THERAPEUTIC ADVANCES in
Infectious Disease

Original Research

Exploring pregnant women's experiences with dapivirine vaginal ring insertion during the MTN-042/DELIVER study in Uganda: a description of secondary data

Ther Adv Infect Dis

2025, Vol. 12: 1–9

DOI: 10.1177/20499361251332750

Joselyne Nansimbe, Brenda Gati Mirembe, Phionah Kibalama Ssemambo, Annette Miwanda Ssekasi, Rose Byogero, Justine Nalwoga and Clemensia Nakabiito

Abstract

Background: Involving pregnant women in HIV prevention trials is key to ensuring that they benefit from efficacious products. MTN-042/DELIVER was a phase IIIb, open-label, multi-site, randomized safety study, the first of its kind to enroll HIV-negative pregnant women into a prevention trial using oral Truvada® once daily and the Dapivirine Vaginal Ring (DVR) every month. There is limited data on pregnant women's experiences with ring insertion, which we explored.

Objectives: To explore the experiences of pregnant women with DVR insertion during the MTN-042/DELIVER study at MU-JHU Care Limited in Kampala, Uganda.

Design: A description of secondary data from the MTN-042/DELIVER study.

Methods: Participant randomization was to either *DVR* or *Truvada* in varying ratios into three successive cohorts (based on gestational age). Ring self-insertion was required at enrolment and every 4 weeks until delivery. Pre-insertion counselling and supervised ring placement assessment were done. Enrollment data were collected to include counselling sessions, insertion tactics, ring self-insertion scores (Very difficult: 3+ attempts and/or pain, severe discomfort, Difficult: 2 attempts and/or moderate discomfort, Easy: 1 attempt with some ring repositioning and/or mild discomfort, Very easy: Smooth insertion and positioning in one attempt with no discomfort), assistance during insertion, encountered challenges and ring expulsion during use.

Results: Out of 154 participants, 73% were randomized to the ring. At enrolment, all participants attempted self-insertion. Only one participant required additional counselling. The squatting position was uniformly favoured. Across all cohorts, 95% of participants had easy/very easy ring self-insertion. Five percent had difficult ring self-insertion, with some variations across cohorts. Challenges included difficulty in folding, gripping, inserting the ring far enough, requiring multiple attempts and reluctance to insert it. No expulsions during ring use were reported.

Conclusion: Most pregnant women managed to insert the Ring themselves. However, participants above 36 weeks required more help with ring insertion compared to others. This suggests that it may be beneficial to encourage pregnant women to start using this HIV prevention method early in pregnancy, to minimize potential initial insertion challenges in late pregnancy.

Trial registration: The primary study, MTN-042/DELIVER is registered as ID NCT03965923 at https://www.ClinicalTrials.gov.

Keywords: dapivirine vaginal ring insertion, HIV prevention, Kampala, MTN-042 study, pregnant women, Uganda

Received: 16 September 2024; revised manuscript accepted: 20 March 2025.

Correspondence to:
Joselyne Nansimbe
Makerere University–John Hopkins University Research Collaboration, Upper Mulago Hill Road, P.O. Box 23491, Kampala, Central 256, Uganda
jnansimbe5@gmail.com; jnansimbe@mujhu.org

Brenda Gati Mirembe
Phionah Kibalama Ssemambo
Annette Miwanda Ssekasi
Rose Byogero
Justine Nalwoga
Clemensia Nakabiito
Makerere University–John Hopkins University Research Collaboration, Kampala, Central, Uganda

Introduction

The HIV pandemic continues to pose a major public health challenge, particularly in sub-Saharan Africa, where reproductive-age women are disproportionately impacted by HIV-1, comprising 56% of adults living with the virus in sub-Saharan Africa.[1] Globally, 44% of all newly acquired HIV infections were among females and girls of all ages in 2023. In sub-Saharan Africa, women and girls of all ages accounted for 62% of all new HIV infections.[2] AIDS-related illnesses remain the second leading cause of death for young women aged 15–24 years in Africa.[1] These data clearly show that women of child-bearing potential living in sub-Saharan Africa are at high risk of HIV acquisition.

The biological as well as behaviour changes during and after pregnancy may further increase a woman's risk for HIV. This, in turn, poses a risk of vertical transmission of HIV to the unborn child. Pregnancy produces a two-fold increased risk for HIV acquisition,[3] a recent analysis found that the per-sexual act probability of acquiring HIV increased steadily during pregnancy and within 6 weeks following delivery.[4,5]

While pregnant women are among those most in need of safe and effective HIV prevention and treatment, research during pregnancy has been limited. Prior clinical trials of antiretroviral (ARV) drug use during pregnancy have primarily focused on treatment and/or prevention of vertical transmission of HIV in women known to have acquired HIV.[6] However, unintended pregnancy is common, at approximately 40% globally, which calls for a great need for HIV prevention technology during pregnancy.[7]

Reported rates of vertical transmission of HIV range from 15% to over 45% in the absence of any initiative and vary across countries. This transmission may occur during pregnancy, labour, delivery or breastfeeding.[8] Almost half of new infections among children were due to their mothers not receiving ARV therapy during pregnancy or breastfeeding and 21% were due to mothers seroconverting during pregnancy or breastfeeding.[9] This underscores the urgent need for HIV prevention technology during these critical stages in the lifetime of women.

MTN-042/DELIVER study was one of the first HIV prevention trials among pregnant women aimed at providing critically needed evidence about safely using the Dapivirine Vaginal Ring (DVR) and pre-exposure prophylaxis (PrEP) taken orally while pregnant.[10]

Prior to MTN-042, other HIV prevention studies were conducted among non-gravid women who tested negative for HIV. The HOPE and ASPIRE studies, for example, were two clinical trials that were phase III in nature. They showed that using a 25 mg monthly DVR was well tolerated and efficacious compared to placebo, reducing HIV-1 incidence by approximately 30% compared with placebo. The high uptake and adherence to the DVR throughout the studies suggested potential for acceptability and practicability of this option for HIV prevention among African women.[11]

Pregnant participants in a qualitative study on the acceptability of the DVR and Daily Oral PrEP recognized that consistent and correct use of the DVR provided protection for them and their unborn children.[12]

DVR, a novel HIV prevention method, offers women a discreet and self-administered option for reducing their risk of HIV infection.[13] However, the introduction of any new biomedical initiative must be accompanied by an understanding of user experiences, particularly in populations with specific physiological needs, such as pregnant women. Although there is acceptability data on the use of the DVR in non-pregnant women,[14–16] there is limited data on its acceptability and usability among pregnant women, particularly regarding their experiences with self-insertion.

As part of the MTN-042 study, this assessment aimed at addressing this gap by exploring pregnant women's experiences with DVR insertion. It provided crucial insights into how pregnant women interact with the DVR, including the ease of self-insertion, the effectiveness of pre-insertion counselling and the challenges faced during the insertion process.

The results offer important implications for the timing of initiation and support strategies for DVR use among pregnant women. Understanding these experiences is vital for optimizing the use of the DVR as a key HIV prevention method in this vulnerable population.

Methods

Study design, setting and population

Data extraction was done from the MTN-042/DELIVER study, a phase IIIb, open-label, multisite, randomized safety clinical trial for the use of DVR and Truvada® during pregnancy. Study sites were Uganda, Zimbabwe, Malawi and South Africa. The MTN-042 study was conducted between February 2020 and May 2024.

Potential participants for the MTN-042/DELIVER study were identified via:

1. The antenatal clinics through the facility-based contact persons.
2. The community through contact persons, Community Advisory Board (CAB) members and Village Health Teams (VHTs) who are most influential in the community.
3. Snowballing through former MTN-043 participants (a sister study on HIV prevention among breastfeeding women) for Cohorts 1–3, and already enrolled MTN-042 participants for Cohorts 2–3.

Recruitment strategies were:

1. Intensive engagement of community (CAB members, VHTs and community influencers) and health-based contact persons.
2. Community educators reported at the ANC site by 7.00 am to receive referred mothers and also to sensitize them.
3. Priority was given to male partners who accompanied their wives to receive study information.
4. Providers of scan services in the community referred presumptively eligible pregnant women.
5. Former MTN 042/MTN 043 participants referred potential participants.
6. The MTN-042/DELIVER and MTN-043/B-PROTECTED HIV prevention study video was viewed during sensitization.
7. Reference to the gestational age table/calendar showing gestation weeks enabled the team not to miss any identified potential mothers.

The overall study population comprised healthy, HIV-uninfected pregnant females, 18–40 (inclusive) years old, with an uncomplicated singleton pregnancy who were willing to be randomized to study product, and their infants.

Infants were prospectively selected for inclusion in the MTN-042 study when their mothers were enrolled. They entered the study when they were born and were followed up to 1 year of age. During follow-up, they were evaluated for adverse events and drug levels associated with study product exposure during pregnancy.

Potential participants were identified during their routine antenatal care visits at the study-specified health facilities. Following pre-screening activities, potential participants were referred to the study site for possible screening. Upon fulfilment of eligibility criteria, participants were randomized in a stepwise fashion into three successive cohorts based on their weeks of amenorrhoea as follows: Cohort 1: 36–37 weeks, Cohort 2: 30–35 weeks and Cohort 3: 12–29 weeks.

Randomization was in varying ratios of 2:1 for Cohorts 1 and 2, and 4:1 for Cohort 3, onto the DVR and oral Truvada respectively. One group was enrolled at a time, beginning with women late in pregnancy, when the potential risks from drug exposure are lowest, and only proceeding to the next group if an independent review of study data deemed it was safe to do so. In total, 558 participants were enrolled across all three cohorts.

The DVR-004 is an off-white matrix ring, containing 25 mg of DPV dispersed in a platinum-catalysed silicone elastomer. The DPV molecule was originally developed as an oral ARV agent by Janssen Sciences Ireland UC, which conducted the early, non-clinical and clinical development. DPV, also known as TMC-120, a substituted diaminopyrimidine derivative, is a tight binding nonnucleoside reverse transcriptase inhibitor with potent antiviral activity against HIV-1.[17]

Following randomization to the DVR, the clinician made a request to the Pharmacy through a prescription note for the DVR to be dispensed. This request was delivered to the Pharmacy through the runner. Upon receipt of a correctly completed and signed prescription or product request slip, the Pharmacist of Record prepared the requested study product as documented on the prescription or request slip. He then dispensed the study product, and the runner transported it

to the clinic in a cooler box. Acknowledgement of receipt was done by the clinician accordingly.

Following adherence counselling with the study counsellor, the participant was then sent to the clinician, who assessed the participant's understanding of DVR use as well as readiness to insert it.

The participant was then guided on DVR insertion procedures by the clinician, which included: washing hands prior to touching it, positioning during insertion and confirmation that the ring was rightly placed. This was followed by DVR self-insertion under supervision.

Assessment of correct insertion was done by the clinician and closing instructions were given, which included: Avoiding vaginal douching and use of any vaginal medications, and not removing the DVR except in cases where labour is confirmed. They were further instructed to immediately contact the study staff in case of any accidental DVR expulsions, for timely replacement.

Further to this, they were supplied with ziplock bags for storing the DVR where applicable and have it returned to the clinic at the earliest opportunity.

The used DVRs were stored during the study and periodically shipped for measurement of drug level concentrations, which served as an indicator for participants' adherence to the study product.

For our assessment, we considered only the Ugandan site, MU-JHU Care Limited in Kampala, which had a total of 154 participants across all Cohorts, of which 112 were randomized to the DVR.

Study procedures

Upon randomization, DVR self-insertion was a requirement at enrollment and every 4 weeks until delivery. The study product was discontinued upon delivery. Pre-insertion counselling and supervised ring placement assessment were done.

We collected data from Enrollment visits of all participants who were randomized to the DVR from several sources, including Chart notes, Counselling notes forms and Electronic Case report forms for DVR insertion and removal.

We summarized the data per Cohort in Microsoft Excel to include counselling sessions, insertion tactics, ring self-insertion scores, assistance during insertion, encountered challenges and ring expulsion during use.

The Ring insertion scores were as follows: *Very difficult*: 3+ attempts and/or pain, severe discomfort, *Difficult*: 2 attempts and/or moderate discomfort, *Easy*: 1 attempt with some ring repositioning and/or mild discomfort, *Very easy*: Smooth insertion and positioning in one attempt with no discomfort.

Statistical analysis

We analysed the data to compare DVR self-insertion experiences across the different cohorts. This included calculating the percentages of participants in each self-insertion score category (Very Easy, Easy, Difficult, Very Difficult) within each cohort, using the total number of DVR users in each Cohort as the denominator.

We also computed the overall percentage of participants for each score as a proportion of the total number of DVR users.

We summarized the number of pre-counselling sessions that were required for each participant prior to DVR self-insertion at enrollment, DVR insertion tactics, including position and any DVR expulsions.

We also summarized the challenges faced by DVR users during self-insertion in general.

Ethical considerations

MTN-042/DELIVER Study was approved by the Joint Clinical Research Center Institutional Review Board (JCRCIRB), Uganda National Council for Science and Technology (UNCST), Johns Hopkins School of Medicine Institutional Review Board (JHMIRB) and National Drug Authority (NDA) prior to implementation.

The Primary Institutional Review Board, JCRC IRB assigned the MTN 042/DELIVER study approval number *JC1719*, UNCST, *HS 2699* and NDA, *CTA-0121*.

All the study participants gave their written informed consent prior to any involvement in study activities.

Table 1. DVR insertion scores by cohort.

Study participants	Cohort 1	Cohort 2	Cohort 3	Total
Eligible gestational age at enrolment	36–37 weeks 44 (100%)	30–35 weeks 42 (100%)	12–29 weeks 68 (100%)	All Cohorts 154 (100%)
No. ring users	29 (65.9%)	28 (66.7%)	55 (81%)	112 (73%)
Self-insertion score,* *N* (%)				
Very easy	2 (7%)	18 (64%)	13(24%)	33 (30%)
Easy	23 (79.3%)	10 (35.7%)	40 (72.7%)	73 (65%)
Difficult	4 (13.8%)	0 (0%)	2 (3.6%)	6 (5%)
Very difficult	0 (0%)	0 (0%)	0 (0%)	0 (0%)

*Among ring users. Question was: *How easy or hard is it for you to insert the Dapivirine Vaginal Ring?*

Permission to do this assessment was granted by the Microbicides Trials Network (MTN), the Sponsors of the MTN-042/DELIVER study. A description of the main study, MTN-042, is available on https://www.ClinicalTrials.gov, as required US law.

The reporting of this article conforms to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement.[18]

Results

Out of 154 participants enrolled at the MU-JHU site, 112 (73%) were randomized to the ring (29 in Cohort 1, 28 in Cohort 2 and 55 in Cohort 3; see Table 1). We extracted enrollment data for all the participants on the DVR. No data was found to be missing.

DVR self-insertion

At enrollment, all participants (100%) attempted self-insertion, none of the women randomized to the DVR refused to use it.

Pre-insertion counselling

All the participants underwent pre-insertion counselling, and out of these, only one participant (0.89%) required additional counselling. This participant had not fully understood the instructions on proper usage of the DVR. This was noted at the point of supervised DVR insertion. Upon additional counselling on the usage of the DVR, she managed to self-insert it.

The rest (99.91%) had a single pre-insertion counselling session at enrollment before DVR self-insertion. These sessions included issues of disclosure to the partner where applicable, study procedures, adherence counselling and HIV risk reduction counselling.

DVR insertion position

The squatting position was uniformly favoured by all participants in the three cohorts. The other two, that is, standing with one leg raised and lying down positions, were not popular among the participants.

DVR insertion scores

Across all the cohorts, 95% of participants had easy/very easy ring self-insertion. Five percent had difficult ring self-insertion, with some variations across cohorts. Participants in Cohort 1 experienced more difficulty with DVR self-insertion compared to those in Cohort 2 and Cohort 3 (see Table 1).

DVR insertion challenges

Challenges included difficulty in folding, gripping, inserting the ring far enough, requiring multiple attempts and reluctance to insert it.

DVR expulsions

No expulsions during ring use were reported. Participants reported no DVR removal between visits. They had supervised removal during their scheduled study visits.

Discussion

There is still limited research and data on DVR insertion experiences of study participants involved in HIV prevention trials, more so pregnant women who were only recently included in clinical trials. This assessment was set out to explore pregnant women's experiences with DVR self-insertion during the MTN-042/ DELIVER study at MU-JHU in Kampala, Uganda.

For our study, pre-insertion counselling sessions were held at every visit until delivery. This not only built the confidence of the participants at every DVR insertion session but also boosted their adherence to the study product. The fact that no participants declined self-insertion suggests that with adequate counselling and support, pregnant women are willing and able to engage with this HIV prevention method.

As observed in our study, individual education and counselling at enrollment and throughout study participation were found to build confidence for self-insertion and strengthened adherence in one of the DVR studies involving non-pregnant women.[14] The sessions which included site-specific group activities, such as social gatherings, on-site lab visits or male partner meetings, motivated adherence and created opportunities to address women's concerns about the DVR or study procedures while promoting correct use.[14]

The squatting position was uniformly favoured by all participants in the three cohorts. This suggests that pregnant women, regardless of gestational age, may find this position the most comfortable and effective for self-insertion. This preference for squatting could be important for informing future counselling and instructional materials for pregnant women considering DVR use. No studies have been done yet to explore positioning during DVR insertion in pregnancy, yet this data is vital for guiding pregnant women on DVR insertion at various stages of their pregnancy.

Across all the cohorts, 95% of participants had easy/very easy DVR self-insertion. This was higher than in another African study, where 81% of participants successfully inserted the DVR on the first attempt at the clinic. Most women were comfortable using the DVR, and very few ($\leqslant$2%) reported feeling it during daily activities or experiencing any physical or emotional issues related to it.[19]

From our assessment, the challenges faced during DVR insertion included difficulty in folding, gripping, inserting the ring far enough, requiring multiple attempts and reluctance to insert it. Despite these challenges, participants inserted the DVR themselves with support from study staff, participants gradually became familiar with using the DVR as the trial progressed. Similar studies found that staff and peer support helped participants find the DVR easy to use and integrate into their daily lives.[20]

In this study, there were no DVR expulsions during use, unlike the ASPIRE study where participants simultaneously described frequent reasons for removing it, such as for sex or menses.[21] In another clinical trial in several sub-Saharan African countries, the DVR was easy to use, with low rates of expulsions and removals. Expulsions were more common during the early stages of use, often happening during urination or defecation. Over time, expulsions became less frequent, but ring removals increased. The most common reason for removing the ring was to sterilize it, despite advice from research staff not to do so.[22]

In a DVR study in South Africa and Uganda, participants experienced both accidental expulsions and intentional removals of the DVR. However, intentional removals were more common, emphasizing the need for adherence counselling.[23] Some participants reported removing the DVR intentionally, with some doing it repeatedly and others only once, similar to findings in other studies.[24]

Various factors influencing intentional DVR removal have been noted in other studies.[25] These include discomfort, removing the ring to sterilize it, during bathing, or because of menstruation,[23] which were all not the case for our assessment.

The differences between our study and the rest could be due to the variation in the pre-insertion counselling approach. Furthermore, the MTN-042 study participants were pregnant. Since pregnancy is a time when the risk of getting HIV is higher,[3] our participants could have been more cautious and feared to remove the DVR. In addition, the absence of menses among our study participants could have contributed to retention of the DVR throughout the study.

Study strengths and limitations

Our study utilized data from a rigorous phase IIIb, open-label, multi-site, randomized safety study, which ensured high-quality data through its robust methodology.

We collected data from multiple sources, including chart notes, counselling notes and electronic case report forms for DVR insertion. This provided us with a comprehensive overview of DVR self-insertion experiences. This triangulation of data sources enhanced the reliability of our findings.

The study specifically focused on pregnant women, a population historically underrepresented in clinical trials, contributing valuable data on the feasibility and usability of the DVR during pregnancy.

The findings were from a Research Trial that had significant support for DVR insertion which may not be generalizable to other programmatic DVR use in routine antenatal care.

Our assessment was limited to Uganda; therefore, we cannot generalize our findings to all the other countries. However, our findings offer very useful insights and/information.

Conclusion

The findings from this study provide valuable insights into the experiences of pregnant women with self-insertion of the DVR during the MTN-042/DELIVER study at MU-JHU. The high rate of participation and successful self-insertion across all cohorts underscore the usability of DVR use in this vulnerable population. While challenges were minimal, they were more prevalent among women above 36 weeks, which suggests that it may be beneficial to encourage pregnant women to start using this HIV prevention method early in pregnancy, to minimize potential initial insertion challenges in late pregnancy.

The results contribute to the growing body of evidence supporting the use of DVRs as a viable HIV prevention method for pregnant women.

Declarations

Ethics approval and consent to participate

This assessment was done from the MTN-042/DELIVER study, which had ethical approval from all the regulatory authorities, that is, the Joint Clinical Research Center Institutional Review Board (JCRCIRB) – *JC1719*, Uganda National Council for Science and Technology (UNCST) – *HS 2699* and the National Drug Authority (NDA) – *CTA-0121*. Permission to do this assessment was granted by the Microbicides Trials Network (MTN), the Sponsors of the MTN-042/DELIVER study. All participants gave written informed consent before taking part in any study activities.

Consent for publication

Not applicable.

Author contributions

Joselyne Nansimbe: Conceptualization; Formal analysis; Investigation; Methodology; Project administration; Resources; Writing – original draft; Writing – review & editing.

Brenda Gati Mirembe: Conceptualization; Formal analysis; Methodology; Supervision; Writing – review & editing.

Phionah Kibalama Ssemambo: Investigation; Methodology; Writing – review & editing.

Annette Miwanda Ssekasi: Investigation; Methodology; Writing – review & editing.

Rose Byogero: Investigation; Methodology; Writing – review & editing.

Justine Nalwoga: Investigation; Methodology; Writing – review & editing.

Clemensia Nakabiito: Conceptualization; Investigation; Methodology; Project administration; Supervision; Writing – review & editing.

Acknowledgements

The authors thank the Microbicides Trials Network (MTN) leadership for funding the MTN-042/DELIVER study, without which we would not have managed to make this assessment and the MTN-042/DELIVER study staff at MU-JHU Care Limited who contributed to the primary data collection process.

Funding

The authors received no financial support for the research, authorship and/or publication of this article.

Competing interests

The authors declare that there is no conflict of interest.

Availability of data

The data used in the study is available upon request from the corresponding author.

Availability of data and materials

This article is reporting a secondary data analysis from the MTN-042/DELIVER Study, registration ID NCT03965923 at https://www.ClinicalTrials.gov.

ORCID iD

Joselyne Nansimbe https://orcid.org/0009-0001-4975-3789

References

1. Marsh K, Eaton JW, Mahy M, et al. Global, regional and country-level 90–90–90 estimates for 2018: assessing progress towards the 2020 target. *AIDS* 2019; 33: S213–S226.
2. UNAIDS. Global HIV statistics, https://www.unaids.org/sites/default/files/media_asset/UNAIDS_FactSheet_en.pdf (2024, accessed 27 August 2024).
3. Gray RH, Li X, Kigozi G, et al. Increased risk of incident HIV during pregnancy in Rakai, Uganda: a prospective study. *Lancet* 2005; 366(9492): 1182–1188.
4. Thomson K, Hughes J, Baeten J, et al. Increased risk of female HIV-1 acquisition throughout pregnancy and postpartum: a prospective per-coital act analysis among women with HIV-1 infected partners. *J Infect Dis* 2018; 218(1): 16–25.
5. Birkhead GS, Pulver WP, Warren BL, et al. Acquiring human immunodeficiency virus during pregnancy and mother-to-child transmission in New York: 2002–2006. *Obstet Gynecol* 2010; 115(6): 1247–1255.
6. World Health Organization. *Antiretroviral drugs for treating pregnant women and preventing HIV infection in infants in resource-limited settings: towards universal access: recommendations for a public health approach*. Geneva: World Health Organization, 2006.
7. Sedgh G, Singh S and Hussain R. Intended and unintended pregnancies worldwide in 2012 and recent trends. *Stud Fam Plann* 2014;45(3):301-14.
8. WHO. Mother-to-child transmission of HIV, https://www.who.int/teams/global-hiv-hepatitis-and-stis-programmes/hiv/prevention/mother-to-child-transmission-of-hiv (2024, accessed 30 August 2024).
9. UNAIDS (2023) *The path that ends AIDS: global AIDS update 2023*. Geneva: Joint United Nations Programme on HIV/AIDS (UNAIDS).
10. Bunge K, Balkus JE, Fairlie L, et al. DELIVER: a safety study of a dapivirine vaginal ring and oral PrEP for the prevention of HIV during pregnancy. *J Acquir Immune Defic Syndr* 2024; 95: 65–73.
11. Baeten JM, Palanee-Phillips T, Mgodi NM, et al. Safety, uptake, and use of a dapivirine vaginal ring for HIV-1 prevention in African women (HOPE): an open-label, extension study. *Lancet HIV* 2021; 8(2): e87–e95.
12. Young AM, Stoner MCD, Mathebula F, et al. Acceptability of the dapivirine vaginal ring and daily oral pre-exposure prophylaxis (PrEP) during pregnancy in Malawi, South Africa, Uganda, and Zimbabwe. *AIDS Behav* 2024; 28(11): 3615–3628.
13. Bhavaraju N, Shears K, Schwartz K, et al. Introducing the dapivirine vaginal ring in sub-Saharan Africa: what can we learn from oral PrEP? *Curr HIV/AIDS Rep* 2021; 18(6): 508–517.
14. Montgomery ET, van der Straten A, Chitukuta M, et al. Acceptability and use of a dapivirine vaginal ring in a phase III trial. *AIDS* 2017; 31(8): 1159–1167.
15. Mayo AJ, Browne EN, Montgomery ET, et al. Acceptability of the dapivirine vaginal ring for HIV-1 prevention and association with adherence in a phase III trial. *AIDS Behav* 2021; 25: 2430–2440.
16. Nel A, Bekker L-G, Bukusi E, et al. Safety, acceptability and adherence of dapivirine vaginal ring in a microbicide clinical trial conducted in multiple countries in sub-Saharan Africa. *PLoS One* 2016; 11(3): e0147743.
17. Microbicide Trials Network. Grant numbers: UM1AI068633, UM1AI068615, UM1AI106707. Pittsburgh, PA: Microbicide Trials Network, 2017.
18. Von Elm E, Altman DG, Egger M, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *Lancet* 2007; 370(9596): 1453–1457.
19. van der Straten A, Montgomery ET, Cheng H, et al. High acceptability of a vaginal ring intended as a microbicide delivery method for HIV prevention in African women. *AIDS Behav* 2012; 16(7): 1775–1786.
20. Montgomery ET, van der Straten A, et al. Acceptability and use of a dapivirine vaginal ring in a phase III trial. *AIDS* 2017; 31(8): 1159–1167.

21. Montgomery ET, Stadler J, Naidoo S, et al. Reasons for nonadherence to the dapivirine vaginal ring: narrative explanations of objective drug-level results. *AIDS* 2018; 32(11): 1517–1525.

22. Nel A, Bekker LG, Bukusi E, et al. Safety, acceptability and adherence of dapivirine vaginal ring in a microbicide clinical trial conducted in multiple countries in sub-Saharan Africa. *PLoS One* 2016; 11(3): e0147743.

23. Milford C, Ramlal H, Mofokeng R, et al. Self-reported removal and expulsion of the dapivirine vaginal ring: qualitative reports from female ring users and their male partners in the Ring Study (IPM 027). *BMC Public Health* 2024; 24(1): 1458.

24. Montgomery ET, van der Straten A, Chitukuta M, et al. Acceptability and use of a dapivirine vaginal ring in a phase III trial. *AIDS* 2017; 31(8): 1159–1167.

25. Mensch BS, van der Straten A and Katzen LL. Acceptability in microbicide and PrEP trials: current status and a reconceptualization. *Curr Opin HIV AIDS* 2012; 7(6): 534–541.