Implementing Biomedical HIV Prevention Trials for Youth

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The Adolescent HIV Prevention Agenda
Global Epidemiology

- As of 2007, 1.2 billion young people between 15-24 in the world
- 10 million were living with HIV
- MSM are driving the epidemics in North and Latin America, Central and Western Europe, and Oceania
- Sub-saharan Africa – young women bear the burden
- IVDU driving the epidemic in Eastern Europe and some parts of Asia
- UNAIDS estimates that 1 million new infections occur in 15-24 year olds
  - 40% of new infections
Domestic Epidemiology

- Youth are at the epicenter of the HIV epidemic in the United States.
- One-third of new infections occur before the age of 30.
- In the <30 age category:
  - 75% of new infections are in males with >80% in MSM risk category.
  - For females >80% are in high risk heterosexual sex category.
- Disproportionate impact of the HIV epidemic on minority communities.
  - Fastest growing segment is the YMSM of color, particularly AA.

Note. Data statistically adjusted for reporting delays and redistribution of cases in persons initially reported without an identified risk.
Once Upon a Time...

- Adolescent Medicine Trials Network for HIV/AIDS Interventions (ATN) – funded by NICHD, with supplemental funds from NIMH & NIDA

- ATN 082 – The Acceptability and Feasibility of a Pre-exposure Prophylaxis (PrEP) Trial with YMSM

- An exploratory mixed-methods research study combining an efficacious behavioral HIV prevention intervention with a biomedical intervention (PrEP)

- Random assignment to one of three arms: 1) daily Truvada as PrEP, 2) a placebo control, or 3) a “no pill” control for 24 weeks.
Specific Aims

- **Aim 1**: To evaluate the specific components of a PrEP delivery protocol that would be necessary to include in a future effectiveness trial for YMSM.

- **Aim 2**: To examine the acceptability, feasibility, and short term reduction in sexual risk behaviors of a combined bio-behavioral HIV risk reduction intervention compared with a placebo control and a behavioral intervention alone (“no pill”).

- **Aim 3**: To explore the acceptability and feasibility of PrEP as a component of a comprehensive HIV risk reduction intervention for YMSM.

- Target N=100; age range 18-22
Why Combination HIV Prevention?

- An ethical responsibility to provide effective risk reduction education to all participants given their high HIV risk.

- For adolescent and young adult MSM, the use of PrEP may be most useful in preventing HIV infection during the high risk years of youth.

- PrEP in youth may be a time-limited strategy that can bridge the developmental period between sexual debut and adulthood.

- The inclusion of a behavioral intervention builds behavioral skills to reduce risk when not taking PrEP.

- Many Men, Many Voices (3MV) – efficacious group-level intervention that addresses behavioral, social and other factors influencing the HIV/STI risk among MSM of color (Wilton et al., 2009).
Meetings with opinion leaders and key stakeholders in community

“Should we include all YMSM in this study or just YMSM of color?”

Group strongly in favor of targeting YMSM of color, cited a history of underrepresentation in research and overrepresentation in the HIV epidemic.

Strong sentiment to advocate for the need for HIV interventions in the African-American community.

Participants agreed that other racial/ethnic groups could be included, if this improved the research design, as long as people of color were strongly represented.
But the resistance begins...

**Internal:**
- Appropriate time?
  - “There is also a growing concern that prevention strategies that rely on adherence are doomed to be ineffective (herpes suppression and microbicide trials). This raises the question whether we should be pushing this trial on a vulnerable population at this time before more safety data and efficacy data are available”
- Focus on YMSM of color
- Need for placebo and no pill arms
- Cost

**External:**
- Need to use actual drug to study PrEP
  - “Taking the study drug as directed and especially not as directed may pose risks to the subjects or the people with whom they share the drug. Because of this, the Board would like to hear why you cannot learn the acceptability and feasibility by giving a sham study drug that would not pose these risks.”
- Focus on youth
- Value of pilot acceptability trial
<table>
<thead>
<tr>
<th>Month/Year</th>
<th>Step in Approval Process</th>
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<tbody>
<tr>
<td>December 2007</td>
<td>Concept capsule submitted to Leadership Group for discussion</td>
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<tr>
<td>September 2008</td>
<td>ATN Executive Committee reviews and approves resources</td>
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<tr>
<td>October 2008 –</td>
<td>Program Review</td>
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<td>December 2008</td>
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<tr>
<td>January 2009 –</td>
<td>Protocol Development</td>
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<tr>
<td>August 2009</td>
<td></td>
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<tr>
<td>October 2009</td>
<td>IRB approval – 3 months contingency</td>
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<tr>
<td>November 2009</td>
<td>First participants enrolled</td>
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Project PrEPare Chicago

PrEPared!

STRONG!
SMART!
SEXY!

Project PrEPare
Rethinking Prevention
Recruiting Youth \( (n=753) \)

- Screened ineligible at initial contact by PDA \( (n=512) \)
  - Age \(<18\) \( (n=38) \)
  - Age \(>22\) \( (n=68) \)
  - Reported no UAI \( (n=235) \)
  - Job obligations only \( (n=38) \)
  - Plans to relocate only \( (n=36) \)
  - Both plans to relocate and job obligations \( (n=25) \)
  - Not interested \( (n=33) \)
  - HIV positive by self report \( (n=28) \)

- Screened eligible at initial contact by PDA \( (n=241) \)
  - Randomized \( (n=58) \)
  - Not randomized \( (n=183) \)
  - Relocated \( (n=2) \)
  - Did not return for final screening visit \( (n=168) \)
  - Found ineligible at final screening visit \( (n=9) \)
  - Decided to attend college \( (n=1) \)
  - Unable to locate \( (n=2) \)
68 participants were enrolled
Of the 68, 10 were discontinued prior to randomization.
Average age was ~20 (range 18-22)
~55% Black, 40% Latino, 5% Mixed/Other
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<tr>
<th></th>
<th>Arm A</th>
<th>Arm B</th>
<th>No Pill</th>
<th>Total</th>
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<tr>
<td><strong>Expected Visits</strong></td>
<td>129</td>
<td>134</td>
<td>133</td>
<td>396</td>
</tr>
<tr>
<td><strong>Actual Visits</strong></td>
<td>117</td>
<td>119</td>
<td>120</td>
<td>356</td>
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<tr>
<td><strong>Overall Retention</strong></td>
<td><strong>90.7%</strong></td>
<td><strong>88.8%</strong></td>
<td><strong>90.2%</strong></td>
<td><strong>89.9%</strong></td>
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Inclusion of 16 and 17 year olds

- Groundbreaking efficacy data (CAPRISA 004) on antiretroviral prevention = proof of concept; growing safety data from adult trials of oral PrEP. Promising iPrEx data anticipated.
- FDA expanded indication of tenofovir down to age 12
- No expedited AE in 082; study drug well tolerated
- High interest in participation from 16-17 yr/old focus group participants
- Supportive interactions with parents of participants
- Young MSM will ultimately be a target population for PrEP
**Consent Issues for Adolescent MSM**

- **Waiver of Parental Consent**
  - Avoids selection bias of only recruiting youth whose parents are both aware of and comfortable with their sexual orientation.
  - Youth who stand to benefit most from HIV prevention interventions are represented in the trials of those interventions.
  - Common practice in the area of LGBT research
Consent Issues for Adolescent MSM (cont’d)

Protection of Youth

- Ask for parental permission first, but allow participation for youth who indicate that requiring permission would potentially place them at risk for harm.
- Establish a Youth Advocate/Ombudsman to protect youth from untoward pressure by the research team:
  - decide that waiving parental permission is not reasonable for a particular youth;
  - decide that a particular youth should not participate because of physical or mental health problems that might be exacerbated by participation.
A Tale of Two Studies
The Impact of iPrEx

- Evidence for the biological plausibility of PrEP among young MSM

- Placebo vs. drug arms no longer equal
  - Unethical to keep participants on placebo

- ATN DSMB Recommended Actions:
  - Unblind all Project PrEPare participants
  - Those on Truvada can finish out study
  - Those on placebo or no pill are invited to “roll over” into the Truvada arm

- Resources have been secured to allow all of our participants to enroll into iPrEx OLE! – many thanks to the Office of AIDS Research and NICHD
## Lessons Learned – Challenges and Solutions

1. Garnering support for trials with youth can be difficult - Research with youth elicits strong reactions from reviewers and ethics panels

2. Youth are transient - identifying eligible participants is the easy part

3. Youth will not conform to your schedule, you will have to conform to theirs

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<thead>
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<th>1.</th>
<th>Educate, advocate and seek consultation</th>
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<td>a)</td>
<td>When in doubt...ask the COMMUNITY</td>
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<th>2.</th>
<th>Stay close, use multiple methods, don’t give up</th>
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<td>a)</td>
<td>Successful retention (within study visit windows) requires frequent contact</td>
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| 3. | Flexibility, flexibility, flexibility |

Lessons Learned - Successes

- Successfully recruited and retained a young, racially diverse cohort in a domestic PrEP trial
- Built strong, supportive collaborations with community members, public health officials, youth groups, and the media
- Combination HIV prevention trial led by a behavioral scientist and a physician
- Pushed the adolescent HIV agenda
- We had FUN!!
Final Thoughts...

- Must be “youth friendly”
- Be willing to be “sized-up” – trust is key for adolescents
- Embrace the drama
- Design trials for youth – don’t try to fit them into adult or pediatric trials
- Remember…it’s all about THEM!
Most importantly, we would like to thank the young men who participated in this study for their willingness to share their lives and their time with us.

My Co-Investigators – Margo Bell, MD, George Siberry, MD, Michelle Lally, MD, Isa Fernandez, PhD, & Craig Wilson, MD – and especially our Project Director, Keith Green.

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