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Statins: are they appropriate for all patients?



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Despite the COVID-19 pandemic, atherosclerotic cardiovascular disease remains the primary cause of death, responsible for more than 18 million deaths annually worldwide. Atherosclerotic cardiovascular disease is often assumed to be a disease of affluent, industrialised countries. However, most deaths occur in low-income and middle-income countries and mortality from this disease, although plateauing in high-income countries, is expected to increase over the next few decades.¹

Although atherosclerotic cardiovascular disease is multifactorial, elevated lipid concentrations, particularly low-density lipoprotein (LDL) cholesterol, is the pivotal risk factor for atherosclerosis.² Statins effectively lower LDL cholesterol concentrations and large multicentre statin trials have conclusively shown that such a reduction decreases both morbidity and mortality and that the reduction in risk is proportional to the absolute reduction in LDL cholesterol.³ Statin therapy reduces the risk of major vascular events such as myocardial infarction and stroke by about a quarter for each 1 mmol/L reduction in LDL cholesterol per year of statin use and larger absolute benefits accrue with prolonged treatment.⁴ Lowering LDL cholesterol with statin therapy in people considered at low risk of atherosclerotic cardiovascular disease also lowers the risk of major vascular events, and the benefit of statin therapy markedly exceeds the harm.⁵ Used appropriately, statin therapy could prevent a large proportion of the global burden of cardiovascular disease. As a result, statins were added to the WHO Essential Medicines List in 2007. However, despite the overwhelming clinical evidence and international guideline recommendations, LDL cholesterol concentrations are infrequently measured and elevated LDL cholesterol concentrations are not being addressed or treated in patients with established atherosclerotic cardiovascular disease, even in high-income countries.⁶

Why the inertia? Unlike conditions such as diabetes, hypercholesterolaemia is an asymptomatic condition and there is no symptomatic benefit from taking statins. In high-income countries where perceived side-effects from statins, often from misinformation, are frequently the reason for non-compliance, in low-income and middle-income countries, non-compliance can arise

from lack of awareness and understanding of the need for statin therapy by health-care personnel and patients.

Additionally, unlike measuring blood pressure, measurement of LDL cholesterol requires a blood sample, which is often not done, particularly in primary care clinics in rural communities. As a result, conditions such as familial hypercholesterolaemia (characterised by LDL cholesterol concentrations that are elevated two-fold or greater from birth) and, if untreated, premature atherosclerotic cardiovascular disease, remain largely undiagnosed and untreated.⁷ With an estimated prevalence of 1 in 300 worldwide, there are more than 30 million people with familial hypercholesterolaemia globally, at least half of whom reside in low-income or middle-income countries.⁸ On the African continent alone there are more than 4 million people with familial hypercholesterolaemia, most of whom are undiagnosed and untreated. Because lifelong exposure to elevated LDL cholesterol in familial hypercholesterolaemia increases the chances of a cardiovascular event, statin therapy needs to be initiated as early as possible.

Although diet, lifestyle, and other atherosclerotic cardiovascular disease risk factors such as cigarette smoking and hypertension must be addressed, lipid-lowering therapy with statins, which are now inexpensive and universally available, is underutilised. In *The Lancet Global Health*, Maja Marcus and colleagues⁹ report that this is particularly the case in 41 geographically and economically diverse low-income and middle-income countries, where 1 in 10 people who were eligible for primary prevention (8.0%, 95% CI 6.9–9.3) and 1 in 5 people with established atherosclerotic cardiovascular disease were prescribed statins.⁹

The UN's third Sustainable Development Goal tabled in 2015 included a target to reduce premature mortality from non-communicable chronic diseases by a third by 2030.¹⁰ To achieve this goal, governmental priorities need to change and substantial health-care system reform is needed, particularly for the most clinically vulnerable people living in low-income and middle-income countries. Additionally, health-care workers need to be educated about the importance of LDL cholesterol testing and appropriate treatment if these concentrations are found to be elevated. With wider

use of even modest doses of statins, the cardiovascular burden could be substantially diminished both in urban and rural communities. Furthermore, with the low cost of generic statins, this strategy is likely to be cost effective.

Although we are not recommending the use of statins for all patients to achieve a reduction in cardiovascular burden, statin therapy should be considered for all patients with established atherosclerotic cardiovascular disease or those at a high risk of developing the condition. Increasing awareness and education of the importance of screening for elevated LDL cholesterol concentrations must be prioritised, particularly in low-income and middle-income countries, which now carry the highest burden of cardiovascular disease cases worldwide.

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