# HIV/Sexual Health Clinical Education Session

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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

*The Lancet HIV* has an Impact Factor of 9·842

# 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 FEMPrEP 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

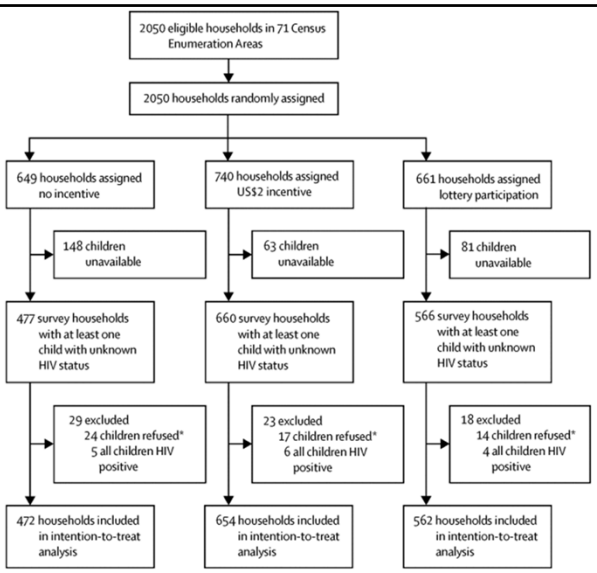


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Figure. Study profile

Child unavailable refers to a child that was absent at initial household visits and absent at two further visits or household head reporting that the child was expected to be absent for more than 2 weeks. *The households remained in the analysis as other children in the household participated.

# Results – *what actually occurred?*

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

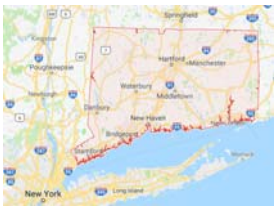
| | At least one child went to clinic | Crude OR (95% CI) | p value | Adjusted OR (95% CI)* | p value |
|---|---|---|---|---|---|
| No incentive (N=472) | 93 (20%) | 1 | .. | 1 | .. |
| US$2 (N=654) | 316 (48%) | 3·81 (2·90–5·01) | <0·0001 | 3·67 (2·77–4·85) | <0·0001 |
| Lottery (N=562) | 223 (40%) | 2·68 (2·02–3·56) | <0·0001 | 2·66 (2·00–3·55) | <0·0001 |

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?*

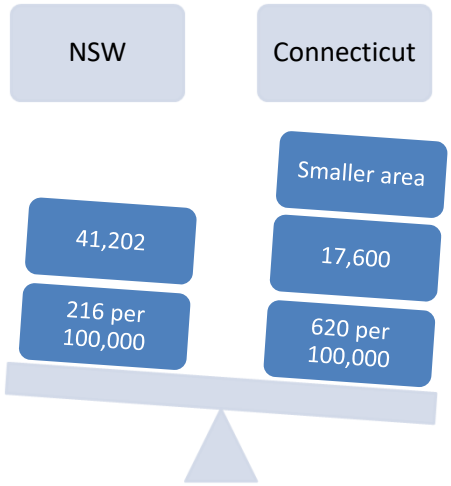
- Financial incentives show promise
- More research:
  - durability,
  - Sustainability
  - cost effectiveness
  - Scalability
  - Ease of implementation



**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

| | 0–14 days | 15–30 days | 31–90 days | 91–180 days | 181–365 days |
|---|---|---|---|---|---|
| Number of cases eligible for analysis | 3181 | 3064 | 2581 | 2065 | 1470 |
| Number of cases with first viral load drawn during the post-release time window | 672/3181 (21%) | 394/3064 (13%) | 683/2581 (27%) | 295/2065 (14%) | 122/1470 (8%) |
| Number of cases with ≥400 viral copies per mL at first viral load* | 173/672 (26%) | 132/394 (34%) | 266/683 (39%) | 113/295 (38%) | 73/122 (60%) |
| Number of cases with <400 viral copies per mL at first viral load* | 492/672 (73%) | 256/394 (65%) | 409/683 (60%) | 177/295 (60%) | 49/122 (40%) |
| Number of cases with first viral load drawn during an earlier time window | Not applicable | 648/3064 (21%) | 883/2581 (34%) | 1282/2065 (62%) | 1138/1470 (77%) |

Data are n or n/N (%).

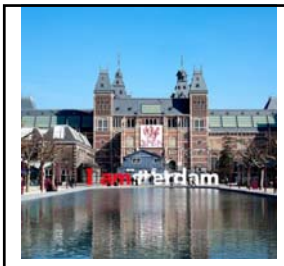
* Values might not sum to 100% because a small number (<2%) of viral load values were unreported during each time window.

## Results – *what did they find?*

- Factors positively associated with LTC within 14 days:
  - Intermediate incarceration (31-365days) 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

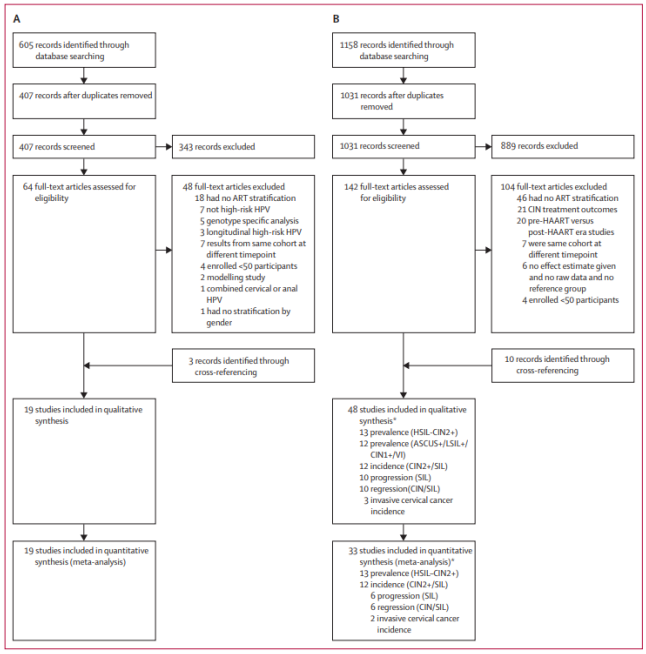


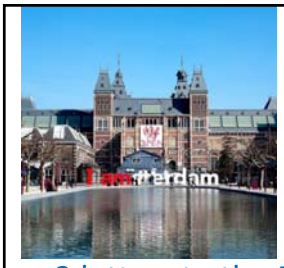

**Figure 1: Study selection for outcomes of high-risk HPV (A) and cervical lesions (B)**
HPV=human papillomavirus. HAART=highly active antiretroviral therapy. CIN=cervical intraepithelial neoplasia. SIL=squamous intraepithelial lesions. HSIL=high-grade SIL. LSIL=low-grade SIL. ASCUS= atypical squamous cells of undetermined significance. *Some studies contributed to more than one outcome (ie, incidence and progression, or progression and regression). Individual studies are summarised in table 1.

## 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[1]
- 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

## ‹sting and linkage to HIV care in ıina: a cluster-randomised trial

Zunyu Wu et al

### Background – *why do this study?*

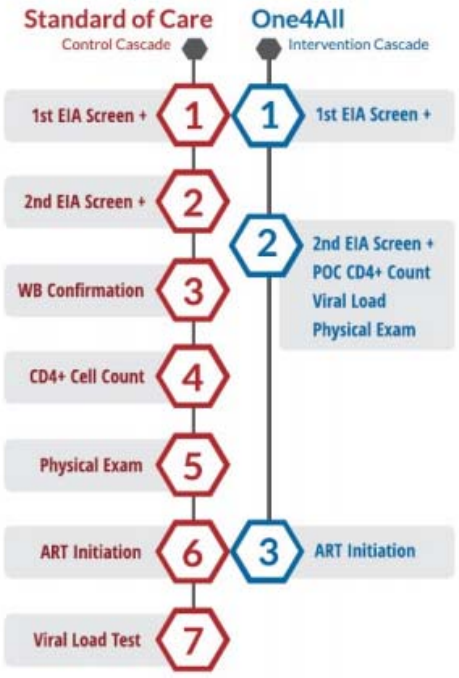
- Implementation or operational research
- Early ART initiation slows disease progression and prevents onward transmission
- What screening processes improve time to initiation of ART?

### 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 elligible 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



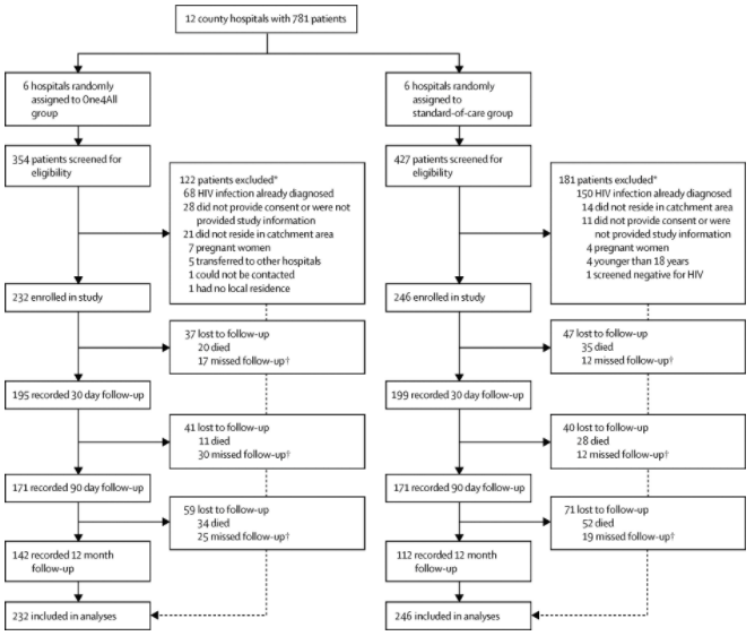
## Method – *what did they do?*

- 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

## 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?*




## 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

| | Testing completeness, 30 days | | ART initiation, 90 days | | Viral suppression, 12 months | | Mortality, 12 months (adjusted for CD4 count) | | Mortality, 12 months (unadjusted for CD4 count) | |
|---|---|---|---|---|---|---|---|---|---|---|
| | OR (95% CI) | p value | OR (95% CI) | p value | OR (95% CI) | p value | HR (95% CI) | p value | HR (95% CI) | p value |
| Group | | | | | | | | | | |
| One4All | 19·94 (3·86–103·04) | 0·0004 | 3·49 (1·37–8·86) | 0·0087 | 1·59 (0·92–2·73) | 0·094 | 0·62 (0·28–1·36) | 0·23 | 0·44 (0·19–1·01) | 0·053 |
| Standard-of-care | 1 | .. | 1 | .. | 1 | .. | 1 | .. | 1 | .. |

# Results – *what did they find?*

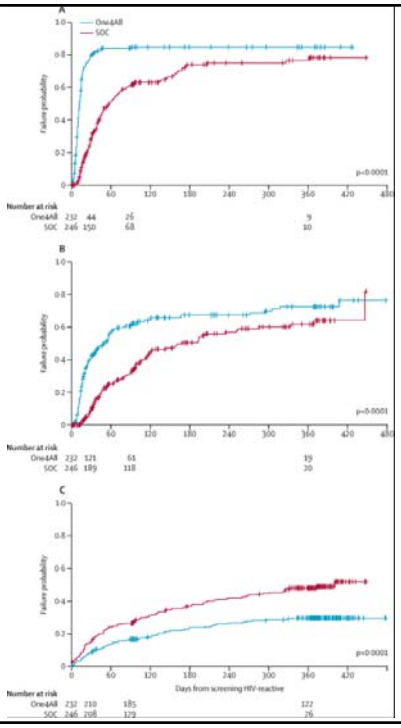


Figure 3. Kaplan-Meier plot for time to testing completeness (A), ART initiation (B), and death (C) from HIV screening

## Results – *what did they find?*

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## 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