A Demonstration Open Label Study to Assess the Acceptability, Safety and Use of Truvada Pre-exposure Prophylaxis in Healthy, HIV-Uninfected Adolescents, 15-19 Years of Age.

PLUSHILLS

NIH Grant #: R01AI094586, NCT02213328

Background

• Blinded and open label studies among adults support the efficacy of TDF/FTC for HIV prevention

• No PrEP data available on heterosexual adolescents or adolescents in Africa, to date

• Additional safety and behavioural data in adolescents are needed to support a PrEP indication

• Inform policy for future roll out of PrEP in AGYW
The Pluspills Study

- A Demonstration Open Label Study to Assess the Acceptability, Safety and Use of Truvada Pre-exposure Prophylaxis in Healthy, HIV-Uninfected Adolescents, 15-19 Years of Age.
- 150 participants
- (under IND)
Primary Objective

• To evaluate the acceptability, safety and use of a daily regimen of oral PrEP (FTC/TDF), as a component of a comprehensive HIV prevention package
• Prevention package included: HIV testing, STI management, risk reduction counselling, access to condoms, PEP and referral for male circumcision
• Grades 2, 3 and 4 adverse events according to healthy volunteer tables.
Secondary and Exploratory Objectives

• Secondary
  – Adherence
  – Sexual behaviours: measure any change in sexual activity, perceptions of sexual risk, risk compensation, and condom use
  – Participants’ and Partners’ attitudes

• Exploratory
  – HIV incidence
  – Effect of biofeedback on adherence
  – Sexual activity and Prep usage
Clinical Eligibility

• **HIV uninfected** based on testing performed by study staff at screening and enrollment

• **Sexually active**, as defined as a minimum of one act of (penile vaginal) sexual intercourse in the last 12 months, per self-report

• **Negative pregnancy** test at screening and enrollment and per participant report, does not intend to become pregnant in the next 12 months

• Using an effective method of *contraception* at enrolment, and intending to use a effective method for the study duration.
Study Design

Basic Package: HCT, MMC, PEP, condoms
Female condoms

Choice of daily, weekly or no SMSs

Adherence clubs

150 Healthy 15-19yo, Sexually active
40:60 M:F Masiphumelele and Soweto

0 Mo
Screen, enroll. Package + PrEP

1 Mo
Screen, enroll. Package + PrEP

2 Mo
Screen, enroll. Package + PrEP

3 Mo
Choice: package +/- PrEP
Acceptability
Reasons for choice

6 Mo
Choice: package +/- PrEP
Acceptability
Reasons for choice

9 Mo
Choice: package +/- PrEP
Acceptability
Reasons for choice

12 Mo
Final Visit

DBS + real time FB vs none

DBS + real time FB vs none

DBS + real time FB vs none

DBS + real time FB vs none

DBS + real time FB vs none

DBS + real time FB vs none
Study Sites - South Africa

Masiphumelele, Cape Town

Soweto, Johannesburg
Community Engagement and ICF process

• Sites worked with HAVEG to develop resources that ensure that the ethico-legal framework for adolescent research was implemented

• Community engagement, outreach and education

• Adolescent friendly services

• Parental/Guardian consent and Adolescent assent/consent

• Development of ICF materials and translation into local languages.
Study Overview

Screened

Started in March 2015
N=244
Cape Town n=96
Soweto n=148

Excluded

N=96
Cape Town n = 21, Soweto n = 75
Not interested: 27
Not sexually active: 23
Pregnant: 8
HIV +: 3, Hep B SAg +: 2
Other: 33

Enrolled

Completed March 2015
N=148
Cape Town n = 75
Soweto n =73

Excluded

N=1
Reason: underage
### Baseline Demographics

<table>
<thead>
<tr>
<th>Demographics</th>
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<tbody>
<tr>
<td>Median Age</td>
<td>18 years</td>
</tr>
<tr>
<td>Female / Male ratio</td>
<td>99/ 49</td>
</tr>
<tr>
<td>Completed Grade 12</td>
<td>23%</td>
</tr>
<tr>
<td>Living with parents/ family</td>
<td>90%</td>
</tr>
<tr>
<td>Median age of Sexual Debut</td>
<td>14.5 years</td>
</tr>
<tr>
<td>Partner &gt; 5 years older</td>
<td>22%</td>
</tr>
<tr>
<td>Transactional Sex</td>
<td>3%</td>
</tr>
<tr>
<td>Had anal sex</td>
<td>6%</td>
</tr>
<tr>
<td>Condom at last sex act</td>
<td>74%</td>
</tr>
<tr>
<td>Always use a condom</td>
<td>34%</td>
</tr>
<tr>
<td>Alcohol in last 12 months</td>
<td>57%</td>
</tr>
<tr>
<td>Recreational drugs in last 12 months</td>
<td>15%</td>
</tr>
<tr>
<td>Any STI at screening</td>
<td>41%</td>
</tr>
</tbody>
</table>

#### Age by Gender

- **15**: Male 0, Female 10
- **16**: Male 10, Female 10
- **17**: Male 10, Female 10
- **18**: Male 20, Female 40
- **19**: Male 20, Female 40
Safety

• Well-tolerated overall
  11% (n= 16) participants experienced a grade 2 or 3 related side effect
  **Grade 2:**
  – 4 headaches
  – 4 nausea and vomiting
  – 2 abdominal pain
  – 2 diarrhea
  – 2 skin rash

**Grade 3**
  – Two Grade 3 adverse events (weight loss) in 2 participants deemed related to study drug
  – Grade 3 weight loss = 10-19%

• No abnormal Creatinine / LFT’s

• 18% of participants opted out of PrEP at 12 weeks with about a third citing side effects as the reason for stopping. A further 20% opted out at week 24 or 36.
41% of participants had an STI at screening, 28% at week 12 and 38% at week 48.
Herpes incidence: 8.3 per 100 person years (95% CI: 4.31 – 16)
STI by Gender

- Baseline: 51% Female, 20% Male
- Week 12: 35% Female, 14% Male
- Week 48: 50% Female, 18% Male
HIV Incidence

• One seroconversion
• HIV incidence 0.76 per100 person years (95% CI: 0.1-5.37)
• 19 year old woman who had opted out of PrEP 24 weeks prior to diagnosis.
Plasma TDF levels

% Participants with TDF in plasma

One third of participants persisted with PrEP
Unknown if these were the most at risk participants
## Factors predicting adherence

<table>
<thead>
<tr>
<th>Factor</th>
<th>OR</th>
<th>P value</th>
<th>Confidence interval</th>
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<tbody>
<tr>
<td>Time in weeks</td>
<td>0.89</td>
<td>0.001</td>
<td>0.87-0.94</td>
</tr>
<tr>
<td>Age</td>
<td>0.73</td>
<td>0.01</td>
<td>0.57-0.94</td>
</tr>
<tr>
<td>Gender</td>
<td>0.79</td>
<td>0.4</td>
<td>0.43 – 1.45</td>
</tr>
<tr>
<td>Site</td>
<td>2.0</td>
<td>0.02</td>
<td>1.11- 3.61</td>
</tr>
</tbody>
</table>

### Plasma TDF ≥ 10

**Mixed methods logistic regression model**

**Young women were not less adherent than young men**
Motivators

- Perceived Risk
- Determination to remain HIV negative
- Desire
- Family/Friends
- Protection
- Reimbursement

It was easy for me to participate because I know us teenagers are not perfect, we do things, we party and I thought I needed PrEP, so it was easy for me.

I said knowing that you are safe, even if you do a little mistake you know that you are safe.
Adherence Facilitators

• Adherence Clubs
• Drug Results
• Pill returns
Support for Youth

- Parents
- Family
- Celebrities
- Friends
- Partners
- Other participants
- Counsellors
- Staff
Take home points

• Adolescents in South Africa are still at high risk for HIV
• Pluspills was a self selected cohort appropriate for combination prevention
• Adherence to programming notoriously difficult for adolescents worldwide.
• PrEP was reasonably well tolerated with minimal safety concerns
• PrEP usage and adherence diminished over time with less frequent visits (fatigue or some other factor)
• Women may have out performed young men
• There was an unexpectedly low HIV incidence despite high STI rates which remained constant
• Opportunity to engage on ethical norms in adolescent research.
Conclusions

• South African adolescents need access to PrEP with tailored adherence support and augmented visit schedules.

• More research on persistence is needed.

• Other less frequent dosing strategies may also benefit in the future.
The 3P study
Next Steps

• Focusing on simple and clear messaging for both PrEP users and their parents/partners/peers
• Accept that PrEP will not be for everyone
• Understanding adherence vs effective use
• Making HIV prevention a lifestyle choice
Acknowledgements

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