

CONTACT: Lisa Rossi  
+1-412-916-3315 (mobile)  
rossil@upmc.edu

**FOR IMMEDIATE RELEASE**

**First Comparison Between Injectable Contraceptives DMPA and NET-EN Suggests Some Women Using DMPA Were at Higher Risk of Acquiring HIV**

*Planned analysis of data from HIV prevention trial VOICE involved more than 3,000 women in South Africa*

**BOSTON, March 4, 2014** – Women who used an injectable contraceptive called DMPA were more likely to acquire HIV than women using a similar product called NET-EN, according to a secondary analysis of data from a large HIV prevention trial called [VOICE](#), researchers from the National Institutes of Health-funded [Microbicide Trials Network](#) (MTN) reported today at the 21<sup>st</sup> [Conference on Retroviruses and Opportunistic Infections](#) (CROI) in Boston.

An unexpected finding in the study was that the combination of being positive for herpes simplex virus type 2 (HSV-2) and using DMPA for contraception was associated with a higher risk of HIV compared to women using NET-EN and who were also HSV-2 positive. Among HSV-2 negative women, however, there was no difference in HIV risk between those using DMPA and those using NET-EN. HSV-2, the most common form of genital herpes, is prevalent among sexually active adults worldwide but particularly widespread in sub-Saharan Africa and also thought to play a role in that region's high rates of HIV. Nearly half of all women in VOICE tested positive for HSV-2 at enrollment.

“It’s very important to acknowledge that this was an observational study. Women weren’t randomized to contraceptive methods, so it’s possible that behavioral or other factors were responsible for what we saw in this analysis. While we saw more HIV infections in this particular group of women in VOICE, this subgroup was small and the finding needs to be taken within a much larger context of research on the impact of contraception on women’s health,” said Lisa Noguchi, C.N.M., M.S.N., who is MTN’s scientific director for pregnancy research and led the current study.

MTN researchers conducted the analysis to investigate the relationship between injectable contraceptives and the risk of acquiring HIV. While some studies have suggested women who use DMPA are at increased risk of HIV compared to those not using a hormonal method, a number of other studies have shown no association. Few studies have separately examined the impact of NET-EN on HIV risk. The new analysis of VOICE data is the first head-to-head observational study to directly compare differences in HIV risk between users of DMPA and NET-EN.

DMPA, or depot medroxyprogesterone acetate, and NET-EN, short for norethisterone enanthate, are progestin-only hormonal contraceptives. DMPA (widely known by its marketed name Depo-Provera<sup>®</sup>) is administered every three months, while NET-EN (or Noristerat<sup>®</sup>) is given every two months. Both types of injectable contraception are highly effective for the prevention of pregnancy and typically more effective than oral contraceptive pills.

VOICE – Vaginal and Oral Interventions to Control the Epidemic – was designed to test the safety and effectiveness of different antiretroviral (ARV) approaches for preventing HIV in women. It was conducted between 2009 and 2012 among 5,029 women from 15 sites in South Africa, Uganda and Zimbabwe. In this planned secondary analysis of HIV risk, MTN researchers focused only on the women enrolled at VOICE’s 11 sites in South Africa, where both injectable contraceptives are popular methods of birth control.

The primary results of VOICE, which were reported at last year's CROI meeting, found none of the products tested (tenofovir tablets, Truvada<sup>®</sup> tablets and tenofovir gel) was effective in preventing HIV and that most participants had not used their assigned product daily as recommended. Younger, unmarried women were least likely to use study product, and were also most likely to acquire HIV, with HIV incidence in this group approaching 10 percent at some study sites in South Africa, a rate considerably higher than expected. The overall HIV incidence, which reflects the number of women who become newly infected for every 100 participants in a given year, was 5.7 percent overall, double what had been anticipated.

As with any HIV prevention trial testing an unproven biomedical intervention, VOICE enrolled only women willing to use effective contraception throughout their participation. In this context, the secondary analysis of data offers new insight about the role of injectable contraceptives and other factors that may have placed women at particular HIV risk.

Among the 4,077 women enrolled in VOICE in South Africa, 3,163 (78 percent) who used an injectable method were included in the analysis, with 2,055 (65 percent) of those who ever used DMPA and 1,363 (43 percent) who ever used NET-EN (a small percentage used both methods at different times). With 204 women acquiring HIV across both groups, the HIV incidence for women using either injectable contraceptive was 7.1 percent. Yet, compared to NET-EN, HIV risk was significantly higher among users of DMPA – 8 percent incidence versus 5.4 – with 150 HIV infections in women using DMPA and 54 in women using NET-EN.

Compared to NET-EN users, DMPA users tended to be slightly older, less likely to report having multiple partners (or that their partner had multiple partners) and to also be HSV-2 positive. In fact, when the researchers took into account whether or not women were HSV-2 positive, the difference was two-fold. Among 1,032 HSV-2 positive women having ever used DMPA, 95 acquired HIV, an incidence rate of 10 percent. In contrast, the HIV incidence was 5 percent among the 537 HSV-2 positive NET-EN users, in whom 20 acquired HIV during VOICE. However, among those women who were HSV-2 negative, DMPA and NET-EN users did not differ significantly in their risk of acquiring HIV during the study.

“One of the reasons we undertook this analysis was to help provide context to questions about injectable contraception and HIV acquisition. Unfortunately, many African women live in areas where there is not only high HIV incidence but also high rates of maternal mortality. Using effective contraception can be a life-saving choice, so comparing family planning methods to each other, rather than nothing at all, is worthwhile. Meeting the health needs of women in this region means ensuring that women can access a variety of safe and effective methods to prevent pregnancy and to protect against HIV,” said Ms. Noguchi.

The [World Health Organization](#) (WHO) recommends that women using progestin-only injectable contraception be strongly advised to always use condoms. At the same time, the WHO makes clear the need to both expand the contraceptive method mix and engage in more research on the relationship between hormonal contraception and HIV.

In recent years, the MTN has taken to diversifying the range of effective contraceptive methods available to study participants. In May 2012, the MTN formed the Contraception Action Team to help site staff gain the necessary training for providing a variety of methods, including the copper intrauterine device (IUD) and implants, directly at the clinic. The momentum had already begun when in July 2012 the MTN launched [ASPIRE](#), a Phase III trial of the dapivirine ring. Of the more than 2,100 women from Malawi, South Africa, Uganda and Zimbabwe who have enrolled to date, fewer than half are using an injectable contraceptive, whereas in VOICE, 71 percent of women chose this method. And while oral hormonal contraception was the choice of 22 percent of women in VOICE, only 8 percent of ASPIRE participants are choosing to use the pill, typically a less effective method than the IUD, implants or injectables. Most notable has been the uptake of the IUD. During VOICE, only eight participants (less than 1 percent) of the 5,029 women used an IUD, while more than 22 percent of ASPIRE participants have chosen to use an IUD for contraception. Other long-acting contraceptives such as hormonal implants were used by only 5 percent of VOICE participants; in ASPIRE, the use of these methods has tripled.

“What our trial sites have accomplished is nothing short of amazing. They have broken down a barrier of sorts, by providing women with the contraceptive choices they deserve and enhancing the capacity of their staff in the delivery of a broader range of reproductive health services. With so many women choosing IUDs, and implants in our study, we’ll also be able to collect data that may help in understanding the potential impact of a range of contraceptive methods on HIV risk,” noted Sharon Hillier, Ph.D., of the University of Pittsburgh School of Medicine, who is co-principal investigator of the MTN and a driving force behind the formation of MTN’s Contraception Action Team.

In addition to Ms. Noguchi, other authors of the study presented at CROI are Barbra Richardson, Ph.D. (University of Washington); Zvavahera Mike Chirenje, M.D. (University of Zimbabwe); Gita Ramjee, Ph.D. (Medical Research Council of South Africa); Gonasagrie Nair, M.B.Ch.B. (Centre for the AIDS Programme Research in South Africa); Thesla Palanee, Ph.D. (Wits Reproductive Health and HIV Institute); Pearl Selepe, M.B.Ch.B. (Aurum Institute); Ravindre Panchia, MBBCh (Perinatal HIV Research Unit, University of the Witwatersrand); Kaila Gomez, M.P.M. (FHI 360); and Jeanne Marrazzo, M.D., M.P.H. (University of Washington).

###

This work was supported funded by the U.S. National Institutes of Health grants UM1AI068633, UM1AI068615, UM1AI106707. Additional support was provided by the Johns Hopkins Training Program in Sexually Transmitted Infections (T32AI050056), the Mary B. Meyer Award and the Ruth Freeman Memorial Award.

#### About VOICE

*VOICE, also known as MTN-003, is a flagship study of the Microbicide Trials Network. The study began September 2009 and completed follow-up of all participants in August 2012. VOICE was led by Zvavahera Mike Chirenje, M.D., from the University of Zimbabwe in Harare; and Jeanne Marrazzo, M.D., M.P.H., from the University of Washington in Seattle. The study products were provided by Gilead Sciences, Inc., of Foster City, Calif., and by CONRAD, of Arlington, Va. Viread (oral tenofovir) and Truvada are registered trademarks of Gilead Sciences. In 2006, Gilead assigned a royalty-free license for tenofovir gel to CONRAD and the International Partnership for Microbicides of Silver Spring, Md. More information about VOICE and related sub-studies can be found at <http://www.mtnstopshiv.org/news/studies/mtn003>*

#### About the MTN

*The Microbicide Trials Network (MTN) is an HIV/AIDS clinical trials network established in 2006 by the National Institute of Allergy and Infectious Diseases with co-funding from the Eunice Kennedy Shriver National Institute of Child Health and Human Development and the National Institute of Mental Health, all components of the U.S. National Institutes of Health. Based at Magee-Womens Research Institute and the University of Pittsburgh, the MTN brings together international investigators and community and industry partners whose work is focused on the development and rigorous evaluation of promising microbicides – products applied inside the vagina or rectum that are intended to prevent the sexual transmission of HIV – from the earliest phases of clinical study to large-scale trials that support potential licensure of these products for widespread use. More information about the MTN is available at <http://www.mtnstopshiv.org/>*

4-March-2014