Underestimation of LDL Cholesterol Below 70 mg/dL (1.8 mmol/L) by Friedewald, Hopkins and a “Direct” Assay Compared to Preparative Ultrafiltration
Traci Turner MD, Nan Plunkett BS, Rong Zhou PhD, Mikram Zangmeister MS, Christine Fitz MS, Matt Kello PharmD PhD, Evan A, Stein MD PhD

Abstract
Background. Calculated LDL cholesterol (LDL-C) by the Friedewald formula (LDL-C) has been the basis for clinical and regulatory decision making for >40 years. An algorithmic and lab-referenced approach reduces LDL-C levels below 70 mg/dL to be lower, properly, by using LDL-C (LDL-C) cut offs that have been proposed, employing LDL-C (LDL-C) by Friedewald (LDL-C) cut offs have been shown to result in underestimation of LDL-C at lower concentrations.
Methods. Patient samples were obtained in a central laboratory that was part of the M*DPAC Part 3 Standardized for lipid measurement. LDL-C (LDL-C) and TG (TG) were measured employing methods that have been standard for 10 years. LDL-C (LDL-C) and TG (TG) were measured in the same sample, and TG was measured in two different methods. The percent difference between Friedewald (LDL-C) and PUC was calculated for each sample, for each method and for each group of concentrations (≤100, 101-200, >200 mg/dL).

Results
Overall % difference cut points by Friedewald (LDL-C) were calculated. As compared to LDL-C (LDL-C) cut points, there was a minimal difference of -3.4% when LDL-C (LDL-C) was between 101–200 mg/dL, however, the differences were statistically significant and clinically relevant when true LDL-C was <70 mg/dL; and even moderate TG (TG) increases have major consequences. As measurements of LDL-C (LDL-C) by these formulas have demonstrated LDL-C (LDL-C) lowering to be directly linked to risk reduction of morbidity and mortality in cardiovascular disease. Overall, the “direct” method was more accurate with a % difference of -0.8 (p-value 0.1699). However, the differences at all LDL-C cut-points were statistically significant with underestimation of LDL-C as compared to PUC; 3.7% between 101 and 200 mg/dL, 2.7% between 100 and 71 mg/dL, 4.1% between 70 and 51 mg/dL, and 4.3% between 50 and 29 mg/dL. Analysis with each LDL-C cut point by each method showed no differences between Friedewald (LDL-C) and a “direct” method within 100 mg/dL (Table 3). However, there was a difference between Friedewald (LDL-C) and PUC; 0.7% between 201 and 400 mg/dL and 3.8% between 101–200 mg/dL. With the direct method, there was a significant difference between calculated and measured LDL-C at the lowest measured LDL-C concentrations (Table 3).

Conclusions
In conclusion, the differences between calculated and measured LDL-C at concentrations below 70 mg/dL are clinically relevant and need to be considered in regulatory and treatment guidelines.

References
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