# A Closer Look at the Long-Term Impact of HIV Cure Research

Scientists are getting a better sense of the risks and benefits of treatment interruptions in cure research.

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People living with HIV who underwent an analytical treatment interruption (ATI) in pursuit of an HIV cure were four times more likely to be hospitalized for non-AIDS-defining illnesses—especially cancer, liver and kidney disease—in the years following resumption of HIV treatment, according to an analysis published in the journal AIDS.

However, people undergoing an ATI were less likely to be hospitalized for cardiovascular events, non-AIDS-defining infections or neuropsychiatric causes.

The study informs the ongoing discussion among HIV researchers and people living with HIV about how to study functional HIV cure approaches while also protecting the health of people who volunteer to participate. Antiretroviral therapy keeps HIV under control as long as people are taking it, so it's necessary to stop treatment to see whether a cure intervention works. During an ATI, viral load is monitored frequently, and antiretrovirals are resumed if it rises above a specified level.

Previous research found that closely monitored treatment interruptions weren't associated with any increase in hospitalizations for non-AIDS conditions within the first three to four years after resuming treatment. Another study suggested that viral load rebound was as quick for people on new HIV medications and those taking older generations of treatment. However, Lorna Leal, MD PhD, of the Hospital Clínic de Barcelona at the University of Barcelona, and colleagues wanted to see what the impact was long term.

Leal and colleagues looked at the 136 people with HIV who underwent an ATI in 10 cure studies in Barcelona between 1999 and 2018. As a control group, they also included 45 people who did not stop treatment. They then tracked hospital admissions since trial inclusion, looking for admissions for non-AIDS-defining diseases. These included non-AIDS-defining cancers, neuropsychiatric conditions, heart disease, non-AIDS-defining infections, liver disease and end-stage kidney disease. People with hepatitis C were excluded from the analysis, and researchers excluded all other medical conditions that might have caused a hospital admission.

Nearly two out of three participants were gay men. The median age was 40 years, and they had been living with HIV for a median of 21 years at the time of the analysis. They had been on antiretroviral treatment for a median of 14 years and had an undetectable viral load for 12 of those years. The men were good candidates for analytical treatment interruption by modern standards, given that their lowest-ever CD4 count was pretty high—a median of 430—and their peak viral load was just 36,447, which indicates that their HIV was detected early and they started treatment fast. These numbers were similar  in the treatment interruption and control arms.

When those who underwent a treatment interruption restarted treatment, their CD4 count, at 470, was slightly higher than it was when they first initiated HIV care all those years ago, and their viral load was lower, at 24,642 copies.

Over the ensuing years, one in three participants (38%) overall were admitted to the hospital for a non-AIDS-defining illness at least once, and five participants died. But when the researchers compared people who underwent an ATI and those who did not, they found stark differences. Nearly twice as many people undergoing an ATI had a health event—43% versus 23%. When they isolated events that occurred only after treatment resumed, the odds of future hospitalizations rose to 2.43, and this happened a median of just five years after treatment resumption.

Hospitalizations for conditions like non-AIDS-defining cancers were markedly more likely among people in the ATI group: 18 of the 19 such hospitalizations were among people who interrupted treatment. All of the seven hospitalizations for liver-related and all of the eight kidney-related hospitalizations occurred among people in the ATI group. However, more people who stayed on treatment continuously experienced cardiovascular events (39% in the control group compared with 29% in the ATI group) and non-AIDS-defining infections. Nearly half of people in the control group were hospitalized for non-AIDS-defining infections, while such infections accounted for just a quarter of hospitalizations in the ATI group.

In the end, after adjusting for possible confounders, such as age and sex, people who underwent ATI were four times more likely to be hospitalized at least once with non-AIDS events than their peers who didn’t.

Of course, one study of fewer than 200 participants at one hospital isn’t the final word on ATI health effects, wrote Leal and colleagues. But it is important information for people considering joining HIV cure trials. And it’s important as researchers continue to design HIV cure studies. For instance, a previous study found that once people’s viral load hit 400 or more, their chances of having a cardiac event rose dramatically. That was in the short term. The study authors said this finding “is complementary” to the current study’s findings.

“In any case, further studies should be taken to confirm our results,” wrote Leal and colleagues. “If confirmed, these data could have a significant impact on functional cure clinical trials.”

Click here to read the study abstract.

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