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- U.S. Agency for International Development (USAID) Technical Brief: "[Hormonal contraception and HIV](#)"
- World Health Organization (WHO) Technical Statement: "[Hormonal contraception and HIV](#)"

Hormonal Contraceptives and HIV Risk—Emerging Evidence in Context (Updated July 2012)

Background

An October 2011 analysis by a group of researchers, led by Renee Heffron of the University of Washington and published in *Lancet Infectious Diseases*, found two-fold increases in the risks of both HIV acquisition and HIV transmission among women in HIV-discordant couples using hormonal contraceptives, particularly the progestin-only injectable, compared with women not using hormonal contraceptives.¹ Another analysis of the data used in the Heffron study found that pregnancy itself doubles the risk of transmitting HIV and that pregnancy also doubles risk of acquiring HIV (though largely because of differences between pregnant and nonpregnant women in age, contraceptive use and sex unprotected by condoms), findings that, if accurate, have serious implications of their own.²

Following these new findings, the World Health Organization (WHO) convened a technical consultation regarding hormonal contraception and HIV acquisition, progression and transmission. It was recognized that this issue was likely to be of particular concern in countries where women not only face high risk of maternal mortality and morbidity, but also high risk of HIV infection.^{3,4} Voluntary contraception is crucial for women who have or are at risk of HIV because it helps women avoid unintended pregnancy and its health risks.^{5,6} In Sub-Saharan Africa, where HIV infection rates are especially high, hormonal contraceptives are the most commonly used methods: Twelve million women use injectable contraceptives and eight million use oral contraceptives; another 11 million women rely on nonhormonal methods—condoms, sterilization or IUDs.⁷

Recommendations by authoritative public health agencies

The World Health Organization convened a technical consultation from January 31 to February 1, 2012, which issued a technical statement saying that: "After detailed deliberation ... the group concluded that the World Health Organization should continue to recommend that there are no restrictions ... on the use of any hormonal contraceptive method for women living with HIV or at high risk of HIV."⁸ The group's detailed recommendations are below:

Recommendations for women at high risk of HIV infection:

- *Women at high risk of HIV can continue to use all existing hormonal contraceptive methods without restriction.*
- *It is critically important that women at risk of HIV infection have access to and use condoms, male or female, and where appropriate, other measures to prevent and reduce their risk of HIV infection and sexually transmitted infections (STIs).*

- *Because of the inconclusive nature of the body of evidence on progestogen-only injectable contraception and risk of HIV acquisition, women using progestogen-only injectable contraception should be strongly advised to also always use condoms, male or female, and other preventive measures. Condoms must be used consistently and correctly to prevent infection.*

Recommendations for women living with HIV infection:

- *Women living with HIV can continue to use all existing hormonal contraceptive methods without restriction.*
- *Consistent and correct use of condoms, male or female, is critical for prevention of HIV transmission to non-infected sexual partners.*
- *Voluntary use of contraception by HIV-positive women who wish to prevent pregnancy continues to be an important strategy for the reduction of mother-to-child HIV transmission.*

The U.S. Centers for Disease Control and Prevention (CDC) conducted its own analysis and, consistent with the WHO, concluded that the use of hormonal contraceptives is safe for women who are HIV-positive or at high risk for HIV infection, while strongly encouraging condom use and other measures to prevent HIV.⁹

Similarly, the U.S. Agency for International Development (USAID) affirmed the WHO recommendations and, in a February 2012 communication to the field, stated that no changes should be made to programs on the ground.¹⁰

About the study by Heffron et al.

Numerous analyses have tried to ascertain whether hormonal contraceptives lead to increased risk of HIV acquisition or transmission. There are several mechanisms by which hormonal contraceptives could theoretically increase the risk of HIV acquisition or transmission, but data supporting many of these are limited and inconclusive. Systematic reviews of these studies have concluded that the weight of evidence suggests no relationship between hormonal contraceptive use and HIV acquisition or transmission and that there is need for conclusive research to be undertaken.¹¹⁻¹⁵

Heffron and colleagues analyzed data from women and men in HIV discordant couples. These data were collected as part of studies designed for purposes other than assessing links between hormonal contraceptive use (or pregnancy) on HIV acquisition and transmission. Most (88%) of the couples for whom data were available were participants in a randomized placebo-controlled trial—conducted in 14 locations within seven Sub-Saharan African countries—assessing the efficacy of acyclovir in preventing HIV infection associated with herpes simplex infection.^{16,17} Data for the other 12% of couples in the analysis came from a parallel observational study of immune correlates of HIV protection at two of the same study sites.

Participants in these studies were provided with comprehensive HIV-prevention services, including risk-reduction counseling for individuals and couples, free condoms and STI treatment. They were offered contraceptives on a voluntary basis at the study site or on referral, or both. Every three months, women were asked what contraceptive method, if any, they were using, and women and their partners were tested to identify new HIV infections. The analysis compared new HIV infection rates in three-month periods during which women at some point used a hormonal method to rates in three-month periods during which women used no hormonal method (i.e., either used no contraceptive at all or relied on condoms alone, tubal sterilization or hysterectomy). Most couples in both groups reported using condoms. Women in a minority (29%) of couples used hormonal contraceptives at least once during the study. Most hormonal method use was of the progestin-only injectable. Data on adherence to method use requirements and brand of contraception were not collected.

Since participants were not randomly assigned to contraceptive use and method type, the researchers used statistical techniques to attempt to adjust for differences between hormonal method users and nonusers. They adjusted for age, HIV viral load at enrollment, sex without a condom and pregnancy, which were the only available study variables reported to have substantial effects on the relationship between contraceptive use and HIV infection. Two forms of statistical modeling (Cox proportional hazards regression and marginal structural modeling) produced similar results, indicating higher HIV acquisition and transmission rates during periods when hormonal contraceptives were used than during periods with no hormonal method use. The elevated risks were statistically significant among those using progestin-only hormonal methods. Although the estimates for oral contraceptive pills were also elevated, they were not statistically significant, possibly due to the small number of women in the analysis using that method.

This study has a number of strengths,¹⁸ including studying discordant couples in which there was clear risk of the HIV-negative person becoming infected, use of genetic sequencing to identify and include only cases of HIV transmission from study women to their partners, inclusion of participants from a range of countries and study sites in Sub-Saharan Africa, a prospective design with frequent assessment of contraceptive use and use of two different types of statistical analysis.

It also has a number of limitations. For example, women were not randomized according to contraceptive method use; statistical methods and variables collected in the study may not adequately adjust for differences between those who used hormonal methods and those who did not, including possible differences in sexual behavior and condom use; the measure of use of a hormonal method at the three-month visit may not represent use at the time the infection occurred; and some variables, including hormonal contraceptive use and condom use, may not have been accurately reported by respondents. These and other issues will need exploration in the evaluation of the Heffron et al. study. However, many such limitations are inherent in secondary analysis of observational data. New research is needed to know for sure whether hormonal contraceptive use is an independent factor in HIV acquisition and transmission.

For questions, please contact:

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