HIV PREVENTION: REVOLUTION THROUGH INNOVATION

IAS 2019 POST-CONFERENCE WEBINAR

30 January 2020
HIV Prevention Updates - IAS 2019

Kenneth Ngure MPH, MSc, PhD
GC Member – Africa
School of Public Health
Jomo Kenyatta University (JKUAT)
HIV Testing
Reaching the untested

Social Network and Index Testing Strategy

RESULTS

- Index testing among men (25-50 years):
  - Elicitation Ratio – 1:1.8
  - HIV Positivity yield – 41%
  - Index ART Linkage – 81%
- Index testing among adolescents and young people (10-24 years):
  - Elicitation Ratio 1:1.4
  - HIV Positivity yield: 32%
  - Index ART Linkage: 85%
- Of the 3,567 HIV positives:
  - 41% were women, 25+ years
  - 36% were men, 25+ years
  - 15% were adolescent girls and young women
  - 5% were adolescent boys and young men
  - 3% were under 10 years old

Intervention in Zambia to increase testing among those less likely to test

- 21 Community liaison officers and 157 lay counsellors were recruited, trained and deployed to offer index testing

Index clients identified through SNS or clients in ART care
Engaging men in HIV testing and care

- Rapid oral or blood-based HIV self-testing kits are now available in many settings.
- HIV self-tests have potential to improve uptake of testing and engagement in care among harder-to-reach groups.
- Choice of 2 HIVST options: oral-fluid or blood-based testing.
- 4,495 test kits distributed, 92% to men.
- Take-away self-testers: 4% HIV positive, 81% linked to care, 73% started ART.
- Rapid HIVST distribution with non-intensive staff support is a feasible, acceptable approach to identify HIV+ men and link them to care and ART in South Africa.

Shapiro, WEAC0202
Peer distribution

Burundi: HIVST introduced December 2018

- Peer outreach has the potential to reach key populations who may not be in touch with facility-based health services.
- 22% of HIV diagnoses in FSW June 2018-March 2019 by HIVST, 35% in MSM.
- Challenge: delay between reactive and confirmatory result.
- HIVST improves uptake of HIV testing among key populations who rarely or never tested.
- More widespread implementation of HIVST with high-risk populations could accelerate progress toward 95-95-95 goals.

Gashobotse, WEAC0203
Oral PrEP
Increased incidence of sexually transmitted infections (STIs) in Prevenir

<table>
<thead>
<tr>
<th></th>
<th>Incidence rate per 100 p.y. (95% CI)</th>
<th>Increase in incidence per year</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anal gonorrhoea</td>
<td>27 (24-29)</td>
<td>+48%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Any STI</td>
<td>86 (82-90)</td>
<td>+38%</td>
<td>&lt;0.001</td>
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- **Prevenir**: prospective cohort (Paris), 3,057 enrolled to daily or on-demand PrEP.
- 15% changed dosing pattern.
- No difference in adverse events or lab abnormalities by regimen (3 discontinuations due to GI adverse events).
- 2,208 person-years follow-up.
- 2 infections (0.09/100 person-years) in men who had discontinued PrEP.
- Estimated 143 HIV infections averted.
- Incidence of viral hepatitis: 1.04 /100 person-years

Molina, TUAC0202
Sexually transmitted infections (STIs) in the era of PrEP

• Is PrEP associated with increases in STIs?
  – Concurrent increases in STIs; rates of bacterial STIs increasing over time; however, rises pre-date PrEP use.
  – Some but inconsistent evidence of risk compensation.
  – PrEP availability is uncovering the hidden epidemic of STIs in some populations.

• Implications for STI control:
  – Improve and move beyond syndromic STI management.
  – Integrate point of care STI tests and revise WHO syndromic algorithms for women.
  – Make sensitive STI diagnostic tests affordable e.g. Xpert.
  – Increasing investment in PrEP programmes could benefit STI control.
  – Evaluate innovative STI interventions such as post-exposure, on-demand doxycycline in PrEP users.
  – Invest in STI vaccines – especially important with growth of gonococcal resistance.
PrEP programme design

A peer-based online social network intervention to facilitate PrEP adoption among young Black/Latinx men who have sex with men in New York City

RESULTS
N=155 enrolled

Feasibility:
- Rapid recruitment/enrollment
- >90% Retention at 12 weeks
- >85% liked, commented, loved ≥ 1 post
- Each post viewed by ~40-50% of participants

Acceptability:
- 82% would continue participating,
- 78% reported high satisfaction
- 75% would recommend friends to participate

Involving the community is critical for programmatic success

Patel, MOPDD0203
Tutu Teen Truck: HIV testing, PrEP and contraception

- **ECHO study** in 7829 women desiring contraception (63% < 25 years) showed very high efficacy of 3 modes (Depo Provera, copper intrauterine device or levonorgestrel implant) in sub-Saharan Africa.
- **BUT:** very high HIV incidence (3.81% per year), very high STI incidence despite syndromic management.
- **High need** for integration of HIV prevention, sexual and reproductive health rights (SRHR) services.
- **POWER study:** delivery of PrEP, contraception and HIV testing to adolescent girls and young women through mobile service
  - Initiation of PrEP and contraception correlated in this population
  - Adolescent girls and young women who were using contraception were significantly more likely to initiate PrEP on the same day compared to those who declined PrEP
- **High-quality contraceptive services** can be delivered in HIV contexts.

Onono, MOAX0103LB; Deese, LBPEB16 Rousseau, TUPEC479
Example of product stigma:

“I have kept it a secret because the bottle is similar to that of ARVs. Someone who doesn’t know about PrEP could think you have HIV…”

(20 year old, female PrEP user)
Dapivirine Ring
Dapivirine ring: MTN-025/HOPE

- MTN-025/HOPE – open-label extension study of dapivirine ring for HIV prevention, to assess adherence and safety
- Population: HIV-negative women previously enrolled in MTN-020 ASPIRE.
- Enrolled in Malawi, South Africa, Uganda, Zimbabwe.
- 12-month follow-up, 1,456 women.
- 73% of women accepted ring at all follow-up visits.
- Observed HIV incidence lower than the placebo group in ASPIRE.
New prevention products in the pipeline
DISCOVER trial: TAF/FTC as PrEP

- DISCOVER: randomised comparison of TDF/FTC (Truvada) vs TAF/FTC (Descovy).
- TAF/FTC non-inferior but a trend towards fewer infections in the TAF arm – why?
- Post-hoc analysis:
  - No differences in sexual behaviour or adherence between arms.
  - Faster achievement of optimal drug concentrations in the TAF/FTC arm.
  - Higher proportion in TAF arm achieved TFV-DP levels in PBMCs >EC90 by week 4 (98% vs 64%).
  - F/TAF achieved EC90 within 1–2 hrs of first dose vs 3 days of daily doses of F/TDF.

spinner, TUAC0403LB
Long-acting injectable antiretrovirals for prevention:

- Long-acting cabotegravir (CAB LA) – integrase inhibitor, injectable half-life 45-60 days.
- HPTN 083 and 084: phase 2b/3 studies evaluating the safety and efficacy of CAB LA compared to TDF/FTC for PrEP in HIV-negative men who have sex with men/transgender women (083) and cisgender women (084).
- Randomized, placebo-controlled studies.
- 5-week induction phase: oral CAB or TDF/FTC.
- Phase 2: two injections 4 weeks apart, then every 8 weeks, 3.5 years follow-up.
- Completion of recruitment projected in April 2020.
- HPTN 084: 3,200 women at higher risk of HIV infection in southern and eastern Africa.
- Does a long-acting injectable have a prolonged sub-therapeutic pharmacokinetic tail if dosing is interrupted / terminated?

Long-acting cabotegravir: dosing schedule in HPTN 083 and 084
Islatravir implant

**Implant dimensions**

- Islatravir (formerly MK-8591) is a nucleoside reverse transcriptase translocation inhibitor (NRTTI) with long half-life (120-177 hrs in PBMCs), achieves similar concentrations in plasma and rectal, vaginal tissues.
- High barrier to resistance due to multiple sites of action.
- Safety and tolerability of two islatravir-eluting implants (54 and 62mg) tested in 12-week placebo-controlled phase 1 study in 16 HIV-negative subjects.
- Both implants had concentrations above PK threshold at 12 weeks; 62 mg implant will continue to release through 52 weeks.
- Potential advantages of implants: removable, consistent and predictable drug delivery.
- BUT an implant requires a surgical procedure, is regulated as both drug and device, difficulty in moving to generic marketplace.
Broadly neutralising antibodies (bnAbs):

- Antibodies that have been shown to neutralize a wide range of HIV isolates.
- First generation products: monoclonal antibodies targeting CD4 binding site of HIV gp120.
- VRC01 being evaluated in 2 phase 2b randomised trials (Antibody-Mediated Prevention, AMP studies):
  - HVTN 704 / HPTN 085: 2,700 men who have sex with men and transgender women in the Americas
  - HVTN 703 / HPTN 081: 1,900 women in sub-Saharan Africa
- Next generation products: monoclonal antibodies targeting multiple sites:
  - VRCO7-523LS - 5- to 8-fold increased potency in vitro compared to VRC01.
- Trispecific antibodies: Combining multiple bnAbs with specificities against different epitopes into a single molecule has the potential to:
  - Improve efficacy
  - Simplify prevention and treatment regimens
  - Streamline the regulatory pathway to a licensed drug
- The goal of these studies is to identify the best regimens for moving to a licensure trial.
Acknowledgments

• All Study Participants
• All the IAS presenters for sharing their slides
• IAS Toolkits
  – Track C: Prevention Science
  – Track D: Social Behavioral and Implementation Science
Thank you