National Health Laboratory Service (NHLS) changes the method of LDL-cholesterol calculation in South Africa

To the Editor: Low-density lipoprotein cholesterol (LDL-C) is the main target for lipid-lowering therapies and preventing cardiovascular disease.[1-6]

Clinicians rely heavily on LDL-C. Statin and non-statin therapy for LDL-C reduction has been shown in randomised controlled trials and meta-analyses to lower the relative risk of atherosclerotic cardiovascular disease (ASCVD) by 20 - 25%,[7] demonstrating the importance of accurate LDL-C to guide therapy.[8] If LDL-C is a primary target in dyslipidaemia, we need accurate, precise and affordable assessment.

ApoB100 is a test that is more specific and precise. However, only private sector laboratories offer the apoB100 assay.[9,10] LDL-C is generally calculated (c-LDL-C) using the Friedewald equation, while some laboratories routinely measure LDL-C (d-LDL-C) with a direct assay. Calculating LDL-C is a simple cost-free way to determine routine LDL-C by subtracting high-density lipoprotein (HDL-C) and triglycerides (TG) from total cholesterol[11,12] when TG is <4.5 mmol/L. The Friedewald equation is inaccurate when TG is >4.5 mmol/L or with new lipid-lowering therapies that lower the LDL-C levels to <1.8 mmol/L. The Friedewald equation showed poor performance in large varied South African (SA) cohorts, including children and patients with diabetes, particularly in samples with hypertriglyceridaemia (TG >4.5 mmol/L).[13,14]

The Friedewald equation has, to date, been the only equation used in SA laboratories for routine calculation of LDL-C with TG <4.5 mmol/L. Hypertriglyceridaemic samples are referred for direct assay, and this increases turnaround time and has logistical obstacles. In SA, using big data analysis, differences in instrument performance are also of concern.[13-15] The Friedewald equation performed poorly when compared with the direct LDL-C assay in an outpatient cohort, misclassifying 12% of all patients across different LDL-C cut-offs.[13]

Dissatisfaction with the performance of the Friedewald equation has led to the development of newer equations, of which two have been found to be robust and accurate. These are the Martin-Hopkins equation and the Sampson-NIH equation samples.[16,17] These equations performed better than the Friedewald equation in recent SA cohorts, including diabetics and children.[13,14]

The newer equation published by Sampson *et al.*[18] improves accuracy with low LDL-C and hypertriglyceridaemia samples, as these are problematic with the Friedewald equation.[18] The National Health Laboratory Service (NHLS) chemistry expert committee has implemented the Sampson-NIH2 equation to modernise practice and report more accurate patient results.

The superiority of the newer equations is undeniable, and private sector laboratories and clinicians need to adopt one of the newer equations. The Martin-Hopkins equation shows excellent comparability with a direct assay, as demonstrated extensively internationally[16,19,20] and locally.[13,14] The Sampson-NIH and extended Martin-Hopkins demonstrate favourable comparability with direct LDL-C with triglyceride levels up to 9 mmol/L, but this still warrants further investigation in SA cohorts. Reducing the need for direct LDL-C assays will reduce the overall cost of a lipid profile and assist in lowering laboratory expenditure. The Friedewald equation is no longer fit for purpose, and laboratories should switch to one of the newer equations.

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