



Clinical Coordinating Center Massachusetts General Hospital 55 Fruit Street, 5LON207 Boston, MA 02114 **Data Coordinating Center**Massachusetts General Hospital
165 Cambridge Street Suite 400
Boston, MA 02114

Factors Associated with Systemic Immune Activation Indices in a Global Primary Cardiovascular Disease Prevention Cohort of People with HIV on Antiretroviral Therapy

Sara E. Looby, Amy Kantor, Heather Ribaudo, Markella Zanni, and colleagues Published in Clinical Infectious Diseases Journal, 2022

Background

People with HIV on antiretroviral therapy (ART) face increased risks of developing heart disease as compared to people without HIV. Heart disease risk among people with HIV is believed to relate both to traditional heart disease risk factors (like high blood pressure, cigarette smoking) and also to increased inflammation. Inflammation, which represents the body's response to infection or injury, tends to be higher among individuals with (vs. without HIV).

Goals of the Study

The current investigation examined factors associated with levels of two markers of inflammation – soluble CD14 and oxidized LDL – among a group of people with HIV participating in the REPRIEVE trial. REPRIEVE is a global clinical research study testing whether treatment with a statin medication helps prevent heart disease among people with HIV. Statin medications are best known for lowering levels of LDL cholesterol, but these medications have also been shown to reduce levels of inflammation among people with HIV.

> The participants:

- o 4907 people with HIV on antiretroviral therapy who have no known heart disease
- o Average age: 50 years
- o 38% female, 48% Black or African American

> The main results

- O When we looked at levels of inflammation in the whole group by sex, age, and region of residence, higher levels of soluble CD14 were associated with female sex and residence in South Asia or Sub-Saharan Africa while higher levels of oxidized LDL were associated with residence in high-income regions.
- When we looked at levels of inflammation in the whole group adjusting for many possible related factors, we noticed the following:

REPRIEVE Trial Website: reprievetrial.org



Clinical Coordinating Center Massachusetts General Hospital 55 Fruit Street, 5LON207 Boston, MA 02114 **Data Coordinating Center**Massachusetts General Hospital
165 Cambridge Street Suite 400
Boston, MA 02114

- For soluble CD14: Female sex, white race (among people living in high-income regions), and current use of NRTI+NNRTI ART were associated with higher levels of soluble CD14 while higher body mass index (a measure of overweight/obesity) and current use of NRTI+INSTI ART regimens were associated with lower levels of soluble CD14.
- <u>For oxidized LDL:</u> Male sex, residence in high-income regions, white race (among those in high-income regions), and higher body mass index were associated with higher levels of oxidized LDL.
- o When we looked at levels of inflammation specifically among women, being post-menopausal was associated with increased levels of soluble CD14 but not with increased levels of oxidized LDL.

Key take-away points:

- Levels of different inflammatory markers are influenced in different ways by the same factors (for example, sex and body mass index). Recognizing this point is important to anticipating that levels of markers may differ for women vs. men and that one single intervention may not affect all inflammatory markers the same way.
- o The fact that women's reproductive aging (transitioning to menopause) relates to a key marker of inflammation may help explain, to a small extent, a way in which menopause may increase women's risk of heart disease (that is, through pathways of inflammation).

Future studies may help us understand:

- o Ways that medications such as statins and changes in behavior (for example, healthy diet) influence levels of inflammation markers.
- O Whether lowering levels of these key inflammation markers helps protect against heart disease among people with HIV, possibly with different effects in females and males.

REPRIEVE Trial Website: reprievetrial.org