IAS Educational Fund Meeting

Mexico City, Mexico
April 17th 2018

Anton Pozniak
Self-Testing
eSTAMP, USA

**METHOD/DESIGN**
- Online provision of self-testing to MSM
  - engages men who have not previously tested and facilitates regular testing
- Randomised study of 2,665 MSM recruited online
- Receive 4+ self-testing kits in the mail and access to usual services vs access to usual services

**RESULTS**
- 17% never previously tested
- Tested at least three times in 12 months: 79% vs 22%
  - Among men who had never previously tested: 70% vs 7%
- New HIV diagnoses: 22 vs 11
  - Linkage to care: 72% vs 91% (difference not statistically significant)

- Community organisation in the UK encourages MSM to order self-test kits online - high demand, high user satisfaction, 92% with reactive results report linking to care
METHOD/DESIGN
National HIV self-testing service, delivered online to MSM and Black Africans 24th June - 5th Aug 2016

RESULTS
4,879 kits ordered,
3,021 people (62%) informed us of their result.
19% had never had an HIV test before and a further 37% had last tested >1 year ago
24 HIV positive, all MSM
Contact was made with 22 (92%) all of whom had accessed confirmatory testing and HIV services

602 people responded to the survey.
98% would use the service again,
91% felt self testing encouraged them to test and
91% were happy with the support they received
Treatment as Prevention

Is U=U for Anal Sex

Opposites Attract

METHODS

- Opposites Attract followed 343 serodiscordant MSM couples in Australia, Thailand and Brazil who were not consistently using condoms
- 591 couple years of follow up from 343 couples; 16,889 sexual acts when condoms were not used
- HIV-positive partners had viral load <200 copies/ml during 98% of follow up

RESULTS

No new HIV infections genetically linked to main partner

- Incidence per 100 years of couple follow up = 0 (95%CI: 0 to 0.62)
- Three new HIV infections in participants, each from an outside partner (60% of couples reported sex outside the main relationship)
- “Our results provide strong support for the hypothesis that undetectable viral load prevents HIV transmission in homosexual men.”
Oral PrEP

Roll Out of PrEP

- PrEP is being effectively scaled up, mostly in countries where research was conducted (e.g. USA, France, Australia)
- Elsewhere much has been achieved without government support, through community and online mobilisation
- It’s important to focus on what the ‘consumer’ wants
  - As seen in contraception, choice of method and choice of model of service delivery
- Urgently need to scale up PrEP implementation in at-risk populations

*Yellow countries have some form of PrEP programming; blue countries do not.*
Oral PrEP

On Demand Regimen

• Sub-group analysis of IPERGAY - men having ‘infrequent’ sex
  - (median pill use 9.5 pills/month, covering 5 sex acts/month)
  - HIV incidence: 0% vs 9.3% in placebo arm; 100% relative risk reduction
• Researchers concluded that “on-demand PrEP is an adequate alternative to daily PrEP for MSM with high risk but infrequent sexual intercourse”

☑ 2 tablets 2-24 hours before sex
☑ 1 tablet 24 hours later
☑ 1 tablet 48 hours after first intake

4 pills of TDF/FTC taken over 3 days to cover one sexual intercourse
PrEP implementation experience in France

- 3,405 people took TDF/FTC PrEP between January 2016 and February 2017
- 97% MSM and all clinically evaluated to be at high risk of acquiring HIV*
- 57% used on-demand regimen, 42% daily regimen
- Four HIV infections - two detected during first weeks of PrEP initiation, two after stopping PrEP
- Data demonstrates that on-demand regimen is robust in the context of national PrEP roll out

*High risk of acquiring HIV -
- MSM or TG individuals having condomless anal sex with 2+ partners in last 6 months; or episodes of STIs in last 12 months; or multiple PEP prescriptions in last 12 months; or chemsex.
- OR other persons, on case by case basis.
On Demand or Daily?

- Qualitative study (AMPPrEP) in Dutch MSM explored reasons why men chose on demand or daily regimens.
- At baseline, 273 men chose daily and 103 chose on demand.
- Conclusion: give PrEP users a choice between regimens; allow choices to change as circumstances evolve.

### Reasons to choose daily or on-demand PrEP

<table>
<thead>
<tr>
<th></th>
<th>Daily PrEP (N=420)</th>
<th>n (%)</th>
<th>Event-driven PrEP (N=206)</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Expected adherence</strong></td>
<td>Need for daily structure</td>
<td>133 (32%)</td>
<td>Issues with daily PrEP adherence</td>
<td>20 (10%)</td>
</tr>
<tr>
<td></td>
<td>Issues with event-driven PrEP adherence</td>
<td>129 (31%)</td>
<td></td>
<td></td>
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<tr>
<td><strong>Perceived HIV risk</strong></td>
<td>Unplanned/frequent sex</td>
<td>79 (19%)</td>
<td>Sex is planned</td>
<td>87 (42%)</td>
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<td></td>
<td></td>
<td></td>
<td>Low frequency of HIV risk</td>
<td>57 (28%)</td>
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<tr>
<td><strong>Expected safety of the other regimen</strong></td>
<td>Fear of side-effects related to event-driven PrEP reinitiation</td>
<td>5 (1%)</td>
<td>Toxicity and burden of daily medication</td>
<td>38 (19%)</td>
</tr>
<tr>
<td></td>
<td>Fear of resistance development with event-driven PrEP</td>
<td>2 (&lt;1%)</td>
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</table>
Early data on safety and acceptability of oral TDF/FTC PrEP in sexually active South African adolescents (15-19 years)

- 148 participants (99 female)
- Open-label demonstration study: daily PrEP + HIV prevention support
- PrEP was reasonably well tolerated with minimal safety concerns
- One HIV infection, in a 19 year old who had stopped PrEP 24 weeks previously
- Adherence decreased over time and with less frequent study visits:
  - Week 12 (monthly visits), 57% had detectable tenofovir
  - Week 48 (visits every 3 months), 38% had detectable tenofovir
- Side-effects and perceived side-effects were an important reason for PrEP discontinuations
- Conclusion: South African adolescents need access to PrEP with tailored adherence support and frequent clinic visits
Injectable Cabotegravir
(strand-transfer integrase inhibitor)

- HPTN077: double-blind, randomised, placebo-controlled, phase II tolerability and pharmacokinetics study
- 199 male and female participants at low risk of HIV, assigned 3:1 to cabotegravir or placebo
  - Cohort 1: 800mg every 12 weeks
  - Cohort 2: 600mg every 8 weeks
- Adverse events: injection site pain (34% vs 2%) and headache (15% vs 2%)
  - Study withdrawals due to adverse events: 7.9% vs 2.1%
- Pharmacokinetic analyses: 600mg 8 week injections consistently met pre-specified pharmacokinetic targets for both sexes; are being evaluated in Phase 3 efficacy studies
New PrEP Agents

Rilvirepine & MK-8591 (Long-acting injectable formulations of ARV agents)

- **Rilpivirine** long-acting injection, phase 1 study: safe and achieves significant drug accumulation in plasma, rectal, and female genital tract tissue
  - Viral inhibition of clades B (HIV-1_{BaL}) and wild type clade C (G147-1) rectal explant infection persisted up to 4 months after the last injection, but cervical explant infection was only suppressed at one time point
- **MK-8591** once-weekly oral agent (nucleoside *reverse transcriptase translocation inhibitor*) was completely protective against repeated low-dose rectal SIV challenge in macaques
Why do we need DSD?

• Progress towards HIV epidemic control:
  – 19.5 million individuals accessing ART worldwide
  – 1.8 million new HIV infections each year
  – 1 million deaths from HIV-related disease each year

• Our successes are due to the public health approach (consistent package of care, decentralised delivery model) enabling scale-up of services

• Challenges to reaching 90-90-90 goals:
  – Expanding ART coverage
  – Achieving high quality care
  – Improving efficiency

• There are structural, psychosocial and behavioural obstacles to successful engagement in care

• DSD can address these challenges and reduce gaps in outcomes
Differentiated Service Delivery

Why do we need DSD?

• DSD is a client-centred approach that simplifies and adapts HIV services
  – Tailor services to recipients of care: modulate the frequency, location and content of service provision
• For example, multi-month prescribing (MMP): people with less complex care needs are prescribed several months ARVs at a time
  – Monthly clinic visits can be difficult to manage for patients: transport costs, time away from education/work, etc.
  – Frees up staff capacity for patients who are starting treatment, have co-morbidities, or are unwell
Differentiated Service Delivery

Why do we need DSD?

• DSD implementation studies should focus on adapting DSD to specific populations
  – For example, poor engagement of men with services and worse clinical outcomes for men. Could tailored interventions for men help reduce gender disparities?

• Need to evolve our public health approach into a new model, a model of ‘precision public health’.
Reducing Stigma

- Integrated stigma mitigation interventions for female sex workers and men who have sex with men in Senegal (24 months)
- Interventions: peer-led community groups, training of healthcare workers in service provision for key populations, peer-to-peer anonymous referral system to health services and prevention
- Interim data up to month 15:
  - Large reductions in *anticipated* healthcare stigma
  - Some reductions in *experienced* healthcare stigma
  - Low uptake of ART in HIV-positive MSM - results reinforce the need for stigma mitigation interventions to be combined with HIV prevention and treatment interventions for key populations

Anticipated and experienced stigma for MSM
Providing Stigma-Free Services

• How to provide stigma-free HIV services to female sex workers in Botswana?
  – Accept each sex worker as a human being
  – Don’t ask unnecessary or intrusive questions
  – Respect confidentiality when counselling
  – Assess all the person’s needs and make referrals for non-health issues (e.g. legal needs)
  – Sensitise other professionals to FSW’s needs
  – Be creative to overcome barriers:
    • e.g. ensure women get ID cards so can access ART
    • e.g. be trained to give emergency ART prescriptions
• In the speaker’s programme, 90% retention among 159 FSW enrolled on ART
Treatment
TB and INSTIS-a problem with rifampicin

Raltegravir- REFLATE Study

VL outcomes
INSPIRING Study: Safety and Efficacy of Dolutegravin-Based ART in TB/HIV Co-infected Adults at Week 24

Dooley KE et al. CROI 2018 #33.

Proportion of Participants With HIV-1 RNA <50 copies/mL, % (95% CI)

- DTG (n=69): 81 (72, 90)
- EFV (n=44): 89 (79, 98)

Modified FDA snapshot analysis (ITT-E)

Week

0 4 8 12 16 20 24 28

Percentage, %

50mg BID DTG

Target $C_{\text{min}} = 300$ ng/mL
REALITY Study: raltegravir-intensified quadruple therapy in first-line antiretroviral therapy -

IRIS

NO evidence that 12 weeks’ RAL intensification impacted incidence or case-fatality of IRIS

89 vs 86 Cases

Mortality

HIV RNA < 50 copies/mL (95% CI)

Mean change in CD4/mm³ at W48: + 163 vs + 148 (p = 0.04)
Switch when undetectable
2017 Guidelines 2 drug switch included

- Switch safely and for a good reason
  - Consider ART history, genotype, interactions, co-infection
- Consider efficacy-based triple therapy switch
- **Multiple studies PI/r or NNRTI to INSTI non inferior**

Also Consider efficacy-based 2DR switch

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<thead>
<tr>
<th>3TC + PI/r based:</th>
<th>3TC + PI/r based:</th>
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<tbody>
<tr>
<td></td>
<td>DRV/r + 3TC</td>
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<tr>
<td></td>
<td>ATV/r + 3TC</td>
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<tr>
<td></td>
<td>LPV/r + 3TC</td>
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<tr>
<td><strong>INSTI + NNRTI</strong></td>
<td><strong>INSTI + NNRTI</strong></td>
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<tr>
<td></td>
<td>DTG + RPV</td>
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</table>
INSTI to INSTI 3 Drug Switch!
Bictegravir/F/TAF from DTG and ABC/3TC

- Switching to B/F/TAF was noninferior to remaining on DTG/ABC/3TC
- No resistance in either treatment arm

Virologic Outcome

<table>
<thead>
<tr>
<th>Patients, %</th>
<th>HIV-1 RNA ≥50 c/mL</th>
<th>HIV-1 RNA &lt;50 c/mL</th>
<th>No Virologic Data</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>3/282</td>
<td>264/282</td>
<td>15/282</td>
</tr>
<tr>
<td></td>
<td>1/281</td>
<td>267/281</td>
<td>13/281</td>
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</tbody>
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Treatment Difference in RNA ≥50, % (95.002% CI)

- Favors B/F/TAF
- Favors DTG/ABC/3TC
Switch to 2 Drug Therapy
From Suppressive ART to DTG + RPV Wk 48

• 1 pt with at Wk 36 in DTG + RPV arm had K101K/E (1.2-fold RPV change)
  – Resuppressed with continued DTG + RPV
  – No INSTI resistance

• AE rates generally similar between treatment arms through Wk 52

Llibre JM, et al. CROI 2017. Abstract 44LB.
Switching
When VL is known to be Detectable

Need Viral Load-PLUS resistance test to do this

Can switch to boosted PI and recycle nucleosides
- Earnest and Second Line

Can switch to DTG and one active nucleoside- Dawning
- need resistance testing or treatment history to determine this
DAWNING trial

Evaluated safety and efficacy of DTG + 2 NRTIs vs LPV/RTV + 2 NRTIs in patients failing first-line therapy of an NNRTI + 2 NRTIs

NEED at least one fully active NRTI based on viral resistance testing

Aboud et al. IAS 2017; Paris. TUAB0105LB
“This was the first conference in which we can see the combination of prevention and treatment at the population level and see how it works... It works beautifully.”

François Dabis, French National Agency for Research on AIDS and Viral Hepatitis (ANRS)