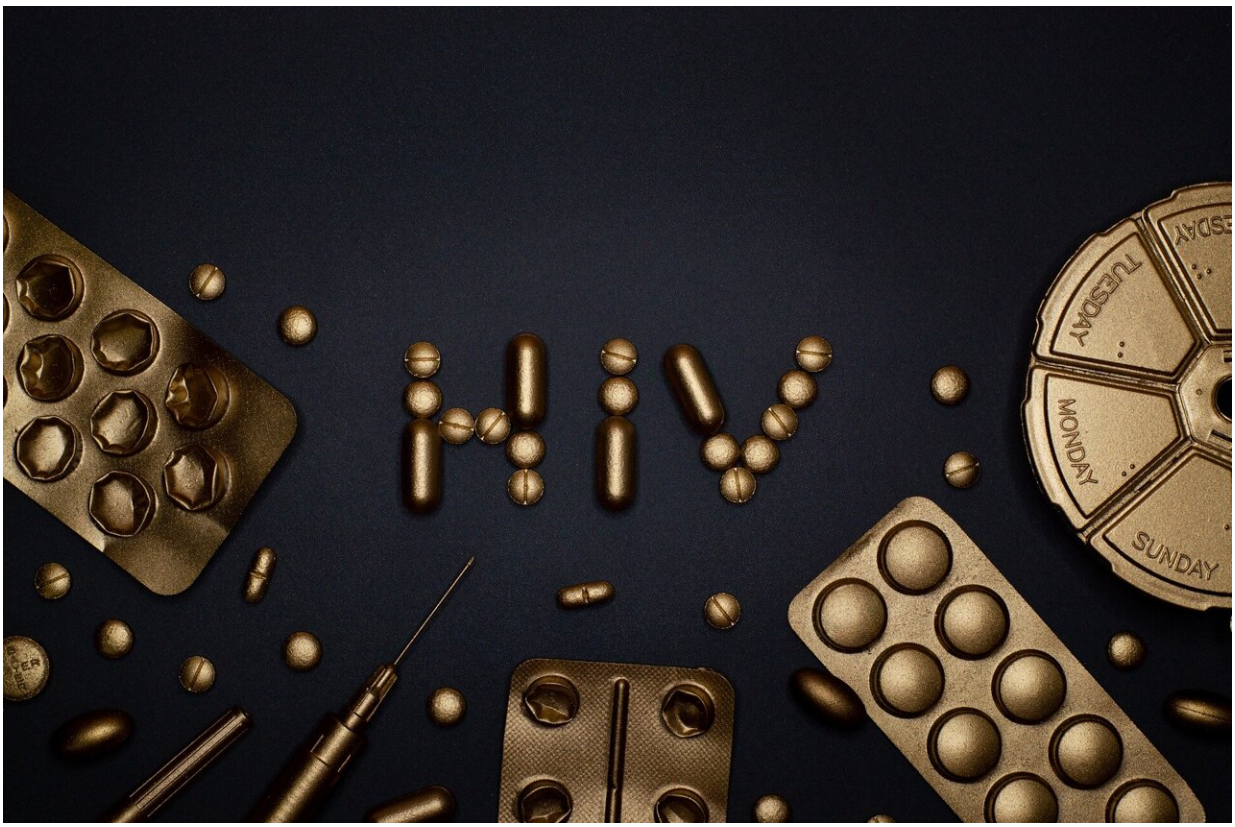
Medical Xpress

Daily statin medication reduces risk of major cardiovascular events by more than one-third in people living with HIV

July 24 2023, by Noah Brown



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The risk of cardiovascular diseases, including myocardial infarction and stroke, has been shown to be roughly twice as high in people living with

HIV than the general population, creating an urgent need to test prevention strategies to ensure healthier, longer lives.

In the first large-scale global clinical trial, Randomized Trial to Prevent Vascular Events in HIV (REPRIEVE), to test a primary cardiovascular prevention strategy in individuals living with HIV, investigators from Massachusetts General Hospital (MGH), a founding member of Mass General Brigham (MGB), found that HIV positive participants who took a daily statin decreased their risk of major adverse cardiovascular events (MACE) by more than a third, and reduced rates of MACE or death by over 20%. The findings are published in the *New England Journal of Medicine*.

"This study offers a major step in addressing the unacceptable burden of heart disease among individuals living with HIV and an important opportunity to develop a cardiovascular disease prevention strategy uniquely tailored for this at risk population," says Steven K. Grinspoon MD, the study chair, chief of the MGH Metabolism Unit and director of the Nutrition Obesity Research Center at Harvard, who also directed the study's Clinical Coordinating Center.

People living with HIV can live longer and healthier lives thanks to decades of research and treatment advances. However, premature heart disease and other chronic conditions have emerged as leading causes of illness and death, in part because people living with HIV frequently have increased inflammation and activation of their immune systems.

Statins are known to lower cholesterol and prevent cardiovascular disease for those at risk in the general population. In addition, statins are known to reduce key inflammatory pathways. But questions have remained on whether statins would have the same beneficial impact on people living with HIV and at risk for premature cardiovascular disease.

The REPRIEVE trial began in 2015 and enrolled 7,769 participants from 145 sites in 12 countries, including in North America, South America, the Caribbean, Asia, Sub Saharan Africa, and Europe.

The primary entry criteria included HIV positive adults between 40 to 75 years of age, on an antiretroviral therapy regimen, without known cardiovascular disease and at low to moderate risk for cardiovascular disease by traditional risk scoring, when statins would not routinely be prescribed.

About two-thirds of participants were non-white, and 31% were female, reflecting the diversity of the global HIV population.

Trial participants were randomly assigned to receive a daily oral 4 mg dose of pitavastatin calcium—a statin considered safe for use with all prescribed antiretroviral therapy regimens—or a placebo pill that contained no medication. They were monitored for major adverse cardiovascular events and adverse reactions to pitavastatin. Side effects for participants were similar to those in the general population taking statin therapy.

The research team found that HIV positive participants enrolled in the trial who took a daily statin lowered their risk of major adverse cardiovascular events within five years by 35%. Those in the statin group also reduced their risk of cardiovascular events or premature death by 21%. Benefits of statin therapy were generally similar across global burden of disease regions and by sex.

This past March, after a planned interim analysis of the REPRIEVE data, the Data Safety and Monitoring Board (DSMB) determined the benefits of daily statin use in HIV positive participants outweighed any risks and recommended that the study terminate early, after five years of follow up.

This 35% reduction in cardiovascular events within five years among those who took statins "was beyond what we expected—a very robust signal," Grinspoon says. "The findings suggest that adding on a statin may have additional effect beyond LDL (low density lipoprotein) cholesterol-lowering among people with HIV who are on antiretroviral therapy, including potential effects on inflammatory and -immune pathways activated in HIV and that may help explain the extra benefits of this treatment approach," Grinspoon says.

While the results of REPRIEVE could improve the health of this population for years to come, researchers called for additional studies to examine how well our current risk prediction tools can be used to accurately predict cardiovascular disease in people with HIV and the specific contribution of inflammation in this population.

Given these latest results, Grinspoon noted that starting a patient with HIV on a statin remains "an individualized decision." But the data certainly suggests that there's a clear benefit to patients aged 40 to 75 who have moderate-to-low risk and a normal LDL. "I hope guidelines will be expanded to incorporate this group," he says.

More information: Steven K. Grinspoon et al, Pitavastatin to Prevent Cardiovascular Disease in HIV Infection, *New England Journal of Medicine* (2023). DOI: 10.1056/NEJMoa2304146

Provided by Massachusetts General Hospital