Understanding the Impact of an HIV Intervention Package for Adolescents

Faikah Bruce
Supervisors: Dr. Leigh Johnson (UCT - CIDER) and Prof. Alex Welte (SU - SACEMA)
Understanding the Impact of an HIV Intervention Package for Adolescents

Contents

• Introduction
• Literature Review
• Model
  - Baseline Characteristics
  - Modelling Sexual Behaviour
  - Model Calibration
  - Clinical Trial Simulation
• Results
• Conclusion
Introduction

Aims and Objectives

• Model the impact of an intervention package on HIV incidence for adolescents in a hypothetical trial
• The model must be able to determine
  - The HIV incidence without any intervention - compare relevant HIV data
  - The mean relative risk of HIV infection depending which components are included in the intervention package
• Clinical trial simulation
  - To assist with the design of a RCT
  - Optimal sample size to detect statistically significant effect
Literature Review

- **Adolescent sexual behaviour:** Heterosexual transmission is the most common mode of HIV transmission among adolescents
  - Age of sexual debut, sexual frequency, partnership formation and dissolution, age-mixing, condom use

- **Male Circumcision:** practice norms - traditional mc & non-traditional mc
  - Reduced risk associated with mc found in the 3 randomized control trials

<table>
<thead>
<tr>
<th>Study</th>
<th>Location</th>
<th>Relative Risk (95% C.I.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Auvert et. al. (2005)</td>
<td>Orange Farm, S.A.</td>
<td>0.40 (0.25 - 0.70)</td>
</tr>
<tr>
<td>Grey et. al. (2007)</td>
<td>Rakai, Uganda</td>
<td>0.49 (0.30 - 0.83)</td>
</tr>
<tr>
<td>Bailey et. al. (2007)</td>
<td>Kisumu, Kenya</td>
<td>0.47 (0.28 - 0.78)</td>
</tr>
</tbody>
</table>
Literature Review

- **Vaginal Microbicides**: formulations – gels; creams; films; rings

<table>
<thead>
<tr>
<th>Study</th>
<th>Location</th>
<th>Protective Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPRISA004</td>
<td>South Africa</td>
<td>39% (95% C.I. 6 - 60)</td>
</tr>
<tr>
<td>VOICE (MTN-003)</td>
<td>S.A., Zimbabwe, Uganda</td>
<td>No statistically significant results</td>
</tr>
</tbody>
</table>

- **Pre-Exposure Prophylaxis:**

<table>
<thead>
<tr>
<th>Study (Group)</th>
<th>Location</th>
<th>Results</th>
</tr>
</thead>
</table>
| iPrEX : (MSM)                         | Peru, Ecuador, Brazil, United States, Thailand and South Africa | Protective effect:  
  • 44% (95% C.I. 15-63)                                                |
| FEM-PrEP : (Women)                    | Sub-Saharan Africa                                     | No significant result - trial stopped                                   |
| Partners PrEP Study : (HIV1-serodiscordant heterosexual couples) | Kenya, Uganda                                        | Risk reduction of HIV incidence:  
  • TDF arm - 67% (95% C.I. 44–81)  
  • TDF-FTC arm - 75% (95% C.I. 55–87) |
Model Structure

• **Stochastic Model**
  • Individual-based simulation
  • Static model

• **Individuals within the model population are stratified by**
  • Sex: Male or Female
  • Age: 10 - 19 years
Understanding the Impact of an HIV Intervention Package for Adolescents

Methodology

Baseline Characteristics

Individual’s characteristics

- Sex: male or female
- Age: 10 -19 years
- Age of circumcision
- Age of sexual debut
- Risk level
- HIV status
- Number of partners
Age of circumcision

• **Traditional circumcision setting**
  - Related the probability of being circumcised to the age of the individual – Weibull Distribution - Connolly et al. 2008

• **Non-traditional circumcision setting**
  - No age of circumcision was assigned
Baseline Characteristics

Age of sexual debut

- Related the probability of being sexually active to the age of the individual – Weibull Distribution

  - LoveLife survey 2003 - Pettifor et al. 2004
  - National Communication survey 2009 - Johnson et al. 2010
Baseline Characteristics

Risk level

- High risk
  - Logit function - 35% in males and 25% in females - Johnson et al. (2009)
  - Negative association between age of sexual debut, $s$, and the level of risk behaviour

- Low risk
Baseline Characteristics

HIV status

- Log-normal distribution - Williams et al. (2000)

- Adjusted to determine HIV prevalence in sexually experienced youth

- Data - Lovelife survey - Pettifor et al. (2004)
**Baseline Characteristics**

**Number of partners**

- Multi-state model of sexual behaviour

![Diagram](image)

- Johnson et al. (2009); Jewkes et al. (2001).

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Description</th>
<th>Males</th>
<th>Females</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\lambda_i$</td>
<td>Rate of partnership formation</td>
<td>7.3</td>
<td>1.39</td>
</tr>
<tr>
<td>$\Theta_i$</td>
<td>Propensity for concurrent partners</td>
<td>0.6</td>
<td>4</td>
</tr>
<tr>
<td>$\mu_i$</td>
<td>Rate of partnership dissolution</td>
<td>2</td>
<td>2</td>
</tr>
</tbody>
</table>
Partner’s Characteristics

- **Sex**
- **Age**
  - Average partner age difference of 3 years
  - Assumed male’s age is greater than female’s age
  - Age difference is assumed to follow a gamma distribution
- **HIV status**
  - Simulated in the same manner as for individual
Modelling Sexual Behaviour

- Time to their next possible event, then which event it could be.
  - Circumcision: age of circumcision
  - Rate of partnership formation:
    - Rate of partnership dissolution:
  - Rate of HIV infection:

- Annual rate of sex acts
- HIV transmission rate
- Efficacy of condom
- Probability of condom usage
- Efficacy of MC
### Model Structure

- Parameter estimates

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Description</th>
<th>Sex</th>
<th>Estimate</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \theta_i(1) )</td>
<td>Rate of partnership formation</td>
<td>M/F</td>
<td>As before</td>
<td>Johnson et al. (2009)</td>
</tr>
<tr>
<td>( \theta_i(2) )</td>
<td>Rate of partnership dissolution</td>
<td>M/F</td>
<td>As before</td>
<td>Johnson et al. (2009)</td>
</tr>
<tr>
<td>( \beta_i )</td>
<td>Probability of HIV transmission per act of unprotected sex</td>
<td>M \rightarrow F, F \rightarrow M</td>
<td>0.0128, 0.04</td>
<td>Baeten et al. (2005) Pettifor et al. (2007)</td>
</tr>
<tr>
<td>( \gamma )</td>
<td>Probability of condom usage</td>
<td>M/F</td>
<td>0.6</td>
<td>Shisana et al. (2009) Johnson et al. (2010)</td>
</tr>
</tbody>
</table>
Model Calibration

Model Estimates of HIV Incidence - 50 000 individuals over 4 years

- HRSC 2002-2005
- HSRC 2005-2008

<table>
<thead>
<tr>
<th></th>
<th>Males</th>
<th>Females</th>
<th>All</th>
</tr>
</thead>
<tbody>
<tr>
<td>Simulated Incidence</td>
<td>1.20</td>
<td>4.30</td>
<td>2.67</td>
</tr>
<tr>
<td>HSRC 2002-2005</td>
<td>0.5</td>
<td>5.5</td>
<td>2.0</td>
</tr>
<tr>
<td>HSRC 2005-2008</td>
<td>0.8</td>
<td>2.2</td>
<td>1.3</td>
</tr>
</tbody>
</table>

Age Group: 15-24 years
Model Calibration

Model Estimates of HIV Incidence - 50 000 individuals over 4 years

- STI-HIV model
- ASSA2003 model
Clinical Trial Simulation

• HIV negative individuals aged 15–18 years over a 3 year trial period
• Intervention options :
  - Males – MMC and PrEP
  - Females – PrEP, Vaginal Gel or Vaginal Ring
• Level of Condom Use
  - \( p \)th quantile of the \textbf{beta distribution} using the \textbf{inverse of the cumulative density function}
    • Mean: \( \eta = 0.60 \)
    • Variance: \( \kappa = 0.15 \)
Clinical Trial Simulation

- Modelling the Acceptability and Uptake of Interventions
  - Positive correlation to level of condom use

- Modelling of Adherence to Interventions
  - Correlation to level of acceptability

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Mean Acceptability</th>
<th>Mean Adherence</th>
<th>Efficacy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Male</td>
<td>Female</td>
<td>Male</td>
</tr>
<tr>
<td>MMC</td>
<td>Trad: 0.1</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td>Non-Trad: 0.8</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>PrEP</td>
<td>0.7</td>
<td>0.7</td>
<td>0.9</td>
</tr>
<tr>
<td>V - Gel</td>
<td>NA</td>
<td>0.7</td>
<td>NA</td>
</tr>
<tr>
<td>V - Ring</td>
<td>NA</td>
<td>NA</td>
<td>0.7</td>
</tr>
</tbody>
</table>
Clinical Trial Simulation

• Modelling the HIV Incidence in Trial
  - Modelling sexual behaviour
    • Intervention Arm
      \[ \vartheta_i(3) = n \beta_i (1 - S_{con,i}E)(1 - \phi_i)(1 - S_{adh,i}^I \varepsilon_i^I) \]
    • Control Arm
      \[ \vartheta_i(3) = n \beta_i (1 - S_{con,i}E)(1 - \phi_i) \]

• Relative Risk, with 95% C.I.
Results

RCT - Full Package

• Sample size: 2000
  - 1000 - Intervention arm
  - 1000 - Control arm

• Simulations: 1000

• Interventions:
  - MMC
  - PrEP
  - VM - Gel
  - VM - Ring

Understanding the Impact of an HIV Intervention Package for Adolescents
Sensitivity Analyses

Different Packages

• **Package 1:** Full Package
  - **GEL**

• **Package 2:** No PrEP

• **Package 3:** No GEL

• **Package 4:** No RING

Results

<table>
<thead>
<tr>
<th>Package</th>
<th>Total</th>
<th>Female</th>
<th>Male</th>
</tr>
</thead>
<tbody>
<tr>
<td>Package 1</td>
<td>0.61</td>
<td>0.70</td>
<td>0.45</td>
</tr>
<tr>
<td>Package 2</td>
<td>0.71</td>
<td>0.69</td>
<td>0.81</td>
</tr>
<tr>
<td>Package 3</td>
<td>0.60</td>
<td>0.68</td>
<td>0.44</td>
</tr>
<tr>
<td>Package 4</td>
<td>0.59</td>
<td>0.67</td>
<td>0.43</td>
</tr>
</tbody>
</table>
Sensitivity Analyses

Different Sample Sizes

- **Sample Size:** 500
- **Sample Size:** 2000

**Power**

- Detect 80% power, with $\alpha=0.05$, expected HIV incidence over 3 years of $0.050379$, and a mean relative risk of HIV infection of $0.6$: sample size required $\approx 1550$ per arm
Understanding the Impact of an HIV Intervention Package for Adolescents

Results

Sensitivity Analyses

Negative correlation between level of condom use and acceptability of other interventions

• Positive Correlation
• Negative Correlation

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>Female</th>
<th>Male</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive Correlation</td>
<td>0.61</td>
<td>0.70</td>
<td>0.45</td>
</tr>
<tr>
<td>Negative Correlation</td>
<td>0.56</td>
<td>0.66</td>
<td>0.36</td>
</tr>
</tbody>
</table>
Conclusion

• The model assists with the design of a RCT

• Sensitivity analyses
  - Components to include package to achieve greatest effectiveness
  - Sample size requirements for an optimally powered trial

• Limitations of the model
  - No variation in the HIV transmission rate
  - True dynamics of relationships are complex – only allowed for 2 behavioural states, with a max number of 2 partners in high risk level

• Future Work
  - Population-level impact
  - Impact of drug-related resistance of PrEP and vaginal microbicides
Thank you!
Baseline Characteristics

Age of circumcision

- Traditional circumcision setting
  - Related the probability of being circumcised to the age of the individual – Weibull Distribution - Connolly et al. 2008 (HSRC2002)
  - Non-traditional circumcision setting
    - No age of circumcision was assigned

Age of sexual debut

- Related the probability of being sexually active to the age of the individual – Weibull Distribution
  - LoveLife survey 2003 - Pettifor et al. 2004
  - National Communication survey 2009 - Johnson et al. 2010
Baseline Characteristics

Risk level

- High risk
  - Logit function - 35% in males and 25% in females - Johnson et al. (2009)
  - Negative association between age of sexual debut, s, and the level of risk behaviour
- Low risk

HIV status

- Log-normal distribution - Williams et al. (2000)
  - Adjusted to determine HIV prevalence in sexually experienced youth
- Data - Lovelife survey 2003
Baseline Characteristics

Age of sexual debut

- Related the probability of being sexually active to the age of the individual – Weibull Distribution

- LoveLife survey 2003 - Pettifor et al. 2004
- National Communication survey 2009 - Johnson et al. 2010
Understanding the Impact of an HIV Intervention Package for Adolescents

Methodology

Baseline Characteristics

Risk level

• High risk
  • Logit function - 35% in males and 25% in females - Johnson et al. (2009)
  • Negative association between age of sexual debut, s, and the level of risk behaviour

• Low risk
Baseline Characteristics

HIV status

- Log-normal distribution - Williams et al. (2000)

- Adjusted to determine HIV prevalence in sexually experienced youth

- Data - Lovelife survey - Pettifor et al. (2004)
Model Calibration

Model Estimates of HIV Incidence - 50,000 individuals over 4 years

- STI-HIV model
- ASSA2003 model