

SMART Study: Viral Loads and Inflammation Explain Increased Cardio Risk

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Untreated HIV may increase the risk of artery blockage and blood clots, according to new data from the international Strategies for the Management of Anti-Retroviral Therapy (SMART) [published](#) October 21 in the online journal *PLoS Medicine*. According to the SMART authors, a high viral load is associated with increases in specific proteins that have been linked to blood vessel inflammation and may explain higher rates of [cardiovascular disease](#) among HIV-positive people not on antiretroviral (ARV) treatment in the study.

Much has been written about the greater risk of heart attacks and deaths among people who interrupted or delayed ARV therapy in the [SMART study](#). SMART compared people who remained on continuous ARV therapy with people who either delayed or stopped treatment until their CD4 counts fell below 250 cells. The study's authors have suggested that uncontrolled HIV replication while people were off ARV therapy over-stimulated the body's defense mechanisms, ultimately increasing the risk of cardiovascular disease. However, the exact mechanism by which this would have occurred has not been proved.

To determine the role of inflammatory markers in the risk of cardiovascular disease and deaths, Lewis Kuller, MD, PhD, from the University of Pittsburgh in Pennsylvania and his SMART colleagues examined stored blood samples from SMART study participants.

Kuller's team first compared the levels of the six proteins between the 85 people who died of any cause in the study with the levels of 170 survivors of similar ages and other characteristics. The team found that three proteins—hsCRP, IL-6 and D-dimer—were significantly higher in those who died than in the survivors.

The team then looked for the relationship between these three inflammatory proteins and whether people remained on continuous treatment, with undetectable viral loads, or were off treatment, and thus had elevated viral loads. Higher levels of IL-6 and D-dimer, both of which have been tied to artery blockage (arteriosclerosis) and blood clots (thrombosis), were much more common in people with high viral loads.

The authors write that the association between deaths and the proteins IL-6 and D-dimer was

particularly strong in the SMART study, even more so than in other studies that have examined the role of these inflammatory markers and cardiovascular disease and deaths in HIV-negative people. Moreover, because high IL-6 and D-dimer levels were more likely to be seen in people with higher viral loads, the authors state that viral replication most likely drives inflammation, which in turn is strongly associated with deaths. Kuller and his colleagues suggest that further research be conducted to confirm these results and to explore whether limiting inflammation could reduce the risk of death in people with HIV.

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