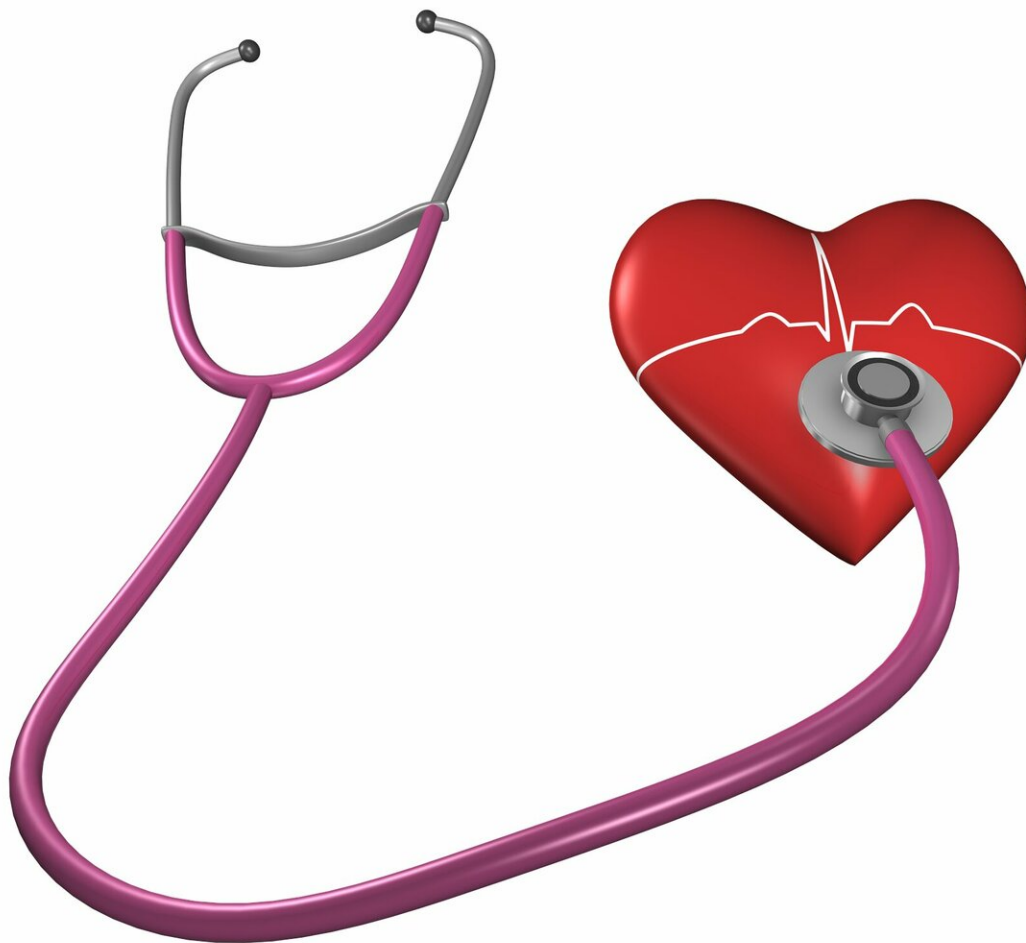


Cholesterol drug combinations could cut health risk for European patients

August 28 2020, by Ryan O'hare



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New findings from a large European study of patients in 18 countries, including the UK, show that while many patients are able to reduce their risk through taking statins, those at the highest risk of cardiovascular events may benefit from combinations of lipid-lowering therapies.

According to the authors, the study highlights a gap between current clinical guidelines and clinical practice for [cholesterol](#) management across Europe. They explain that even among patients who are already receiving optimal doses of statins, greater use of other, non-[statin](#) cholesterol-lowering drugs could help to further reduce [cholesterol levels](#) and potentially improve health outcomes for those most at risk.

The findings, which will be presented at the virtual meeting of the [European Society of Cardiology 2020](#), are published in the journal *European Journal of Preventive Cardiology*.

Professor Kausik Ray, from Imperial's School of Public Health, who led the DA VINCI study, said: "In order to tackle the burden of cardiovascular disease, a global approach is needed. After diet and lifestyle, cholesterol lowering with medications is a key approach to lowering risk of heart disease and strokes. Based on trial data we have compelling evidence that lower cholesterol levels benefit those at highest risk particularly.

"Though statins are first line treatment, it is clear from our contemporary study that statins alone even when optimally used will not help the majority of patients achieve European Society of Cardiology cholesterol goals. Only one in five very-high risk patients achieve 2019 recommended goals and to improve this will require use of combination

therapy of more than one drug. Currently less than 10% of very-high risk patients in Europe receive some form of combination therapy, 9% with ezetimibe and 1% with PCSK9 inhibitors."

High levels of low-density lipoprotein (LDL) cholesterol, or so-called 'bad' cholesterol, in the blood are a known risk factor for cardiovascular disease. While diet and lifestyle are important factors in reducing LDL cholesterol, many patients are at increased risk—such as those with diabetes, inherited conditions or who have previously had heart attack or stroke—and are prescribed cholesterol-lowering drugs, like statins, to reduce their cholesterol.

But a number of other classes of cholesterol-lowering drugs are available, which act on different elements of the body's cholesterol-metabolism. These treatments, such as ezetimibe, bempedoic acid, or PCSK9 inhibitors, can be used in combination with statins to further reduce LDL-cholesterol levels.

In the DA VINCI study, a consortium of researchers led by the Imperial Clinical Trials Unit at Imperial College London looked at patients across Europe who were prescribed lipid-lowering therapies.

In total 5888 patients, enrolled across 18 countries, provided information at doctor's appointment or in hospital to manage cardiovascular conditions. Information included lifestyle factors, previous cardiovascular events (such as heart attack or stroke) as well as measures of their current LDL cholesterol levels and any current lipid-lowering medications.

Current guidelines from the European Society of Cardiology (ESC)/European Atherosclerosis Society (EAS) recommend statins as first-line treatment for lowering LDL cholesterol. The guidance also recommends goals based on risk groupings, such as a target of 50%

reduction in LDL-C levels in very-high risk patients and achieving LDL-C levels below 1.4mmol/L, in order to reduce the risk of additional cardiovascular events.

In the DA VINCI study the team reviewed how lipid-lowering therapies were used in primary and secondary care and the attainment of cholesterol reduction goals set out by the guidelines.

Analysis revealed that 84% of patients¹ received statins as their primary lipid-lowering therapy only, with high intensity statins used in approximately one-quarter (28%)² of patients. Just 9% of patients were prescribed ezetimibe with moderate intensity statins and just 1% of patients used PCSK9 inhibitors in combination with statins and/or ezetimibe.

They found that overall, less than half of patients were achieving the most recent cholesterol-lowering goals set out by guidelines. Among patients receiving high-intensity statins, 2019 LDL-C goals were achieved in 22% of patients with established cardiovascular disease. However, among the patients receiving statins with a PCSK9 inhibitor about two thirds attained the new lower ESC recommended cholesterol goals.

According to the authors, the findings highlight the potential for combinations of lipid lowering drugs to help close the gap and reduce the risk for millions of patients across Europe. They explain that reducing LDL cholesterol levels in very-high risk patients (from the observed levels of above 2mmol/L to below 1.4 mmol/L) could offer an 11% relative reduction in cardiovascular events and 5% relative reduction in mortality.

The authors add that untreated lipid levels were not available and so they were unable to quantify to what extent the ~50% LDL-C reduction from

baseline was achieved, but used high-intensity statin use as proxy. They add that physician choice of LLT, pre-treatment LDL cholesterol levels and local prescribing restrictions could have influenced our observations.

Professor Ray added: "Over the last 15 years we have seen improvements in guideline implementation and control of cardiovascular risk factors. These were based on better first line treatment such as statins. Now, with lowering of cholesterol goals, our data suggest this will not be enough and we need to think about cholesterol in the same way as we look at blood pressure where often combinations of treatments are needed to optimise targets."

More information: 'EU-Wide Cross-Sectional Observational Study of Lipid-Modifying Therapy Use in Secondary and Primary Care – the DA VINCI study' by Kausik Ray et al. is published in *European Journal of Preventive Cardiology*.

The findings will be presented at the European Society of Cardiology Congress 2020.

Provided by Imperial College London

Citation: Cholesterol drug combinations could cut health risk for European patients (2020, August 28) retrieved 25 April 2024 from <https://medicalxpress.com/news/2020-08-cholesterol-drug-combinations-health-european.html>

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