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10,000-plus medical charts provides comparator for HIV prevention study in pregnant women
Records review conducted in four African countries published in PLOS ONE will help determine safety of PrEP and dapivirine ring in DELIVER; includes data seldom collected in these countries

PITTSBURGH --31 March 2021 – A detailed examination of more than 10,000 medical records at maternity clinics and hospitals in urban Malawi, South Africa, Uganda and Zimbabwe has yielded important insight about pregnancy and neonatal outcomes in these communities as well as the frequency with which different complications occur. The findings, which were published in [PLOS ONE](#), include data not often available or reported in much of eastern and southern Africa.

The medical chart review was undertaken by researchers from the National Institutes of Health-funded Microbicide Trials Network (MTN) in preparation for the [DELIVER](#) (MTN-042) study, now underway, that is evaluating the safety of two HIV prevention methods in pregnant women– a daily antiretroviral pill called Truvada[®], an approach known as oral PrEP (short for pre-exposure prophylaxis) and the monthly [dapivirine vaginal ring](#).

Though most pregnancies are “uneventful,” pregnancy is not without risks, and, as such, it is expected that there will be participants in DELIVER who experience complications, some of which may be serious. Because there is no placebo group in DELIVER– all women will use an active product – researchers needed a frame of reference for determining whether the particular complications or adverse events observed among women in the study are occurring with similar frequency to what would be expected for women in that region generally, or occurring more often, which would suggest the use of either PrEP or the dapivirine ring as the reason.

The medical chart review was conducted over a period of approximately eight weeks at nine healthcare facilities – the same hospitals and clinics where participants enrolling in DELIVER would be giving birth –in Blantyre, Malawi; Kampala, Uganda; Johannesburg, South Africa; and in Harare and nearby Chitungwiza, Zimbabwe.

Researchers confined their review to records of women who had delivered within the previous seven days, taking note of the pregnancy outcome (whether it was a full-term live birth, premature birth or stillborn), the method of delivery (vaginal or Cesarean) and the infant’s birth weight. Also documented was whether the record included a diagnosis for any of the complications to be monitored in DELIVER. Many of these are complications of the type not routinely monitored by national programs or included in comprehensive surveillance-like studies in these settings. As such, the data collected through the medical chart review fills important gaps in information regarding the prevalence of these complications at the local level, in particular, complications associated with high blood pressure, or so-called hypertensive disorders of pregnancy (gestational hypertension, eclampsia and preeclampsia); postpartum endometritis, an infection in the uterus that develops after childbirth; chorioamnionitis, an infection in the uterus affecting the amniotic sac or its membranes; and postpartum hemorrhage, or excessive bleeding after childbirth.

While national data exists for pregnancy outcomes generally, some of the findings from the chart review suggest these may not necessarily reflect what is happening at the local level. At some sites, for example, rates of premature births and stillbirths were found to be higher than what would be expected according to the national data.

“We now have a good idea of background rates for the specific pregnancy complications and outcomes that we are monitoring in DELIVER, and, importantly, in the very same communities where the study is being conducted, which will be extremely useful in our evaluation of the safety of the ring and PrEP during pregnancy. We hope this data can also be of benefit to local health authorities and other research groups who are evaluating novel interventions during pregnancy” said Jennifer Balkus, Ph.D., M.P.H., assistant professor, department of epidemiology, University of Washington in Seattle, and the paper’s lead author.

The chart review, which was designed and conducted as a sub-study of DELIVER (and called MTN-042B), was approved by local ethics committees responsible for research oversight. Each of the research sites also obtained the permission of the participating hospitals and clinics to access medical records. In total, 10,138 medical records were examined. Research teams had no interaction with patients or the clinical staff caring for them.

MTN-042B began in August 2019 and was completed in March 2020, just one month after the first site started enrolling participants into the DELIVER study. To date, more than 140 participants have been enrolled.

DELIVER is being conducted in a step-wise, backward fashion, enrolling one group of women at a time, beginning with 150 women who are late in pregnancy (36-37 weeks, or about 8-9 months pregnant) when it is believed use of PrEP or the ring would pose the least risk. Interim reviews of study data by an independent panel of experts will take place after each group to determine whether it is safe to proceed to the next phase, using as a basis of comparison the background rates of complications and outcomes provided through the medical records review as well as an extensive review of published reports and scientific literature for studies taking place in Malawi, South Africa, Uganda and Zimbabwe within the past 20 years.

The first of these interim reviews is expected to take place in the coming months, after the last participant in group one has given birth.

DELIVER will provide the kind of information that national programs, health care providers and women themselves need to make informed decisions about whether to use Truvada as PrEP or the dapivirine ring during pregnancy, when a women’s chances of acquiring HIV are up to three times greater than at any other time during their lives.

Both products have been found to be well tolerated and to reduce the risk of HIV in clinical trials involving nonpregnant women. PrEP is approved in several countries, and data thus far suggests it is safe to use during pregnancy, though more information about its safety is needed. The monthly dapivirine ring is a new HIV prevention method, which last year received a positive opinion from the European Medicines Agency for its use among cisgender women ages 18 and older in developing countries, and soon after, was added to the World Health Organization (WHO) list of pre-qualified medicines. In addition, WHO’s updated guidelines for HIV prevention, published in March 2021, recommend the ring as an additional HIV prevention choice for women at substantial risk of HIV. IPM is seeking approval of the ring in eastern and southern Africa, with the first of these decisions possibly by mid-year. IPM is also seeking regulatory approval from the US Food and Drug Administration. Compared with Truvada, much less is known about the ring’s safety during pregnancy.

The clinical research sites (CRSs) conducting DELIVER also conducted the medical chart reviews for the MTN-042B sub-study. These are the College of Medicine-Johns Hopkins University Research Project in Blantyre, Malawi; Makerere University-Johns Hopkins University (MU-JHU) Research Collaboration in Kampala, Uganda; Wits Reproductive Health and HIV Institute (Wits RHI) Shandukani Research Centre in Johannesburg, South Africa; and the University of Zimbabwe Clinical Trials Research Centre (UZ-CTRC) Zengeza CRS in Harare. A similar study involving breastfeeding mothers and their babies, called [B-PROTECTED](#) (MTN-043), is also being conducted at these sites.

In addition to Dr. Balkus, other authors of the PLOS ONE paper include DELIVER protocol chairs Bonus Makanani (College of Medicine-Johns Hopkins Research Project, Blantyre, Malawi) and Katherine E. Bunge

(University of Pittsburgh); and protocol co-chair, Lee Fairlie (Wits RHI, University of the Witwatersrand, South Africa); as well as Nyaradzo Mgodzi and Felix Mhlanga (UZ-CTRC, Harare, Zimbabwe); Clemensia Nakabiito (MU-JHU, , Kampala, Uganda); Ashley Mayo (FHI 360); Moni Neradilek and Tanya Harrell (Vaccine and Infectious Diseases Division, Fred Hutchinson Cancer Research Center, Seattle); and Jeanna Piper (National Institute of Allergy and Infectious Diseases, Division of AIDS).

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Summary of MTN-042B results

MTN-042B involved a review of medical charts for women who delivered within the last seven days and was conducted over a period of approximately eight weeks at nine facilities in Blantyre, Malawi; Johannesburg, South Africa; Kampala, Uganda; and Harare and Chitungwiza, Zimbabwe. Full results are published in PLOS ONE and available here: <https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0248423>. The following is a summary of some of the key findings:

- Of the 10,138 medical records examined, 13.6 percent included a diagnosis of HIV. Overall, most pregnancies (97 percent) resulted in single births, and 73 percent were vaginal deliveries
- Most pregnancies (81 percent) resulted in the birth of a full-term baby; 13 percent of infants were born prematurely (before 37 weeks gestation) and 4.1 percent were stillborn, with rates that ranged from 3.1 to 5.5 percent across the four sites – all higher than the national stillborn birth rates for each country of about 2 percent. Likewise, while the lowest pre-term birth rate was in Kampala at 10.7 percent, and the highest was in Johannesburg, at 21.6 percent – both are rates that are higher than the 6.6 and 12.4 percent national estimates for Uganda and South Africa, respectively.
- Of the 9,767 live births (both full and pre-term births), 15.5 percent (1,539) were infants of low birthweight, weighing 2500 grams or less. Two percent of infants (192) died within seven days after birth.
- Gestational hypertension – a form of high blood pressure that develops later in pregnancy – was the most common pregnancy complication, which was noted in 4.4 percent of the charts reviewed, though rates varied by site. The lowest prevalence was seen in Kampala, Uganda (about 1 percent) and the highest prevalence was in Chitungwiza and Harare, Zimbabwe (9.3 percent). Preeclampsia and eclampsia, which are more serious hypertension-related complications, occurred in 4.3 percent and 0.6 percent of pregnancies, respectively. The second most common pregnancy complication was postpartum hemorrhage, reported in 3.2 percent of pregnancies. Other complications of interest to the research team – unexplained fever, chorioamnionitis and postpartum endometritis – each were reported in less than 1 percent of records.
- There were seven instances of maternal death, all of which occurred in Blantyre, accounting for less than 1 percent of pregnancies.

More information about DELIVER (MTN-042) and the MTN-042B sub-study are at <https://mtnstopshiv.org/news/studies/mtn042>; <https://mtnstopshiv.org/research/studies/mtn-042> and <https://mtnstopshiv.org/research/studies/mtn-042b> or click [here](#) to watch a short video. For more information about the dapivirine ring go to www.ipmglobal.org.

The MTN is supported by U.S. National Institutes of Health grants UM1AI068633, UM1AI068615 and UM1AI106707.

About the Microbicide Trials Network

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 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 www.mtnstopshiv.org/.

31-March-2021