Dapivirine Vaginal Ring Pre-exposure Prophylaxis for HIV Prevention in South Africa

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# Background

- A vaginal ring (VR) containing dapivirine (DPV) is under evaluation for pre-exposure prophylaxis (PrEP) for HIV prevention among women.
- The potential impact and cost-effectiveness of DPV PrEP scale-up are unknown.
- Cross-resistance is common between DPV and first-line antiretroviral therapy (ART) in resource-limited settings.

# Methods

## Model overview
- We refined a deterministic mathematical model to simulate the HIV epidemic in KwaZulu-Natal, South Africa with the scale-up of DPV VR PrEP.
- The model population was stratified by gender, age, sexual behavior, HIV status and disease progression, male medical circumcision (MMC) status, ART or PrEP use, and drug sensitivity of HIV in blood and genital compartments.
- The model was calibrated to HIV prevalence and incidence data from KwaZulu-Natal using a Bayesian framework.

## Interventions
1. **Baseline:** ART + MMC scale-up.
   - ART reaching 80% of HIV+ persons with CD4 ≤ 500 cells/µL by 2020.
   - MMC reaching 80% of men by 2017.
2. **Unprioritized PrEP:** Baseline + 5.5% overall PrEP coverage.
3. **Age-prioritized PrEP:** Baseline + 15% overall PrEP coverage.
   - a) DPV VR PrEP scale-up reaching 5%–8% of women aged 15–24.
   - b) DPV VR PrEP scale-up reaching 15%–85% of women aged 20–29.
   - DPV VR PrEP scale-up reaching 50%–90% of female sex workers (FSWs).

## Cost-effectiveness Analysis Characteristics
- **Perspective:** modified societal.
- **Time horizon:** 2017–2027.
- **Discount rate:** 3% per year.

## Model Analyses
- **Base case analyses:** interventions simulated using input point estimates (Table 1).
- **Uncertainty analyses:** multivariate analyses of 10,000 simulations per intervention, using randomly sampled inputs (Table 1).

## Results

### HIV Drug Resistance
- ART scale-up in the baseline scenario without PrEP produced 476,019 prevalent drug-resistant infections in 2027.
- PrEP scale-up decreased prevalent drug-resistant infections in base case simulations (Figure 4).
- Decreases in drug resistance diminished by 2%–12% when in addition to blood, resistance was also tracked in the genital compartment.

### Uncertainty Analyses
- Risk-prioritized PrEP was cost-saving in all simulations (Figure 5).
- Age-prioritized PrEP was more likely to be cost-effective at ages 20–29 vs. 15–24.
- Unprioritized PrEP was the least likely to be cost-effective.
- At a willingness-to-pay threshold of $7,500 (~South Africa’s GDP), PrEP’s probability of cost-effectiveness was 74% when prioritized.
  - 81% when prioritized to women 15–24.
  - 98% when prioritized to women 20–29.
  - 100% when prioritized to FSWs.

### Table 1. Key Model Inputs

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Base case</th>
<th>Range</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>DPV average adherence</td>
<td>47%–57%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>High adherence scenario</td>
<td>76.1%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low adherence scenario</td>
<td>20.9%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PrEP efficacy against wild-type HIV</td>
<td>90%</td>
<td>57%–98%</td>
<td></td>
</tr>
<tr>
<td>PrEP efficacy against PPV-resistant HIV, relative to wild-type</td>
<td>100%</td>
<td>50%–100%</td>
<td></td>
</tr>
<tr>
<td>Cross-resistance prevalence</td>
<td>80%</td>
<td>70%–100%</td>
<td></td>
</tr>
<tr>
<td>% of ART-resistant HIV that is cross-resistant to PrEP</td>
<td>None</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Resistance time of drug concentrations after ring removal</td>
<td>1–3 days</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cost-per-PrEP, per person-year</td>
<td>$15</td>
<td>$60–$150</td>
<td></td>
</tr>
<tr>
<td>Art cost, per person-year</td>
<td>$750</td>
<td>$560–$1,040</td>
<td></td>
</tr>
<tr>
<td>MNC cost, per surgery</td>
<td>$110</td>
<td>$70–$150</td>
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</tbody>
</table>

### Figure 1. Cumulative (unadjusted) infections prevented by PrEP. Unprioritized and age-prioritized PrEP strategies covered 15% of uninfected adults aged 15–54.

### Figure 2. Incremental healthcare costs of PrEP strategies. Unprioritized and age-prioritized PrEP strategies covered 15% of uninfected adults aged 15–54.

### Figure 3. Cost-effectiveness frontier for PrEP strategies. 2.5%, 5%, 10% and 15% overall coverage levels are shown for unprioritized and age-prioritized PrEP. Cost-effectiveness ratios (relative to basecase) are reported for 15% overall coverage.

### Table 2. Median (interquartile range) outcomes of PrEP scale-up.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Method</th>
<th>PrEP to women 15–24</th>
<th>PrEP to women 20–29</th>
<th>PrEP to FSWs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infections prevented</td>
<td>$6,747</td>
<td>$5,200</td>
<td>$3,309</td>
<td></td>
</tr>
<tr>
<td>Incremental cost, millions $</td>
<td>$2,213</td>
<td>$2,209</td>
<td>$192</td>
<td></td>
</tr>
<tr>
<td>Cost per infection prevented</td>
<td>($2,491–$5,737)</td>
<td>($4,180–$6,448)</td>
<td>($2,300–$4,462)</td>
<td></td>
</tr>
</tbody>
</table>

### Conclusions
- DPV VR PrEP could have considerable impact on HIV prevention at compelling economic value when prioritized to women by age.
- DPV VR PrEP could decrease drug resistance, even if adherence is modest.

### Acknowledgements
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