

Women May Naturally Control HIV Better Than Men

Study suggests women may be better candidates for functional cure strategies that aim to prevent viral rebound after stopping antiretrovirals.

October 2, 2025 By [Liz Highleyman](#)

The HIV viral reservoir in males and females differs in ways that may enable women to control the virus better than men, according to a study published in [Science Translational Medicine](#). Women and men showed marked differences in the composition of the viral reservoir and immune responses against HIV.

“Collectively, these data suggest a stronger ability of the female immune system to drive immune selection of HIV-1 reservoir cells during antiretroviral therapy, putatively because of improved innate immune function,” the study authors concluded.

[Antiretroviral therapy](#) (ART) can keep HIV replication suppressed long-term, but the virus inserts its genetic blueprints—known as a provirus—into the DNA of human cells, establishing a long-lasting reservoir that is impervious to the medications. These latent proviruses can lie dormant in resting CD4 T cells indefinitely, but they usually start churning out new virus soon after treatment is stopped, making a cure nearly impossible.

Only 10 people are known to have been [cured of HIV after stem cell transplants](#) for cancer treatment. In addition, a small proportion of people, known as elite controllers, appear to [control the virus naturally](#), while a larger group of [post-treatment controllers](#) remain in remission after stopping antiretrovirals.

Previous studies and anecdotal reports suggest that women tend to have slower viral rebound after treatment interruption, and they are more likely to be elite controllers or experience post-treatment control. On the other hand, there is also evidence that boys exposed to HIV before birth [may be more likely than girls to control HIV](#) after stopping antiretrovirals.

Xu Yu, MD, of the Ragon Institute of Massachusetts General Hospital, MIT and Harvard, and colleagues sought to better understand these sex differences by comparing the viral reservoir and immune responses in men and women. Results were [previously presented](#) in part at last year’s Conference on Retroviruses and Opportunistic Infections (CROI 2024).

The study included 35 cisgender men and 30 postmenopausal cisgender women who had been on suppressive antiretroviral treatment for a median of 20 years. The researchers analyzed more than 4,000 HIV genomes. One limitation of the study is that it only looked at HIV reservoir cells in peripheral blood, which might not fully reflect reservoir characteristics in lymphoid tissues that are the source of viral rebound after ART interruption.

The researchers observed “profound sex-specific differences in viral reservoir cell structure and composition.” Notably, the reservoir in women showed less genetic complexity, or reduced diversity. While the overall frequency of intact and defective proviral genomes did not differ significantly between males and females, women were more likely to have intact proviruses inserted in transcriptionally silent parts of their chromosomes where they could not reactivate. This suggests that women might be better candidates for “block and lock” functional cure strategies that aim to keep latent virus from rebounding after stopping antiretrovirals.

“We propose that these structural differences in the viral reservoir cell profile in females result from sex-specific immune selection forces, implying that the female immune system is more effective in driving immune selection pressure within the viral reservoir cell pool,” the study authors wrote.

Women showed evidence of more effective innate immune responses against the virus, specifically more natural killer cells with enhanced functionality. However, this study did not find a notable association between HIV-specific T cells and features of the viral reservoir, which “casts doubt on the ability of virus-specific T cells to effectively engage viral reservoir cells during suppressive ART.” The researchers also did not see sex-specific differences in viral reactivation in the laboratory, but they noted that current in vitro viral outgrowth assays have limited usefulness for assessing the reservoir.

Intact HIV proviruses from women had fewer killer T cell resistance mutations, which “might suggest a more effective immune control at early stages of infection before ART initiation in females, resulting in reduced viral turnover with fewer opportunities for viral sequence adaptation” to T-cell immune pressure, the authors suggested. This hypothesis is supported by prior studies showing a lower viral set-point in untreated women compared with men. Alternatively, limited mutations could reflect more potent immune clearance of intact proviruses during long durations of suppressive ART in women.

The reasons for these sex differences are unclear, but male and female sex hormones or sex-related chromosome variations may play a role. All the women in this study were postmenopausal at the time of the analysis, though they acquired HIV and established a viral reservoir some two decades earlier. “It is possible that sex-dependent immune effects on the viral reservoir cell pool might materialize differently during infancy, adolescence and young adulthood,” the authors wrote. To learn more, future research should include female as well as male participants at all stages of life.

“The HIV reservoir in women is associated with features of deeper latency; therefore, women may

be primed to achieve a state of HIV control, and the inclusion of women in cure studies should be a priority,” lead study author Toong Seng Tan, of the Ragon Institute, said during his CROI 2024 presentation.

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