echo
Evidence for Contraceptive Options & HIV Outcomes

PHOTO CREDIT: JESSICA SCRANTON | FHI 360

The Evidence for Contraceptive Options and HIV Outcomes (ECHO) Study is an open-label randomised clinical trial comparing three highly effective, reversible methods of contraception — a progestogen-only injectable called depot-medroxyprogesterone acetate (DMPA), a levonorgestrel implant and the non-hormonal copper intrauterine device — to evaluate whether there is any difference in the risk of acquiring HIV infection among users of these methods.

WHY ECHO IS NEEDED

More than 150 million women worldwide use various hormonal contraceptives for family planning. In sub-Saharan Africa, progestogen-only injectables are the most commonly used method. By enabling women to avoid high-risk pregnancies, injectables and other modern methods of contraception help prevent hundreds of thousands of maternal and infant deaths every year.

There is evidence from observational studies that use of progestogen-only injectable methods — particularly DMPA — is associated with an increased risk of acquiring HIV infection, but uncertainty remains about whether DMPA use actually causes increased risk. These studies have a number of limitations; most were designed to answer different questions and may be biased because they could not control for other important factors affecting women's risk of HIV infection.

Given the widespread use of DMPA in areas of high HIV incidence, the question of whether DMPA increases women's risk of HIV is a critical public health issue requiring the strongest evidence possible. Women need to know whether using DMPA or other methods affects their risk of acquiring HIV so they can make informed choices about contraception.

WHO GUIDANCE

The World Health Organization (WHO) has convened experts to consider systematic reviews of the latest data on the safety of hormonal contraception three times since 2012. In March 2017, they concluded that the available evidence continues to indicate an association between use of progestogen-only injectables and an increased risk of acquiring HIV; however, it is unknown whether the associations seen in observational studies were due to a true biological effect or the limitations of such studies.

The WHO recommends that long-acting progestogen-only injectables should remain accessible to women at high risk of HIV, "because the advantages of these methods generally outweigh the possible increased risk of HIV acquisition." However, women at high risk of HIV who choose to use these methods should be counselled about the possible increased risk of HIV and how to reduce this risk.

ECHO STUDY SITES

SOUTH AFRICA

Aurum Institute, Klerksdorp

Effective Care Research Unit, East London

Emavundleni Research Centre, Cape Town

Madibeng Centre for Research, Brits

MatCH Research Commercial City, Durban

MatCH Research Edendale, Pietermaritzburg

Qhakaza Mbokodo Research Clinic, Ladysmith

Setshaba Research Centre, Soshanguve

Wits RHI/University of the Witwatersrand, Johannesburg

KENYA

KEMRI Research Care Training Program Study Centre, Kisumu

ESWATINI

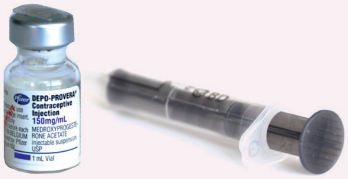
Family Life Association of Swaziland – ICAP, Manzini

ZAMBIA

University of North Carolina's Division of Global Women's Health – Kamwala Clinic, Lusaka

CONTRACEPTIVES BEING USED IN THE ECHO STUDY

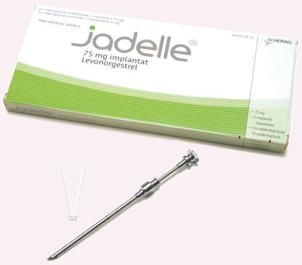
DMPA



- Is the most widely used progestogen-only injectable
- Given every 3 months
- Benefits include privacy, no daily action required and no interference with sex; protects against endometrial cancer and uterine fibroids
- Side effects include irregular, infrequent or prolonged menstrual bleeding initially, followed by infrequent or no bleeding
- Return of fertility may be delayed by 6-9 months after the last injection

LEVONORGESTREL IMPLANT (JADELLE)

- Consists of two thin, flexible rods filled with a progestogen (levonorgestrel) that are inserted just under the skin of the upper arm
- Once inserted, lasts up to 5 years
- Benefits include privacy, no daily action required and no interference with sex
- Side effects include prolonged or irregular menstrual bleeding, or both, and application site reactions
- Can be removed at any time, with a rapid return to fertility



COPPER IUD

- Is a small, flexible plastic frame with copper sleeves or wire around it
- Once inserted, lasts up to 10-12 years
- Benefits include privacy, no daily action required and no interference with sex; may provide some protection against endometrial and cervical cancer
- Changes in menstrual bleeding (heavier periods and more menstrual cramps) are common, especially in the first 3 to 6 months of use
- Can be removed at any time, with a rapid return to fertility

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The WHO guidance highlights the continued importance of randomised clinical trials to clarify whether the use of progestogen injectables causes an increased risk of acquiring HIV. The ECHO Study is the first large-scale randomised clinical trial to address this critical public health question.

TRIAL OVERVIEW

The ECHO Study is a multi-center, multi-country, open-label, randomised clinical trial designed to fill an important gap in HIV and reproductive health research by providing conclusive information about the comparative risks and benefits of three highly effective contraceptive methods.

- A total of 7,830 sexually active HIV-negative women ages 16 to 35 were enrolled at 12 study sites in Kenya, South Africa, eSwatini and Zambia.
- Participants were randomly assigned to use one of three contraceptive methods: DMPA, a progestogen implant containing levonorgestrel or the copper intrauterine device (IUD).
- Investigators will analyse HIV acquisition, pregnancy, method continuation and complications associated with contraceptive use among participants.
- Participants were expected to attend quarterly visits for up to 18 months.
- The participating women were encouraged to remain on their assigned methods for the duration of the study but could change methods if they wished.
- Women who wanted to join the study learned about the study procedures and the risks and benefits of participation through a consent process designed to ensure that their participation was informed and voluntary.
- Results, expected in mid-2019, will help guide the implementation of safe, effective policies and services that will enable women at high risk of HIV to make fully informed choices about contraception and HIV prevention.

COLLABORATING INSTITUTIONS

FHI 360, the University of Washington and the Wits Reproductive Health and HIV Institute (RHI) coordinate the ECHO Study, in partnership with the WHO and research institutions in Kenya, South Africa, eSwatini and Zambia.

The ECHO Study is funded by a consortium of donors, including the Bill & Melinda Gates Foundation, the US Agency for International Development (USAID), the Swedish International Development Cooperation Agency, the United Nations Population Fund and the Medical Research Council of South Africa. In addition, USAID and the South African government donated the contraceptives used in the study.

For more information on the ECHO Study, see http://echo-consortium.com/.