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Please contact may.wang@ashm.org.au for details.
Presenter

• Vickie Knight, Sydney Sexual Health Clinic

*Lancet HIV*
Lancet HIV

Vickie Knight, CNC Sydney Sexual Health Centre
Daily and non-daily pre-exposure prophylaxis in African women: a randomised, open-label, phase 2 trial
Bekker et al on behalf of the HPTN 067 (ADAPT) study team

Background – why do this study?
- Study designed in 2010
- PrEP daily dosing based on dosing intervals of Rx
- Study team concerned daily dosing wouldn’t match risk events
- VOICE and FEMPPrEP showed no prevention effectiveness

Hypothesis – what did they think the outcome would be?
Less frequent PrEP might be:
- sufficient for prevention
- result in lower drug costs
- result in less side effects and
- this may increase adherence and use
Method – what did they do?

- Women
- Directly observed dosing for 5 weeks
- Then assigned to:
  - daily;
  - time-driven (twice a week plus a post-sex dose); or
  - event-driven (one tablet both before and after sex).

Results – what actually occurred?

Daily dosing resulted in:
- higher coverage of sex events
- increased adherence & augmented drug concentrations more than either time-driven or event-driven dosing
Implications – *what does all this mean for us?*

- Countered earlier evidence
- When PrEP offered in open lable fashion most women attempted to use PrEP as assigned.

**Economic incentives for HIV testing by adolescents in Zimbabwe: a randomised controlled trial**

*Katharina Kranzer et al*

**Background – *why do this study?***

- HIV testing is entry point to HIV care
- Uptake of testing & ARV coverage are lower in older children/adolescents than adults
- 2 RCTs & 2 OS – all showed increase uptake of HIV testing
- None done in older children or adolescents
Hypothesis – *what did they think the outcome would be?*

- Incentives would increase testing uptake
- If testing uptake was increased ARV coverage might improve

Method – *what did they do?*

- RCT
- Nested in home HIV prevalence study
- Households with eligible children randomised:
  - No incentive
  - Fixed USD$2 incentive
  - Participate in $5 or $10 lottery
- if they attended for HIV testing
- Compared incentives group to non-incentives group
Results – what actually occurred?

Table 2. Effect of provision of and type of incentives on uptake of HIV testing at household level

<table>
<thead>
<tr>
<th>At least one child went to clinic</th>
<th>Crude OR (95% CI)</th>
<th>p value</th>
<th>Adjusted OR (95% CI)*</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No incentive (N=472)</td>
<td>93 (20%)</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>US$2 (N=654)</td>
<td>316 (48%)</td>
<td>3.81 (2.90–5.01)</td>
<td>&lt;0.0001</td>
<td>3.67 (2.77–4.85)</td>
</tr>
<tr>
<td>Lottery (N=562)</td>
<td>223 (40%)</td>
<td>2.68 (2.02–3.66)</td>
<td>&lt;0.0001</td>
<td>2.66 (2.00–3.55)</td>
</tr>
</tbody>
</table>

OR=odds ratio.

* Adjusted for community and number of children in household as fixed effects and for research assistant as a random effect.
Implications – what does all this mean for us?

• Financial incentives show promise
• More research:
  – durability,
  – Sustainability
  – cost effectiveness
  – Scalability
  – Ease of implementation

Predictors of linkage to HIV care and viral suppression after release from jails and prisons: a retrospective cohort study Kelsey BLoeliger et al

Background – why do this study?

• USA has highest incarceration rate of any country
• 12 million transition annually
• 1/6 of PLWH passing through
• Incarceration provides opportunity for engagement
• However, poor HIV treatment outcomes after release
AIM – what did they want to achieve?

- Assess post-release linkage to care
Method – what did they do?

- Retrospective cohort study
- LTC = VL in 14 and in 30 days after release
- Secondary outcome of UDVL

Results – what did they find?

Table 1. Time to linkage to care as measured by first HIV viral load drawn after release from prison or jail

<table>
<thead>
<tr>
<th></th>
<th>0-14 days</th>
<th>15-30 days</th>
<th>31-90 days</th>
<th>91-180 days</th>
<th>181-365 days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of cases eligible for analysis</td>
<td>3181</td>
<td>3064</td>
<td>2581</td>
<td>2065</td>
<td>1470</td>
</tr>
<tr>
<td>Number of cases with first viral load drawn during the post-release time window</td>
<td>672/3101 (21%)</td>
<td>394/664 (13%)</td>
<td>683/2581 (27%)</td>
<td>295/2065 (14%)</td>
<td>122/1470 (8%)</td>
</tr>
<tr>
<td>Number of cases with &gt;400 viral copies per mL at first viral load</td>
<td>173/672 (20%)</td>
<td>132/394 (24%)</td>
<td>266/683 (39%)</td>
<td>113/295 (30%)</td>
<td>73/122 (50%)</td>
</tr>
<tr>
<td>Number of cases with &lt;400 viral copies per mL at first viral load</td>
<td>492/672 (73%)</td>
<td>256/394 (65%)</td>
<td>499/683 (60%)</td>
<td>177/295 (60%)</td>
<td>49/122 (49%)</td>
</tr>
<tr>
<td>Number of cases with first viral load drawn during an earlier time window</td>
<td>Not applicable</td>
<td>648/564 (21%)</td>
<td>883/2581 (34%)</td>
<td>1282/2665 (62%)</td>
<td>1138/1470 (77%)</td>
</tr>
</tbody>
</table>

Data are n or n/N (%)).

* Values might not sum to 100% because a small number (<2%) of viral load values were unreported during each time window.
Results – what did they find?

• Factors positively associated with LTC within 14 days:
  – Intermediate incarceration (31-365 days) AOR 1.52, CI:1.19-1.95
  – Transitional case management (AOR 1.65, CI:1.36-1.99)
  – Receipt of ARVs during incarceration (AOR 1.39, CI:1.11-1.74)
  – 2 or more comorbidities AOR 1.86, 1.48-2.36

• Factors negatively associated
  – Reincarceration (AOR 0.70, 0.56-0.88)
  – Conditional release (AOR 0.62, 0.50-0.78)

Implications – what does all this mean for us?

• LTC after release is suboptimal in this area
• LTC improves when medical, psych & case management needs are addressed before release
• Integrated programmes aligning justice and health have great potential to improve long-term HIV Rx outcomes
The effect of ART on cervical cancer precursor lesions

Henry J Cde Vries Renske D M Steenbergen

Background – why do this study?

• Higher prevalence of genital high-risk oncogenic HPV infection
• More likely to have persistent infection
• More likely progression of CIN lesions
• Effect of ART on these is not well established
  – Conflicting evidence in research

Method – what did they do?

• Searched MEDLINE/Embase for articles 1996-May 2017 which reported the association of ART with:
  – prevalence of high-risk HPV or prevalence,
  – incidence, progression, or regression of histological (CIN)
  – cytological (squamous intraepithelial lesions [SIL]) cervical abnormalities, or
  – incidence of invasive cervical cancer.

• Found 31 studies
Results – what did they find?

- Women living with HIV on ART had
  - Lower prevalence of HR HPV (AOR 0.83, 0.70-0.99)
  - Some evidence association with lower prevalence of HSIL-CIN2+ (0.65, 0.40-1.06)

- ART associated with:
  - decreased risk of HSIL-CIN2 (0.59, 0.40-0.87)
  - SIL progression aHR 0.64, 0.54-0.75
  - Increased likelihood SIL/CIN regression (1.54, 1.30-1.82)
Implications – what does all this mean for us?

- Early ART likely to reduce incidence and progression of SIL/CIN
- Ultimately reduce incidence of Cx CA
- Need more cohort studies to confirm possible effect

Wild-type HIV infection despite PrEP: a lot to learn from a case report

2 letters to the Editor and 1 response
- Hoornenborg et al, 1st case report of HIV acquisition despite good levels of PrEP in DBS
- Stopped PrEP
- Didn’t start ARVs
- No HIV provirus in peripheral blood
- Meaning HIV was probably contained in the mucosa
- Localised infection is associated with better outcomes
- Advocate starting ARVs at seroconversion rather than waiting for definitive diagnosis
Testing and linkage to HIV care in China: a cluster-randomised trial
Zunyu Wu et al

Background – why do this study?

• Implementation or operational research
• Early ART initiation slows disease progression and prevents onward transmission
• What screening processes improve time to initiation of ART?

Background – why do this study?

• Many patients lost at each step of HIV care cascade
• Current standard is complex
• Some parts of China only 43% receive confirmatory testing
• Only 57% of confirmed cases receive CD4 count within 6 months
• CD4 counts used to determine ART eligibility
• Meaning 80% newly diagnosed eligible for ART were not engaged in timely treatment
Method – what did they do?

- Cluster RCT in 12 hospitals in Guangxi
- Chose 12 most similar hospitals
- Assigned 1:1 One4All or standard of care
- >18 years identified as HIV positive
- Intervention (One4All)
  - rapid HIV testing & CD4 counts, VL testing
  - To promote fast Dx and staging and immediate ART
- Standard of care
Method – **what did they do?**

- **Primary outcome**
  - Completeness of testing by 30 days from initial HIV-reactive screening

- **Secondary outcome**
  - ART initiation within 90 days from initial HIV-reactive screening

- **Tertiary outcomes**
  - Viral suppression
  - Mortality at 12 months

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Method – **what did they do?**

- Sample size calculation
- Intention to treat analysis
- Categorical variables - $\chi^2$
- Continuous variables - $t$ test adjusted for clustering
- Kaplan-Meier analyses for time to testing completeness, initiation of ART, and death.
- Created a fixed multivariate Cox model
- Follow-up commenced Feb 2014 & completed Jan 2016.
Results – what did they find?

- Male (78%)
- Worked as farmers or labourers (95%)
- Self-reported as heterosexual (97%)
- Median age 55
- More in intervention group had middle school education (p=0.0498)
- No other differences between groups
- 76% of intervention group & 63% in SOC group achieved testing completeness
Results – what did they find?

Table 2. Multivariate models of patients having 30 day testing completeness, 90 day ART initiation, 12 month viral suppression, and 12 month mortality, controlling for hospital clustering

<table>
<thead>
<tr>
<th>Group</th>
<th>Testing completeness, 30 days</th>
<th>ART initiation, 90 days</th>
<th>Viral suppression, 12 months</th>
<th>Mortality, 12 months (adjusted for CD4 count)</th>
<th>Mortality, 12 months (unadjusted for CD4 count)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR (95% CI)</td>
<td>p value (95% CI)</td>
<td>OR (95% CI)</td>
<td>HR (95% CI)</td>
<td>p value (95% CI)</td>
</tr>
<tr>
<td>One4All</td>
<td>19.94</td>
<td>0.0004</td>
<td>3.49</td>
<td>0.0087</td>
<td>1.59</td>
</tr>
<tr>
<td></td>
<td>(3.86–103.04)</td>
<td>(1.37–10.70)</td>
<td>(0.92–27.3)</td>
<td>(0.28–13.6)</td>
<td>(0.23–1.01)</td>
</tr>
<tr>
<td>Standard-of-care</td>
<td>1</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
</tr>
</tbody>
</table>

Figure 3. Kaplan-Meier plot for time to testing completeness (A), ART initiation (B), and death (C) from HIV screening.
Results – what did they find?

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• Self-reported as heterosexual (97%)
• Median age 55
• More in intervention group had middle school education (p=0.0498)
• No other differences between groups
• 76% of intervention group & 63% in SOC group achieved testing completeness

Conclusions

• 20 times increased testing completeness
• 3.5 x increased ART initiation
• Cut mortality by more than half
• Global consensus that combining streamlining of testing with linkage to ART can improve clinical outcomes
• This is likely to reduce transmission
• Can we get enough coverage to make a difference?
Critique

• Good study
• Very important topic requiring investigation
  • Sophisticated example of implementation science
  • rigorous & relevant, providing a new path to improve HIV outcomes and reduce infectiousness of people with HIV infection
• Scientifically sound