Table 1.
Baseline characteristics

<table>
<thead>
<tr>
<th>Demographic</th>
<th>2% PRO2000 (n=2734)</th>
<th>0.5% PRO2000 (n=3326)</th>
<th>Placebo (n=3325)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>15–24</td>
<td>1022/2734 (37%)</td>
<td>1249/3326 (38%)</td>
<td>1267/3324 (38%)</td>
</tr>
<tr>
<td>25–34</td>
<td>955/2734 (35%)</td>
<td>1076/3326 (32%)</td>
<td>1096/3324 (33%)</td>
</tr>
<tr>
<td>35–44</td>
<td>532/2734 (19%)</td>
<td>723/3326 (22%)</td>
<td>702/3324 (21%)</td>
</tr>
<tr>
<td>≥45</td>
<td>225/2734 (8%)</td>
<td>278/3326 (8%)</td>
<td>259/3324 (8%)</td>
</tr>
<tr>
<td>Education</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>177/2734 (6%)</td>
<td>240/3326 (7%)</td>
<td>233/3324 (7%)</td>
</tr>
<tr>
<td>Primary</td>
<td>1927/2734 (70%)</td>
<td>2309/3326 (69%)</td>
<td>2271/3324 (68%)</td>
</tr>
<tr>
<td>Secondary or higher</td>
<td>630/2734 (23%)</td>
<td>777/3326 (23%)</td>
<td>820/3324 (25%)</td>
</tr>
<tr>
<td>Medical history (ever)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-menstrual bleeding</td>
<td>266/2734 (10%)</td>
<td>339/3326 (10%)</td>
<td>307/3325 (9%)</td>
</tr>
<tr>
<td>Sores or ulcers</td>
<td>294/2734 (11%)</td>
<td>357/3326 (11%)</td>
<td>342/3325 (10%)</td>
</tr>
<tr>
<td>Unusual genital discomfort</td>
<td>656/2734 (24%)</td>
<td>786/3326 (24%)</td>
<td>820/3325 (25%)</td>
</tr>
<tr>
<td>Unusual genital discharge</td>
<td>686/2734 (25%)</td>
<td>796/3326 (24%)</td>
<td>820/3325 (25%)</td>
</tr>
<tr>
<td>Pain during sex</td>
<td>140/2734 (5%)</td>
<td>181/3326 (5%)</td>
<td>163/3325 (5%)</td>
</tr>
<tr>
<td>Other genital disorders</td>
<td>22/2734 (1%)</td>
<td>21/3326 (1%)</td>
<td>28/3325 (1%)</td>
</tr>
<tr>
<td>Positive laboratory results</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chlamydia trachomatis</td>
<td>202/2698 (7%)</td>
<td>256/3293 (8%)</td>
<td>266/3295 (8%)</td>
</tr>
<tr>
<td>Neisseria gonorrhoeae</td>
<td>93/2698 (3%)</td>
<td>110/3293 (3%)</td>
<td>119/3295 (4%)</td>
</tr>
<tr>
<td>Herpes simplex virus type 2 seropositive</td>
<td>1622/2725 (60%)</td>
<td>2029/3312 (61%)</td>
<td>1982/3311 (60%)</td>
</tr>
<tr>
<td>Syphilis†</td>
<td>106/2726 (4%)</td>
<td>116/3300 (4%)</td>
<td>137/3304 (4%)</td>
</tr>
<tr>
<td>Trichomonas vaginalis</td>
<td>268/2723 (10%)</td>
<td>312/3314 (9%)</td>
<td>314/3311 (9%)</td>
</tr>
<tr>
<td>Behavioural</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Effective contraception‡</td>
<td>1514/2732 (55%)</td>
<td>1850/3326 (56%)</td>
<td>1873/3325 (56%)</td>
</tr>
<tr>
<td>Sex acts in previous week</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>542/2732 (20%)</td>
<td>627/3326 (19%)</td>
<td>610/3325 (19%)</td>
</tr>
<tr>
<td>1</td>
<td>433/2732 (16%)</td>
<td>573/3326 (17%)</td>
<td>534/3325 (17%)</td>
</tr>
<tr>
<td>≥2</td>
<td>1754/2732 (64%)</td>
<td>2124/3326 (64%)</td>
<td>2178/3325 (64%)</td>
</tr>
<tr>
<td>Missing/unknown</td>
<td>3/2732 (&lt;1%)</td>
<td>2/3326 (&lt;1%)</td>
<td>3/3325 (&lt;1%)</td>
</tr>
<tr>
<td>Partners in previous week (median [IQR])</td>
<td>1 (1–1)</td>
<td>1 (1–1)</td>
<td>1 (1–1)</td>
</tr>
<tr>
<td>Condom use at last sex act</td>
<td>1500/2732 (55%)</td>
<td>1894/3326 (57%)</td>
<td>1826/3325 (55%)</td>
</tr>
<tr>
<td>Anal sex in previous 4 weeks</td>
<td>28/2732 (1%)</td>
<td>42/3326 (1%)</td>
<td>31/3325 (1%)</td>
</tr>
</tbody>
</table>

Data are n/n of participants with reported data (%) unless otherwise stated.

* 2% PRO2000 gel was discontinued Feb 14, 2008.
† Active syphilis was defined on the basis of rapid plasma reagin titre.
‡ Sterilisation, intrauterine contraceptive device, or use of injected, implanted, or oral contraception.
Table 2.

Primary efficacy outcome: HIV-1 incidence in the primary and secondary efficacy analyses

<table>
<thead>
<tr>
<th>End of study</th>
<th>Censored at 2% PRO2000 gel discontinuation, Feb 14, 2008</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0·5% PRO2000 (n=3326)</td>
</tr>
<tr>
<td>Participants</td>
<td>3156</td>
</tr>
<tr>
<td>Woman-years of follow-up</td>
<td>2873</td>
</tr>
<tr>
<td>Seroconversions</td>
<td>130</td>
</tr>
<tr>
<td>Incidence†</td>
<td>4·5 (3·8–5·4)</td>
</tr>
<tr>
<td>Hazard ratio</td>
<td>1·05 (0·82–1·34)</td>
</tr>
<tr>
<td>p value</td>
<td>0·71</td>
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</tbody>
</table>

**Secondary efficacy analysis‡**

<table>
<thead>
<tr>
<th></th>
<th>0·5% PRO2000 (n=3326)</th>
<th>Placebo (n=3325)</th>
<th>2% PRO2000 (n=2732)</th>
<th>0·5% PRO2000 (n=2732)</th>
<th>Placebo (n=2722)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Participants</td>
<td>3156</td>
<td>3112</td>
<td>2591</td>
<td>2587</td>
<td>2543</td>
</tr>
<tr>
<td>Woman-years of follow-up</td>
<td>3133</td>
<td>3099</td>
<td>1847</td>
<td>1846</td>
<td>1832</td>
</tr>
<tr>
<td>Seroconversions</td>
<td>145</td>
<td>143</td>
<td>86</td>
<td>70</td>
<td>77</td>
</tr>
<tr>
<td>Incidence†</td>
<td>4·6 (3·9–5·4)</td>
<td>4·6 (3·9–5·4)</td>
<td>4·7 (3·8–5·8)</td>
<td>3·8 (3·0–4·8)</td>
<td>4·2 (3·4–5·3)</td>
</tr>
<tr>
<td>Hazard ratio</td>
<td>1·00 (0·79–1·26)</td>
<td>1</td>
<td>1·11 (0·82–1·51)</td>
<td>0·90 (0·65–1·24)</td>
<td>1</td>
</tr>
<tr>
<td>p value</td>
<td>0·99</td>
<td>..</td>
<td>0·50</td>
<td>0·53</td>
<td>..</td>
</tr>
</tbody>
</table>

Data are n or n (95% CI) unless otherwise stated. ..=not applicable.

* All enrolled participants, excluding those with HIV-1 infection at enrolment, those without follow-up data for HIV-1 infection, and censored at 52 weeks (plus 6 week window for final visit) or pregnancy.
‡ Equivalent to primary efficacy analysis, but not censored for pregnancy or at week 52.
† Per 100 woman-years.
Table 3.

Secondary efficacy outcomes

<table>
<thead>
<tr>
<th></th>
<th>End of study</th>
<th>Censored at 2% PRO2000 gel discontinuation, Feb 14, 2008</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0·5% PRO2000 (n=3326)</td>
<td>Placebo (n=3325)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Herpes simplex virus type 2</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infection by week 40</td>
<td>59/890 (6·6%)</td>
<td>66/907 (7·3%)</td>
</tr>
<tr>
<td>Odds ratio</td>
<td>0·90 (0·63–1·30)</td>
<td>1</td>
</tr>
<tr>
<td>p value</td>
<td>0·59</td>
<td>..</td>
</tr>
<tr>
<td>Infection by week 52</td>
<td>109/919 (11·9%)</td>
<td>115/888 (13·0%)</td>
</tr>
<tr>
<td>Odds ratio</td>
<td>0·90 (0·68–1·20)</td>
<td>1</td>
</tr>
<tr>
<td>p value</td>
<td>0·48</td>
<td>..</td>
</tr>
<tr>
<td><strong>Neisseria gonorrhoeae</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infection at week 24 (±4 weeks)</td>
<td>77/2674 (2·9%)</td>
<td>74/2597 (2·9%)</td>
</tr>
<tr>
<td>Odds ratio</td>
<td>1·01 (0·73–1·40)</td>
<td>1</td>
</tr>
<tr>
<td>p value</td>
<td>0·95</td>
<td>..</td>
</tr>
<tr>
<td><strong>Chlamydia trachomatis</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infection at week 24 (±4 weeks)</td>
<td>159/2674 (6·0%)</td>
<td>164/2597 (6·3%)</td>
</tr>
<tr>
<td>Odds ratio</td>
<td>0·94 (0·75–1·17)</td>
<td>1</td>
</tr>
<tr>
<td>p value</td>
<td>0·58</td>
<td>..</td>
</tr>
</tbody>
</table>

Data are n/n (%) or n (95% CI) unless otherwise stated. ..=not applicable.
## Table 4.

Reported serious adverse events, selected genital adverse events, and primary safety events

<table>
<thead>
<tr>
<th></th>
<th>End of study</th>
<th>Censored at 2% PRO2000 gel discontinuation Feb 14, 2008</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0·5% PRO2000 (n=3326)</td>
<td>Placebo (n=3325)</td>
</tr>
<tr>
<td>Attended at least one visit after enrolment</td>
<td>3258</td>
<td>3223</td>
</tr>
<tr>
<td>Primary safety events*</td>
<td>163</td>
<td>137</td>
</tr>
<tr>
<td>Woman-years of follow-up</td>
<td>3349</td>
<td>3317</td>
</tr>
<tr>
<td>Primary safety event (first)</td>
<td>154</td>
<td>128</td>
</tr>
<tr>
<td>Incidence†</td>
<td>4·6 (3·9–5·4)</td>
<td>3·9 (3·2–4·6)</td>
</tr>
<tr>
<td>Hazard ratio</td>
<td>1·18 (0·93–1·49)</td>
<td>1</td>
</tr>
<tr>
<td>p value</td>
<td>0·17</td>
<td>..</td>
</tr>
</tbody>
</table>

### Adverse events

<table>
<thead>
<tr>
<th></th>
<th>0·5% PRO2000</th>
<th>Placebo</th>
<th>2% PRO2000</th>
<th>0·5% PRO2000</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-menstrual bleeding</td>
<td>551 (17%)</td>
<td>527 (16%)</td>
<td>320 (13%)</td>
<td>339 (13%)</td>
<td>318 (13%)</td>
</tr>
<tr>
<td>Ulcers (internal)</td>
<td>32 (1%)</td>
<td>38 (1%)</td>
<td>20 (1%)</td>
<td>22 (1%)</td>
<td>25 (1%)</td>
</tr>
<tr>
<td>Ulcers (external)</td>
<td>161 (5%)</td>
<td>157 (5%)</td>
<td>121 (5%)</td>
<td>111 (4%)</td>
<td>116 (5%)</td>
</tr>
<tr>
<td>Oedema (internal)</td>
<td>11 (&lt;1%)</td>
<td>15 (&lt;1%)</td>
<td>5 (&lt;1%)</td>
<td>5 (&lt;1%)</td>
<td>9 (&lt;1%)</td>
</tr>
<tr>
<td>Oedema (external)</td>
<td>8 (&lt;1%)</td>
<td>5 (&lt;1%)</td>
<td>6 (&lt;1%)</td>
<td>3 (&lt;1%)</td>
<td>5 (&lt;1%)</td>
</tr>
<tr>
<td>Erythema (internal)</td>
<td>201 (6%)</td>
<td>201 (6%)</td>
<td>134 (5%)</td>
<td>117 (5%)</td>
<td>122 (5%)</td>
</tr>
<tr>
<td>Erythema (external)</td>
<td>54 (2%)</td>
<td>35 (1%)</td>
<td>39 (2%)</td>
<td>32 (1%)</td>
<td>29 (1%)</td>
</tr>
<tr>
<td>Itching</td>
<td>349 (11%)</td>
<td>310 (10%)</td>
<td>214 (9%)</td>
<td>247 (10%)</td>
<td>232 (9%)</td>
</tr>
<tr>
<td>Burning</td>
<td>72 (2%)</td>
<td>56 (2%)</td>
<td>52 (2%)</td>
<td>53 (2%)</td>
<td>46 (2%)</td>
</tr>
<tr>
<td>Other genital events</td>
<td>379 (12%)</td>
<td>356 (11%)</td>
<td>232 (9%)</td>
<td>241 (10%)</td>
<td>239 (10%)</td>
</tr>
<tr>
<td>Other non-genital events</td>
<td>685 (21%)</td>
<td>631 (20%)</td>
<td>442 (18%)</td>
<td>435 (17%)</td>
<td>424 (17%)</td>
</tr>
</tbody>
</table>

### Serious adverse events‡

<table>
<thead>
<tr>
<th></th>
<th>0·5% PRO2000</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deaths</td>
<td>9 (&lt;1%)</td>
<td>5 (&lt;1%)</td>
</tr>
<tr>
<td>Other serious adverse events</td>
<td>142 (4%)</td>
<td>119 (4%)</td>
</tr>
</tbody>
</table>

Data are n (%) or n (95% CI). ..=not applicable.

* Defined as adverse events of grade 3 or more reported any time after enrolment. For women with more than one event, the time-to-event analysis uses the first event only.
† Per 100 woman-years.
‡ Serious adverse events were death, an immediate threat to life, admission to hospital, disability, congenital abnormality, vaginal oedema with sloughing, profuse non-menstrual bleeding, and cervical or gynaecological cancer.
§ Two additional deaths were reported after Feb 14, 2008.