

# Research on hormonal contraception and HIV acquisition

FHI 360 has been a leader in research on the relationship between hormonal contraception and HIV acquisition for more than two decades. With that relationship still unclear, FHI 360 and colleagues will report the results of a large meta-analysis, based on individual participant data from 18 prospective studies, at the 2014 International AIDS Conference in Melbourne, Australia. In partnership with the World Health Organization, the Wits Reproductive Health and HIV Institute and the University of Washington, FHI 360 will also help lead a randomized controlled trial to provide a more definitive answer to this important reproductive health question.

Worldwide, more than 150 million women use hormonal contraceptives, most commonly either combined oral contraceptives (COCs) or progestin-only injectable contraceptives such as depot-medroxyprogesterone acetate (DMPA). Despite the popularity and effectiveness of these methods, some studies suggest that use, particularly of DMPA, might be associated with an increased risk of acquiring HIV from an infected partner. The results of research on this issue have been conflicting and inconclusive.

## Observational analyses of HIV acquisition

FHI 360 has conducted multiple studies on hormonal contraception and HIV acquisition, including the largest prospective study designed specifically to evaluate the relationship between COC and DMPA use and HIV acquisition.<sup>1</sup> With funding from the U.S. National Institute of Human Development, the study took place over four years among some 6,100 family planning clients in Thailand, Uganda and Zimbabwe. The results, published in 2007, found no overall association between the use of either COCs or DMPA and acquisition. A reanalysis of the data using advanced statistical techniques to better control for confounding biases, however, found an increased risk of HIV associated with DMPA use but not with COC use.<sup>2</sup>

In 2011, an observational analysis from an HIV prevention trial identified an association between DMPA use and HIV acquisition.<sup>3</sup> Conducted by the University of Washington and colleagues among 3,790 HIV-serodiscordant couples in seven African countries, the study suggested that DMPA use could double the risk of HIV acquisition.

A subsequent systematic review of all the available observational data on hormonal contraception and HIV acquisition concluded that some, but not all, of the data suggest an association between DMPA use and HIV acquisition.<sup>4</sup>

## World Health Organization recommendations

Following two expert consultations and a thorough review of the evidence on hormonal contraception and HIV acquisition, the World Health Organization (WHO) came to a similar conclusion. In a statement issued in 2012, WHO continued to advise that women who are at high risk of HIV or who are already infected with the virus can safely use hormonal contraceptives to prevent pregnancy. However, the WHO statement specified that women who use progestin-only injectables, such as DMPA, are strongly advised to also use condoms.

WHO also recommended that higher-quality clinical studies were needed to improve the evidence on hormonal contraception and HIV acquisition. Observational studies cannot establish a direct cause-and-effect relationship between hormonal contraceptive use and acquisition. Only a randomized controlled trial can determine whether a causal link between the two exists.

## Meta-analysis of individual participant data

To provide more compelling evidence, FHI 360 performed a meta-analysis of individual participant data on hormonal contraception and HIV acquisition from 18 prospective studies and HIV prevention trials in sub-Saharan Africa. Examining data from individual participants can help overcome some of the methodological challenges of simply combining estimates of the effects from multiple studies.

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For the meta-analysis, data from more than 37,000 women from sub-Saharan Africa were used to evaluate whether hormonal contraceptive use was associated with a risk of HIV acquisition. The data were also used to determine if age or the presence of herpes simplex virus type-2 affected a possible association and to directly compare the risks of HIV acquisition among the three hormonal methods — COCs, DMPA and the injectable norethisterone enanthate (NET-EN). The results will be released in July 2014 at the 20th International AIDS Conference in Melbourne, Australia.

### Randomized controlled trial of HIV acquisition

In 2013, FHI 360, the Wits Reproductive Health and HIV Institute, the University of Washington and WHO organized the Evidence for Contraceptive Options and HIV Outcomes (ECHO) consortium to plan a randomized controlled trial of hormonal contraception and HIV. Representatives of the Statistical Center for HIV/AIDS Research & Prevention, the University of Fort Hare and the University of the Witwatersrand in South Africa, the International Centre for Reproductive Health in Kenya, the Kenya Medical Research Institute and the University of Zimbabwe also participate in this ongoing consortium.

The ECHO trial will enroll from 14 sites in east and southern Africa approximately 8,600 HIV-negative women who desire contraception. The women will be openly randomized to use DMPA, a levonorgestrel implant or the copper intrauterine device and will be followed for an average of 15 months. The researchers will then compare the rates of HIV acquisition among the three groups of women. Rates of pregnancy, contraceptive method continuation and contraceptive method-related adverse events will also be reported. The trial will take approximately four years to complete, with enrollment expected to begin in early 2015.

Further clarification on hormonal contraception and HIV acquisition is crucial for improving family planning policies and programs, HIV prevention strategies and the health of millions worldwide.

### REFERENCES

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