The impact of hormonal contraception on HIV susceptibility

Renee Heffron, MPH, PhD

Department of Global Health
International Clinical Research Center
University of Washington

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Presentation outline

• Hormonal contraception
• Hormonal contraception & HIV-1 risk
• Implications for a potential association between injectable contraception and HIV-1
• Future directions
Background on hormonal contraception
Hormonal contraception is very important

• Contributes to:
  – Reductions in maternal mortality
  – Improvements in maternal health
  – Improvements in child health

• Used by >140 million women worldwide

• Method mix differs by geographic area

• Unmet need for contraception is large in some regions
**Contraception reduces maternal mortality**


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**Expected reduction in maternal deaths if unmet needs for contraception are fulfilled**

Simulation results, presented at the aggregated level, of number of maternal deaths per year if anticipated contraceptive demand is met (red bars) or not met (blue bars).
Contraceptive use at enrollment into the Partners in Prevention HSV/HIV Transmission Study

Heffron et al. STD. 2010
Serum progestin levels in different hormonal contraceptives

![Graph showing serum concentration of progestin (ng/mL) over a nine-month period for different contraceptives.](image)

**Source:**
Hormonal contraception & HIV-1
Epidemiologic questions

How are people who get HIV-1 different from people who don’t get HIV-1?

Does hormonal contraception increase a woman’s risk of acquiring HIV-1?

- Is the increase in risk driven by sexual behavior or by biological effects (or both)?
- Is there one particular hormonal contraceptive method that increases risk?
- If there is an increase in risk, how does it balance with the benefits of hormonal contraceptives?
Biologic effects of hormonal contraceptives could increase HIV-1 susceptibility

- Changes to cervical ectopy and cervical mucous
- Change thickness of vaginal wall
- Change in immune function
Published studies of injectable contraceptive use and HIV-1 risk

*Includes 2 types of injectables – DMPA and Net-En; All other studies include only injectable DMPA
Common limitations from prospective studies

- Small sample size
- Long follow up time between study visits
- Poor follow up rates
- Inability to distinguish between types of hormonal contraceptives
- No or not enough adjustment for confounding factors
- Self report of contraceptive use and sexual behavior
Relationship of hormonal contraception, condoms, and HIV-1

- Hormonal contraception 3 months ago
- Condom use 3 months ago

Diagram shows relationships between hormonal contraception, condoms, and HIV-1.
Highest quality published studies of injectable contraceptives and HIV-1 risk

*Includes 2 types of injectables – DMPA and Net-En; All other studies include only injectable DMPA
Partners in Prevention study of hormonal contraceptive use and HIV-1 risk among women

Heffron et al. 2012

- Prospective cohort study of 1314 HIV-1 uninfected women in serodiscordant partnerships from East and southern Africa (14 sites, 7 countries)
- All women knew their study partner was HIV-1 infected; clinical and behavioral data collected from HIV-1 infected partners
- Quarterly follow up visits for ≤24 months
- 24-month retention: >90%
- Statistical models controlled for age, plasma viral load of the HIV-1 infected partner, any unprotected sex and pregnancy
- Multiple statistical methods and sensitivity analyses produced consistent results
Contraception and HIV-1 acquisition among women in the Partners in Prevention study

<table>
<thead>
<tr>
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<th>Adjusted** Cox PH regression analysis</th>
<th>Adjusted** marginal structural model analysis</th>
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<tbody>
<tr>
<td></td>
<td>Incidence rate*</td>
<td>HR (95% CI)</td>
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<tr>
<td></td>
<td></td>
<td>p-value</td>
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<tr>
<td>No hormonal contraception</td>
<td>3.78</td>
<td>1.00</td>
</tr>
<tr>
<td>Injectable</td>
<td>6.85</td>
<td>2.05 (1.04-4.04)</td>
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*per 100 person years
**Adjusted for age, enrollment plasma viral load level of the HIV-1 infected partner and time dependent unprotected sex and pregnancy.

After detailed, prolonged deliberation...

...the group agreed that the data were not sufficiently conclusive to change current guidance.

However, because of the inconclusive nature of the evidence, women using progestogen-only injectable contraception should be strongly advised to also always use condoms...

Expansion of contraceptive method mix and further research on the relationship between hormonal contraception and HIV infection is essential.
Summary of current understanding

Possible HIV-1 risk with some hormonal contraceptives + Uncertainty in data + Tremendous benefit of hormonal contraceptives

Public health conundrum
Implications of a potential hormonal contraception – HIV-1 association
Intersection of injectable hormonal contraceptive use and HIV-1 prevalence

Future directions for work on hormonal contraception and the risk of HIV-1 infection
What do we need to do to get a more clear answer?

- More research
  - Randomized trial
  - Observational analyses
  - Biologic studies

- No more research
  - Change the method mix
  - Increase HIV-1 testing
  - Implement antiretroviral-based HIV-1 prevention strategies
  - Integrate family planning and HIV-1 services
Conclusions

• In regions with high HIV-1 risk and use of injectable contraception, understanding the impact of hormonal contraception on HIV-1 risk is one of the most important questions in women’s health today

• Top priorities in research include conducting a high quality randomized trial

• Integration of reproductive health and HIV-1 prevention programs is extremely important
<table>
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<th>Session Title</th>
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<tr>
<td>Start Making Sense: Weighing the Evidence on Hormonal Contraception and HIV (satellite)</td>
<td>Sunday, 9am, Mini room 4</td>
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<td>Hormonal contraception and HIV: An evolving controversy (oral abstracts)</td>
<td>Wednesday, 14:30, Session room 2</td>
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<tr>
<td>Hormonal contraception: The role of fertility choice in HIV prevention (symposia)</td>
<td>Thursday, 11:00, GV Session room 2</td>
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<tr>
<td>Late breaker abstract: Method of hormonal contraception is associated with lower tenofovir concentration in healthy women (MTN-001): implications for pre-exposure prophylaxis</td>
<td>FRLBC03</td>
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<tr>
<td>Multiple poster presentations</td>
<td>Search “contraception” in the Programme-at-a-Glance</td>
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Acknowledgements

Study participants and staff

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Partners in Prevention HSV/HIV Transmission Study Team

University of Washington Coordinating Center and Central Laboratories - Seattle, WA

Connie Celum, Anna Wald, Jairam Lingappa, Jared Baeten, Mary Campbell, Lawrence Corey, Robert Coombs, James Hughes, Amalia Magaret, M.Juliana McElrath, Rhoda Morrow, James Mullins

Site Principal Investigators

Botswana: Max Essex, Joseph Makhema


Rwanda: Etienne Karita, Kayitesi Kayitenkore, Susan Allen

South Africa: David Coetzee, Guy de Bruyn, Sinead Delany-Moretwe, Glenda Gray, James McIntyre, Helen Rees

Tanzania: Rachel Manongi, Saidi Kapiga

Uganda: Elly Katabira, Allan Ronald

Zambia: Mubiana Inambao, William Kanweka, Bellington Vwalika, Susan Allen