

# New drugs could reduce risk of heart disease when added to statins

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Credit: Medical Research Council

New drugs that lower levels of triglycerides (a type of fat) in blood could further reduce the risk of heart attack when added to statins. These new drugs, which are in various stages of development, could also reduce blood glucose levels and the risk of diabetes, according to a new genetic study from the Medical Research Council Epidemiology Unit at the University of Cambridge.

MRC scientists behind the research, published today in *JAMA Cardiology*, suggest these new drugs – lipoprotein lipase enhancers – could be paired with statins, the current gold standard for high

cholesterol treatment, or other cholesterol lowering agents. Their findings, which stem from a type of genetic study which aims to simulate a clinical trial, hold promise for clinicians and pharmaceutical companies that are considering testing the efficacy of these novel drugs.

Dr Luca A. Lotta, Senior Clinical Investigator at the MRC Epidemiology Unit, said: "Our study suggests that these new [triglyceride](#)-lowering agents could give additional benefits to patients with heart disease when added to statins. This combination could prevent more heart attacks as well as reduce the risk of developing type 2 diabetes."

Heart disease is a significant problem in the UK, tied to more than a quarter of all deaths in the country, according to 2018 estimates. One of the major factors leading to heart disease is high levels of low-density lipoprotein or LDL cholesterol, often referred to as "bad cholesterol".

Statins are widely prescribed to lower LDL levels and are effective at preventing heart disease. Some people who are treated with statins will still encounter heart attacks, which has been partly linked to raised levels of triglycerides in their blood.

Normally, our bodies can break down triglycerides with a protein called lipoprotein lipase or LPL. In recent years, scientists and drug developers have tapped into this, developing several new agents that enhance the activity of this enzyme. However, these drugs are still in pre-clinical or early clinical stages of development.

In theory, these new heart drugs could be used in combination with statins and other cholesterol-lowering agents, but there hasn't been a large-scale trial to show their efficacy. MRC scientists used genetic data to gain insights into their likely efficacy and safety in advance of a large-scale trial.

The new research studied the genetics of some 400,000 people from the UK Biobank, EPIC-InterAct, and EPIC-Norfolk studies. Scientists used an approach called Mendelian randomisation, which uses naturally occurring genetic differences to simulate the effects of a clinical trial, to study the likely effects of statins and these novel LPL-enhancing drugs.

Some people have variation in their DNA that naturally increases the effectiveness of LPL, mimicking the effect that would be observed if the LPL-enhancing drugs were used.

In this study, people who carried both triglyceride-lowering DNA variants in the LPL gene and cholesterol-lowering variants in several other genes (simulating the protective effect of statins) had a lower risk of [heart disease](#) compared with people with only one of either of these sets of DNA variants.

The researchers believe these drugs could mitigate some of the potential side effects of statins, too. For some people, statins can increase the risk of developing type 2 diabetes – 50 to 100 new cases for every 10,000 patients treated. The scientists found that those with LPL gene variants had a lower risk of type 2 diabetes in all study groups, suggesting that these [new drugs](#) may improve blood glucose control when paired with statins.

Dr Lotta said: "We're using genetics to gain insight and help to predict the likely result of future trials. Studies that simulate clinical trials are invaluable because large-scale trials are expensive, take years to conduct and considerable resources – scientists need strong evidence of a drug's likelihood of success before it gets to the trial stage."

Clinical trials are costly endeavours but emerging findings indicate the odds of successful drug development are increased when knowledge about these novel agents is bolstered by genetic studies. To empower

these studies, the MRC, pharmaceutical companies, and other funders have invested in large genetic resources including the recent announcement of a consortium of companies to sequence the DNA of all participants of the UK Biobank, a study of 500,000 people from the general UK population.

**More information:** Lucca Lotta et al. Association of Genetically Enhanced Lipoprotein Lipase–Mediated Lipolysis and Low-Density Lipoprotein Cholesterol–Lowering Alleles With Risk of Coronary Disease and Type 2 Diabetes. *JAMA Cardiol.* Published online September 19, 2018. [DOI: 10.1001/jamacardio.2018.2866](https://doi.org/10.1001/jamacardio.2018.2866)

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