PrEP Implementation: One Perspective

Jared Baeten MD PhD
Departments of Global Health, Medicine, and Epidemiology
University of Washington

Controlling the HIV Epidemic with Antiretrovirals: From Consensus to Implementation
London, September 2013
Disclosures

• I have received research funding related to PrEP, antiretroviral treatment for HIV prevention, and microbicides from the US National Institutes of Health, the United States Agency for International Development, and the Bill & Melinda Gates Foundation.

• For some research studies, medication has been donated by Gilead Sciences.

• I have no other financial conflicts of interest.
After the RCTs, the US FDA, and all the commentary on PrEP, moving to implementation is something like this…

Photo from the post-airport security area, Milwaukee, USA airport
Perspective on PrEP implementation

What are the questions?

What is the interface with ART for prevention?

What are the risks?
Perspective on PrEP implementation

What are the questions?

What is the interface with ART for prevention?

What are the risks?
What are the questions?

• The transition from clinical trials to delivery opens up an entirely new set of questions, with new expectations and different approaches to quantify and measure success.
<table>
<thead>
<tr>
<th>Topic</th>
<th>Question</th>
</tr>
</thead>
<tbody>
<tr>
<td>Delivery</td>
<td>How to deliver and how to deliver at scale?</td>
</tr>
</tbody>
</table>

- PrEP demonstration projects suggest some possible models of delivery and various populations (CSW, MSM, couples) but not the totality of how PrEP could be delivered.
- What is the capacity to add PrEP to primary & specialty health services?
## Uptake

<table>
<thead>
<tr>
<th>Topic</th>
<th>Question</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uptake</td>
<td>Who/how to prioritize? Do those who might benefit most want it?</td>
</tr>
</tbody>
</table>

- What are tools for providers to identify those appropriate for PrEP?
  - How to ask about risk, how to offer PrEP
  - Objective tools may help – eg couples risk score *(Kahle JAIDS 2013)*

- Initial data suggest that demand is there *when PrEP is known*:
  - In San Francisco, waiting list of >50 for demo project
  - In Kenya/Uganda, demo project uptake >90%
## Adherence

<table>
<thead>
<tr>
<th>Topic</th>
<th>Question</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adherence</td>
<td>What is the expectation for adherence? How to maximize?</td>
</tr>
</tbody>
</table>

- In contrast to clinical trials, which expected 100% sustained adherence, implementation will focus on those who continue PrEP interest and return for refills. Arguably:
  - Those who don’t use PrEP won’t come back = no benefit but also no programmatic costs. [PrEP takers]
  - Those who use PrEP will achieve prevention benefits (like with every other prevention strategy…) [nontakers]
Risks

<table>
<thead>
<tr>
<th>Topic</th>
<th>Question</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risks</td>
<td>Sexual behavior/STIs? Antiretroviral resistance?</td>
</tr>
</tbody>
</table>

- Empiric data needed much more than hypotheses.
- In Partners PrEP Study, no increase in unprotected sex, pregnancy, STIs after July 2011 (when placebo arm stopped):

![Average frequency of unprotected sex, before & after July 2011](image)

Mugwanya et al., ISSTDR 2013
### Impact

<table>
<thead>
<tr>
<th>Topic</th>
<th>Question</th>
</tr>
</thead>
<tbody>
<tr>
<td>Impact</td>
<td>Programmatic success? HIV incidence? Costs?</td>
</tr>
</tbody>
</table>

- How is programmatic success defined for PrEP? With the recognition that PrEP is not for everyone and certainly not forever.

- What can be done to define the PrEP cascade: HIV testing → linkage to prevention services → initiation and sustained use of PrEP and other prevention options → support for PrEP discontinuation
## Implementation questions

<table>
<thead>
<tr>
<th>Topic</th>
<th>Question</th>
</tr>
</thead>
<tbody>
<tr>
<td>Delivery</td>
<td>How to deliver and how to deliver at scale?</td>
</tr>
<tr>
<td>Uptake</td>
<td>Who/how to prioritize? Do those who might benefit most want it?</td>
</tr>
<tr>
<td>Adherence</td>
<td>What is the expectation for adherence? How to maximize?</td>
</tr>
<tr>
<td>Risks</td>
<td>Sexual behavior/STIs? Antiretroviral resistance?</td>
</tr>
<tr>
<td>Impact</td>
<td>Programmatic success? HIV incidence? Costs?</td>
</tr>
</tbody>
</table>

**HIV**

CONTROLLING THE HIV EPIDEMIC WITH ANTIRETROVIRALS

Treatment as Prevention and Pre-Exposure Prophylaxis
Perspective on PrEP implementation

What are the questions?
What is the interface with ART for prevention?
What are the risks?
Implementation questions apply to ART and PrEP in similar ways

<table>
<thead>
<tr>
<th>Topic</th>
<th>Question</th>
</tr>
</thead>
<tbody>
<tr>
<td>Delivery</td>
<td>How to deliver and how to deliver at scale?</td>
</tr>
<tr>
<td>Uptake</td>
<td>Who/how to prioritize? Do those who might benefit most want it?</td>
</tr>
<tr>
<td>Adherence</td>
<td>How is adherence? How to maximize?</td>
</tr>
<tr>
<td>Risks</td>
<td>Sexual behavior/STIs? Antiretroviral resistance?</td>
</tr>
<tr>
<td>Impact</td>
<td>Programmatic success? HIV incidence? Costs?</td>
</tr>
</tbody>
</table>
Debate about how to balance ART & PrEP

Uganda rejects HIV prevention tool on moral grounds

New HIV policy spells doom for discordant couples – activists

Couples who had hoped to benefit from pre-exposure prophylaxis will have to look to other means for protection against HIV newvision

By Francis Kagolo

The 4,758 HIV sero-discordant couples who participated in a research about Pre-exposure Prophylaxis (PrEP) hoped that the strategy would reduce new infections if adopted.

However, their wishes withered when the health ministry announced last week that it had rejected the HIV prevention strategy citing high costs and fears that it would increase promiscuity.
PrEP & ART: synergy in delivery

• For HIV serodiscordant couples:
  • Not all HIV+ partners will choose to or can start ART immediately and staged use of PrEP, as a bridge to ART, might be effective and cost-effective (Hallet et al. PLoS Med 2011; Mitchell et al. STI World Congress 2013)

• For populations:
  • Risk-targeted PrEP adds to ART (Ying et al. STI World Congress 2013)
  • Demonstration projects delivering both PrEP + maximal push for ART must be prioritized: MSM (e.g., with syphilis), FSW, others
Partners Demonstration Project

- **Goal:** to understand prevention preferences, uptake of ART and PrEP, adherence, & risk behavior among high risk HIV serodiscordant couples

- **Design:** Prospective observational study of 1000 HIV serodiscordant couples in Kenya and Uganda with quarterly follow up for 2 years

- **Setting:** Kenyan and Ugandan HIV care centers

- **Delivery:** PrEP is offered as a ‘bridge’ to ART use
  - PrEP discontinuation recommended after 6 months of sustained ART use the HIV infected partner
Partners Demonstration Project: optimizing PrEP & ART for couples

- Recruit higher-risk HIV-1 serodiscordant couples
- Offer/refer for ART for HIV-1\(^+\) partners according to current national guidelines

**Prioritization**

- Accepts ART:
  - Offer PrEP for 6 months to HIV-1\(^-\) partner
  - Continue to counsel HIV-1\(^+\) partner on ART

- Declines ART:
  - Offer PrEP to HIV-1\(^-\) partner

- Not yet eligible for ART:
  - Offer PrEP to HIV-1\(^-\) partner
  - Follow HIV-1\(^+\) partner and refer for ART when eligible
Changing the conversation

How do we talk about the benefits for ART and PrEP?

(after years of telling people not to get HIV because antiretrovirals are awful)

‘If I am given antiretrovirals I will think I am nearing the grave’: Kenyan HIV serodiscordant couples’ attitudes regarding early initiation of antiretroviral therapy

Kathryn Curran\textsuperscript{a,b}, Kenneth Ngure\textsuperscript{b,e,f}, Bettina Shell-Duncan\textsuperscript{b,c}, Sophie Vusha\textsuperscript{f}, Nelly R. Mugo\textsuperscript{b,g}, Renee Heffron\textsuperscript{b}, Connie Celum\textsuperscript{a,b,f} and Jared M. Baeten\textsuperscript{a,b,d}
Message synergy

• ART
  Treatment is health-preserving and not reflecting late-stage sickness.

• PrEP
  PrEP is health-preserving, use is not life-long – months/years of greatest risk (“seasons of PrEP” – like contraception) might avoid 40+ years of ART

• Both ART and PrEP
  We need messages that have fewer academic caveats and that better respond to patient needs.
Perspective on PrEP implementation

What are the questions?

What is the interface with ART for prevention?

What are the risks?
Looking back…

“The potential short term gains … may be far outweighed …. In Africa, a higher proportion of patients are likely to fall into the category of potential poor adherers unless resource intensive adherence programmes are available.”

Stevens et al. BMJ 2004

Pre-determining failure (in this case, for ART roll-out) has not been productive in the past…
Looking ahead…

New options may be on the horizon…

… Or, they may be a long way off
The risk: doing, but not enough

• Persistent / increasing HIV incidence in the era of high ART access in high income settings (example from UK below) illustrate that standard approaches are not enough.

The risk: doing, but not enough

• Persistent / increasing HIV incidence in the era of high ART access in high income settings (example from UK below) illustrate that standard approaches are not enough.

• Accepting cascades of lost opportunities in treatment and prevention (or recreating in new settings) cannot happen.
The risk: doing, but not enough

- Persistent / increasing HIV incidence in the era of high ART access in high income settings (example from UK below) illustrate that standard approaches are not enough.
- Accepting cascades of lost opportunities in treatment and prevention (or recreating in new settings) cannot happen.
- Risk is an ever-increasing treatment need, without turning off the tap of new infections.

UNAIDS 2011
In summary: PrEP implementation

New/different questions

Parallels and synergies with ART for prevention

There are risks in doing, but real risks in not doing enough
Change does not happen instantly…

Diffusion of innovation is a process.

Good science, clear messages, cross-cutting advocacy, and a strong public health focus may help accelerate change in this field.
Thank you

- **University of Washington**: Connie Celum, Deborah Donnell, ICRC team
- **Partners PrEP Study and Partners Demonstration Project Teams**:  
  - Eldoret, Kenya (Moi U, Indiana U): Edwin Were, Ken Fife  
  - Jinja, Uganda (Makarere U, UW): Patrick Ndase, Elly Katabira  
  - Kabwohe, Uganda (KCRC): Elioda Tumwesigye, Stephen Asiimwe, Rogers Twesigye  
  - Kampala, Uganda (Makarere U): Elly Katabira, Allan Ronald, Edith Nakku-Joloba, Nulu Bulya  
  - Kisumu, Kenya (KEMRI, UCSF): Elizabeth Bukusi, Craig Cohen, Josephine Odoyo  
  - Mbale, Uganda (TASO, CDC): Jonathan Wangisi, Jim Campbell, Jordan Tappero  
  - Nairobi, Kenya (KNH/U Nairobi, UW): James Kiarie, Carey Farquhar, Grace John-Stewart  
  - Thika, Kenya (KNH/U Nairobi, UW): Nelly Mugo, Kenneth Ngure  
  - Tororo, Uganda (CDC, TASO): Jim Campbell, Jonathan Wangisi, Jordan Tappero
- **Adherence & Modeling (Harvard/MGH/Johns Hopkins/Imperial)**: David Bangsberg, Jessica Haberer, Tim Hallett, Craig Hendrix, Norma Ware, Monique Wyatt, Steve Safren, Christina Psaros
- **MTN**: Thes Palanee, Katie Schwartz, Lydia Soto-Torres, Sharon Hillier, Ian McGowan, ASPIRE/MTN Team
- **Funders**: Bill & Melinda Gates Foundation (OPP47674, OOP52516, OPP1056051); US National Institutes of Health (R01 MH095507, R21 NR012663, R01 AI096968, R01 MH098744, R21 AI104449, R21 HD074439, UM1 AI068633); US Agency for International Development (AID-OAA-A-12-00023)
- **Research participants**