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PrEParing for choice in a new era of HIV prevention

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In this edition of *Lancet HIV*, Gonasagrie Nair, Connie Celum, and colleagues[1] report the findings from the REACH trial, which investigated the safety of, adherence to, and preferences for HIV pre-exposure prophylaxis (PrEP) among adolescent girls and young women (AGYW). Conducted in three African countries, this study employed a smart cross-over design to gain new insights about PrEP use in this vulnerable population. Participants, aged 16-21, agreed to take oral daily emtricitabine/tenofovir disoproxil fumarate (FTC/TDF) and use the dapivirine vaginal ring for six months each. The sequence of these PrEP assignments was randomly allocated, after which participants transitioned to a six-month "product choice" period where they could continue with a preferred PrEP modality or no PrEP at all.

The REACH trial was rigorously conducted, with an impressive 94% retention at 72 weeks of follow-up. Over the course of the study, product adherence remained high. Based on pharmacologic measures, nearly 60% of women had tenofovir diphosphate levels consistent with four or more doses per week. A similar proportion of vaginal rings had residual drug levels consistent with continuous use. Both products were found to be safe and well-tolerated, though a higher frequency of Grade ≥2 adverse events were reported during oral PrEP use. Only one participant formally discontinued study product. Four participants acquired HIV, two while taking oral PrEP and two while using the dapivirine ring. According to pharmacologic evaluations, all seroconversions occurred during periods of low to no product use.

The inclusion of the product choice period within REACH—where participants made informed choices about future PrEP use—provides unique insights about preference. The vast majority (>95%) elected to continue some form of PrEP, with two-thirds selecting the dapivirine ring. Although a modest proportion (13%) switched products over the ensuing six months, initial choices remained relative stable. Given the limited use of vaginal ring devices to date in Africa—whether for HIV prevention, contraception, or other indications—this finding was somewhat surprising. It highlights how first-hand experiences with PrEP, in this case through the assigned evaluation periods, can introduce new delivery modalities and potentially increase downstream persistence and adherence.

By empowering individuals to select PrEP modalities that best align with their individual needs, product choice adds an important new dimension to the field of HIV prevention. Choice may be especially important for AGYW, a population that has experienced

suboptimal outcomes across the PrEP cascade. Results from the PrEP Implementation for Young Women and Adolescents (PrIYA) Program in Kenya, for example, found that only 16% of AGYW accepted daily oral PrEP when offered and, among those individuals, only 29% returned for a refill in the weeks following initiation.[2] In programmatic contexts, reported PrEP use has been even lower.[3] Given well-documented challenges to daily pill-taking,[4] there is optimism that newer formulations—including the dapivirine vaginal ring and injectable cabotegravir—can directly address barriers to PrEP utilization among AGYW.

How should choice be implemented into existing PrEP programs in sub-Saharan Africa? Important lessons can be learned from the contraception literature, where choice has been a cornerstone of service delivery for decades. Availability of different contraceptive methods has led to increases in modern contraceptive prevalence,[5] a population metric that reflects both uptake and sustained use. However, availability of different options does not automatically translate into informed choice. A recent study conducted in Burkina Faso, for example, found that nearly 40% of contraceptive users were using a method that did not match their preferences, even when their preferred method was available.[6] Misalignment between contraceptive preferences and use can increase the likelihood of discontinuation and risk of unintended pregnancy.[7] This can be driven by directive counseling, which may emphasize provider beliefs over individual client needs, compromise service quality, and unintentionally foster coercive dynamics.[8]

To fully realize the potential of choice in this new era of HIV prevention, it is essential that client priorities, needs, and preferences are placed at the center of service delivery. Efforts are already underway to support person-centered PrEP decision-making, with promising early results[9,10] These decision support tools should be refined to support longitudinal decision-making and adapted to include new modalities and formulations. Ultimately, choice can be a powerful strategy to enhance PrEP outcomes, but deliberate care is needed to ensure full, free, and informed decisions.

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