Adolescent PrEP Delivery: Strategies and Tools to Maximize Adherence

Young Women in Africa

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Disclosures

- I have no conflicts to declare
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- Consulting: Merck, Natera
Outline

• Why are young African women a high priority population for PrEP?
• Adherence
  • Clinical trials vs cohorts vs demonstration projects
  • Oral tenofovir/emtricitabine, dapivirine ring
• Lessons learned thus far
• Factors related to adherence
• Promising interventions
• Ongoing/planned studies
• Summary
Why young African women and PrEP?

• By 2050, the number of Africans <18 years old may be >1 billion (!)

• Young women <25 years old...
  • Account for 3 of ~4 million young people in sub-Saharan Africa who are living with HIV
  • Have one of the highest HIV incidence rates globally (>5%)

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Estimates</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Women:</strong></td>
<td></td>
</tr>
<tr>
<td>15–19 years old</td>
<td>140,000</td>
</tr>
<tr>
<td>20–24 years old</td>
<td>770,000</td>
</tr>
<tr>
<td><strong>Men:</strong></td>
<td></td>
</tr>
<tr>
<td>15–19 years old</td>
<td>0</td>
</tr>
<tr>
<td>20–24 years old</td>
<td>40,000</td>
</tr>
<tr>
<td><strong>Countries:</strong></td>
<td></td>
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<tr>
<td>Kenya, Lesotho, Mozambique, South Africa, Swaziland.</td>
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</tbody>
</table>

(Godfrey, UNAIDS 2015)
Why young African women and PrEP?

• High risk factors
  • Biological (e.g., concurrent STIs, pregnancy)
  • Behavioral (e.g., older partners, inability to control condom use)
  • Structural (e.g., poverty, power dynamics)

• PrEP is the only completely woman-controlled form of HIV prevention
Why are we talking about adherence?

• Oral tenofovir/emtricitabine has been shown to be a very effective method for prevention of HIV acquisition

• However...
  Only when taken

• “Drugs don’t work if you don’t take them”
  ~C. Everett Koop, Former US Surgeon General
Reductions in HIV incidence versus adherence

Pearson correlation = 0.88, p<0.001

Note: Diameter of circles is proportional to number of HIV infections in the control group.

(Slide from J. Baeten)
ADAPT (HPTN 067)

- Young women in South Africa
- Comparison of oral PrEP dosing, using plasma tenofovir and real-time adherence monitoring
  - Daily
  - Intermittent weekly with an additional dose at the time of sex
  - Coitally-dependent dosing
- Daily dosing resulted in better coverage of sex acts and higher adherence (79% versus 63% versus 53%, plasma at week 30)
- Daily dosing may foster better habit formation and provide the most forgiveness for missed doses

(Bekker, CROI 2015)
ASPIRE (MTN 020) and the Ring Study (IMP)

(Baeten, NEJM 2016; Nel, NEJM 2016; slide from J. Baeten)
Adherence in ASPIRE

HIV protection differed by age

Women age 25 or older had substantial HIV protection while those younger than age 25 had no significant reduction in HIV incidence.

- < 25 years: 10% reduction
- > 25 years: 61% reduction

This difference in HIV protection was associated with differences in adherence.

More dapivirine released = more use = more protection

(Slide from J. Baeten)
## Differences among studies to date

<table>
<thead>
<tr>
<th></th>
<th>Clinical trials</th>
<th>Demonstration projects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Design</td>
<td>Randomized including placebo</td>
<td>Open label</td>
</tr>
<tr>
<td>Known efficacy</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Product</td>
<td>A lot of uncertainty</td>
<td>More confidence</td>
</tr>
<tr>
<td>Goal</td>
<td>Efficacy and safety</td>
<td>Uptake and use when given the opportunity</td>
</tr>
</tbody>
</table>

*(Amico/Stirratt, CID 2014)*
Lessons learned from VOICE and FEM-PrEP

• These trials did **not** find that women do not want PrEP
• Rather, many...
  • Encountered barriers to use
  • Desired more directive feedback

*(van der Straten, JIAS & PLoS One 2014; Corneli, JAIDS 2015)*
Prevention-effective adherence

• Prevention-effective adherence: alignment of adherence and risk for HIV acquisition

Prevention-effective adherence paradigm: Success is achieved because PrEP is used during all episodes of HIV exposure. Adherence to PrEP may be periodic and mapped to periods of risk.

- Adherence behavior
- HIV exposure over time

• PrEP use in this way can be highly efficient: maximal protection with minimal individual burden and cost
• May be particularly relevant (and challenging) for youth

(Waberer, AIDS 2015)
Individuals take PrEP relative to self-perceived risk

- Partners PrEP Study *(Donnell, JAIDS 2014)*
- Partners Demonstration Project *(Haberer, JIAS 2017; Haberer, JAIDS 2017)*
- Need a better understanding of motivations and barriers
- May be particularly important early in PrEP use given developmental stage of this population (e.g., getting through early side effects to achieve longer term goals)

*(Celum, JIAS 2015)*
Partners Demonstration Project

- Periodic SMS surveys
- Mean adherence was 92% on surveys with risk versus 84% on surveys without risk (p=0.001)

(Haberer, JAIDS 2017)
What are the issues for young women and PrEP?

Socio-ecological framework

Structural factors

Community

Individual
Individual factors

• Lack of adequate information about PrEP
• Lack of familiarity pill taking and/or preventive care
• Prioritization of HIV prevention and/or chaotic lifestyle
• Normal adolescent/youth development
  • Lag between emotional and cognitive control maturation
  • Risk perception and behavioral decision-making (optimism bias)
  • Evolving ability to weigh short-term intimacy and pleasure rewards versus longer term health promotion benefits (present-bias)
• Depression
• Alcohol use

(Celum, JIAS 2015; Rapoff 1999; Weinstein, Science 1989; Nakimuli-Mpungu, AIDS Behav 2012)
Community factors

• Stigma (e.g., perception as ART, sex worker)
• Peers
• Sexual partners
• Gender-based violence
• Family
• Community leaders

Structural factors

• Getting to clinic
• Lack of youth-friendly services
  • Physical space
  • Provider attitudes
• Revised legislation

(Hosek, JIAS 2016)
Potential interventions

• Individual factors
  - Educational campaigns
  - Demand creation

{Thinking creatively about what HIV means, what PrEP means, and what fits within the lives of young women}

• SMS for establishing adherence habits and support
• Enhanced counseling (e.g., cognitive behavioral therapy, motivational interviewing) within scalable models
Potential interventions

• Community factors
  • Educational campaigns
  • Address social norms
  • Engaging peers, male partners, community leaders and parents

• Structural factors
  • Alternate delivery designs (e.g., youth-friendly services; mobile delivery; combination with family planning)
  • Provider attitudes
  • Legislation for women <18 years in some settings
<table>
<thead>
<tr>
<th>Study</th>
<th>Type</th>
<th>Location</th>
<th>Objective adherence measures</th>
<th>Features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liverpool VCT/SWOP Kenya</td>
<td>Oral</td>
<td>Kenya</td>
<td>Electronic monitoring (MEMS)</td>
<td>Combination prevention, health system including cost</td>
</tr>
<tr>
<td>HPTN 082 (HERS Study)</td>
<td>Oral</td>
<td>South Africa, Zimbabwe</td>
<td>Plasma tenofovir</td>
<td>Scalable adherence support interventions</td>
</tr>
<tr>
<td>POWER</td>
<td>Oral</td>
<td>South Africa, Kenya</td>
<td>DBS, pharmacy refills</td>
<td>Comparison of delivery models</td>
</tr>
<tr>
<td>3 Ps for Prevention</td>
<td>Oral</td>
<td>South Africa</td>
<td>DBS</td>
<td>Conditional incentives; demand creation</td>
</tr>
<tr>
<td>Church of Scotland Hospital PrEP Project</td>
<td>Oral</td>
<td>South Africa</td>
<td>?</td>
<td>Pregnancy</td>
</tr>
<tr>
<td>UNICEF PrEP Demonstration Project</td>
<td>Oral</td>
<td>South Africa, Brazil, Thailand</td>
<td>?</td>
<td>Address regulatory, structural, and capacity challenges</td>
</tr>
<tr>
<td>Bridge to Scale Implementation Project</td>
<td>Oral</td>
<td>Kenya</td>
<td>?</td>
<td>Scalable model</td>
</tr>
<tr>
<td>EMPOWER</td>
<td>Oral</td>
<td>South Africa, Tanzania</td>
<td>?</td>
<td>Combination prevention, including GBV, social norms</td>
</tr>
<tr>
<td>DREAMS</td>
<td>Oral</td>
<td>Kenya, S. Africa, Zim, Swaziland, Uganda</td>
<td>?</td>
<td>Varied, broad-based interventions</td>
</tr>
</tbody>
</table>
### Ongoing/planned cohort studies *(AVAC web site; CT.gov)*

<table>
<thead>
<tr>
<th>Study</th>
<th>Type of PrEP</th>
<th>Location</th>
<th>Adherence measure</th>
<th>Features</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHAMPS Pills Plus</td>
<td>Oral</td>
<td>South Africa</td>
<td>DBS</td>
<td>Tailored support (SMS, adherence clubs, real-time feedback on DBS)</td>
</tr>
<tr>
<td>MTN 025 (HOPE Study)</td>
<td>Ring</td>
<td>Malawi, South Africa, Uganda</td>
<td>Residual in ring</td>
<td>Includes “decliner population”</td>
</tr>
<tr>
<td>MTN 034 (REACH Study)</td>
<td>Ring, oral (cross-over)</td>
<td>South Africa, Kenya, Zimbabwe</td>
<td>DBS, residual in ring</td>
<td>Adolescents 16-17 years old</td>
</tr>
<tr>
<td>CAPRISA 082</td>
<td>Oral</td>
<td>South Africa</td>
<td>Drug testing</td>
<td>Risk perception, acceptability of prevention options</td>
</tr>
<tr>
<td>IMPAACT 2009/DAIDS 30030</td>
<td>Oral</td>
<td>Zimbabwe, South Africa, Malawi, Uganda</td>
<td>DBS</td>
<td>Includes pregnancy outcomes</td>
</tr>
<tr>
<td>MPYA</td>
<td>Oral</td>
<td>Kenya</td>
<td>Electronic monitors, DBS</td>
<td>Real-time adherence monitoring, SMS reminders, risk assessments, “decliner” population</td>
</tr>
</tbody>
</table>
Monitoring Pre-Exposure Prophylaxis in Young Adult (MPYA) Women

• Prospective cohort with embedded randomized trial of SMS reminders
• Study sites: Thika and Kisumu, Kenya
• Funding: NIMH (R01MH109309; RFA: Innovative Measures of Oral Medication Adherence for HIV Treatment and Prevention)
• PIs: Haberer, Baeten, Mugo, Bukusi
MPYA procedures

• Target enrollment: 314 women, ages 18-24
• Two years of follow-up with quarterly visits
• Adherence measured with Wisepill
• Questionnaires: individual and community barriers
• Weekly SMS surveys of sexual behavior, risk perception starting at 6 months
• In depth qualitative interviews in 50 women at 0, 3 and 12 months
• Supplement to assess women who do not choose to enroll, as well as influence of peers, male partners and community leaders/parents
Summary

• PrEP (oral or ring) may be a great HIV prevention option for many young women in Africa
• We need to pay attention to the interests, challenges, and skills of this population
• Many studies are ongoing to answer questions about effective means for delivery
• Good adherence monitoring will be critical to see benefits, especially as most studies are not powered for effectiveness
Acknowledgments

• Jared Baeten, Connie Celum
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• Study staff and participants

Thank you for your attention!

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MPYA team: Kisumu

MPYA team: Thika