HIV prevention in young women – designing combination prevention approaches

Sinead Delany-Moretlwe
HIV and Women workshop, Boston, Feb 2016
Overview

• Syndemics of HIV and gender-based violence (GBV)

• GBV increases HIV risk

• GBV has marked impact on continuum of HIV prevention, treatment and care continuum

• Linking programme responses to HIV and GBV for adolescent girls and young women
One-third of new infections globally occur in young African women.

Estimated number of new HIV infections per week among young women aged 15-24 years in East and Southern Africa, 2012

Data source: UNAIDS 2013

Over 7,000 new HIV infections every week among young women globally.
Fast track HIV prevention for young women

- By 2050, Sub-Saharan Africa is project to have more adolescents than any other region
- This represents an absolute increased in the HIV susceptible population
- More will need to be done to achieve the Fast Track targets by 2030

Population of adolescents 10-19 years old in millions, by region, 1950-2010

*Source: UNICEF, 2012*
“There is no policy for progress more effective than the empowerment of women and girls. Study after study has taught us that no other policy is as likely to raise economic productivity, or to reduce infant and maternal mortality. No other policy is as sure to improve nutrition and promote health -- including the prevention of HIV/AIDS...”

Kofi Annan, 2005
Gender and HIV risk

Underlying → Proximate factors → Biological factors → HIV infection

**Structural**
- Poverty
- Gender inequality
- Low social power
- Education
- Access to quality health services

**Behavioural**
- Early sexual debut
- Age-disparate partnerships
- Concurrent sexual partners
- Transactional sex
- Low condom use
- Alcohol abuse

**Biological**
- STIs
- Genital inflammation
- Intimate partner violence
- Hormones
- Partner circumcision
- Partner HIV viral load

High prevalence of past-year intimate partner violence, among ever-partnered women (15-19 years)

Prevalence (%)

Source: Decker, 2014

IPV and non-partner sexual violence associated with a range of poor health outcomes

Heise, 2014; Day, 2005
Young key populations experience high rates of partner violence and sexual assault

- **Sex workers**
  - Life time prevalence of any violence 45-75%
  - Young trafficked sex workers may experience rape to coerce them to sell sex

- **PWID**
  - Sexual assault associated with drug use (own or partner)

*Source: Delany-Morelwe, 2015*
Intimate partner violence is associated with HIV acquisition

- Cohort studies from sub-Saharan suggest that
  - physical (pooled OR 1.22; 95% CI 1.01-1.46),
  - sexual (OR 1.77, 95% CI 1.0-3.15) or
  - any type of violence (OR 1.28, 95% CI 1.0-1.64) are associated with an increased risk of HIV acquisition (Li, 2014)

- Estimates of population attributable fraction 12-22% of incident HIV infection
  - Not only sexual violence important
  - Physical violence, verbal abuse and highly unequal relationships associated with HIV acquisition (Jewkes, 2010; Kouyoumdjian, 2013; Durevall, 2014)
Intimate partner violence induces immune dysregulation

Direct mechanism
• Genital injury and exposure to HIV/STI as a result of sexual violence can induce inflammation, immune activation

Indirect mechanism
• Physical abuse, emotional abuse associated with up/down regulation of host genital immunology immune responses
  • Women who experienced IPV were at increased risk of acquiring HIV with increasingly severe violence associated with increased risk of infection.
  • Higher rates of depression and lower T-cell function in women who experience chronic abuse.
  • PTSD associated with dysregulation of cortisol pathways, fight or flight responses.
  • Reduced ability to suppress HSV-1 reactivation in physically and emotionally abused women compared to non-abused controls

• It might not all be about sexual violence
• Potentially important in the maturing genital tract of young women

Source: Garcia-Linares, 2004; Klot, 2012; Ghosh, 2015;
The effect of age-disparate partnerships

Africa Centre identified phylogenetically linked HIV transmission networks in Hlabisa

High HIV incidence men
Mean age 27 years (range 23-35 years)

Very young women acquire HIV from men, on average, 8 years older

Men and women > 24 years usually acquire HIV from similarly aged partners

High HIV risk women
Mean age 18 years (range 16-23 years)

High HIV prevalence women
Mean age 26 years (range 24-29 years)

When teen women reach mid-20s they continue the cycle

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ART for prevention – reducing infectiousness

- Men lower testing uptake \( (HSRC, 2012) \)
- Men presented significantly later for treatment \( (Cornell, 2012) \)
  - lower median CD4+ cell counts
  - More likely to be classified WHO stage III/IV
- Men more likely to be truly lost to follow up at 3 years

UNAIDS, 2013
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Intimate partner violence may increase HIV transmission

- Anticipated IPV is associated with refusing **HIV testing**
  - Stigma, fear of disclosure to partner major barrier to uptake of PMTCT ART
- Physical IPV lowers uptake of **antenatal care**
- Male involvement predicts better **adherence to NVP**
- History of violence decreases women’s **breastfeeding**

- Anticipated violence lengthens time to **linkage to care**
- History of physical or sexual IPV decreases **ART uptake**
- Current IPV is linked to poor **ART adherence**
- GBV associated with poor **HIV outcomes**
  - Lower CD4+ counts, increased virologic failure and OI

**Studies with HIV-positive Women**

Source: Gourlay, 2013; Hatcher, 2013
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Until recently, few HIV prevention methods under direct control of young women

PrEP should be offered to individuals at substantial risk for HIV infection...
PrEP – the evidence

• PrEP works when taken
  • Systematic review and meta-analysis of 18 studies found PrEP effective
  • Protection did not vary by age, gender, regimen, dosing or mode of HIV acquisition
  • Protection strongly correlated with adherence
    • In trials with adherence ≥80%, HIV risk was ↓ by 70%

PK studies show lower concentrations in cervical vs. rectal compartment with oral PrEP
  • Greater requirement for consistent adherence in women?
  • Effects of STIs/genital inflammation?

Poor partnership dynamics influence adherence

• Male partners’ understanding/support of the trial and study products had a significant influence on women’s use of PrEP
  • Fear of disclosure to partner
  • Disclosure however associated with better adherence

• ART use perceived to be associated with HIV illness by male partners;
  • unintentional disclosure occasionally led to relationship conflicts
  • Concerns about potential stigma led to concealed use of study products and lower adherence;

Source: Marrazzo, 2015; Montgomery, 2014; van der Straten, 2014a; van der Straten, 2014b Stadler, 2014; Succop, 2014; Mngadi, 2014
Trials ≠ “real life”

- What PrEP-takers say PrEP offers
  - Decreased anxiety
  - Increased communication, disclosure, trust
  - Increased self-efficacy
  - Increased sexual pleasure & intimacy

- Sex workers
  - Fear of violence may motivate PrEP use
  - Also observed in FACTS 001

- Need to understand how young women will incorporate oral PrEP into their every day lives, and what support is required

Source: Gilmore, 2014; Ware, 2012; Ware 2014; Eakle, personal communication
HPTN 067/ADAPT Study: Comparison of daily & non-daily PrEP dosing in African women

Bekker, CROI 2015 978LB

• 179 women in Cape Town; 6 wks of DOT then randomized to daily, or twice weekly with a post-sex boost or event-driven oral PrEP

• Adherence (measured by Wisepill & tenofovir levels) & coverage of sex acts highest with daily dosing
  – 75% of sex acts with daily vs 48% with twice weekly/sex boost dose & 52% with event-driven dosing
  – In the daily dosing study arm, 93% of the women had drug in their plasma at week 10, and 79% at week 30

• Additional studies are needed to understand the package of adherence support for young women in these settings

• Median age 26 years (range 18-52),
• 80% were unmarried
• 83% unemployed
PrEP demonstration projects in Africa

Models suggest PrEP will be cost-effective, but concerns that slow uptake, poor adherence and risk compensation will undermine gains

- How do we respond to the potential for gender violence to undermine oral PrEP?
- What can we learn now, while we wait for new products to be developed?
- How can we begin to make PrEP part of a comprehensive package?

<table>
<thead>
<tr>
<th>Population</th>
<th>Location</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female sex workers</td>
<td>Zimbabwe, South Africa, Benin, Senegal, Kenya (n=5)</td>
</tr>
<tr>
<td>Adolescent girls and young women</td>
<td>South Africa, Zimbabwe, Tanzania, Kenya (n=7)</td>
</tr>
<tr>
<td>HIV serodiscordant couples/Adult populations</td>
<td>Kenya, Botswana, Nigeria, Mozambique (n=4)</td>
</tr>
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Source: AVAC, 2015
Health system challenges

• Launch prototype for future product introduction.

• Product attributes will define levels of provider and user effort, and service delivery channels.

• PrEP will require a programmatic “home” for introduction.
  • ART has been procured and administered through treatment programmes,
  • But HIV prevention activities are shared across many programmes.

• Prospect of the expansion of options over the next few years rather than decades.
  • Managing simultaneous introductions of new technologies into services that have not traditionally provided ART or associated monitoring will require significant planning and coordination of stakeholders.

• Cost is a significant consideration
  • Need to leverage programme synergies
Prevention of violence against women and girls – the evidence for LMIC

- Men and boys gender norms programming
- Economic empowerment

- One-stop crisis centres
- Women’s police stations
- Perpetrator programmes
- Social marketing
- Alternative rights of passage
- Home visitation
- Infrastructure/transport
- ICT services

- Awareness raising campaigns
- Personnel training
- Justice and law enforcement responses

- Community mobilisation
- Empowerment training for women and girls
- Group training for women and men
- Microfinance/cash transfers + gender training

Source: Ellsberg, 2014
Implications for HIV programming

<table>
<thead>
<tr>
<th>IMAGE trial, South Africa</th>
<th>SASA! Uganda</th>
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</thead>
<tbody>
<tr>
<td>• Microfinance +/- gender empowerment CRCT</td>
<td>• CRCT of community mobilisation</td>
</tr>
<tr>
<td>• ↓ past year IPV by 55%</td>
<td>• ↓ physical IPV</td>
</tr>
<tr>
<td>• Improved HIV communication</td>
<td>• ↓ sexual IPV</td>
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<tr>
<td>• 25% less unprotected sex</td>
<td>• ↓ partner concurrency in men</td>
</tr>
<tr>
<td>• 64% higher HCT</td>
<td>• HIV incidence not measured</td>
</tr>
<tr>
<td>• No impact on incidence</td>
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<tr>
<th>Swa Koteka (HPTN 068), South Africa</th>
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<tr>
<td>• RCT of CT conditioned on 80% school attendance</td>
<td>Similar modalities used/planned for use across programmes – Co-financing?</td>
</tr>
<tr>
<td>• ↓ IPV by 28% at any visit</td>
<td></td>
</tr>
<tr>
<td>• ↓ having a sex partner and unprotected sex</td>
<td></td>
</tr>
<tr>
<td>• No effect on HIV or HSV-2</td>
<td></td>
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<tr>
<td>• School enrolment protective</td>
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Source: Pronyk, 2006; Ambramsky, 2015; Pettifor, 2015
The health sector has a responsibility to respond to violence, and global guidelines already exist

- Abused women more likely to seek health services
- Most women attend health services at some point, especially sexual and reproductive health
- If health workers know about a history of violence they can give better services for women
  - Identify women in danger before violence escalates
  - Provide appropriate clinical care
  - Reduce negative health outcomes of VAW
    - Including poor HIV outcomes
  - Assist survivors to access help/services/protections
  - Improve sexual, reproductive health and HIV outcomes
- Human rights obligations to the highest standard of health care

Source: Garcia-Moreno, 2014
Combining IPV prevention activities with existing HIV services – the SHARE trial

**Design:** Cluster randomized trial (CRT) that built on previously conducted CRT completed in Rakai

**Research Aims:** To assess impact of intervention on:
1. Past year emotional, physical and sexual IPV
2. Direct and indirect risk behaviors in the pathway between IPV and HIV infection (IP rape, number of non-marital sex partners, condom use, alcohol use before sex, discussion of condom use and HIV results disclosure)
3. HIV incidence
SHARE: integrating IPV prevention activities with existing HIV services

**RHSP’s HIV/ART Services**

- HIV counseling and testing
- Health education
- ART services
- ART adherence support services

**Added SHARE Activities**

- Trained HCT counselors to:
  1. Screen/handle IPV
  2. Use 2 screening and brief intervention tools to address IPV

- Trained RHSP health educators to incorporate messages about IPV in HIV education

- Trained ART counselors to screen for / handle cases of IPV

- Support groups for HIV+ women experiencing and/or at risk for IPV

Wagman, 2014
SHARE: main findings

• Exposure to SHARE was associated with significant:
  • Reductions in past year sexual IPV, physical IPV and forced sex as reported by women
  • 33% reduction in HIV incidence (more pronounced in men)
    • Ongoing exposure required to sustain effect
  • Increases in disclosure of HIV results

• Exposure to SHARE was NOT associated with:
  • Reductions in men’s reports of perpetrating IPV
  • Changes in reports of alcohol use at sex, number of sex partners, condom use
How is DREAMS different than other PEPFAR activities for AGYW?

- Focus in areas of highest HIV burden areas
- Combination prevention
- Move towards the evidence-base
- PrEP
Conclusions

• The syndemic effects of HIV and gender inequality and violence create conditions of hypervulnerability in young women in southern Africa

• Young women’s choices may be constrained, even when they intend to act in ways that promote HIV prevention

• Oral PrEP is a vanguard product; there is much we still need to learn about delivery within the health system

• While the evidence base is small, promising approaches suggest that it is possible to achieve reductions in violence and HIV within programmatic timeframes
  • These can result in programme efficiency as well as health and social good
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