Urgent appeal to implement pre-exposure prophylaxis for pregnant and breastfeeding women in South Africa

In this editorial, we appeal to the South African (SA) National and Provincial Departments of Health to urgently implement preexposure prophylaxis (PrEP) for pregnant and breastfeeding women at risk of HIV acquisition, in view of the persistent and unacceptably high rate of maternal HIV infection and transmission in SA.

High HIV incidence among young women persists during pregnancy and postpartum, and there is evidence that HIV acquisition risk increases by >2-fold during pregnancy and the postpartum period. Acute maternal HIV infection is associated with increased vertical transmission risk, making prevention of HIV among pregnant and breastfeeding women a national health priority.

SA has the highest number of people living with HIV in the world, with HIV prevalence rates up to 41% in pregnant women. SA is committed to achieving the elimination targets in the World Health Organization (WHO) Last Mile Plan. In January 2015, SA rolled out prevention of mother-to-child transmission (PMTCT) Option B+, which enabled pregnant and breastfeeding women living with HIV (WLHIV) to initiate antiretroviral therapy for life, regardless of baseline CD4 count. Now, over 6 years later, it is critical that we expand the PMTCT guidelines to include not only HIV treatment but primary prevention of HIV in pregnant and breastfeeding women through the use of PrEP.

In the 2019 Antenatal HIV Sentinel Study in SA,^[7] the overall prevalence of HIV in first antenatal care (ANC) visit attendees was 30%, ranging from 40.9% in KwaZulu-Natal to 17.9% in Western Cape Province (Fig. 1). In a recent analysis of the 2017 sentinel survey of >10 000 HIV-infected pregnant women,^[8] the annual HIV incidence was 1.5% (95% confidence interval (CI) 1.2 - 1.7), based on HIV recency testing. The Joint United Nations Programme on HIV and AIDS (UNAIDS) target to reduce the incidence by 75% by 2020 (which is equivalent to reducing the incidence to <1%) has not been met.

There are \sim 1 million live births in SA annually, of which \sim 70% occur in women not living with HIV (n=700 000 live births). Many of these women are at very high risk of HIV acquisition and subsequent vertical transmission. These women have the right to access PrEP to protect them against HIV during this high-risk period. Currently in SA, \sim 1 in 3 infant infections arise from maternal seroconversion during pregnancy or breastfeeding. SA will continue to struggle to reach the elimination goals unless the government ensures that women at risk can access an effective biomedical prevention option during their pregnancy and breastfeeding journey.

Since 2017, the WHO, the US President's Emergency Plan for AIDS Relief (PEPFAR) and several national HIV programmes have recommended offering daily oral tenofovir disoproxil fumarate (TDF)-based PrEP to pregnant and breastfeeding women at substantial risk for HIV,^[10-12] based on a large body of safety data from WLHIV who used TDF for HIV treatment during pregnancy and breastfeeding.^[10,11,13] Oral TDF-based PrEP is being scaled up among pregnant and breastfeeding women in sub-Saharan Africa, with notable implementation successes in Kenya and ongoing demonstration projects in SA, Lesotho, Malawi, Zambia and Zimbabwe.^[10,14-18] Although SA's PMTCT policies mention PrEP as an option, they refer clinicians to PrEP guidelines that remain unclear about PrEP in pregnancy and limit initiation to doctors, leaving clinicians on their own to make decisions about how to proceed.^[19,20]

Demonstration studies in SA have reported high acceptability and feasibility of integrating PrEP into antenatal and postnatal care. A recent study in Cape Town demonstrated that >85% of HIV-uninfected women accepted PrEP at their first ANC visit, and >70% continued on PrEP at month 1, and 60% at month 3. Those who were at higher risk, e.g. were diagnosed with a sexually transmitted infection, had a partner living with HIV or had >1 sex partners, were more likely to continue on PrEP. This study also demonstrated

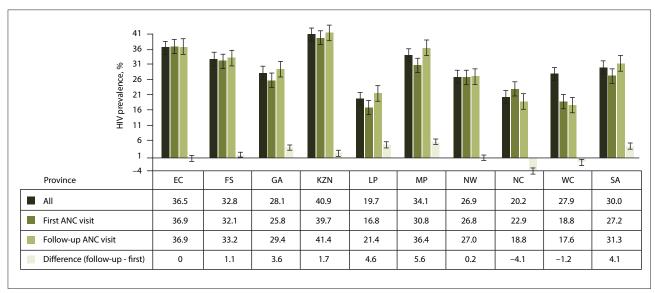


Fig. 1. HIV prevalence among first ANC visit attendees, follow-up ANC visit attendees and overall by province in the 2019 HIV Sentinel Survey, South Africa. [8] (EC = Eastern Cape; FS = Free State; GA = Gauteng; KZN = KwaZulu-Natal; LP = Limpopo; MP = Mpumalanga; NW = North West; NC = Northern Cape; WC = Western Cape; SA = South Africa; ANC = antenatal care.)

the safety of providing PrEP in this population, in line with other studies in the region. [14,21] Antenatal care uptake in SA is high, reaching >95%, creating a perfect opportunity to offer PrEP to women engaging in these routine services, including priority groups such as adolescent girls and young women and serodiscordant couples. Expanding PrEP implementation to include pregnant and breastfeeding women will further support SA's efforts to reach its ambitious PrEP uptake goals.

We call on the National and Provincial Departments of Health to urgently action the following steps:

- Implement PrEP prescription for pregnant and breastfeeding
- Allow nurse-initiation and management of ART (NIMART) trained nurses and midwives to prescribe PrEP in ANC and postnatal settings
- Include PrEP as part of the updated PMTCT guidelines for HIVuninfected women at substantial risk
- Simplify PrEP guidelines to ensure that it is provided on the same day as ANC to at-risk women, along with counselling on how best to ensure adherence to the daily pill.

Not offering PrEP to women not living with HIV but who are at risk of HIV acquisition, including those in serodiscordant relationships or with partners of unknown serostatus, undermines the efficacy of all the government's PMTCT efforts. It is urgent and overdue to implement PrEP in pregnancy and during breastfeeding. Doing so will align with the national PTMCT policy of 'strengthening antenatal and postnatal care for both HIV-negative and positive mothers'. Failure to do so in the face of proven prevention interventions allows ongoing avoidable HIV infection among women in SA, with the added high risk of transmission to their offspring.

Dvora L Joseph Davey

Department of Epidemiology, Fielding School of Public Health, University of California, Los Angeles, California, USA; Division of Epidemiology and Biostatistics, School of Public Health and Family Medicine, Faculty of Health Sciences, University of Cape Town, South Africa dvora.josephdavey@uct.ac.za

Natasha Davies

Anova Health, Johannesburg, South Africa

Yvette Raphael

Advocacy for Prevention of HIV and AIDS (APHA), Johannesburg, South Africa

Yogan Pillay

Center for Global Health Innovation, Georgetown University, Washington, DC, USA

Linda-Gail Bekker

Desmond Tutu HIV Centre, University of Cape Town, South Africa

- Drake AL, Wagner A, Richardson B, John-Stewart G. Incident HIV during pregnancy and postpartum and risk of mother-to-child HIV transmission: A systematic review and meta-analysis. PLoS Med 2014;11(2):e1001608. https://doi.org/10.1371/journal.pmed.1001608
- Thomson KA, Hughes J, Baeten JM, et al. Increased risk of HIV acquisition among women throughout
 pregnancy and during the postpartum period: A prospective per-coital-act analysis among women with
 HIV-infected partners. J Infect Dis 2018;218(1):16-25. https://doi.org/10.1093/infdis/jiy113
- Graybill LA, Kasaro M, Freeborn K, et al. Incident HIV among pregnant and breast-feeding women in sub-Saharan Africa: A systematic review and meta-analysis. AIDS (London, England) 2020;34(5):761-776. https://doi.org/10.1097/qad.000000000002487
- https://doi.org/10.1097/qad.0000000000002487

 4. Joseph Davey DL, Nyemba DC, Gomba Y, et al. Prevalence and correlates of sexually transmitted infections in pregnancy in HIV-infected and uninfected women in Cape Town, South Africa. PLoS ONE 2019;14(7):e0218349. https://doi.org/10.1371/journal.pone.0218349
- Joseph Davey D, Farley E, Gomba Y, Coates T, Myer L. Sexual risk during pregnancy and postpartum periods among HIV-infected and -uninfected South African women: Implications for primary and secondary HIV prevention interventions. PLoS ONE 2018;13(3):e0192982. https://doi.org/10.1371/journal.pone.0192982
- Moodley D, Esterhuizen T, Reddy L, et al. Incident HIV infection in pregnant and lactating women and its effect on mother-to-child transmission in South Africa. J Infect Dis 2011;203(9):1231-1234. https://doi. org/10.1093/infdis/jir017
- Woldesenbet SA, Kufa T, Lombard C, et al. The 2017 National Antenatal Sentinel HIV Survey, South Africa. National Department of Health, July 2019. https://www.nicd.ac.za/wp-content/uploads/2019/07/ Antenatal survey-report 24 July 19 pdf (accessed 5 October 2021).
- Woldesenbet S, Kufa-Chakezha T, Lombard C, et al. Recent HIV infection among pregnant women in the 2017 antenatal sentinel cross-sectional survey. South Africa: Assay-based incidence measurement. PLoS ONE 2021;16(4):e0249953. https://doi.org/10.1371/journal.pone.0249953
- Dinh TH, Delaney KP, Goga Å, et al. Impact of maternal HIV seroconversion during pregnancy on early mother to child transmission of HIV (MTCT) measured at 4 - 8 weeks postpartum in South Africa 2011 -2012: A national population-based evaluation. PLoS ONE 2015;10(5):e0125525. https://doi.org/10.1371/ journal.pone.0125525
- Joseph Davey DL, Pintye J, Baeten JM, et al. Emerging evidence from a systematic review of safety of preexposure prophylaxis for pregnant and postpartum women: Where are we now and where are we heading?
 J Int AIDS Soc 2020;23(1):e25426. https://doi.org/10.1002/jia2.25426
 Stalter RM, Pintye J, Mugwanya KK. Safety review of tenofovir disoproxil fumarate/emtricitabine pre-
- Stalter RM, Pintye J, Mugwanya KK. Safety review of tenofovir disoproxil fumarate/emtricitabine preexposure prophylaxis for pregnant women at risk of HIV infection. Expert Opin Drug Saf 2021 (epub 28 May 2021). https://doi.org/10.1080/14740338.2021.1931680
 World Health Organization. Preventing HIV during pregnancy and breastfeeding in the context of pre-
- World Health Organization. Preventing HIV during pregnancy and breastleeding in the context of preexposure prophylaxis (PrEP). Policy brief, 1 July 2017. https://www.who.int/publications/i/item/WHO-HIV-2017.09 (accessed 1 October 2021).
- Mofenson LM, Baggaley RC, Mameletzis I. Tenofovir disoproxil fumarate safety for women and their infants during pregnancy and breastfeeding. AIDS (London, England) 2017;31(2):213-32. https://doi. org/10.1097/QAD.000000000001313
- Joseph Davey DI., Mvududu R, Mashele N, et al. Early pre-exposure prophylaxis (PrEP) discontinuation among pregnant and postpartum women: Implications for maternal PrEP roll out in South Africa. medRxiv 2021 (epub 4 May 2021). https://doi.org/10.1101/2021.05.04.21256514
- Pintye J, Joseph Davey DL, Wagner AD, et al. Defining gaps in pre-exposure prophylaxis delivery for pregnant and post-partum women in high-burden settings using an implementation science framework. Lancet HIV 2020;7(8):e582-e592. https://doi.org/10.1016/s2352-3018(20)30102-8
 Bekker L-G, Brown B, Joseph-Davey D, et al. Southern African guidelines on the safe, easy and effective
- Bekker L-G, Brown B, Joseph-Davey D, et al. Southern African guidelines on the safe, easy and effective use of pre-exposure prophylaxis: 2020. South Afr J HIV Med 2020;21(1):a1152. https://doi.org/10.4102/ sajihivmed.v21i1.1152
- Kinuthia J, Pintye J, Abuna F, et al. Pre-exposure prophylaxis uptake and early continuation among pregnant and post-partum women within maternal and child health clinics in Kenya: Results from an implementation programme. Lancet HIV 2020;7(1):e38-e48. https://doi.org/10.1016/S2352-3018(19)30335-2
- Zimba C, Maman S, Rosenberg NE, et al. The landscape for HIV pre-exposure prophylaxis during pregnancy and breastfeeding in Malawi and Zambia: A qualitative study. PLoS ONE 2019;14(10):e0223487. https://doi.org/10.1371/journal.pone.0223487
- National Department of Health, South Africa. South African guidelines for the provision of pre-exposure prophylaxis (PrEP) to persons at substantial risk of HIV infection. 1 January 2020. https://www.prepwatch. org/resource/south-african-guidelines-prep-2020/ (accessed 1 October 2021).
- National Department of Health, South Africa. Guideline for the prevention of mother to child transmission of communicable infections. October 2019. https://www.knowledgehub.org.za/system/ files/elibdownloads/2020-05/PMTCT%20Guideline%2003-2020%20PRINT%20v8.pdf (accessed 1 October 2021).
- Joseph Davey D, Bekker L-G, Mashele N, et al. High initiation and persistence on pre-exposure prophylaxis (PrEP) in HIV-uninfected pregnant women in Cape Town, South Africa. Abstract OA07.05LB. HIVR4P Conference (Virtual), 2020. https://programme.hivr4p.org/Abstract/Abstract/1416 (accessed 5 October 2021).

 $S\ Afr\ Med\ J\ 2021; 111(11): 1038-1039.\ https://doi.org/10.7196/SAMJ. 2021.\ v111i11.16187$