OBJECTIVE

To predict the potential impact of the CAPRISA 004 tenofovir gel microbicide in South Africa in terms of:

- HIV and HSV-2 infections prevented (IP) in men and women
- Women-years on microbicide necessary to prevent one HIV infection

We conduct a two-level spatial analysis. First, we make predictions for the province of KwaZulu-Natal, and then for all 9 provinces in South Africa.

BACKGROUND

- HIV prevalence and antiretroviral therapy (ART) coverage vary across the nine provinces of South Africa (Table 1)
- CAPRISA 004 was designed to assess the effectiveness and safety of a 1% tenofovir gel, vaginal microbicide
- Effectiveness in preventing HIV infection for women in the trial was:
  - 54% in high adherers (i.e. used gel for >80% of sex acts)
  - 38% in intermediate adherers (i.e. used gel for 50-80% of sex acts)
  - 28% in low adherers (i.e. used gel for <50% of sex acts)
  - 39% overall
- Overall effectiveness was 51% in preventing HSV-2 infection in women

Table 1: HIV prevalence and ART coverage among those with CD4 < 350 for the nine provinces of South Africa.

<table>
<thead>
<tr>
<th>Province</th>
<th>HIV prevalence in women</th>
<th>HIV prevalence in men</th>
<th>ART adherence</th>
<th>ART coverage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gauteng</td>
<td>26%</td>
<td>23%</td>
<td>18%</td>
<td>18%</td>
</tr>
<tr>
<td>North West</td>
<td>26%</td>
<td>21%</td>
<td>18%</td>
<td>18%</td>
</tr>
<tr>
<td>Eastern Cape</td>
<td>30%</td>
<td>30%</td>
<td>32%</td>
<td>31%</td>
</tr>
<tr>
<td>Limpopo</td>
<td>30%</td>
<td>30%</td>
<td>32%</td>
<td>31%</td>
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<tr>
<td>Mpumalanga</td>
<td>30%</td>
<td>30%</td>
<td>32%</td>
<td>31%</td>
</tr>
<tr>
<td>Western Cape</td>
<td>30%</td>
<td>30%</td>
<td>32%</td>
<td>31%</td>
</tr>
<tr>
<td>Free State</td>
<td>30%</td>
<td>30%</td>
<td>32%</td>
<td>31%</td>
</tr>
<tr>
<td>North East</td>
<td>30%</td>
<td>30%</td>
<td>32%</td>
<td>31%</td>
</tr>
<tr>
<td>KwaZulu-Natal</td>
<td>30%</td>
<td>30%</td>
<td>32%</td>
<td>31%</td>
</tr>
</tbody>
</table>

METHODS

- We constructed a mathematical model of interacting HIV and HSV-2 epidemics.
- Model assumptions:
  - HSV-2 infection increases risk of acquiring HIV 2-3 fold
  - HSV-2 co-infection increases HIV per-act infectivity 30-70%
  - HIV infection increases duration/frequency of HSV-2 shedding episodes
  - HIV/HSV-2 more transmissible from women to women than men to men
- We calibrated the model to prevalence and incidence data from each of South Africa's nine provinces using Monte Carlo filtering.
- The model predicts the percentage of HIV and HSV-2 infections prevented (IP) from 2012 (when we assume microbicides will be rolled out) to 2022. We included the rollout of ART in South Africa that began in 2004. We use uncertainty and sensitivity analysis.

RESULTS (cont'd)

- Predicted impact of tenofovir gel on HIV incidence in South Africa over 10 years
  - Considerable variation in the number of HIV IP among provinces due to spatial heterogeneity in demographics and HIV prevalence (Figure 3)
  - In each province, number of IP in women greatly exceeds those in men
  - Lowest impact in the Northern Cape with only 5200 and 1600 IP in women and men, respectively
  - Highest impact in KwaZulu-Natal with 156000 and 54000 IP in women and men, respectively

Figure 3: Number of HIV IP over 10 years by tenofovir gel (assuming 54% effectiveness and 90% coverage)

- Estimated number of women-years on microbicide that are necessary to prevent one HIV infection in each of the nine provinces in South Africa
  - Considerable variation among provinces in the number of women-years that are necessary, due to spatial heterogeneity in HIV incidence (Figure 4)
  - Significant gender differences are apparent (Figure 4)
  - The highest number of women-years is in the Western Cape; 445 and 1600 to prevent one infection in women and men, respectively
  - The lowest number of women-years is in KwaZulu-Natal; 113 and 323 to prevent one infection in women and men, respectively

Figure 4: Women-years on microbicide necessary to prevent one HIV infection (assuming 54% effectiveness and 90% coverage)

- Identifying the relationship between HIV incidence and the number of women-years on microbicide that are necessary to prevent one HIV infection
  - The number of women-years that are necessary to prevent one infection decreases exponentially with increasing incidence (Figure 5)
  - The lower the effectiveness of the microbicide, the greater the number of women-years that are necessary to prevent one infection (Figure 5)
  - The number of women-years varies among provinces (Figure 5)

Figure 5: Women-years necessary to prevent one HIV infection as a function of HIV incidence in women (colors represent values for different provinces, red curves are extensions of regression curve for higher incidence values)

- If the tenofovir gel tested in the CAPRISA 004 clinical trial is rolled out in South Africa, our results indicate geographic targeting at the province level would be a very effective control strategy, particularly under financial constraints.

ACKNOWLEDGEMENTS

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