

Comparison of existing methods of low-density lipoprotein cholesterol estimation in patients with type 2 diabetes mellitus

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ABSTRACT

Introduction: Elevated low-density lipoprotein cholesterol (LDL-C) is an important risk factor for atherosclerotic cardiovascular disease (ASCVD). Direct LDL-C measurement is not widely performed. LDL-C is routinely calculated using the Friedewald equation (FLDL), which is inaccurate at high triglyceride (TG) or low LDL-C levels. We aimed to compare this routine method with other estimation methods in patients with type 2 diabetes mellitus (T2DM), who typically have elevated TG levels and ASCVD risk.

Method: We performed a retrospective cohort study on T2DM patients from a multi-institutional diabetes registry in Singapore from 2013 to 2020. LDL-C values estimated by the equations: FLDL, Martin/Hopkins (MLDL) and Sampson (SLDL) were compared using measures of agreement and correlation. Subgroup analysis comparing estimated LDL-C with directly measured LDL-C (DLDL) was conducted in patients from a single institution. Estimated LDL-C was considered discordant if LDL-C was <1.8mmol/L for the index equation and ≥1.8mmol/L for the comparator.

Results: A total of 154,877 patients were included in the final analysis, and 11,475 patients in the subgroup analysis. All 3 equations demonstrated strong overall correlation and goodness-of-fit. Discordance was 4.21% for FLDL-SLDL and 6.55% for FLDL-MLDL. In the subgroup analysis, discordance was 21.57% for DLDL-FLDL, 17.31% for DLDL-SLDL and 14.44% for DLDL-MLDL. All discordance rates increased at TG levels >4.5mmol/L.

Conclusion: We demonstrated strong correlations between newer methods of LDL-C estimation, FLDL, and DLDL. At higher TG concentrations, no equation performed well. The Martin/Hopkins equation had the least discordance with DLDL, and may minimise misclassification compared with the FLDL and SLDL.

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INTRODUCTION

Elevated low-density lipoprotein cholesterol (LDL-C) levels are a major risk factor for the development of atherosclerotic cardiovascular disease (ASCVD). A reduction in LDL-C levels has been shown to significantly reduce the risk of incident ASCVD¹ and

all-cause mortality.² LDL-C levels are hence key treatment targets in the prevention of ASCVD, with a target of <1.8mmol/L for patients with high cardiovascular risk.^{3,4}

Accurate LDL-C measurement is important to guide treatment decisions. The established reference

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CLINICAL IMPACT

What is New

- Current methods of low-density lipoprotein cholesterol (LDL-C) estimation may underestimate LDL-C, especially at higher triglyceride levels.

Clinical Implications

- Such underestimations can lead to undertreatment in patients at high risk of atherosclerotic cardiovascular disease.
- Use of the Martin/Hopkins equation has the potential to minimise the clinical discordance in estimation values compared with the conventional Friedewald equation.

method for measuring LDL-C is the beta-quantification method,⁵ which requires ultracentrifugation followed by polyanion precipitation of high-density lipoprotein cholesterol (HDL-C) and other lipoproteins. This process is time-consuming, costly, and requires equipment not readily available in all routine laboratories.

Clinical laboratories therefore typically estimate LDL-C levels using the Friedewald equation (FLDL): $\text{LDL-C} = \text{total cholesterol (TC)} - \text{HDL-C} - \text{triglycerides (TG)}/2.2$, with all units in mmol/L.⁶ This has been widely adopted both in clinical practice and in research studies.⁵ However, the FLDL has been reported to underestimate LDL-C levels, particularly when LDL-C levels are very low ($<1.0\text{mmol/L}$)⁷ or TG levels are elevated.⁸ Moreover, the equation cannot be used when there is significant hypertriglyceridaemia ($\text{TG} \geq 4.5\text{mmol/L}$) as the assumption of a factor of 5 in the TG:very low-density lipoprotein (VLDL) ratio is no longer valid.⁶

To overcome these limitations, Martin et al. developed an estimation method using an adjustable factor based on strata-specific median TG:VLDL ratios instead of a fixed ratio.⁹ The Martin/Hopkins equation (MLDL) has been reported to be more accurate than the FLDL at lower LDL-C levels,¹⁰ but can overestimate LDL-C levels when TG is high ($>2.8\text{mmol/L}$).¹¹ Sampson et al. therefore developed a novel equation based on a population with a high frequency of hypertriglyceridaemia.¹² The Sampson equation (SLDL) is valid in patients with TG levels up to 9.0mmol/L and has been reported to be more accurate than both FLDL and

MLDL in patients with TG levels $>2.8\text{mmol/L}$.¹¹ In fact, some have reported that the SLDL may still be accurate even with TG levels $>9.0\text{mmol/L}$.¹³ However, not all reports have described concordant findings, with a recent study in a large East Asian population reporting that the MLDL had the greatest accuracy across all TG levels.¹⁴

Patients with diabetes are an important population with high cardiovascular risk in whom appropriate lipid-lowering therapy is crucial. These patients also typically have elevated TG levels when compared to patients without diabetes.¹⁵ Moreover, patients of Asian ethnicities appear to have higher TG levels when compared to their Caucasian counterparts.¹⁶ Underestimation of LDL-C levels when using the conventional FLDL may lead to undertreatment and worse cardiovascular outcomes in this group of patients. We hence compared the correlation and agreement in LDL-C estimated by the FLDL, MLDL and SLDL in a multiethnic Asian population of patients with type 2 diabetes mellitus (T2DM), and to determine if these differences would have any clinical significance in determining intensification of lipid lowering therapy. We also explored the relationship of all 3 equations with directly measured LDL-C (DLDL).

METHOD

Study design and population

We conducted a retrospective cohort study using data from the SingHealth Diabetes Registry (SDR), a multi-institutional diabetes registry in Singapore. It incorporates data from the largest healthcare cluster in Singapore, providing healthcare services to approximately 50% of the national population via a total of 20 healthcare institutions. The structure and data collection for the SDR have been described previously.¹⁷ This study included patients ≥ 18 years of age with T2DM, enrolled between 2013 and 2020. The following data were collected for all patients: demographics (age, sex and ethnicity), weight and body mass index, smoking status, history of hypertension, peripheral vascular disease, ischaemic heart disease and previous ischaemic stroke, current lipid-lowering medications and lipid test results (TC, TG and HDL-C). Patients with any missing demographics or with negative estimated LDL-C values using any of the 3 methods were excluded from analysis. Only the latest lipid test result for each unique patient was included in the analysis.

To determine the accuracy of estimation methods against DLDL, subgroup analysis was also performed on patients from a single institution within the SDR, which had started performing routine DLDL

measurements via a homogenous enzymatic colorimetric assay using the cobas c702 (Roche Diagnostics, Basel, Switzerland) platform from 22 July 2017.¹⁸ In addition to the earlier-mentioned data, DLDL values were also collected for this subset of the population. Patients with lipid test results recorded prior to this date or with missing data, including DLDL measurements, were excluded from this subgroup analysis.

This study utilised anonymised data from the SDR and was granted a waiver for the need to obtain informed consent by the SingHealth Centralised Institutional Review Board.

LDL-C estimation equations

LDL-C values were estimated in mmol/L, using the Friedewald, Martin/Hopkins, and Sampson equations:

$$\begin{aligned} \text{Friedewald:} \quad & \text{FLDL} = \text{Non-HDL-C} - \text{TG}/2.2 \\ \text{Martin/Hopkins:} \quad & \text{MLDL} = \text{Non-HDL-C} - \text{TG}/\text{AF} \\ \text{Sampson:} \quad & \text{SLDL} = \text{TC}/0.948 - \text{HDL-C}/0.971 - \\ & (\text{TG}/3.74 + \text{TG} \times \text{Non-HDL-C}/24.1 \\ & - \text{TG}^2/79.36) - 0.244 \end{aligned}$$

where non-HDL-C is defined as TC-HDL-C, and is the adjustable factor based on the strata-specific median TG:VLDL ratios obtained from the 180-cell table by Martin et al. (converted to mmol/L).⁹

Statistical analysis

The baseline characteristics of the population were described with continuous variables expressed as means and standard deviations, and categorical variables reported as numbers and proportions. LDL-C and other lipid values were reported as medians and interquartile range (IQR) (25th–75th percentile) as their distributions were notably right-skewed.

The distribution of estimated LDL-C values by all 3 equations was described using box and whisker plots stratified by TG values. Overall and strata-specific median estimated LDL-C values were compared with using Mann-Whitney U tests. TG strata were defined firstly at >1.7mmol/L³, being a commonly used treatment threshold in consensus guidelines, and >4.5mmol/L, the traditional upper bound of TG for the FLDL. Ordinary least squares regression was performed to measure the correlation of FLDL versus SLDL, and FLDL vs MLDL, and the results were evaluated using R^2 , root-mean-square-error (RMSE), and the correlation coefficient (r). Goodness-of-fit between observed values and the regression models was also evaluated using R^2 . Agreement between each of the 3 equations was assessed using Bland-Altman plots.

To determine the clinical significance of differences in

estimated LDL-C values, concordance and discordance between the estimated LDL-C values were evaluated categorically within TG strata using a LDL-C threshold of <1.8mmol/L, a common treatment target for patients at high cardiovascular risk.³ Patients with diabetes mellitus are typically considered at minimum to have high, if not very high, cardiovascular risk. LDL-C values using 2 different equations were considered concordant if both estimates were either $\geq 1.8\text{mmol/L}$ or $< 1.8\text{mmol/L}$. As the hypothesis was that FLDL tended to underestimate LDL-C, discordance was defined as an LDL-C value of <1.8mmol/L on the FLDL (reference equation) and an LDL-C value of $\geq 1.8\text{mmol/L}$ on either the SLDL or MLDL, respectively (comparator equations). Discordance was defined unidirectionally since the FLDL or DLDL would typically be conventionally used to make treatment decisions at present. The same methods were used for the subgroup analysis evaluating the correlation of the DLDL with FLDL, SLDL and MLDL. All analyses were performed using Python 3.8 (Python Software Foundation, Delaware, US).

RESULTS

Patient characteristics

A total of 154,877 patients were included in the final analysis, as described in Fig. 1. The baseline characteristics of the study population are summarised in Table 1. Of note, most patients were already on lipid-lowering therapy at the time of inclusion into the study, with statin therapy being the most common therapeutic modality.

Among the original cohort of 154,877 patients, 11,475 patients had DLDL measurements available and were included in the subgroup analysis. Characteristics of patients included in the subgroup analysis were mainly similar to that of the overall sample, apart from a slightly higher rate of prevalent ischaemic heart disease, ischaemic stroke or transient ischaemic attack, and overall cardiovascular disease. Additionally, there was a slightly higher proportion of patients of Malay ethnicity due to the demographic distribution in the local area of the single institution from which patients were recruited. These are shown in Table 1.

Differences between LDL-C estimated by all 3 equations

Bland-Altman plots did not demonstrate significant agreement, as would be expected between 3 equations derived using different models or coefficients (Supplementary Fig. S1). All 3 equations were closely correlated by linear regression regardless of TG strata. However, as expected, a slightly poorer fit was observed

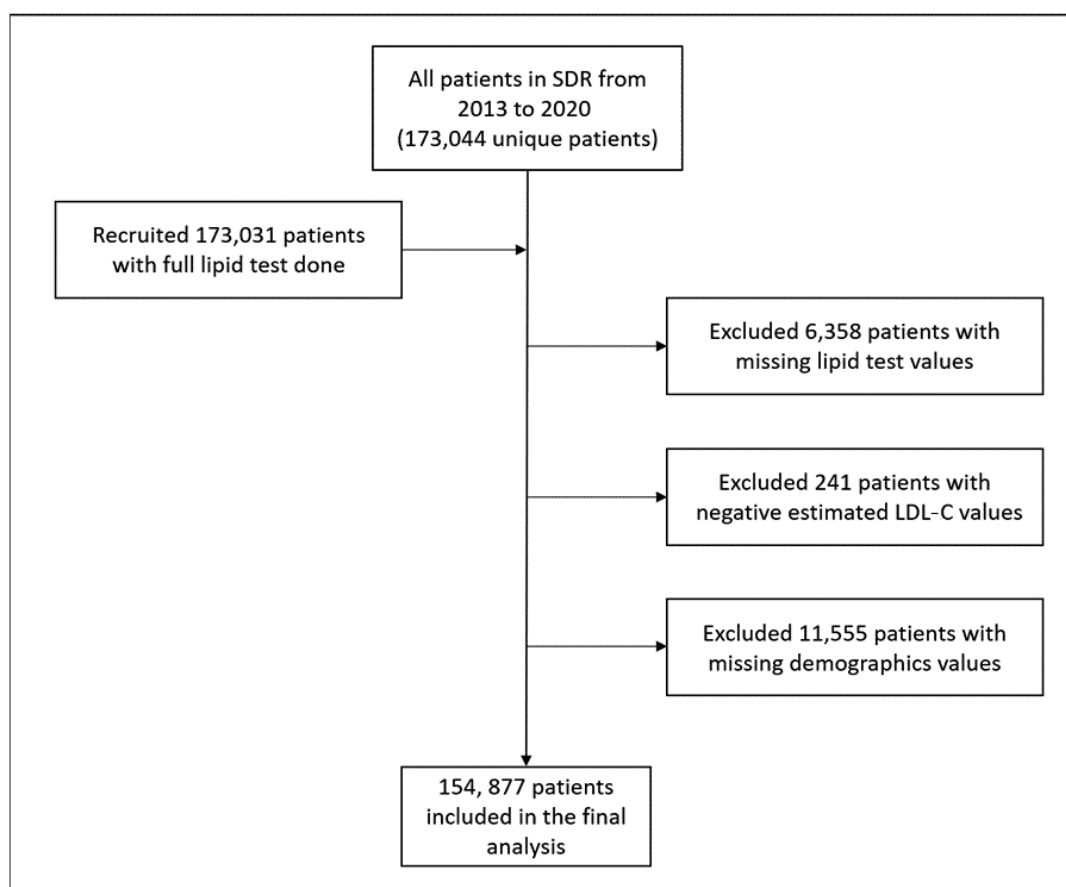


Fig. 1. Flow diagram of participants in the study.

LDL-C: low-density lipoprotein cholesterol; SDR: SingHealth Diabetes Registry

towards higher TG values (RMSE 0.534 and 1.006 for SLDL and MLDL, respectively). While both the SLDL ($R^2=0.990$ and $r=0.995$, $P<0.001$) and MLDL ($R^2=0.964$ and $r=0.982$, $P<0.001$) demonstrated consistently high R^2 and r values above 0.9, the SLDL showed a smaller RMSE (0.111 vs 0.192) and hence a better fit with the FLDL, although the significance of these differences is marginal. These findings are summarised in Table 2. SLDL (median 2.12, IQR 1.68–2.64) and MLDL (median 2.14, IQR 1.72–2.67) tended to estimate higher LDL-C values than the FLDL (median 2.04, IQR 1.61–2.56), as shown in Fig. 2 and described in Supplementary Table S1. The differences between overall and TG strata-specific medians were all statistically significant ($P<0.05$).

Discordance rate between FLDL-SLDL and FLDL-MLDL

The discordance between FLDL-SLDL and FLDL-MLDL for all subjects were 4.21% and 6.55%, respectively. Discordance was relatively low at TG values of $<1.7\text{mmol/L}$, at 2.33% and 2.89%,

respectively. However, at moderate TG values of $1.7\text{--}4.5\text{mmol/L}$, these rose to 8.14% and 14.1% for FLDL-SLDL and FLDL-MLDL, respectively. The discordance rate at TG values above 4.5mmol/L was the highest at 18.81% and 37.55% for FLDL-SLDL and FLDL-MLDL, respectively, as illustrated in Fig. 3.

Comparing all 3 equations against DLDL

All 3 estimation methods were highly correlated with DLDL for low and moderate TG levels, with SLDL ($R^2=0.933$ and $r=0.966$, $P<0.001$) achieving slightly better R^2 and r values than FLDL ($R^2=0.917$ and $r=0.958$, $P<0.001$) and MLDL ($R^2=0.918$ and $r=0.958$, $P<0.001$). However, correlation coefficients were observed to diverge at higher TG levels ($\geq 4.5\text{mmol/L}$), with FLDL performing the worst against DLDL having the smallest R^2 (0.574) and r (0.758) values, and largest RMSE value (1.354). Notably, neither SLDL ($R^2=0.584$, $r=0.764$ and $\text{RMSE}=1.093$, $P<0.001$) nor MLDL ($R^2=0.547$, $r=0.739$ and $\text{RMSE}=1.167$, $P<0.001$) fared much better at this range. These findings are summarised in Table 2. Bland-Altman plots did not

Table 1. Demographic and baseline clinical characteristics of patients.

		Overall sample n=154,877	Subgroup with DLDL n=11,475
Age, median (IQR), years		67.0 (59.0–75.0)	66.0 (58.0–76.0)
Body mass index, median (IQR)		25.7 (22.9–29.1)	26.0 (22.9–29.8)
HbA1c, median (IQR)		6.9 (6.4–7.7)	7.0 (6.2–8.2)
Sex, no. (%)	Male	80,727 (52.1)	6,775 (59.0)
	Female	74,150 (47.9)	4,700 (41.0)
Ethnicity, no. (%)	Chinese	108,314 (69.9)	6,575 (57.3)
	Malay	23,493 (15.2)	2,781 (24.2)
	Indian	16,352 (10.6)	1,122 (9.8)
	Others	6,718 (4.3)	997 (8.7)
Smoking status, no. (%)	Never-smoker	126,589 (81.7)	8,706 (75.9)
	Current smoker	13,919 (9.0)	1,372 (12.0)
	Ex-smoker	3,924 (2.5)	427 (3.7)
	Unknown	10,445 (6.7)	970 (8.5)
Hypertension, no. (%)	Yes	138,608 (89.5)	10,662 (92.9)
	No	16,269 (10.5)	813 (7.1)
Cardiovascular disease, ^a no. (%)	Yes	61,650 (39.8)	7,740 (67.5)
	No	93,227 (60.2)	3,735 (32.5)
Ischaemic heart disease, no. (%)	Yes	42,472 (27.4)	5,647 (49.2)
	No	112,405 (72.6)	5,828 (50.8)
Peripheral vascular disease, no. (%)	Yes	7,925 (5.1)	1,135 (9.9)
	No	146,952 (94.9)	10,340 (90.1)
Ischaemic stroke or TIA, no. (%)	Yes	20,440 (13.2)	3,001 (26.2)
	No	134,437 (86.8)	8,474 (73.8)
Lipid-lowering therapy, ^b no. (%)	Statin	136,105 (97.7)	10,526 (98.4)
	Fibrate	13,461 (9.6)	1,025 (9.6)
	Ezetimibe	4,842 (3.5)	733 (6.9)
	PCSK9 inhibitor	27 (0)	7 (0.1)
	Others	234 (0.2)	22 (0.2)
TG strata, no. (%)	<1.7mmol/L	107,802 (69.6)	7,505 (65.4)
	1.7–4.4mmol/L	45,416 (29.3)	3,729 (32.5)
	≥4.5mmol/L	1,659 (1.1)	241 (2.1)

DLDL: directly measured low-density lipoprotein cholesterol; HbA1c: haemoglobin A1C; IQR: interquartile range; PCSK9: proprotein convertase subtilisin-kexin type 9; TG: triglyceride; TIA: transient ischaemic attack

^a Defined as composite of ischaemic heart disease, peripheral vascular disease, a stroke or transient ischaemic attack.

^b Patients may be on more than one lipid-lowering therapy.

Table 2. Correlations between Friedewald equation (FLDL) with Sampson equation (SLDL) and Martin/Hopkins equation (MLDL), as well as between directly measured LDL-C (DLDL) with FLDL, SLDL and MLDL.

		Overall			TG<1.7			1.7≤TG<4.5			TG≥4.5		
		FLDL	SLDL	MLDL	FLDL	SLDL	MLDL	FLDL	SLDL	MLDL	FLDL	SLDL	MLDL
FLDL	RMSE		0.111	0.192		0.051	0.061		0.160	0.283		SLDL	MLDL
	R ²		0.990	0.964		0.998	0.995		0.997	0.984		0.534	1.006
	r		0.995	0.982		0.999	0.997		0.998	0.992		0.987	0.977
	P value		<0.001	<0.001		<0.001	<0.001		<0.001	<0.001		0.994	0.989
DLDL	RMSE	0.516	0.437	0.424	0.390	0.356	0.369	0.628	0.505	0.437	1.354	<0.001	<0.001
	R ²	0.917	0.933	0.918	0.964	0.967	0.964	0.919	0.925	0.920	0.574	0.584	0.547
	r	0.958	0.966	0.958	0.982	0.983	0.982	0.959	0.962	0.959	0.758	0.764	0.739
	P value	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001

LDL-C: low-density lipoprotein cholesterol; RMSE: root-mean-square-error; TG: triglycerides

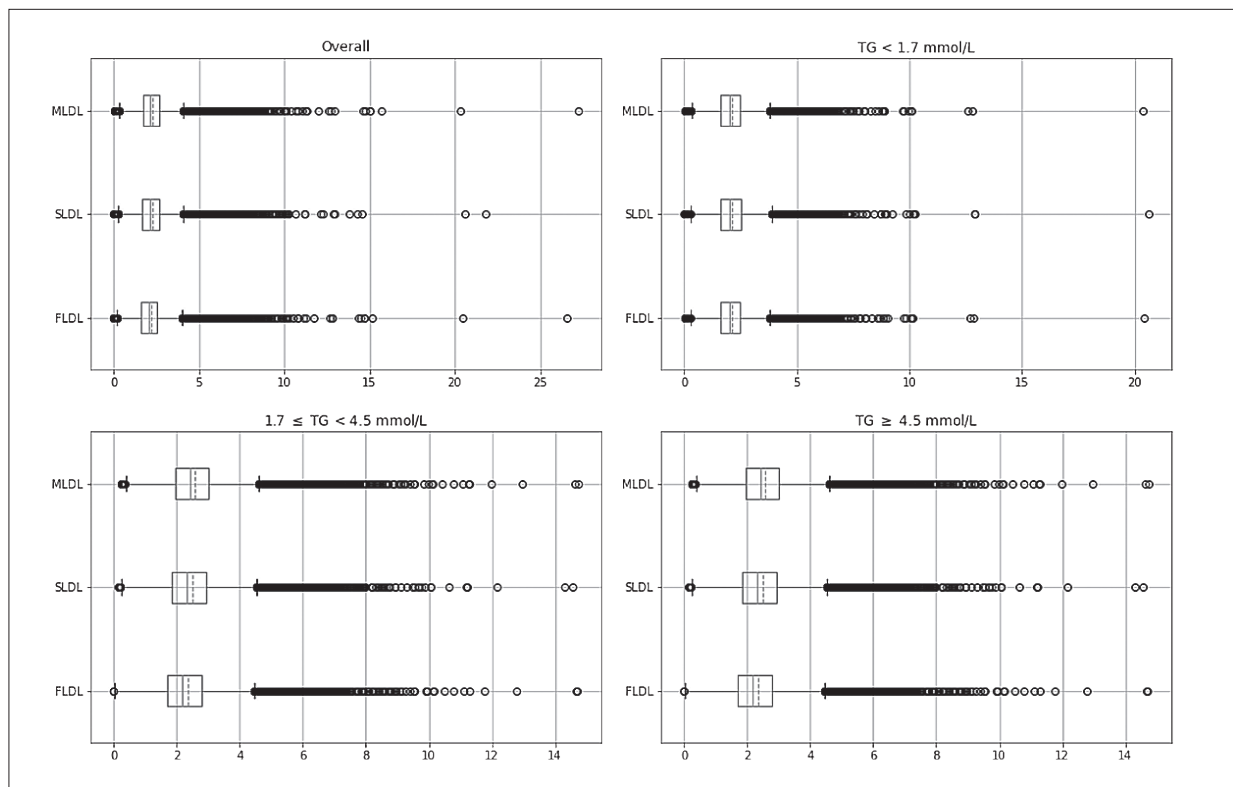


Fig. 2. Distribution of overall and triglyceride strata-specific estimated LDL-C values in the main study population. LDL-C: low-density lipoprotein cholesterol; TG: triglycerides

demonstrate significant agreement as well.

Of note, all 3 equations tended to estimate lower LDL-C values than DLDL across TG strata, except for MLDL at TG values above 4.5mmol/L (which estimated higher LDL-C). These differences were all statistically significant. FLDL tended to estimate the lowest values regardless of TG, followed by SLDL and then MLDL.

The difference in SLDL and MLDL estimated LDL-C was the most pronounced at TG levels above 4.5mmol/L. These are demonstrated in Fig. 4.

Discordance rates were somewhat higher when the DLDL was used as the comparator, with overall rates of 21.57%, 17.31% and 14.44% for the FLDL, SLDL and MLDL, respectively. Even at low TG levels of below

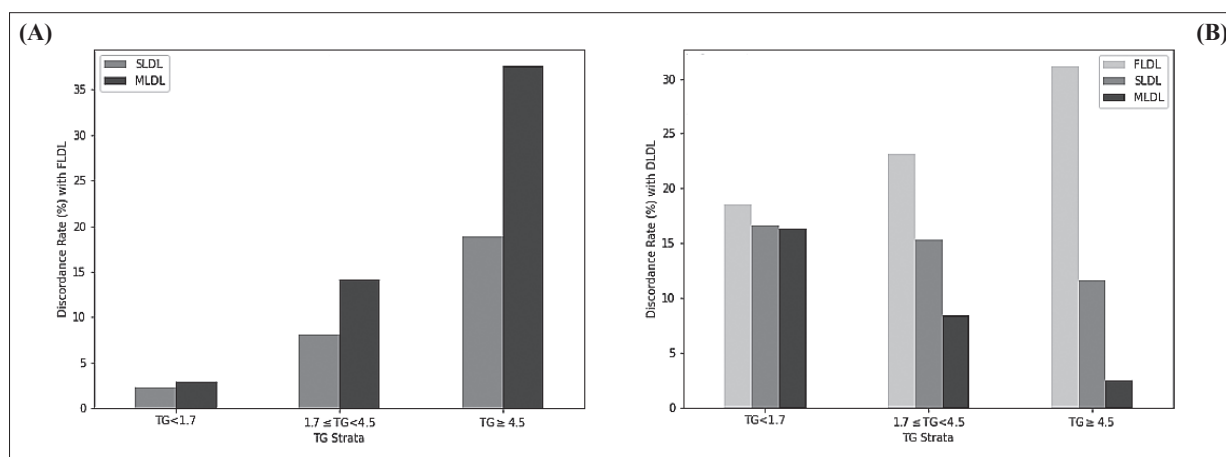


Fig. 3. (A) Discordance rates between Friedewald equation (FLDL) with Sampson equation (SLDL) and Martin/Hopkins equation (MLDL) across all triglyceride (TG) strata. (B) Discordance rates of FLDL, SLDL and MLDL with directly measured LDL-C (DLDL). Estimated low-density lipoprotein cholesterol (LDL-C) was considered discordant if LDL-C was <1.8mmol/L for the index equation and ≥1.8mmol/L for the comparator.

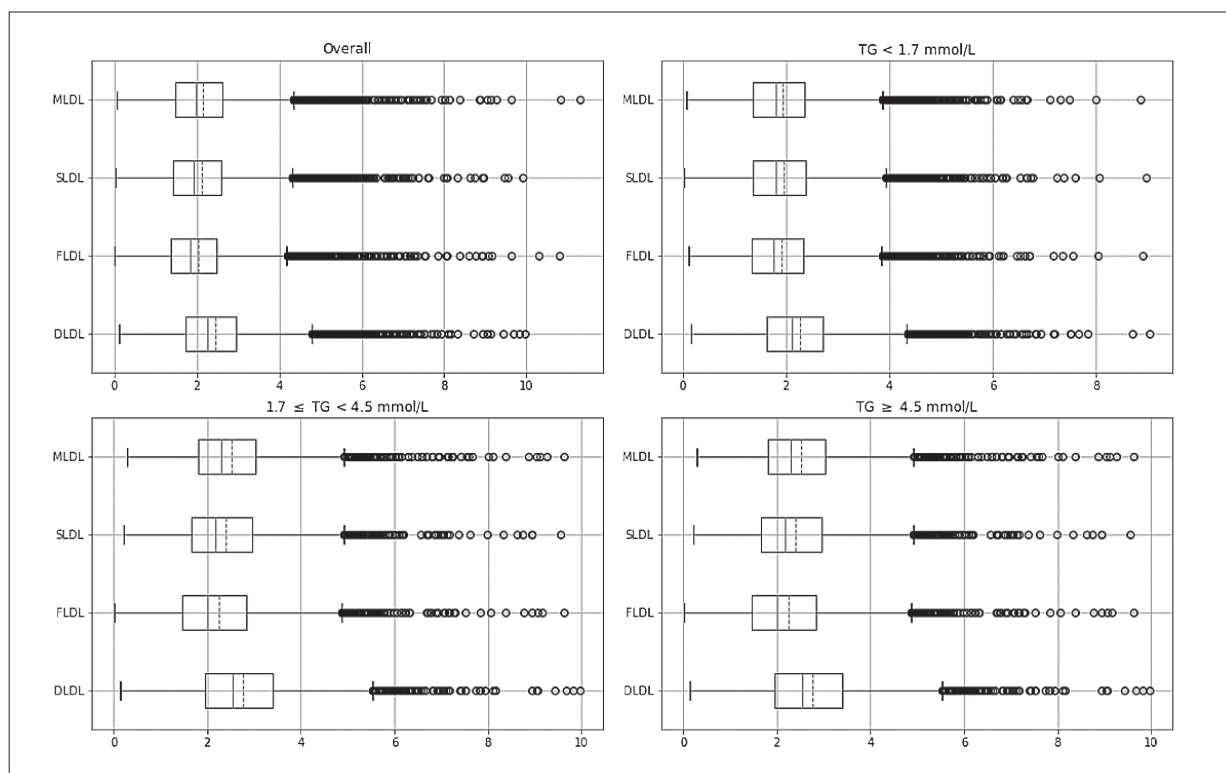


Fig. 4. Distribution of overall and triglyceride (TG) strata-specific estimated low-density lipoprotein cholesterol (LDL-C) values in the subgroup analysis. All 3 equations had lower median values than directly measured LDL-C (DLDL), with Friedewald equation (FLDL) estimating the lowest values across strata. The differences between median estimated LDL-C values and median DLDL values were all statistically significant ($P < 0.05$).

1.7mmol/L, the discordance was still fairly substantial at 19.71%, 17.93% and 17.49%, respectively. As expected, discordance rates rose moving across the TG strata. The MLDL demonstrated the lowest discordance rates within each TG stratum, as shown in Fig. 3.

DISCUSSION

We conducted a large study of 154,877 patients with T2DM, demonstrating the relationship between LDL-C values estimated by the FLDL, MLDL and SLDL. The study population is a uniquely relevant group of patients with both elevated TG levels and high

cardiovascular risk. To our knowledge, this is the first study comparing all 3 equations in this population, as well as against DLDL.

Both the SLDL and MLDL are alternative methods for estimating LDL-C in patients with T2DM, and are closely correlated with the conventional FLDL. In fact, all 3 methods also showed good correlation with DLDL. This is perhaps unsurprising as all 3 equations have the same theoretical basis—both HDL-C and TG are subtracted mathematically (albeit with varying factor coefficients) from the overall cholesterol, just as they are removed via polyanion precipitation and ultracentrifugation, respectively, in the beta-quantification method. There are differences in the correlation coefficients, with the SLDL appearing to demonstrate the best fit with both FLDL and DLDL overall, although the true magnitude of differences in both the correlation and goodness-of-fit (based on r , R^2 and RMSE values) between the equations is marginal.

Additionally, while the equations are closely correlated, none are equivalent to DLDL. The gold standard of LDL-C measurement should remain as beta-quantification. Commercially available homogenous enzymatic colorimetric assays (as used in our study) are an alternative to beta-quantification. These assays utilise a multistep reaction in which cholesterol esterase and oxidase produce hydrogen peroxide from solubilised LDL-C. Hydrogen peroxide reacts with selected reagents in the presence of peroxidase to produce a red-purple dye, which can be measured photometrically at the sub and main wavelengths of 700nm and 600nm, respectively. These assays are reported by the manufacturer to correlate well with beta-quantification and offer advantages including assay validity up to a maximum TG concentration of 23.0mmol/L.¹⁸ However, these are not widely available, particularly in primary care settings. Therefore, these equations still offer a practical alternative to LDL-C measurement.

Unlike the MLDL and FLDL, the SLDL was designed to correlate better with measured LDL-C in hypertriglyceridaemic patients with TG values up to 9.0mmol/L.¹⁹ However, this was not observed in our study. While the SLDL did correlate the best at TG values above >4.5mmol/L, with the highest correlation of 76.4%, this was firstly still much lower than its overall correlation of 96.6%, and secondly only marginally different from that reported for the MLDL (73.9%) and FLDL (75.8%). The goodness-of-fit was also similar for all 3 equations. As such, it remains uncertain which is the best method of LDL-C estimation when TG levels are high. More work including epidemiological studies and clinical intervention studies comparing different

LDL-C estimation methods may be required in this group of patients.

Evaluating the discordance between the equations is important as this reflects a real-world treatment gap. Hypothetically, a patient with an estimated LDL-C of below 1.8mmol/L may not be targeted for more aggressive treatment, where in fact the true LDL-C value may be higher than 1.8mmol/L. This patient would hence be undertreated and exposed to a higher risk of poorer cardiovascular and overall outcomes. It is notable that the discordance between estimation methods can be close to 40% in patients with the highest TG values. This suggests that there may be a large unrecognised proportion of patients with diabetes who may be undertreated, especially when using the traditional Friedewald model. Lipid-lowering therapy is typically safe and effective.³ As such, a method of LDL-C estimation that favours intensification of treatment may be preferred. Similar to previous reports,²⁰ the MLDL had the lowest discordance rates and hence may be considered as the most clinically favourable alternative to the traditional FLDL.

This study has several limitations. Firstly, the SDR only includes patients from 1 of the 3 healthcare clusters in Singapore. However, as previously described, the SingHealth cluster is the largest healthcare cluster in Singapore and is responsible for the medical care of approximately 50% of the national population. As such, these results can still be extrapolated to the national population at large.

Secondly, we used an LDL-C threshold of 1.8mmol/L when defining clinically relevant discordance, in keeping with international guidelines.^{3,21} However, guidelines from Asian societies are heterogenous with respect to treatment targets²² and evidence can be mixed.²³ Indeed, the local guidelines for our study population suggest a more permissive LDL-C target of <2.6mmol/L in high-risk and <2.1mmol/L in very-high-risk patients,²⁴ although this is currently under review. Nevertheless, while the exact value of the treatment target may be debated, it remains clear that lower lipid targets are generally beneficial even in Asian populations,²⁵ and we believe it is likely that there will still be substantial discordance between estimated LDL-C levels even if the LDL-C threshold used may vary slightly.

Lastly, only a subgroup of patients had direct LDL-C measurements. However, we believe this subgroup is largely similar to the overall population, apart from slight differences in ethnic profile and certain prevalent comorbidities at time of enrolment, which would not be expected to significantly affect LDL-C values.

Additionally, direct LDL measurements in the subgroup analysis were conducted using a homogenous enzymatic colorimetric assay. Significant non-selectivity errors have been reported when using this method in general,²⁶ although this particular laboratory has previously reported achieving satisfactory results on this assay when benchmarked on the College of American Pathologists external quality assurance programme.¹⁸

CONCLUSION

In a very large sample of patients with T2DM from an Asian population, we demonstrated strong correlation between newer methods of LDL-C estimation and the traditional FLDL. While the SLDL seemed to perform the best in statistical terms, the practical overall difference between the equations seems to be marginal. However, at higher TG concentrations, no one equation performed very well, suggesting further study may be required in this area. Clinically significant discordance was noted between equations and with DLDL. The use of the MLDL in this population may lead to less misclassification and undertreatment than the FLDL and SLDL.

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