

Even Low-Level Detectable Viral Load Can Lead to Adverse Outcomes

Starting HIV treatment later and having a lower CD4 count were also linked to serious non-AIDS events.

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People with a detectable but low-level HIV viral load are at risk for serious non-AIDS-defining illnesses such as cancer, heart disease and kidney disease, according to study results presented at the [30th Conference on Retroviruses and Opportunistic Infections \(CROI\)](#). This analysis also confirmed that people who start antiretroviral treatment sooner have better outcomes.

It is well known that maintaining viral suppression can halt disease progression, allow CD4 T-cells to recover and eliminate the risk of HIV transmission. Commonly used viral load tests measure down to 50 copies of HIV RNA, the usual threshold for “undetectable.” But many antiretroviral therapy studies define virological treatment failure or non-suppression as a viral load above 200, and the World Health Organization puts the threshold at 1,000. It is estimated that up to 10% of people on antiretroviral treatment sometimes have a detectable viral load between 50 and 200, but the consequences of low-level virus are not fully understood.

Anuradha Ganesan, MD, of the Henry M Jackson Foundation for the Advancement of Military Medicine, and colleagues analyzed the association between low-level viral load and serious non-AIDS events using data from the U.S. Military HIV Natural History Study. This cohort is comprised of military beneficiaries living with HIV who have access to care and antiretroviral medications.

This analysis included more than 2,800 people who started HIV treatment after 1996 and had at least two viral load measurements using a test with a lower limit of detection of 50 copies. As is typical of a U.S. military cohort, more than 90% were men. Just over 40% were Black, 40% were white and 17% were Latino or “other.” The median age was approximately 29 years at the time of HIV diagnosis and 42 years when diagnosed with a serious non-AIDS event. The median CD4 T-cell count at the time of treatment initiation was fairly low, at 370.

Over a median 10 years of follow-up, 8% of participants had a low-level detectable viral load (50 to 200 copies), 4% had high-level viremia (200 to 1,000 copies) and a third had one or more episodes of viral non-suppression or virological failure (at least 200 copies on two consecutive tests or a single measurement above 1,000). In addition, 12% had isolated viral “blips,” or detectable viral load on a single test.

The researchers looked at serious non-AIDS events including cancers, cardiovascular events, and liver and kidney disease. During this period, nearly 14% of participants had one such event, and nearly 8% had two or more. Anal cancer and prostate cancer were the most common malignancies (26 and 23 cases, respectively). Twenty-five people had a myocardial infarction (MI), 54 had coronary heart disease without MI, 23 developed liver cirrhosis and 205 developed moderate or worse chronic kidney disease.

The risk of serious non-AIDS events rose as viral load increased, but even those with low-level detectable virus were not spared. In an adjusted analysis, people with viral non-suppression were 71% more likely, those with high-level viremia were 57% more likely and those with a low-level viral load were 25% more likely to experience such events relative to those with consistent viral suppression.

Although a majority of participants had viral suppression and had experienced good CD4 cell recovery since starting antiretrovirals, the researchers still found that waiting longer to start treatment, having a high viral load at the time of treatment initiation, having a lower CD4 count and having any level of detectable HIV were associated with a greater risk for serious non-AIDS events. In addition, women were more likely than men to experience such events, while those who used integrase inhibitors were less likely compared with those to used other types of antiretrovirals.

Based on these findings, the researchers suggested that the threshold for virological failure or viral non-suppression should perhaps be lowered. “Our results need confirmation, nevertheless, we believe, at a minimum, the presence of [low-level viremia] should necessitate an assessment of adherence and closer follow-up,” they concluded.

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