Increasing options for women – the potential impact of multipurpose prevention technologies for HIV prevention and contraception: a mathematical modelling study.

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• Aim: estimate impact and cost-effectiveness of a dual-use Intra-Vaginal Ring (IVR) for HIV and pregnancy prevention in South Africa.

• South Africa:
  • High prevalence
  • Approximately two thirds of pregnancies are unintended
  • ~14% of married women have unmet need for contraception
Overall findings

• MPT could avert substantial morbidity and maternal mortality in South Africa

• Need to reach those women who are not existing contraceptive users

• Delivery strategy influential determinant of impact

• Given ART widely available, majority of health gain in terms of reproductive health benefits

• Potential to be very cost-effective (according to traditional thresholds)
Mathematical model

• Deterministic, compartmental model of HIV transmission, fertility, contraception and pregnancy outcomes

• Stratified by:
  • Age
  • Sex
  • Behavioural risk group
  • Male circumcision status
  • ART use
  • MPT use
Model calibration
Demography

- Population of South Africa
- Time-varying age- and sex-specific:
  - fertility rates
  - mortality rates
(Obtained from Actuarial Society of South Africa)
- Impact of contraceptive use on:
  - unintended pregnancy
  - unsafe abortion
  - maternal mortality
Population structure
HIV epidemic
ART & male circumcision
Maternal mortality
Analysis
MPT use

• Prioritization by age and risk group
• New users, or displaced – proportion of users who have switched from other methods of contraception
• Adherence:
  • Proportion of sex acts that are protected
  • High - 80-90%

• Mean duration of use 5 years
• Assume that all women who start using the IVR stop using condoms.
• Reduce risk of HIV acquisition and pregnancy
• Efficacy:
  • HIV: 56% - 75%
    • “low” – based on Dapivirine ring
    • “high” – based on Partners PrEP trial result
  • Pregnancy: 92% - 97%
    • “low” – typical use of nuvaring and the NES-EE ring and ethinyl estradiol
    • “high” – long-acting reversible methods (e.g. implants, mirena intra-uterine system)

• (applicable across different formulations of MPT)
## Delivery scenarios

<table>
<thead>
<tr>
<th>Scenario</th>
<th>IVR Coverage and Age Groups of IVR Users</th>
<th>Adherence</th>
<th>Delivery Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>PHC</td>
<td>5% of women aged 15-49 years</td>
<td>80%</td>
<td>Low (Baseline cost of US$16 or US$48 PPY)</td>
</tr>
<tr>
<td>PHC+</td>
<td>5% of women aged 30-49 years. Enhanced coverage (10%) among women aged 15-29 years</td>
<td>80%</td>
<td>Low US$27 or US$82 PPY</td>
</tr>
<tr>
<td>Youth</td>
<td>10% of women aged 15-29 years</td>
<td>90%</td>
<td>High US$43 or US$130 PPY</td>
</tr>
<tr>
<td>WAR</td>
<td>10% of women at greatest risk (i.e. in the group with the highest rates of new sexual partner acquisition in the model) and aged 15-49 years</td>
<td>90%</td>
<td>Very High US$54 or US$163 PPY</td>
</tr>
</tbody>
</table>
Delivery costs

- PHC delivery scenario - $16, $48 per person per year
- Include shipping, delivery costs, clinic costs, HIV testing, and other medical and access costs.

- Vertical delivery systems
  - PHC+ outreach - (1.7 times higher)
  - Women at highest risk (3.4 times higher)
  - Young women - (2.7 times higher)

- Cost-effectiveness:
  - 1* GDP and 3* GDP thresholds
  - Discount rate: 3%
Results
DALYS averted (2018-2025)

- PHC
- PHC+
- Youth
- WAR

DALYS averted range from 20,000 to 140,000.
Cost per DALY averted

Low cost

High cost
Cost effectiveness acceptability curve
Reproductive health outcomes (assuming “low” efficacy ring)

<table>
<thead>
<tr>
<th></th>
<th>50% displacement</th>
<th>New users</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PHC</td>
<td>PHC+</td>
</tr>
<tr>
<td>Infections averted - women</td>
<td>10,717</td>
<td>19,576</td>
</tr>
<tr>
<td>Infections averted - women (%)</td>
<td>1.20</td>
<td>2.19</td>
</tr>
<tr>
<td>Infections averted - total</td>
<td>15,219</td>
<td>28,217</td>
</tr>
<tr>
<td>Infections averted - total (%)</td>
<td>0.97</td>
<td>1.79</td>
</tr>
<tr>
<td>Unintended pregnancies averted</td>
<td>41,496</td>
<td>72,702</td>
</tr>
<tr>
<td>Unintended pregnancies averted (%)</td>
<td>0.76</td>
<td>1.33</td>
</tr>
<tr>
<td>Unsafe abortion averted</td>
<td>5,295</td>
<td>9,277</td>
</tr>
<tr>
<td>Unsafe abortions averted (%)</td>
<td>0.76</td>
<td>1.33</td>
</tr>
<tr>
<td>Maternal deaths averted</td>
<td>82</td>
<td>144</td>
</tr>
<tr>
<td>Maternal deaths averted (%)</td>
<td>0.87</td>
<td>1.54</td>
</tr>
<tr>
<td>Total DALYs averted</td>
<td>26,757</td>
<td>50,108</td>
</tr>
<tr>
<td>IVR spending (low) (US$ millions)</td>
<td>61.21</td>
<td>162.04</td>
</tr>
<tr>
<td>IVR spending (high) (US$ millions)</td>
<td>183.62</td>
<td>486.13</td>
</tr>
<tr>
<td>Cost per DALY averted (low)</td>
<td>1,651</td>
<td>2,607</td>
</tr>
<tr>
<td>Cost per DALY averted (high)</td>
<td>6,226</td>
<td>9,075</td>
</tr>
<tr>
<td>Cost per infection averted (low)</td>
<td>2,903</td>
<td>4,629</td>
</tr>
<tr>
<td>Cost per infection averted (high)</td>
<td>10,946</td>
<td>16,115</td>
</tr>
</tbody>
</table>
## Reproductive health outcomes (assuming “high” efficacy ring)

<table>
<thead>
<tr>
<th></th>
<th>PHC</th>
<th>PHC+</th>
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<th>WAR</th>
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<th>Youth</th>
<th>WAR</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PY on IVR</strong></td>
<td>3,829,883</td>
<td>5,969,342</td>
<td>4,581,248</td>
<td>3,861,733</td>
<td>3,829,913</td>
<td>5,969,435</td>
<td>4,581,336</td>
<td>3,861,117</td>
</tr>
<tr>
<td><strong>Infections averted - women</strong></td>
<td>21,690</td>
<td>39,861</td>
<td>42,336</td>
<td>33,959</td>
<td>21,689</td>
<td>39,859</td>
<td>42,334</td>
<td>33,956</td>
</tr>
<tr>
<td><strong>Infections averted - women (%)</strong></td>
<td>2.42</td>
<td>4.46</td>
<td>4.73</td>
<td>3.80</td>
<td>2.42</td>
<td>4.46</td>
<td>4.73</td>
<td>3.80</td>
</tr>
<tr>
<td><strong>Infections averted - total</strong></td>
<td>31,005</td>
<td>57,769</td>
<td>62,091</td>
<td>50,157</td>
<td>31,004</td>
<td>57,767</td>
<td>62,089</td>
<td>50,155</td>
</tr>
<tr>
<td><strong>Infections averted - total (%)</strong></td>
<td>1.97</td>
<td>3.67</td>
<td>3.95</td>
<td>3.19</td>
<td>1.97</td>
<td>3.67</td>
<td>3.95</td>
<td>3.19</td>
</tr>
<tr>
<td><strong>Unintended pregnancies averted</strong></td>
<td>141,317</td>
<td>247,561</td>
<td>226,771</td>
<td>72,258</td>
<td>181,957</td>
<td>318,763</td>
<td>292,005</td>
<td>93,072</td>
</tr>
<tr>
<td><strong>Unintended pregnancies averted (%)</strong></td>
<td>2.58</td>
<td>4.52</td>
<td>4.14</td>
<td>1.32</td>
<td>3.33</td>
<td>5.83</td>
<td>5.34</td>
<td>1.70</td>
</tr>
<tr>
<td><strong>Unsafe abortion averted</strong></td>
<td>18,032</td>
<td>31,589</td>
<td>28,936</td>
<td>9,220</td>
<td>23,218</td>
<td>40,674</td>
<td>37,260</td>
<td>11,876</td>
</tr>
<tr>
<td><strong>Unsafe abortions averted (%)</strong></td>
<td>2.58</td>
<td>4.52</td>
<td>4.14</td>
<td>1.32</td>
<td>3.33</td>
<td>5.83</td>
<td>5.34</td>
<td>1.70</td>
</tr>
<tr>
<td><strong>Maternal deaths averted</strong></td>
<td>260</td>
<td>455</td>
<td>424</td>
<td>158</td>
<td>328</td>
<td>572</td>
<td>530</td>
<td>191</td>
</tr>
<tr>
<td><strong>Maternal deaths averted (%)</strong></td>
<td>2.78</td>
<td>4.86</td>
<td>4.53</td>
<td>1.68</td>
<td>3.50</td>
<td>6.11</td>
<td>5.66</td>
<td>2.04</td>
</tr>
<tr>
<td><strong>Total DALYs averted</strong></td>
<td>60,099</td>
<td>112,435</td>
<td>118,622</td>
<td>85,524</td>
<td>63,913</td>
<td>119,283</td>
<td>125,044</td>
<td>87,541</td>
</tr>
<tr>
<td><strong>IVR spending (low) (US$ millions)</strong></td>
<td>61.28</td>
<td>162.37</td>
<td>197.91</td>
<td>210.08</td>
<td>61.28</td>
<td>162.37</td>
<td>197.91</td>
<td>210.04</td>
</tr>
<tr>
<td><strong>IVR spending (high) (US$ millions)</strong></td>
<td>183.83</td>
<td>487.10</td>
<td>593.73</td>
<td>630.23</td>
<td>183.84</td>
<td>487.11</td>
<td>593.74</td>
<td>630.13</td>
</tr>
<tr>
<td><strong>Cost per DALY averted (low)</strong></td>
<td>443</td>
<td>873</td>
<td>1,091</td>
<td>1,801</td>
<td>417</td>
<td>823</td>
<td>1,035</td>
<td>1,759</td>
</tr>
<tr>
<td><strong>Cost per DALY averted (high)</strong></td>
<td>2,483</td>
<td>3,761</td>
<td>4,428</td>
<td>6,714</td>
<td>2,334</td>
<td>3,545</td>
<td>4,201</td>
<td>6,558</td>
</tr>
<tr>
<td><strong>Cost per infection averted (low)</strong></td>
<td>859</td>
<td>1,699</td>
<td>2,085</td>
<td>3,071</td>
<td>859</td>
<td>1,699</td>
<td>2,085</td>
<td>3,071</td>
</tr>
<tr>
<td><strong>Cost per infection averted (high)</strong></td>
<td>4,812</td>
<td>7,320</td>
<td>8,460</td>
<td>11,448</td>
<td>4,812</td>
<td>7,320</td>
<td>8,460</td>
<td>11,447</td>
</tr>
</tbody>
</table>
Overall findings

• MPT could avert substantial morbidity and maternal mortality in South Africa

• Need to reach those women who are not existing contraceptive users

• Delivery strategy influential determinant of impact

• Given ART widely available, majority of health gain in terms of reproductive health benefits

• Potential to be very cost-effective (according to traditional thresholds)
Delivery of MPT

• Priority group - women with a dual unmet need for contraception and HIV prevention

• Reaching women who were not existing contraceptive method users improved cost-effectiveness in all scenarios
  • In practice reaching these women may incur higher costs

• Initial product introduction:
  • Settings that currently provide HIV treatment and family planning services
Limitations

• IVR cost could be under-estimated
• Reduced future spending on ART not included
• DALYs do not quantify the full burden of sexual and reproductive ill health
• Emergence of drug resistance following inadvertent use of MPTs when already HIV-infected
• Optimistic assumptions regarding the effectiveness of the IVR for HIV prevention
• With displacement - we do not take into account that injectable contraceptives and oral contraceptive pills would no longer be being paid for through the public healthcare system for these women
  • may be over-stating the additional cost of IVR interventions
• Conservative assumption that all women who start using the IVR stop using condoms
Data requirements

• Cost data
  • Unit cost – per woman per year/ per ring
    • Direct costs
      • Product cost
      • Service provision
    • Indirect costs

• Efficacy

• Adherence & typical patterns of use

• Displacement from other forms of contraception – especially condoms
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