Harmonization of Baseline Lipid Measurements Across WHI Laboratories

WHI measured baseline lipids in plasma at the MRL/PPD central laboratory prior to 2001 and in serum at the University of Minnesota Medical Center (UMMC) central laboratory after December 2010. This introduces potential confounding related to laboratory platform, specimen differences, and time since baseline. Approximately 3,000 paired samples (samples from the same individual) measured at both laboratories were used to generate correction equations to calibrate plasma to serum values. These equations were developed for a published report(1) using plasma measurements from WHI studies W1 and W6, and serum measurements from studies W54, W58, and A422. The equations result in near-perfect alignment between plasma and serum values and across laboratories and time.

Application of the equations may be useful for analyses which include all the baseline lipids available and require a higher degree of accuracy, e.g., classification of participants by baseline lipids or by levels of CVD risk factor score. For other studies, it may be sufficient to note these limitations in the discussion section of the report. The equations are as follows for lipids (all in mg/dL):

Total cholesterol: Total cholesterol serum = 1.03 x total cholesterol plasma

Low-density lipoprotein cholesterol: LDL-C serum = exp{0.471 + 0.923 x log(LDL-C plasma)}

High-density lipoprotein cholesterol: HDL-C serum = exp{0.395 + 0.883 x log(HDL-C plasma)}

Triglycerides: Triglycerides serum = exp{-0.390 + 1.064 x log(Triglycerides plasma)}

The LDL-C correction equation above was developed using LDL-C calculated with the older Friedewald equation (2). Current WHI datasets tabulate uncorrected values for LDL-C calculated with the Friedewald equation where LDL-C = total cholesterol - HDL-C - (triglycerides/5). However, the equation overestimates lower levels of LDL-C and becomes inaccurate at triglyceride levels above 150 mg/dl; it cannot be used at triglyceride levels of 400 mg/dl or above.

Investigators are encouraged to calculate LDL-C using the Modified Sampson-NIH equation by first applying the plasma-to-serum correction equations for measured total cholesterol, HDL-C, and triglycerides; next, calculating non–HDL-C as corrected total cholesterol minus corrected HDL-C; and then applying the Modified Sampson-NIH equation using the corrected values (3). The Modified Sampson-NIH equation is LDL-C = non-HDL-C - TG/8.37 - (TG × non-HDL-C)/2640 + TG^2/17400. The equation is more accurate

than the Friedewald equation at lower LDL-C levels and allows for calculation of LDL-C in samples with triglycerides up to 1000 mg/dl.

Lastly, plasma-to-serum correction equations operationalize earlier WHI guidance on standardizing assays across laboratories; https://www.whi.org/doc/Standardization-of-assays-from-multiple-labs-for-a-given-analyte.pdf.

References:

1.Rossouw, J.E., et al., Influence of Cardiometabolic Status on Cardiovascular Effects of Oral Menopausal Hormone Therapy. Obstet Gynecol, Published online July 24, 2026. doi:10.1097/AOG.0000000000006381

2. Friedewald WT, et al. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. Clin Chem. 1972;18(6):499-502.

3. Sampson, M., et al., A Modified Sampson-NIH Equation with Improved Accuracy for Estimating Low Levels of Low-Density Lipoprotein-Cholesterol. Clin Chem, 2025; 71(11): 1125-1137.