Pre-exposure prophylaxis: Not ready for prime time yet in Africa

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Thanks to Connie Cellum, Helen Rees, Robyn Eackles, Quarraisha Abdool Karim, Alasdair Reid, AVAAC, Gabster Gomez
We agree...

• We need better prevention
• It works! (surprisingly well)
• (if taken)
• (in the real world in gay men, discordant couples)
• It works in women – PARTNERS PrEP
• Incomplete adherence still gives excellent cover
• Resistance almost certainly not a public health issue
• Risk compensation nonsense (like all the other prevention)
All Projects Planned to Deliver PrEP in Africa in 2015

- Senegal Demo Project
- Benin Demo Project
- Nigeria Demo Project
- TDF2 Follow-Up
- Partners PrEP Demo
- LVCT and SWOP
- Mozambique Demo Project
- SAPPH-Ire
- CHAMPS
- TAPS
- iPrEx OLE (completed)

Ongoing projects
Completed projects
But! Let us be clear...

• PrEP needs better justification before we run to governments to fund

• We are proposing an intervention that is:
  • Costly
  • May need access to groups not traditionally easy to reach: sex workers, adolescents, gay men
  • Requires significant engagement with the (unfriendly) health care system
  • Requires fair adherence
  • Side effects an issue
1) Cost...

- It is costly! Especially if not taken
- Secondary consideration – active pharmaceutical ingredients (API) a challenge
- ?TAF an option in future
- Cost of HIV testing a major factor
2) Adherence – the “Achilles heel”
Trials of oral and topical tenofovir-based PrEP show that these strategies reduce risk of HIV infection if they are used correctly and consistently. Higher adherence is directly linked to greater levels of protection.

Source: Salim S. Abdool Karim, CAPRISA
2) Adherence

• High risk gay men, discordant couples, take it well – others less so!

• “Adherence will be better in the real world” – we need this proof

• In many studies – women seemed to take almost NO treatment – waste of money – how do we identify this group?

• No clear adherence measure – MEMS? Blood levels?
3) Finding these groups...

- Sex work remains illegal almost everywhere
- MSM populations – also legal and stigma challenges
- Adolescent girls? – political disaster
- General population – maybe discordant couples (but a huge undertaking)
PrEP Landscape in the U.S.

Challenge: More Persons at Risk for HIV than Persons Evaluated for or Prescribed PrEP

Estimated to be at risk for HIV, N = 500,000

Estimated to have started PrEP, through end 2015

Approximately 14,000 unique individuals had initiated PrEP based on a sample of 39% of all TRUVADA prescriptions through Q1 2015

Estimated to be at risk for HIV, N ≈ 1,232,000

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1 Dawn K. Smith, MD et al, MMWR Morb Mortal Wkly Rep 2015;64:1-6
2 Adapted from Bush, S. et al. IAPAC Adherence 2015; #74
PrEP Landscape in the U.S.
The Prevention Continuum and PrEP Implementation

Identification
Persons at risk for HIV

Linkage
Persons who might benefit from PrEP

Clinical Support
Evaluated for PrEP
Prescribed PrEP
4) Safety?

- Lets say it ONLY causes severe acute renal failure in 1/5,000 – in healthy people? Can we justify that when treatment is so effective and safe? Especially if NNT is high?
- Limited safety data – remember: HIV negatives!
- Requires creatinine clearances – are we brave enough to drop it?
- Hep B bone data
- Repeat HIV testing – how do we do it?
5) Treatment vs Prevention

• Treatment is unbelievably effective – for treatment and prevention
• Life expectancy higher than general population!
• ?just better to treat HIV in a relative few, rather than treating many?
Change in Prevalence over Time for a Cohort of HIV-negative Women

- Status quo (SQ)
- SQ + PrEP
- ART < 350
- ART < 350 + PrEP
- ART < 500
- ART < 500 + PrEP
- Universal coverage

Prevalence (%)

Time in years

0 5 10 15
RCT evidence for preventing sexual HIV transmission - 2014

<table>
<thead>
<tr>
<th>Study</th>
<th>Effect size (CI)</th>
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<tr>
<td>Medical male circumcision (Orange Farm, Rakai, Kisumu)</td>
<td>54% (38; 66)</td>
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<tr>
<td>HIV Vaccine (Thai RV144)</td>
<td>31% (1; 51)</td>
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<tr>
<td>PrEP for discordant couples (Partners PrEP)</td>
<td>73% (49; 85)</td>
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<tr>
<td>PrEP for heterosexuals (Botswana TDF2)</td>
<td>63% (21; 48)</td>
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<tr>
<td>STD treatment (Mwanza)</td>
<td>42% (21; 58)</td>
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<tr>
<td>Microbicide (CAPRISA 004 tenofovir gel)</td>
<td>39% (6; 60)</td>
</tr>
<tr>
<td>Treatment for prevention (HPTN 052)</td>
<td>96% (73; 99)</td>
</tr>
<tr>
<td>PrEP for MSMs (IPREX)</td>
<td>44% (15; 63)</td>
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6) Treatment system is unfriendly?
“Ironically, it may require greater intimacy to discuss sex than to engage in it”

*The Hidden Epidemic*
Institute of Medicine, 1997
6) Treatment system is unfriendly?

- Would you put up with queues, unfriendly staff, drug stock outs etc etc?
- AND you are using precious human resources...
7) Ethics?

• No contest in treatment vs prevention
• HIV negative people have multiple options, HIV positive people only have ART
8) HSV-2?

• Not a good enough reason
Conclusion

- An exciting complex intervention, with high resource requirements
- Cost needs addressing - not just cost of drug
- Access system, and HIV testing need to improve
- Safety considerations should not be dismissed
- Needs careful thought before putting prioritising this