interventions for seronegatives, and potent HIV prevention interventions for seropositives

  – In many cases these “cocktails” may need to involve both behavioral and biological approaches to reducing risk of transmission for both seronegatives and seropositives
Why Prevention with Positives?

- All new HIV infections must involve an HIV seropositive individual.

- Given limited funds, it may be cost-effective to encourage HIV testing and to intervene with individuals who are HIV positive, as well as those who are HIV negative.

- While most HIV positive individuals who know their serostatus reduce their risk levels, some do not.

- In the ART era, prevalence rates for HIV infection will continue to climb. Prevention for positives would seem to make sense.
Estimated HIV Infection Incidence and Prevalence, by Year, 1977-2003, United States

Adults and children estimated to be living with HIV, 2007

**Total: 33 million (30 – 36 million)**

WHO/UNAIDS/Unicef (2008)
Estimated number of adults and children newly infected with HIV 2007

North America
54,000
[9,600 – 130,000]

Caribbean
20,000
[16,000 – 25,000]

Latin America
140,000
[88,000 – 190,000]

Western & Central Europe
27,000
[14,000 – 49,000]

Middle East & North Africa
40,000
[20,000 – 66,000]

Sub-Saharan Africa
1.9 million
[1.6 – 2.1 million]

Eastern Europe & Central Asia
110,000
[67,000 – 180,000]

East Asia
52,000
[29,000 – 84,000]

South & South-East Asia
330,000
[150,000 – 590,000]

Oceania
13,000
[12,000 – 15,000]

Total: 2.7 million (2.2 – 3.2 million)

WHO/UNAIDS/Unicef (2008)
Some interventions for seropositives that may reduce new HIV infections

- **Increased HIV Testing**
  - Identifying Seropositives
  - Effects of Testing On Risk Behavior

- **HIV Care**
  - Effects of Care Initiation & Maintenance on Behavioral and Biologic Risk

- **Initiating ARVs**
  - Effects on Behavioral & Biologic Risk

- **ARV Adherence**
  - Effects of Adherence on:
    - HIV Risk Behavior
    - Biologic risk

- **Traditional Prevention for Positives**
  - Effects on Risk Behavior

- **Next Generation HIV Prevention for Positives Interventions**
HIV Testing

- HIV Testing
- HIV Care
- Initiating ARVs
- Prevention for Positives
- ARV Adherence
- Next Generation HIV Prevention for Positives Interventions
Increased HIV testing: Identifying Seropositives

- **Proportion of PLWH who know their status varies:**
  - About 75% of all PLWH in the US are aware of their status (Marks, Crepaz & Janssen; 2006)
  - The 25% of PLWH who do not know their status may account for over 50% of all new infections annually (Marks, Crepaz & Janssen; 2006)
  - Globally, the proportion of PLWH aware of their HIV status varies (5% - 60%), and a large proportion of PLWH remain unaware of their HIV status (WHO/UNAIDS 2008 Progress Report)
  - It is likely that globally, PLWH who are unaware of their status account for the majority of new HIV infections annually
Increased HIV testing: Identifying Seropositives

• **Availability and uptake of HIV testing**

  – Results from low- to middle-income countries indicate the *median percent of persons ever tested for HIV* who have received their test results is quite low:

  • 10.9% of all women, 10.3% of all men surveyed

  • 3.9% of all women, 3.8% of all men in sub-Saharan Africa

(WHO/UNAIDS 2008 Progress Report)
Increased HIV testing: Identifying Seropositives

- **Availability and uptake of HIV testing**
  - Increased uptake in HIV testing has coincided with the increased availability of ARVs

  - In fact, in low and middle income countries, 43% of those who had ever received an HIV test, had done so in the past year

  - Greater uptake in testing is likely facilitated by increased treatment options, and associated lowering of stigma

(WHO/UNAIDS 2008 Progress Report)
Effects of HIV Testing on *Risk Behavior*

- **Meta analyses examining the effects of HIV testing on subsequent risk behavior find:**
  - Reduced risk behavior among VCT participants compared to non-testers in developing countries (Denison et al., 2008)
  - The largest reductions in sexual risk occur among seropositives and serodiscordant couples post diagnosis (Denison et al., 2008; Weinhardt et al., 1999)
  - Among PLWH who learn their HIV status, sexual risk behaviors with HIV- and status unknown partners are reduced by 68% (Marks et al., 2005)
Effects of HIV Testing on Risk Behavior

- Nevertheless, there are fluctuations in risk behavior over time
  - Studies continue to indicate that proximately 1/3 of PLWH continue to engage in risk behavior post diagnosis (e.g., Crepaz et al., 2002; Kalichman, 2000)
  - Although rates of risk behavior fluctuate, they remain lower than rates observed prior to initial diagnosis (Marks, Crepaz, & Janssen; 2006)
  - A recent review indicates these fluctuations may vary in relation to the stage of the HIV disease (Eaton & Kalichman, 2009)
    - Higher rates of risk behavior during acute infection and prolonged periods of asymptomatic infection
    - Lower rates of risk behavior following initial HIV diagnosis or a formal AIDS diagnosis
HIV Care

HIV Testing

Initiating ARVs

ARV Adherence

Prevention for Positives

Next Generation HIV Prevention for Positives Interventions
Some recent evidence indicates that engagement in HIV care may be associated with:

- Reductions in risk behavior among recently diagnosed PLWH who are successfully linked to primary care (Metsch et al., 2008) and those retained in care over time (Metsch et al., 2008; Takizawa et al., 2007)

- Nevertheless, unsafe injection drug use, sexual behavior and unrecognized STIs continue to be observed in clinical care samples (e.g., Cornman et al., 2008; Ebelding et al., 2000; Fisher et al., 2006; Sarna et al., 2008; Vlahov et al., 2001)

- In general, more research is needed to clarify the relationship between initiating and maintaining clinical care and risk behavior
Effects of Initiation & Maintenance of Care on Biological Risks

• **Being in care can also provide access to ARVS:**
  – Initiation of care facilitates the timely initiation of antiretroviral (ARVs) medications, which can lower risk of transmission

• **Maintaining care can also support biologic benefits**
  – Maintenance of regular care facilitates monitoring of ARVs, viral load, CD4 count, and co-morbid conditions, reducing risk of transmission

• **Regarding PfP, initiation and maintenance of care may have behavioral and biologic impacts on risk behavior and infectiousness** (Temoshok and Wald, 2008)
Initiating ARVs

HIV Testing → HIV Care

Initiating ARVs

ARV Adherence

Prevention for Positives

Next Generation HIV Prevention for Positives Interventions
Effects of Initiating ARVs on Biologic Risk

- ARV’s ability to suppress viral load is associated with a reduction of transmission risk to sexual partners (Lalani & Hicks, 2007)

- Recent mathematical modeling of the effects of ARVs on reducing transmission suggests risk of transmission may be more substantially reduced among serodiscordant heterosexual couples than serodiscordant MSM couples (Wilson et al., 2008)

  - These mathematically modeled effects of reduced transmission are sensitive to changes in risk behavior (e.g., decreased condom use) (McCormick et al., 2006; Wilson et al., 2008)
Effects of Initiating ARVs on Behavioral Risk

Results regarding the effects of ARVs on Behavioral Risk are more complex:

- **Factors associated with no change in behavioral risk**

  - Initiating ARV therapy, or having a suppressed viral load, is not generally associated with increased risk behavior among PLWH in the US or developing countries (e.g., Burman et al., 2008; Crepaz et al., 2004; Kaida et al., 2008; Kennedy et al., 2007; Sarna et al., 2008; Stephensen et al., 2003)

  - Some studies found a decrease in risk behavior among PLWH after initiating ARVs in Africa (Kennedy et al., 2007; Kida et al., 2008; Lutchers; 2008).
Effects of Initiating ARVs on Behavioral Risk

- **Factors related to increased behavioral risk**
  - In both the US and Africa, attitudes about the reduced risk of transmission due to ARVs, or reduced or suppressed viral load (e.g., Crepaz et al., 2004; Cohen et al., 2009; Cox et al., 2008; Huebner & Gerend, 2001; Kaida et al., 2008; Kalichman et al., 2001; Lalani & Hicks, 2007; Ostrow et al., 2002; Vanable et al., 2000)
  - Perceived low viral load, regardless of actual viral load (Stolte et al., 2004)
  - Safer sex fatigue among HIV+ MSM (Cox et al., 2004; Ostrow et al., 2002)
  - Partner’s serostatus (Cox et al., 2004; Luchters et al., 2008)
  - Cohabitation with main partner, fertility desires, non-disclosure, and stigma in developing countries (Kaida et al., 2008; Luchters et al., 2008)
Effects of Initiating ARVs on Behavioral Risk

• In sum, though NOT eliminated, ARVs can reduce the overall biologic risk of transmission.

• Concerning behavioral risk, it is important that HIV prevention efforts with PLWH on ARVs address both attitudinal and other psychosocial factors that can increase risk behavior.
ARV Adherence

HIV Testing → HIV Care

Initiating ARVs

ARV Adherence

Prevention for Positives

Next Generation HIV Prevention for Positives Interventions
Effects of ARV Adherence on HIV Risk Behavior & Biologic Risk

• Exploration of the relationship between adherence to ARVs and behavioral risk suggests some overlap, although more research is needed
  – Findings suggest, achieving optimal adherence may be related to a decrease in sexual risk behavior, while higher rates of risk behavior are often observed among PLWH who are less adherent (e.g., Diamond et al., 2005; Flaks et al., 2003; Kalichman et al., 2008; Wilson et al., 2002)

• Given the potential to transmit resistant virus, the dynamics of risk behavior in the context of varying adherence needs further attention (Remien et al., 2007)
  – For example, Kozal et al. (2004) identified 5% of their clinic-based sample as both treatment resistant and sexually risky. As a group, these folks, reported large numbers of transmission risk events
Effects of ARV Adherence on HIV Risk Behavior & Biologic Risk

• *PLWH who are enrolled in ARV adherence interventions adhere better, have lower viral loads and are less infectious* (Simoni et al., 2006)

• *Thus, interventions aimed at facilitating optimal levels of adherence are a critical component of the PfP portfolio*

• *Adherence promotion interventions and maintenance in care:*
  
  – In combination, *can* work symbiotically to facilitate improved outcomes and reduced infectivity via (Temoshok & Wald, 2008) -
    
    • Viral suppression and reduced risk of transmission
    
    • Regular clinic visits provide opportunity for ongoing treatment and for adherence and risk reduction counseling to occur
Sample ART Adherence Intervention

A CD-Rom Based
ART Adherence Promotion Intervention
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Prevention for Positives

HIV Testing

Initiating ARVs

ARV Adherence

HIV Care

Prevention for Positives

Next Generation HIV Prevention for Positives Interventions
Effects of Prevention for Positives Interventions on HIV Risk Behavior

• Overall, the goal of PfP interventions is to prevent HIV transmission to others and ensure optimal health in PLWH
  – Most behavioral PfP interventions to date focus on safer behavior, which decreases HIV transmission and helps prevent seropositives from acquiring new pathogens
Effects of Prevention for Positives Interventions on HIV Risk Behavior

- **Behavioral Prevention for Positives interventions (PfP) can target a diverse range of preventive behaviors, and support their adoption over the life span**
  - Traditional prevention behaviors
    - e.g., safer sex behaviors, safer needle use, disclosure
  - Harm reduction behaviors
    - e.g., condom use with non-primary partners, strategic sexual positioning, serosorting

- **Given the substantial numbers of people living worldwide with HIV, PfP has the potential to impact the epidemic through behavior change by PLWH who know their status and engage in risky behaviors**
Conceptualizing Risky and Preventive Behavior among Seropositives:

The Information-Motivation-Behavioral Skills Model

- Work on risk dynamics among PLWH has shown that individual levels of HIV prevention information, motivation and behavioral skills are associated with levels of risky and safer sexual behavior.

Three fundamental determinants of HIV-risk and preventive behavior among seropositives.


Effects on HIV Risk Behavior

• Previous Meta-analyses have demonstrated the effectiveness of behaviorally-focused PfP interventions in promoting safer behavior among PLWH who know their status:
  
  – PfP interventions are more effective on average than typical “prevention for negatives” interventions in reducing risk behavior (Crepaz et al., 2006; Johnson et al., 2006)
  
  – Furthermore, the most effective interventions in reducing sexual risk behavior contained Informational, Motivational, and Behavioral Skills (IMB) components (Johnson et al., 2006)
Sample Prevention for Positives
Interventions

Physician-Based Intervention for Seropositives
J. Fisher, PI

Lay Counselor-Based Intervention for Seropositives
J. Fisher, PI
Options: A Clinic-based PfP Intervention

- Options links Prevention for Positives with routine clinical care, and can include both behavioral and biological elements that can impact the risk of transmission.
Options Protocol for Each Patient Visit

• Provider performs medical exam
  – Monitors the effects of ARVs on viral suppression and resistance
  – Addressees other co-morbid conditions that can affect HIV transmission (STI’s, etc.)

• Sets the agenda to discuss safer sex.

• Assesses risk behavior.

• Quickly determines the risk dynamics for a particular patient

• Elicits a menu of specific strategies from the patient for addressing these risk dynamics.

• Negotiates a goal or action plan with the patient.

• Gives a “behavioral prescription” to the patient.
US Options Intervention Outcomes at 18 months

Estimated (GEE) Group Means

- **Significant Time x Condition interaction** \( (b = -0.51, SE = 0.15, p < 0.001) \)
  - Risk behavior was significantly **reduced** in the intervention group \( (b = -0.51, se = 0.23, p < 0.05) \) but significantly **increased** over time in the control group \( (b = 0.51, se = 0.19, p < 0.01) \)

South Africa *Options* Pilot Intervention Outcomes at 6 months

- **Significant Time x Condition interaction** $(b = -2.24, SE = .92, p = .016)$
  - Again, we found a similar pattern of risk behavior being significantly **reduced** in the intervention group $(b = -1.41, se = .65, p < .05)$, and a marginally significant **increase** over time in the control group $(b = .67, se = .34, p = .05)$

South Africa *Options*

- We hope to demonstrate that *Options* is a model for PfP, linking prevention with care, that can be used in the context of ARV rollouts bringing seropositives into care throughout Africa.
Benefits of *Options* as a Clinic-based Prevention for Positives Intervention

- Enables access to large numbers of seropositives

- **Behavioral aspects** of the intervention can be delivered by a variety of health care providers who vary in levels of formal training.

- **Biological aspects of the intervention** require a trained health professional.

- *Options* allows patients to receive ongoing behavioral and biological PfP treatment over extended periods of time.
Next Generation of HIV Prevention for Positives Interventions
Possible Future Directions for Prevention for Positives Interventions

- Future PfP interventions will likely yield greater impact on the epidemic by addressing the unique interface of behavior and biology by including (Temoshok & Wald, 2008):
  
  - Behavioral approaches
    - Safe/safer sex, optimal ARV adherence, and reduction of substance use

  - Medical approaches to deal with biologic risk
    - Effective ART monitoring, viral suppression, monitoring viral resistance, and co-morbid conditions

  - Integrate other services to address conditions that facilitate risk among PLWH
    - e.g., mental health, addiction, and family planning services
Possible Future Directions (continued)

• *Behavioral* PfP components need to be integrated into the current *structural* changes (global scale up of HIV testing and ARV rollout) and *biomedical* advances (ARVs and prophylaxis)
Possible Future Directions (continued)

• In addition to other future directions, PfP needs to be conceptualized, in research and in practice, to include the core elements in the figure below, AND, critically, to ensure the links between them.
Possible Future Directions (continued)

- **Possible strategies to enhance the proposed linkages between these core elements**

  - *Test and Treat (TNT)* facilitating uptake of HIV Testing, early entry into care and aggressive early initiation of ARVS

  - Build in *health literacy* and *system navigation* components to facilitate linkage to care and ARV initiation

  - Enhance *patient self-management* skills to sustain adherence and maintenance of care
Possible Future Directions (continued)

• Expanding opportunities for behavioral PfP interventions to meet the prevention needs of PLWH will require a much broader focus:
  – Implementing behavioral PfP into routine HIV medical care
  – Implementing behavioral PfP into other HIV support services
  – Cross-training providers to address both prevention and adherence, or provide linkages and intensive follow up

• Prevention for Positives interventions need to be ongoing, not one time events, permitting them to respond to individual needs, as they change
Finally, next generation PfP interventions need to be:

- targeted to address any behavioral (e.g., risky sex, drug use, nonadherence) or biological element (e.g., inadequate ARV regimen, co-morbid conditions) or their interaction, which could affect infectivity to others (e.g., viral load, viral resistance).

- Should especially target those who are highly infectious
Possible Future Directions (continued)

• Next generation PfP interventions also need to be:
  – Widely disseminated and linked to other critical medical and social service practices
  – Adapted, implemented, and evaluated to meet the various resource constraints and culturally relevant behavioral and biologic prevention needs in developing nations, as HIV testing and ARV scale-ups gain momentum
Evidence for Reducing Risk of Transmission

HIV Testing
• Behavioral
• Biological

HIV Care
• Behavioral**
• Biological

Initiating ARVs
• Behavioral
• Biological

ARV Adherence Interventions
• Behavioral**
• Biological

Traditional Prevention for Positives Interventions
• Behavioral
• Biological

Next Generation HIV Prevention for Positives Interventions
• Behavioral
• Biological
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