How should we listen to ECHO?

Published Online
June 13, 2019
http://dx.doi.org/10.1016/S0140-6736(19)31387-X

See Online/Articles
http://dx.doi.org/10.1016/S0140-6736(19)31288-7

For many years before the long-awaited results of the study by the Evidence for Contraceptive Options and HIV Outcomes (ECHO) Trial Consortium,[1] observational and laboratory studies suggested that some hormonal contraceptive methods, particularly intramuscular depot medroxyprogesterone acetate (DMPA-IM), might increase women's susceptibility to HIV acquisition.[2] In ECHO, 7829 HIV-seronegative women seeking effective contraception were randomly assigned to receive DMPA-IM, a copper intrauterine device (IUD), or a levonorgestrel (LNG) implant, and followed for 18 months for incident HIV infection. All three methods were highly effective for pregnancy prevention, and, as was anticipated for trial sites in eSwatini, Kenya, South Africa, and Zambia, observed overall HIV incidence was high (3·81 per 100 woman-years [95% CI 3·45–4·21]), despite HIV prevention services provided for all participants. In modified intention-to-treat analyses, hazard ratios for HIV acquisition were 1·04 (96% CI 0·82–1·33, p=0·72) for DMPA-IM versus copper IUD, 1·23 (0·95–1·59, p=0·097) for DMPA-IM versus LNG implant, and 1·18 (0·91–1·53, p=0·19) for copper IUD versus LNG implant.

Thus, none of ECHO's primary intention-to-treat analyses showed a 50% increase in HIV incidence, which the trial was designed to be able to detect. Investigators did acknowledge, however, that even an effect consistent with less than 30% increase in HIV risk (for which ECHO had low statistical power) might be important for individual women at very high HIV risk, in terms of decision making about contraception and HIV prevention. Notably, ECHO successfully answered some but not all questions about potential interactions between contraception and HIV infection. Results do not address the range of methods (eg, etonogestrel implant, subcutaneously administered DMPA, oral contraceptive pills, injectable norethisterone enanthate, combined progestin and oestrogen injectable contraceptives, and hormonal IUDs) not included in the trial because of practicality and programmatic priority; nor can results speak to whether study methods affect risk for HIV acquisition compared with use of no contraceptive method, a design choice already well justified by ECHO investigators.[3] Important clinical and implementation research questions also remain with regard to meeting contraceptive needs of women living with HIV.[4,5]

In July, 2019, ECHO results will be reviewed in the context of the WHO medical eligibility criteria for contraceptive use,[6] and a Guideline Development Group will determine whether or not DMPA-IM will revert from category 2 (advantages of method generally outweigh theoretical or proven risks) to category 1 (no restriction for use) for women at high risk for HIV acquisition.[7] Regardless of the outcome of those deliberations, family planning should remain prioritised as one of public health's most powerful tools against a range of adverse outcomes, including maternal mortality.[8,9] Like immunisation, family planning has had myths and misunderstandings plague its history, and the importance of clear, consistent communication regarding ECHO results and any related updates to the medical eligibility criteria cannot be overemphasised. Coordinated communication planning efforts involving community stakeholders, country governments, advocates, implementing partners, and WHO headquarters and country offices are fortunately already underway.

Ultimately, the response to ECHO results must be centred on and informed by women and girls in Africa, where the trial occurred and where substantial burden persists in unmet need for family planning and HIV prevention, both of which have suffered from siloed approaches to funding and programming. Going forward, health systems need innovative models that more conveniently integrate services according to the preferences of women already too burdened

Jonathan Torgovnik/Getty Images

with unpaid work,[10] and acknowledge the reality of how partners and family members affect women's choices. However, policies and guidelines must reflect women's and girls' right to autonomous decision making over their own bodies, and promote access to comprehensive sexual and reproductive health services. Realisation of this goal does require remedying the inadequate quality of care that discourages many people, especially adolescents, from using such services. Without addressing underlying drivers of poor delivery, experience, and uptake of care, we will not achieve true universal health coverage or the sustainable development goal of good health and wellbeing for all.[11] Gender bias continues to contribute to gaps in resources needed to address these drivers and, consequently, the world is still failing its most vulnerable women and girls.

Although ECHO results are largely reassuring for contraceptive methods included in the trial, a substantial unfinished agenda remains to meet the range of needs of those at risk for unplanned pregnancy and HIV infection, including stronger global and national commitments and accountability for informed choice for family planning and HIV prevention and treatment. Many factors are driving unacceptably high rates of HIV acquisition in young women, but we have good reasons to believe that contraception is not one of them. Decision makers need to listen to the voices of women and girls—who continue to suffer and die not solely as a result of their unconscionable lack of access to high-quality contraceptive and HIV-related care but also to primary care, cancer prevention, mental health, safe abortion, violence prevention, and maternal health services. Therein lies the message we need to hear and amplify as we listen to results of ECHO.

Lisa Miyako Noguchi, Princess Nothemba Simelela
Johns Hopkins Bloomberg School of Public Health, Johns Hopkins University, Baltimore, MD 21205, USA (LMN); and World Health Organization, Geneva, Switzerland (PNS)
lnoguch1@jhu.edu

We declare no competing interests.

1 Evidence for Contraceptive Options and HIV Outcomes (ECHO) Trial Consortium. HIV incidence among women using intramuscular depot medroxyprogesterone acetate, a copper intrauterine device, or a levonorgestrel implant for contraception: a randomised, multicentre, open-label trial. *Lancet* 2019; published online June 13. http://dx.doi.org/10.1016/S0140-6736(19)31288-7.

2 Polis CB, Curtis KM, Hannaford PC, et al. An updated systematic review of epidemiological evidence on hormonal contraceptive methods and HIV acquisition in women. *AIDS* 2016; **30:** 2665–83.

3 Hofmeyr GJ, Morrison CS, Baeten JM, et al. Rationale and design of a multi-center, open-label, randomised clinical trial comparing HIV incidence and contraceptive benefits in women using three commonly-used contraceptive methods (the ECHO study). *Gates Open Res* 2018, **1:** 17.

4 Patel RC, Morroni C, Scarsi KK, et al. Concomitant contraceptive implant and efavirenz use in women living with HIV: perspectives on current evidence and policy implications for family planning and HIV treatment guidelines. *J Int AIDS Soc* 2017, **20:** 21396.

5 Communique of the Kigali Dolutegravir Stakeholder Meeting of African women living with HIV. http://www.afrocab.info/wp-content/uploads/2019/05/Kigali-Communique-.pdf (accessed June 3, 2019).

6 WHO. WHO guidance on contraceptive eligibility for women at high risk of HIV. https://www.who.int/reproductivehealth/publications/contraceptives-methods-hiv/en/ (accessed June 3, 2019).

7 WHO. Hormonal contraceptive eligibility for women at high risk of HIV: Guidance Statement. https://apps.who.int/iris/bitstream/handle/10665/254662/WHO-RHR-17.04-eng.pdf (accessed June 3, 2019).

8 Ahmed S, Li Q, Liu L, Tsui AO. Maternal deaths averted by contraceptive use: an analysis of 172 countries. *Lancet* 2012; **380:** 111–25.

9 Rodriguez M, Reeves M, Caughey A. Evaluating the competing risks of HIV acquisition and maternal mortality in Africa: a decision analysis. *BJOG* 2012; **119:** 1067–73.

10 UN Women. Turning promises into action: gender equality in the 2030 agenda for sustainable development. http://www.unwomen.org/-/media/headquarters/attachments/sections/library/publications/2018/sdg-report-gender-equality-in-the-2030-agenda-for-sustainable-development-2018-en.pdf (accessed June 3, 2019).

11 UN. The Sustainable Development Goals Report 2018. New York, NY: United Nations, 2018.