DOES HORMONAL CONTRACEPTION INCREASE HIV ACQUISITION RISK AMONG ZAMBIAN WOMEN IN DISCORDANT COUPLES?

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The authors have no conflicts of interest due to financial or personal relationships that might be perceived to cause bias.
Hormonal contraception

- Prevents unintended pregnancy\(^1\)
- Prong 2 PMTCT for HIV+ women\(^1\)
- Is widely used in high HIV prevalence areas\(^2\)

Use among married women in Zambia\(^3\):

- 11% OCP
- 9% Injectable
- 0.4% Implant
Hormonal contraceptive methods and risk of HIV acquisition in women: a systematic review of epidemiological evidence

Chelsea B. Polis\textsuperscript{a,b,*}, Sharon J. Phillips\textsuperscript{c}, Kathryn M. Curtis\textsuperscript{d}, Daniel J. Westreich\textsuperscript{c}, Petrus S. Steyn\textsuperscript{c}, Elizabeth Raymond\textsuperscript{f}, Philip Hannaford\textsuperscript{g}, Abigail Norris Turner\textsuperscript{h}

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Chelsea B. Polis\textsuperscript{a,*}, Daniel Westreich\textsuperscript{b,c,*}, Jennifer E. Balkus\textsuperscript{d,e,*}, Renee Heffron\textsuperscript{e,*}, participants of the 2013 HC-HIV Observational Analysis Meeting
Discordant couples identified from couples’ voluntary HIV counseling and testing services in Lusaka from 1994-2012

Eligibility
- M+F- couples with follow-up
- Male partner was not on ART

Followed 3-monthly at the research site
- Contraception methods provided/assessed
- HIV testing of negative partners
CONTRACEPTIVE EXPOSURES

Hormonal methods:
- Implant (Norplant, Jadelle)
- Injectable (150 mg IM DMPA)
- Oral contraceptive pills (OCPs)

Non-hormonal method control:
- Condoms
- Copper intrauterine device (IUD)
- Permanent methods
HIV INFECTION OUTCOMES AMONG WOMEN

- Time to any HIV infection
  - Genetically linked or unlinked to the study partner

- Time to genetically linked HIV infections
Multivariate Cox models

- Potential effect-measure modifiers: genital ulceration, genital inflammation, viral load of HIV+ partner, fertility intentions, age

Sensitivity analyses explored effects of:

- Method exposure/control categories/definitions
- Misclassification of unprotected sex
- Time-dependent confounding (marginal structural models)
# SEROCONVERSION RATES AMONG WOMEN (N = 1,393 COUPLES)

<table>
<thead>
<tr>
<th>METHOD</th>
<th># Infections</th>
<th>CY</th>
<th>Incidence /100 CY</th>
<th>95%CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>TOTAL</td>
<td>252</td>
<td>2842</td>
<td>8.9</td>
<td>7.8</td>
</tr>
<tr>
<td>Non-hormonal methods</td>
<td>153</td>
<td>1902</td>
<td>8.0</td>
<td>6.8</td>
</tr>
<tr>
<td>OCPs</td>
<td>49</td>
<td>425</td>
<td>11.5</td>
<td>8.5</td>
</tr>
<tr>
<td>Injectables</td>
<td>41</td>
<td>392</td>
<td>10.5</td>
<td>7.5</td>
</tr>
<tr>
<td>Implant</td>
<td>9</td>
<td>123</td>
<td>7.3</td>
<td>3.3</td>
</tr>
</tbody>
</table>
### Multivariate Model: Time to Any HIV Seroconversion

<table>
<thead>
<tr>
<th>Method</th>
<th>aHR*</th>
<th>95% CI</th>
<th>p-value (2-tail)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-hormonal methods</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>OCPs</td>
<td>1.3</td>
<td>0.9</td>
<td>1.8</td>
</tr>
<tr>
<td>Injectables</td>
<td>1.2</td>
<td>0.8</td>
<td>1.7</td>
</tr>
<tr>
<td>Implant</td>
<td>1.1</td>
<td>0.5</td>
<td>2.2</td>
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</table>

*Controlling for woman’s:*
- Age (per year increase)
- Literacy in Nyanja
- Genital ulceration and inflammation

Conclusions remained the same when controlling for pregnancy and/or fertility intentions.
Similarly, the results of:

- Multivariate models of linked infections only
  - **Controlling for:** woman’s age, literacy, sperm present on a wet prep, couples’ unprotected sex in past 3 months, genital ulceration/inflammation of female and male partner in past 3 months, man’s viral load at baseline

- All sensitivity analyses

**did not indicate any significant increase in HIV risk for hormonal contraception users.**
# Measures of unprotected sex by method of contraception

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<thead>
<tr>
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<tbody>
<tr>
<td>Incident pregnancy</td>
<td>3%</td>
<td>5%</td>
<td>1%</td>
<td>0%</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Self-reported</td>
<td>29%</td>
<td>37%</td>
<td>34%</td>
<td>18%</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>unprotected sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
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<0.05: OCP vs. non-hormonal methods
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# <0.001: injectables vs. non-hormonal methods
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& <0.001: implant vs. non-hormonal methods
STUDY DESIGN STRENGTHS

- HIV-discordant couple population
  - More homogenous HIV risk, more efficient study
  - Ethical study design: HIV testing partners together

- Methods provided at study site
  - More accurate exposure assessment

- Method use assessed at 3-month intervals
  - Important for capturing high rates of method stopping/switching

- Several time-varying measures of unprotected sex
  - Sperm on a wet prep, self-report, incident STIs, incident pregnancy
CONCLUSIONS & RECOMMENDATIONS

After controlling for sexual behavior and other confounders in this large cohort study, we found no statistically significant association between hormonal contraception and HIV acquisition risk in women.

- Condom use and reinforced condom counseling should always be recommended for women at-risk of HIV.
  - In our study, women at increased risk for unprotected sex were OCP and injectable users.
  - HIV testing of sex partners together is critical to establish HIV risk, ascertain couple fertility intentions, and counsel appropriately.

- We support LARC method promotion and efforts to increase method mix, proven strategies to decrease unintended pregnancy, along with condoms for HIV prevention.
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