

From pregnancy to beyond: renewed emphasis on comprehensive HIV prevention in South Africa

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South Africa continues to document high HIV prevalence, particularly among pregnant women, highlighting significant prevention gaps. This viewpoint triangulates findings from the Sixth South African HIV Prevalence Survey, the 2022 Antenatal HIV Sentinel Survey, and our ongoing “Philani Ndiphile” trial, which is evaluating STI screening algorithms to improve pregnancy outcomes. Despite a recent national decline in antenatal HIV prevalence, the Philani trial recorded an HIV prevalence of 28.6% among pregnant women, mirroring high rates across the Eastern Cape Province. The trial cohort also revealed a significant increasing trend in HIV prevalence with age, from 6% at 18 years to 63% at 43 years, highlighting the need for age-targeted interventions in young women of childbearing age.

National progress toward UNAIDS’ targets for HIV status knowledge and ART initiation is evident; however, viral suppression remains a challenge, reflected in the 20% of Philani participants newly initiated or reinitiated on ART at their first antenatal visit. Efforts to reduce new HIV infections require strengthening, as high incidence rates persist among young women and during pregnancy and postpartum.

Expanding access to oral and long-acting PrEP for pregnant and postpartum women is critical. Current coverage is low, and while new options show promise, implementation guidance remains limited. Socioeconomic factors, such as poverty and intimate partner violence, exacerbate HIV risk. Comprehensive interventions, including educational and vocational support, engaging male partners, and addressing STIs are essential. Continued support from global health partnerships and innovation in prevention strategies are vital to ending the epidemic and ensuring equitable outcomes.

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South Africa remains at the forefront of the HIV epidemic, facing persistent challenges within specific demographics. This viewpoint emphasizes the critical role of pregnant women in HIV prevention and control, extending from pregnancy to nonpregnant females. We integrate findings from the Sixth South African HIV Prevalence, Incidence, and Behavioral and Media Survey [1], the 2022 Antenatal HIV Sentinel Survey [2], and our ongoing clinical trial in Eastern Cape, “Philani Ndiphile” (meaning “Thrive together, for our child to thrive”), which is evaluating the impact of multiple screening algorithms for sexually transmitted infections (STIs) on adverse pregnancy outcomes [3]. We highlight the concerning antenatal HIV burden in South Africa, positioning pregnant women as crucial in the effort to end the HIV epidemic.

Between March 2021 and January 2024, the Philani trial provided HIV testing to 2675 eligible pregnant women (≥ 18 years at first antenatal care visit, < 27 weeks’ gestation) in Buffalo City Metro Health District, Eastern Cape Province. The trial recorded an HIV prevalence of 28.6% [95% confidence interval (95% CI): 26.9–30.4] [4], closely aligned with South Africa’s overall antenatal HIV prevalence of 27.5% (95% CI: 27.0–28.1) [2]. In comparison, the Eastern Cape’s antenatal HIV prevalence was estimated at 32.9%, the second highest among South Africa’s nine provinces [2], exceeding the general prevalence among women (22.3%, 95% CI: 20.8–23.8) and adults aged 15–49 years (17.0%, 95% CI: 16.0–18.0) [1]. There was a 2.5% decline in national antenatal HIV prevalence from 2019 [2], but the survey report attributes it to slight changes in the demographics of the survey respondents rather than a direct result of effective prevention efforts [2].

Among the pregnant women in our Philani trial, we have observed a noteworthy increase in HIV prevalence with age (Fig. 1), ranging from 6% among women aged 18 years to 63% in those aged 43 years. A statistical trend test revealed a slope coefficient of 1.0478, suggesting that the antenatal HIV prevalence increases by about 4.8% for every additional year of age. The sixth national survey similarly reflect this upward trend by age, with prevalence peaking around 41% in women aged 35–39 years [1]. Beyond the chronic nature of HIV infection and improving population survival, factors contributing to the higher prevalence in older pregnant women may include prolonged sexual activity, differing HIV testing behaviors, increased number of sexual partners, and a higher likelihood of encountering partners living with HIV. Current prevention efforts should address unique age-related variabilities to improve outcomes.

An assessment of South African antenatal surveys shows progress toward the first two UNAIDS 95–95–95 targets—HIV status awareness and antiretroviral therapy (ART) initiation—but only two-thirds of pregnant women living with HIV have achieved viral suppression, indicating challenges with the third target [5]. In our Philani trial (Fig. 1), about 20% of women with HIV are not on ART at their first antenatal care visit. ART initiation varies by age, with coverage improving from 60% in 18-year-olds to over 80% in women aged 30 and older, reaching 91% by age 38 and 100% by age 44, though sample sizes for older age groups are small. This trend suggests that age-targeted interventions, toward younger women with HIV in this case, could enhance progress along the care continuum and help achieve viral suppression goals.

South Africa’s progress in reducing new HIV infections among women of reproductive age is insufficient [6], potentially hindering the nation’s ability to meet the WHO’s elimination targets for mother-to-child transmission, which include fewer than 50 new pediatric infections per 100 000 live births and less than 5% transmission during breastfeeding [7]. A cohort study documented an HIV incidence of 4.51 per 100 woman-years among South African women aged 16–35 years [8]. Other data indicate that the risk of HIV acquisition can more than double during pregnancy and postpartum [9]. Effective but comprehensive HIV prevention strategies are urgently needed. Increased healthcare engagement during pregnancy could be leveraged to evaluate and implement tailored prevention programs that retain relevance across the reproductive continuum.

Expanding access to biomedical HIV prevention is critical, starting with the scaled adoption of oral preexposure prophylaxis (PrEP) for pregnant and postpartum women. Despite eligibility for one in three pregnant women in South Africa, the 2022 antenatal survey reported only 6.5% PrEP coverage [2]. Bridging this gap requires prioritizing pregnant and breastfeeding women in the development and roll-out of long-acting PrEP options to address adherence challenges with daily oral PrEP [10]. Recent advocacy is driving more research into the preferences of these historically underserved populations. Cabotegravir (CAB-LA), a bimonthly injectable, is currently the most effective approved option globally, but faces challenges such as accessibility, cost, and limited data on its use during pregnancy and postpartum [11]. The Dapivirine vaginal ring, with modest efficacy (35–50%), is recommended for women at an increased risk in several African countries and has demonstrated some safety from late pregnancy through postpartum.

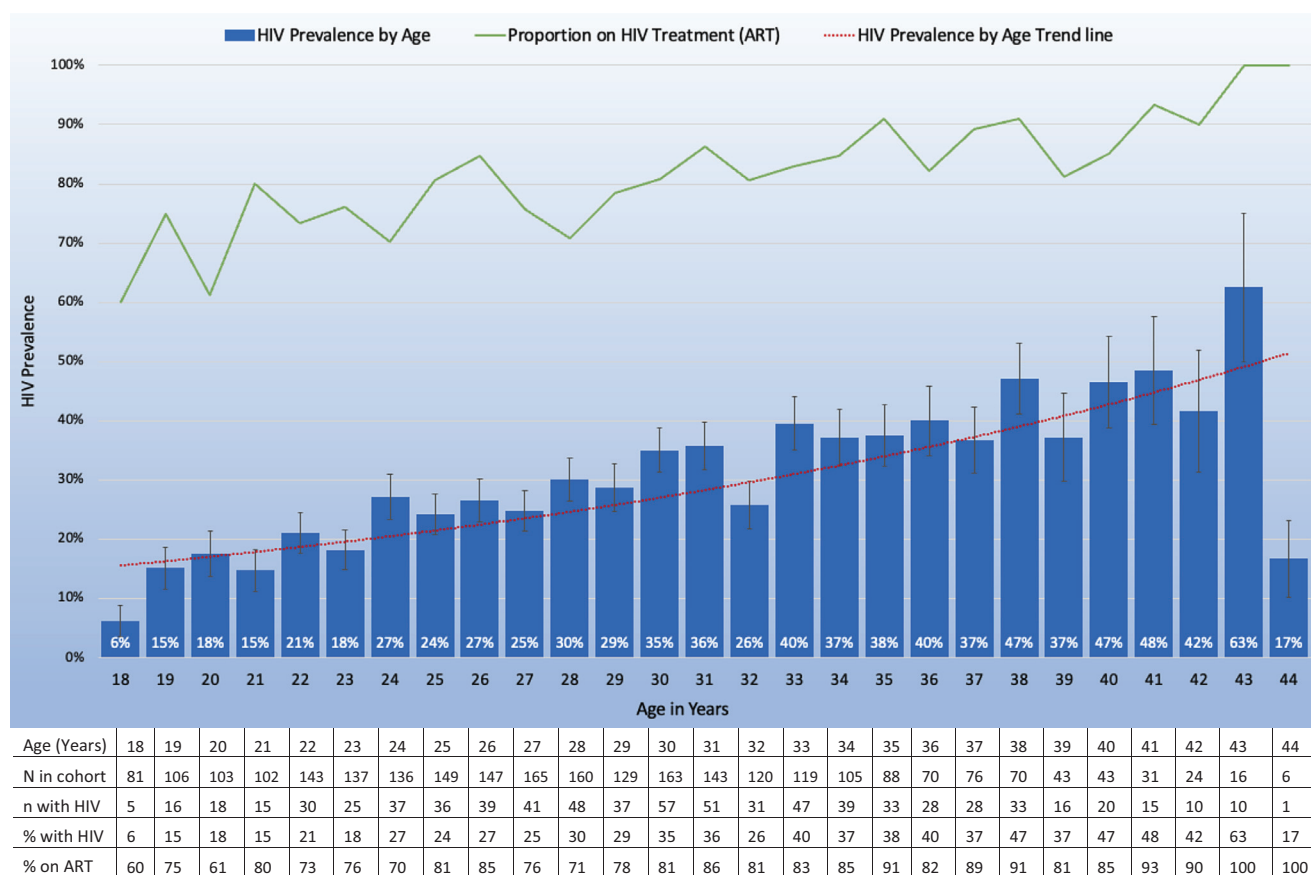


Fig. 1. HIV prevalence and antiretroviral therapy coverage by age among 2675 pregnant women aged 18–44 years in Eastern Cape, South Africa (March 2021–January 2024).

Nevertheless, systemic barriers and sparse implementation data limit its use [12]. Developing acceptable and cost-effective long-acting PrEP options is critical [10]. Several promising candidates, including oral and implant PrEP modalities, are advancing through clinical trials, with Gilead Sciences' twice-yearly injectable Lenacapavir being particularly notable [13]. The Phase III trials among cisgender women in South Africa and Uganda (PURPOSE 1 – NCT04994509) allowed enrollment of pregnant and breastfeeding women from the start. Interim results, announced at the AIDS 2024 conference, showed 100% efficacy for Lenacapavir, significantly outperforming daily oral PrEP options, largely due to suboptimal adherence with the latter. However, data on its safety during pregnancy and lactation are still insufficient.

Meanwhile, socioeconomic and behavioral factors continue to widen disparities among young South African women [14]. Poverty, limited education, and inequitable sexual relationships often lead to power imbalances, increasing vulnerability to STIs and HIV [14]. Intimate partner violence, with a lifetime prevalence ranging from 20 to 50%, also significantly impacts HIV burden and should be addressed [15]. Addressing these issues within antenatal programs could be impactful. The impact of relevant and sustainable educational initiatives that

complement extending school years for female adolescents should be more definitively assessed, as postsecondary education may offer some protection against HIV [16]. Integrating antenatal STI and HIV services is essential for identifying and treating both prevalent and incident STIs, thereby reducing the heightened risk of HIV acquisition and preventing adverse reproductive and fetal outcomes associated with untreated infections [14].

Cash transfers, particularly when linked to education, may empower young African women and potentially reduce HIV transmission risk [17]. However, in economies with high female youth unemployment, initiatives focused solely on subsidizing secondary education may be less effective, potentially leading to risky partnerships even during pregnancy. Vocational programs that provide life skills training and financial literacy alongside cash support hold promise for improving young women's quality of life across sub-Saharan Africa. Assessing their direct impact on HIV outcomes remains challenging due to program heterogeneity and the need for extended monitoring [18].

Efforts to engage men in HIV prevention should be strengthened, including offering partner HIV testing during antenatal visits and linking those who test positive

to care. Culturally competent approaches, supported by implementation research, are necessary to tailor strategies to specific contexts [19]. In high-prevalence settings like South Africa, engagement should extend beyond the partners of women living with HIV to include a broader population of men connected to antenatal and public health services. In parallel, medical male circumcision is a recognized cost-effective method for reducing HIV transmission, with coverage in South Africa increasing from 30% in 2008 to approximately 40% by 2017 [20]. PEPFAR aims for 80% coverage by 2025 in priority districts, targeting a 22% reduction in new infections. However, significant disparities persist, with some districts achieving up to 80% coverage among men aged 15–49 years, while others lag with rates of 3–13% [21]. Antenatal care presents a valuable opportunity to engage men, though cultural and religious beliefs, HIV stigma, healthcare access, and limited peer-to-peer information must be navigated to enhance acceptability [20].

Research validating multifaceted HIV prevention strategies will be beneficial. These layered interventions offer promise, but identifying priority components for each setting is crucial for developing high-impact programs [22]. For example, the DREAMS (Determined, Resilient, Empowered, AIDS-free, Mentored, and Safe) PEPFAR initiative (2016–2018) aimed to reduce new HIV infections by 40% in young women in sub-Saharan Africa through a combination of PrEP, community mobilization, social protection, and risk reduction strategies [22]. However, the impact of DREAMS in South Africa was limited by low uptake of some novel components compared to established initiatives like HIV testing [22,23]. Future multifaceted HIV prevention strategies should be guided by community needs assessments, with pregnancy offering an opportunity to prioritize and evaluate these interventions for women of reproductive age.

In conclusion, our narrative emphasizes the high HIV prevalence among pregnant women in South Africa and the need for both comprehensive and targeted prevention strategies. Addressing the unique needs of younger versus older women, expanding access to effective PrEP options alongside long-acting modalities, and leveraging antenatal care as both entry point and evaluation tool for prevention initiatives are vital steps. Continued global partnerships, such as those with PEPFAR, are essential, with the development of a well tolerated and effective HIV vaccine remaining a key objective. Collaboration, community engagement, and innovation will be pivotal in building a sustainable HIV prevention framework and ensuring no one is left behind.

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Conflicts of interest

There are no conflicts of interest.

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