

IMAP Statement

on the Evidence for Contraceptive Options and HIV Outcomes (ECHO) trial

Robust investigation into the association between use of progestogen-only injectables and increased risk of HIV acquisition was required, which led to the development of the ECHO trial.

This statement was prepared by the International Medical Advisory Panel (IMAP) and was approved in July 2019.

Background

The body of evidence on possible increased risk of HIV acquisition with use of progestogen-only contraception has remained mixed since 1991, with the greatest concern of an increased risk of HIV acquisition centred on the use of intramuscular depot-medroxyprogesterone acetate (DMPA-IM).¹ Data on the risk of HIV acquisition and use of other highly effective contraceptives such as norethisterone enanthate (NET-EN), hormonal implants, and hormonal and non-hormonal IUDs are limited.² And there are no data on subcutaneous DMPA (DMPA-SC) and HIV risk.

In 2016, an updated systematic review of epidemiological evidence on hormonal contraception and HIV acquisition concluded that there was a significant association between the use of DMPA and HIV acquisition and no increased HIV risk with oral contraceptive pills.³ The updated systematic review provided important data regarding DMPA users at high risk of HIV; however, confounding in these observational data could not be excluded.

The historically mixed data and the need to control for confounding required further investigation into the association between use of progestogen-only injectables and increased risk of HIV acquisition, using a more robust research design. This led to the development of the Evidence for Contraceptive Options and HIV Outcomes (ECHO) trial.

The purpose of this statement

This statement's purpose is to share current evidence regarding hormonal contraception and HIV risk, the results of the ECHO trial, and their implications for family planning and HIV prevention. The statement provides recommendations to IPPF Member Associations in light of the trial results; reinforces IPPF's position and commitment to a rights-based approach to sexual and reproductive health (SRH) service provision and counselling; provides clarity on IPPF's position with regard to hormonal contraception and HIV risk; and mitigates misinformation regarding hormonal contraception and HIV risk.

Intended audience

The statement is primarily intended to inform IPPF Member Associations and secretariat staff, and relevant partners, including SRH service delivery organizations, about this prevailing issue.

The ECHO study aimed to determine whether using any of three highly effective reversible contraceptive methods (a progestogen-only injectable, a progestogen implant, and the copper IUD) is linked to an increased risk of HIV acquisition.

The ECHO trial

The ECHO trial is a multi-site, multi-country, open-label randomised clinical trial that was conducted in 12 sites in four countries – Eswatini (Swaziland), Kenya, South Africa, and Zambia – between December 2015 and December 2018.⁴

The study was designed to compare three highly effective reversible methods of contraception – a progestogen-only injectable, intramuscular depot-medroxyprogesterone acetate (DMPA-IM); a progestogen implant (Jadelle®); and the non-hormonal copper intrauterine device (IUD). The study aimed to determine whether using any of these contraceptive methods is linked to an increased risk of HIV acquisition. A total of 7,829 women aged 16–35 years were randomly assigned to one of the three contraceptive methods.

The study was led by FHI 360, Wits Reproductive Health and HIV Institute (Wits RHI), the University of Washington and the World Health Organization (WHO) and supported by the Bill and Melinda Gates Foundation (BMGF), the Swedish International Development Cooperation Agency (Sida), the South African Medical Research Council (SAMRC), the United Nations Population Fund (UNFPA), and the US Agency for International Development (USAID).

The results of the ECHO study were released on 13 June 2019 at the 9th SA AIDS Conference in Durban, South Africa.⁵

Results of the ECHO Trial

Among the 7,829 women who took part in the study, 397 HIV infections occurred, resulting in an overall HIV incidence of 3.81 per 100 woman-years [95% CI 3.45–4.21].

While the HIV incidence was alarmingly high (the study assumed an underlying incidence of 3.5 per 100-woman years), there was no statistical difference in the rate of acquisition of HIV among the women. In other words, women who used DMPA-IM were not at a higher risk of acquiring

HIV than women who used a progestogen implant or the non-hormonal copper IUD. Women aged younger than 25 years or who were HSV-2-seropositive were associated with a higher HIV incidence. Sexually transmitted infections (STIs) such as *C. trachomatis* (chlamydia), *N. gonorrhoeae* (gonorrhoea), and herpes simplex virus (HSV-2) were common in the study population at baseline.

All three methods of contraception included in the study proved to be safe and highly effective for pregnancy prevention, with pregnancy rates of approximately one per cent or less per year when in use.

The ECHO trial did not provide evidence on the risk of acquiring HIV with use of contraceptive methods that were not included in the trial such as combined oral contraceptive pills (COCs), NET-EN, DMPA-SC, etonogestrel (ETG) implant, etc.

Implications of the ECHO trial results

Following its standard practice when important new research findings are published relating to contraceptive safety, WHO will convene a Guideline Development Group to review its existing recommendations concerning women's eligibility for using various contraceptive methods if they are at high risk of HIV. Updated recommendations will be issued by the end of August 2019.

Meanwhile, the robust scientific evidence generated by the ECHO trial underscores the need to provide quality, integrated sexual and reproductive health and HIV services, including ensuring access to HIV testing services and HIV prevention commodities such as male and female condoms, pre-exposure prophylaxis (PrEP), and post-exposure prophylaxis (PEP). Screening, diagnosis, and treatment of other STIs are crucial components of integrated SRH services, as the presence of STIs, such as syphilis or gonorrhoea, greatly increases the risk of acquiring or transmitting HIV.

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Women seeking contraceptive services, particularly in Eastern and Southern Africa, are also at high risk of acquiring HIV and other STIs. Integrated service provision can positively impact contraceptive and HIV prevention outcomes thus reducing unintended pregnancy, unsafe abortion (particularly among women at risk of and living with HIV) and perinatal transmission of HIV; increasing the uptake of HIV testing and promoting dual-method use and dual protection.^{6,7} Integrated service provision also promotes a rights-based approach to health service provision by making services more easily accessible (including prioritizing youth-friendly services), meeting the unmet need for contraceptive services for those most at risk of acquiring HIV, and reducing stigma associated with seeking HIV services.⁸

The ECHO trial also demonstrated the feasibility of delivering highly effective and safe long-acting and reversible contraceptive methods such as the non-hormonal copper IUD and a progestogen implant across multiple settings. This was possible due to the study's investment in training; assurance of provider clinical competency; adequate human resources for contraceptive counselling and management of side effects; and the necessary logistical support, including management of contraceptive commodities.

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Implications for IPPF Member Associations and other SRH service delivery organizations

- *The ECHO trial results showed that there is no statistical difference in the rate of acquisition of HIV among women using the three contraceptives.*

IPPF Member Associations and other SRH service delivery organizations should therefore continue to promote and ensure that women have access to a broad method mix of contraceptives, including progestogen-only injectables and other long-acting and reversible contraceptive methods, which have been proved to be safe and highly effective.

Access to high-quality, affordable SRH services and information, including a broad method mix of contraceptives, is not only essential to preventing pregnancy, but is fundamental to fulfilling the rights and well-being of all people.

- *The high incidence of HIV acquisition among the study participants is alarming, in spite of the provision of an individualized HIV prevention package.*

This finding highlights the need to strengthen prevention of HIV and other STIs through SRHR and HIV services integration and provision of PrEP in countries with high HIV incidence. There are many SRHR and HIV integration resources available to help health service delivery organizations consider models of integration (i.e., integrating contraceptive services into HIV services or vice versa),^{9,10} the policy environment required for successful integration,^{11,12} human resource considerations,¹³ and integrated counselling best practices,^{14,15,16} including important considerations related to hormonal contraception and antiretroviral therapy drug-drug interactions.^{17,18,19}

Implications for women and girls

Women and girls should be supported to make informed decisions about their preferred contraceptive method through counselling and provision of a broad method mix of contraceptives.

Women and girls who are at high risk of acquiring HIV should not be denied hormonal contraceptives if this is their preferred method. They should not only receive comprehensive and accurate information regarding their contraceptive method of choice, but should also be counselled on methods available for HIV and STI prevention,

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such as male and female condoms and PrEP. No hormonal contraceptive method prevents sexually transmitted infections (STIs), including HIV.

According to the WHO Medical Eligibility Criteria (MEC), women at high risk of acquiring HIV can use all methods of contraception, including hormonal contraceptives.²⁰ However, there should be greater focus on dual method use (i.e. use of a barrier method (male or female condom) plus another effective contraceptive) for prevention of unintended pregnancy and STIs, including HIV. Women in the ECHO study demonstrated a high rate of STIs at the start of the study, highlighting the need for increased access to STI prevention counselling and treatment services.

Recommendations and guidance

The translation of the ECHO trial evidence into actionable policy and programmatic guidance will primarily take place at the country level, led by ministries of health and supported by implementing partners such as IPPF Member Associations. There are many ways IPPF Member Associations and other SRH organizations can support country-level planning in response to the trial results.

IPPF Member Associations often participate in and provide technical assistance to national ministries of health SRH working groups. Ministries of health will need to consider if and to what extent their national service delivery guidelines for SRH and HIV prevention services achieve integrated service delivery. They will also need to consider how to reduce barriers for women who are at high risk of acquiring HIV and who wish to prevent an unintended pregnancy. National guidelines and service delivery tools may need to be updated. Ministries of health will need to take the lead at the country level to organize SRH partners to adapt and implement WHO's updated guidance as a result of the ECHO trial. IPPF Member Associations should take every opportunity to participate in and support national guideline review processes in their

countries and advocate for rights-based decisions that advance women's and girls' reproductive choices and ensure access to contraception and HIV services.

Following the release of the ECHO trial results, all Member Associations and other sexual and reproductive health organizations can engage in the following areas:

COMMUNICATION

- Familiarize themselves, including service providers, staff, and volunteers, with the ECHO trial results; the latest updates from WHO on the ECHO trial and hormonal contraception and HIV;²¹ and IPPF's Technical Brief on *Hormonal contraception: Recommendations for women at high risk of HIV*.²²
- Provide accurate information on the ECHO trial, its results, and its implications to all Member Association staff and other key stakeholders.
- Engage with national-level technical working groups to determine if and to what extent national governments are responding to the results of the ECHO trial.
- Determine if any changes to national or implementing partner guidelines or service delivery tools have been made since WHO's update to the MEC in 2017.

ADVOCACY

- Advocate at national and regional levels and to legislative bodies and ministries of health to further support the integration of SRHR and HIV services. Member Associations can support the demonstrated need for an integrated approach to sexual and reproductive health service provision as described in the Guttmacher-*Lancet* Commission report (2018).²³ This should include advocating for the availability of and access to PrEP.

Ministries of health will need to consider if and to what extent their national service delivery guidelines for SRH and HIV prevention services achieve integrated service delivery and take the lead to organize SRH partners to adapt and implement WHO's updated guidance following the ECHO trial.

IPPF Member Associations should take every opportunity to participate in and support national guideline review processes in their countries and advocate for rights-based decisions that advance women's and girls' reproductive choices and ensure access to contraception and HIV services.

- Advocate for comprehensive sexuality education for young people and youth-friendly integrated services. In the study, women aged younger than 25 years were at a greater risk of acquiring HIV.
- Promote clients' right to informed decision-making as a fundamental principle when providing any contraceptive information and services.
- Advocate for availability of the full range of safe, effective and affordable contraceptive methods, ensuring universal coverage and leaving no one behind.
- Ensure that women and girls have access to HIV prevention methods, including male or female condoms and PrEP.
- Sensitize men and boys on the life-saving benefits of their partners using highly effective contraceptive methods, as well as on the benefits of consistent and proper condom use.
- Service providers should:
 - Prioritize a client-centred, rights-based approach to sexual and reproductive health service provision and counselling.
 - Help sexually active individuals make informed decisions by providing accurate and complete information about their contraceptive and HIV/STI prevention options.
 - Never deny women and girls, including those at high risk of HIV, the choice of a contraceptive method.

SERVICE DELIVERY

- Provide accurate, comprehensive, and integrated sexual and reproductive health and HIV prevention information and services. This includes counselling all women, girls, and couples on dual method use if they are at risk of acquiring HIV and other STIs, regardless of the method of their choice.



Dedication

This IMAP statement is dedicated to Dr Ward Cates (1942–2016) who until the time of his passing was the President, Research at FHI 360. Dr Cates was instrumental in mobilizing resources for the ECHO trial. He was a member of IMAP in the early 2000s and contributed to and provided guidance in the drafting of the Third Edition of IPPF's Medical and Service Delivery Guidelines, published in 2004, and many IMAP statements. We wish to recognize Dr Cates for his contributions to the field of sexual and reproductive health and believe he would have been pleased with the results of the ECHO trial.

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Acknowledgements

We would like to express our appreciation to Lindsey Miller for drafting this statement and to Dr Ian Askew, Professor Michael Mbizvo, Dr France Anne Donnay and Janet Meyers for providing technical input and guidance as the lead reviewers. We are also grateful to IPPF colleagues Darcy Weaver, Daniel McCartney, Manuelle Hurwitz, and Yuhsin Huang for reviewing the document; and Sarah Onyango for her review and coordination of the process. Finally, we gratefully acknowledge the support from IPPF's International Medical Advisory Panel (IMAP): Dr Ian Askew, Dr Neelam Bhardwaj, Dr France Anne Donnay, Professor Kristina Gemzell Danielsson, Dr Raffaella Schiavon Ermani, Professor Oladapo Alabi Ladipo, Professor Michael Mbizvo (Chair), Janet Meyers, and Professor Hextan Yuen Sheung Ngan for their valuable and timely guidance and reviews offered during the development process.

WHO WE ARE

The International Planned Parenthood Federation (IPPF) is a global service provider and a leading advocate of sexual and reproductive health and rights for all. We are a worldwide movement of national organizations working with and for communities and individuals.



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Published July 2019