Issues in the development of long-acting PrEP: An advocate’s perspective

Mitchell Warren, Executive Director
IAS ILF Roundtable
March 5, 2018
I read the news today; Oh, boy

Five African Countries Approach Control of Their HIV Epidemics as U.S. Government Launches Bold Strategy to Accelerate Progress

September 19, 2017

The New York Times

In Africa, a Glimpse of Hope for Beating H.I.V.

We Have the Tools to End AIDS Now
Breaking the Cycle of Heterosexual Transmission

Young women acquire HIV from men who are on average 8 years older.

When teen women with HIV reach their mid-20s, if they aren’t on effective ART, then they may transmit to partners of the same age—and vice versa.

Men and women over the age of 24 years usually acquire HIV from similarly aged partners.

Women at high risk of HIV
Mean age: 18 years (range: 16-23 years)

Male populations with high HIV incidence
Mean age: 27 years (range: 23-35 years)

Oral PrEP (and dapivirine ring, if approved) for HIV-negative women

Treatment for men who are living with HIV

Oral PrEP for HIV-negative men

VMMC, especially to prevent infection among men at risk

Treatment for men and women living with HIV

Oral PrEP (and dapivirine ring, if approved) for HIV-negative women

Female populations with high HIV prevalence
Mean age: 26 years (range: 24-29 years)

http://www.avac.org/infographic/breaking-cycle-heterosexual-transmission
### Different Strokes for Different Folks

<table>
<thead>
<tr>
<th>Method</th>
<th>Contraception</th>
<th>HIV Prevention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Behaviour</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Barrier Methods</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Gels</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Rings</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Oral pill</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Injectable</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Implants</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Surgical procedures</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Treatment</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
## Prevention Paradigm 2017 & beyond

### Different Strokes for Different Folks

<table>
<thead>
<tr>
<th>Method</th>
<th>Contraception</th>
<th>HIV Prevention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Behaviour</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Barrier Methods</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Gels</td>
<td>✓</td>
<td>✓ – not registered</td>
</tr>
<tr>
<td>Rings</td>
<td>✓</td>
<td>✓ – with regulatory body</td>
</tr>
<tr>
<td>Oral pill</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Injectables</td>
<td>✓</td>
<td>? – 1 ARV, 1 bNAb, 2 vax in phase 3; others in pre.</td>
</tr>
<tr>
<td>Implants</td>
<td>✓</td>
<td>? – multiple in preclinical</td>
</tr>
<tr>
<td>Surgical procedures</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Treatment</td>
<td></td>
<td>✓</td>
</tr>
</tbody>
</table>
Now What?

- Where is the greatest unmet need for prevention?
- What products will people want AND use?
- What trial designs can best answer the questions fastest and ethically?
- How will we deliver next generation PrEP?
- How to best “balance our portfolio”?
Research in the Post-Placebo Era

**Placebo-Controlled Trial**

- Experimental vs. Placebo

**Double-Dummy Double-Blind***

- DISCOVER (Oral F/TAF)
  - Experimental + Placebo vs. Placebo + Active
- HPTN 083; HPTN 084 (Long-acting Cabotegravir)
  - Injection + Placebo vs. Placebo + Active

**Open-Label With Active Arm***

- Active vs. Experimental

All of these designs are randomized, meaning that participants are assigned to a study arm by chance. This protects against bias, whether the participant knows what he or she is receiving or not.

**Open-Label Extension**

If the experimental product is shown to be safe and effective, trial designers may decide to give all participants access to the active product, or products, if multiple are shown to be safe and effective.

**Product Introduction**

- Licensure
- Demonstration projects
- Rollout
- Scale-up

*AVAC’s Advocate's Guide to Research Terms in the Post-Placebo Era* and *HIV Prevention Trial Terms: An Advocate's Guide*
- Clinical trials are not “real”
- People lie about sex and drugs
- Risk perception is very personal and subjective, and does not necessarily drive product uptake
- We don't know what people want, and they may not either
  - Need ≠ use
  - Demand ≠ use
  - Acceptability ≠ use
  - Access ≠ use
- And it's never just the product...
Or “what keeps me up at night”:

- New world order – and independence of science from political whimsy
- Declaring success too soon…
- …and not planning for success soon enough
- Px focus – in addition to tx, not in opposition to it
- Px R&D focus – when other leaders say “we have all the tools to end”
- Overburdened/exhausted trial communities and stakeholders
- Post-placebo trial designs
- Potential backlash if current wave of trials doesn’t result in product (and meet current expectations) and/or if successful trials are not followed-up
- Move from “user-initiated” to “systemic/health system delivery”
Coalition to Support and Accelerate Prevention Research (CASPR)

Cooperative Agreement No. AID-OAA-A-16-00031
HIV Vaccine and Biomedical Prevention Research Project—Objective 3