

Dietary supplements are just not SPORTing for LDL-cholesterol reduction

SPORT (Supplements, Placebo or Rosuvastatin Study) was conducted to compare the efficacy of low-dose rosuvastatin with a number of supplements marketed as natural alternatives to cholesterol-lowering drugs. A total of 190 adults, without established cardiovascular disease but with elevated LDL-cholesterol, were randomised to rosuvastatin 5 mg daily, placebo or one of six cholesterol-lowering supplements. After 28 days, only the statin had significantly lowered LDL-cholesterol, by 35% compared with placebo. In fact, the garlic supplement increased LDL-cholesterol by 8% ($P=0.01$). Despite the limitations of a small, short-duration study, these findings provide pragmatic information for us to discuss with our patients in primary and secondary care to reinforce the benefits of statins on cardiovascular health compared to commonly used dietary supplements.

Many of my patients place great stock in dietary supplements to reduce their cholesterol as an alternative or addition to modern cholesterol-lowering therapies such as statins. This is partly driven by the nocebo effect of statins: the inverse of the placebo effect, whereby adverse events (such as muscle symptoms) occur due to a belief that the intervention will cause harm. The nocebo effect is multifactorial but strongly influenced by pre-existing health beliefs, as well as the media (including social media).

Both the use of dietary supplements to reduce cholesterol and the nocebo effect of statins are potentially harmful, as we have high-quality evidence demonstrating that statins are efficacious at lowering LDL-cholesterol, and that this translates into a reduction in major adverse cardiovascular events. For every 1 mmol/L reduction in LDL-cholesterol, there is a 22% reduction in the annual rate of major vascular events (Cholesterol Treatment Trialists' Collaboration, 2010). Furthermore, in that study, there was no evidence of any threshold within the cholesterol target range studied, suggesting that reducing LDL-cholesterol by 2–3 mmol/L would reduce annual cardiovascular risk by up to 50%.

The Supplements, Placebo or Rosuvastatin Study (SPORT) was presented at a late-breaking session at the American Heart Association's

Scientific Sessions in November 2022 and simultaneously published in the *Journal of the American College of Cardiology*. It was a single-centre, prospective, randomised, single-blind, eight-arm trial exploring the impact of low-dose rosuvastatin (5 mg daily) versus (in hierarchical order) placebo, fish oil, cinnamon, garlic, turmeric, plant sterols or red yeast rice on lipid and inflammatory biomarkers. A total of 190 adults aged 40–75 years were recruited, all with no history of atherosclerotic cardiovascular disease (i.e. primary prevention) but with LDL-cholesterol levels of 1.8–4.9 mmol/L and at increased 10-year cardiovascular risk.

After 28 days of follow-up, rosuvastatin 5 mg had reduced LDL-cholesterol by 35.2% compared with placebo. In contrast, none of the dietary supplements demonstrated a significant reduction in LDL-cholesterol. Interestingly, garlic demonstrated a significant 7.8% increase in LDL-cholesterol levels. Rosuvastatin also had a benefit on triglyceride and total cholesterol levels. There was no significant difference in high-sensitivity CRP levels in any of the groups after 28 days.

Adverse event rates were similar across all groups. Reassuringly, there were no significant adverse effects observed on liver blood tests, renal function or blood glucose in the rosuvastatin group.



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“Both the use of dietary supplements to reduce cholesterol and the nocebo effect of statins are potentially harmful, as we have high-quality evidence demonstrating that statins are efficacious at lowering LDL-cholesterol.”

The authors do acknowledge that this was a short-duration study with a small sample size, and so it may not fully capture the effects of supplements on lipid biomarkers with longer use. Furthermore, most participants were of white ethnic background, limiting generalisability to other ethnicities. Additionally, the investigators did not explore the impact of combining rosuvastatin with dietary supplements on LDL-cholesterol.

Nevertheless, this high-quality study provides pragmatic information for us to discuss with our patients in primary and secondary care to reinforce the benefits of statins on cardiovascular health compared to commonly used dietary supplements. ■

Cholesterol Treatment Trialists' Collaboration (2010) Efficacy and safety of more intensive lowering of LDL cholesterol: a meta-analysis of data from 170,000 participants in 26 randomised trials. *Lancet* **376**: 1670–81



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