Standards, standards, standards: Who defines standards?

2013 Biomedical HIV Prevention Forum Preconference
Bridget Haire
Since 2005, 10 HIV prevention trials showed positive results

• 3 trials of voluntary medical male circumcision
• 1 trial of a preventive vaccine
• 1 trial of a tenofovir gel as a vaginal microbicide
• 4 trials of oral pre-exposure prophylaxis
• 1 trial that used early antiretroviral therapy in HIV positive participants to prevent transmission to their negative sexual partners
<table>
<thead>
<tr>
<th>Study</th>
<th>Population</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>iPrEX</td>
<td>Men who have sex with men</td>
<td>44% FTC/TDF</td>
</tr>
<tr>
<td>Partners PrEP</td>
<td>Serodiscordant couples</td>
<td>67% TDF</td>
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<tr>
<td></td>
<td></td>
<td>75% FTC/TDF</td>
</tr>
<tr>
<td>TDF-2</td>
<td>Heterosexual people</td>
<td>62% FTC/TDF</td>
</tr>
<tr>
<td>FEM PrEP</td>
<td>Women</td>
<td>Futility FTC/TDF</td>
</tr>
<tr>
<td>VOICE</td>
<td>Women</td>
<td>Futility TDF</td>
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<tr>
<td></td>
<td></td>
<td>Futility TDF gel</td>
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<td></td>
<td></td>
<td>Futility FTC/TDF</td>
</tr>
<tr>
<td>Bangkok PrEP</td>
<td>People who inject drugs**</td>
<td>49% TDF</td>
</tr>
</tbody>
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Overview

• General ethical issues in research
• How the concept of standards underpins many of these issues
• The particular issues facing HIV research ethics in the era of partially protective prevention interventions
• How the definition of particular standards impacts on decision making in HIV prevention research
Ethical issues in research

• Balance of risks of benefits
• Fairness
• Consent
  – Voluntary
  – Sufficient understanding
  – No coercion
• Promote justice, avoid exploitation
  – Reasonable likelihood that the trial community will eventually derive benefit
  – Risks not disproportionate or unreasonable
Most of these issues are grounded in standards

- Assessment of risk – standard of reasonable safety
- Consent
  - People are told what they need to know to voluntarily make a decision about participation
- Promote justice, avoid exploitation
  - Reasonable likelihood that the trial community will eventually derive benefit (post trial access)
‘Hard’ and ‘soft’ standards

• Hard standards are where effective processes exit to check compliance and implementation of a standard
  – National standards ‘policed’ by ethics committees

• Soft standards may be articulated by an authoritative source, but there are no processes regarding compliance and implementation
  – International ethical guidance
Ethical considerations
in biomedical HIV prevention trials
[Additional guidance point added in 2012]

UNAIDS/WHO guidance document
PrEP (FTC/TDF) approved by US FDA for prevention of HIV

- **From:** US Food & Drug Administration
- **When:** 16 July 2012
- **For:** Gilead Sciences oral TDF/FTC in the US
- **What:** Regulatory approval in the US for daily oral TDF/FTC (Truvada) for PrEP in HIV-negative adults
Ipergay

- Tests intermittent PrEP against placebo in gay men/MSM
- France and Canada
- Began in Feb 2012
- No marketing authorisation for PrEP in the European Union
UNAIDS, guidance point 13

• New HIV risk-reduction methods should be added [to the standard of prevention] based on consultation among all research stakeholders including the community, as they are scientifically validated or as they are approved by relevant authorities...
The rationale put forward for retaining the placebo in Ipergay

- Optimal design for ‘rigorous assessment’
- Reduce risk of behavioural disinhibition*
- FTC/TDF has not been evaluated in ‘real life’ conditions in USA
- No detrimental in terms of prevention and health promotion
- *Participants would be no worse off
Rationale for testing intermittent PrEP against continuous PrEP:

- International best practices prevent vulnerable* participants being used to test drugs for those more privileged.
- People enrolled in HIV prevention trials are generally at the highest risk of HIV infection.
- Health equity perspective.
- Best practice standards of care recognize the contribution that research participants make to the research endeavour.
Decision

• The study should continue as designed, using the placebo
• Based upon the Scientific Advisory Committee
• NOT a consensus view – the majority of the community advisory board wanted PrEP access
Advocates need research literacy

• if community groups and the communities they represent are to have meaningful input into standard-setting on important issues like trial design, they need to be well trained and adequately resourced to increase their research literacy
Conclusion (1)

• On the one hand, we want the highest possible protections for research participants. On the other hand, we do need to recognise the very real issues of feasibility involved, and the questions about the willingness of particular national governments to make available newly validated interventions.
• With post-trial access, we need to maximise the benefits and try to avoid gaps between the trial’s end and post-trial provision

• Trial-mediated post-trial access is time limited—need advocacy

• Communities must have a voice in these dialogues

• Community perspectives need to be highly informed and politically adept