COLLEGE of AMERICAN PATHOLOGISTS

Educational Discussion: Accuracy Based Lipids

2019-A

The samples used in the Accuracy-Based Surveys were produced following procedures that minimize matrix effects and produce commutable serum pools with characteristics as close as possible to patient samples. Thus, measurement results can be compared not only within peer-group but also across peer-groups. Furthermore, measurement results reported by participants using the same assay can be considered replicate measurements. Thus, measurement results from participants can be combined to calculate mean bias and imprecision. The measurement variability and accuracy observed in Accuracy-Based Surveys provides information about the variability and accuracy occurring in patient care.

The evaluation criteria listed in the Survey describe the limits for a single measurement. By combining individual measurements, the mean bias and imprecision can be calculated. The results can then be compared to the analytical performance criteria developed by the National Cholesterol Education Program (NCEP), which are listed in Table 1:

Table 1: Maximum allowable bias and imprecision for lipids measurement as suggested by the NCEP and mean bias and imprecision calculated using the all method means averaged across samples

Analyte	NCEP suggested allowable mean bias	NCEP suggested allowable imprecision	ABL-A Mean bias	ABL-A Mean imprecision
Total Cholesterol (TC)	± 3%	≤ 3%	-0.8%	2.3%
HDL-Cholesterol (HDL-C)	± 5%	≤ 4%	0.4%	6.8%
LDL-Cholesterol (LDL-C)	± 4%	≤ 4%	-1.8% (calculated) 4.8% (measured)	4.0% (calculated) 3.3% (measured)
Total Glycerides (TG)	± 5 %	≤ 5 %	0.49%	3.6%

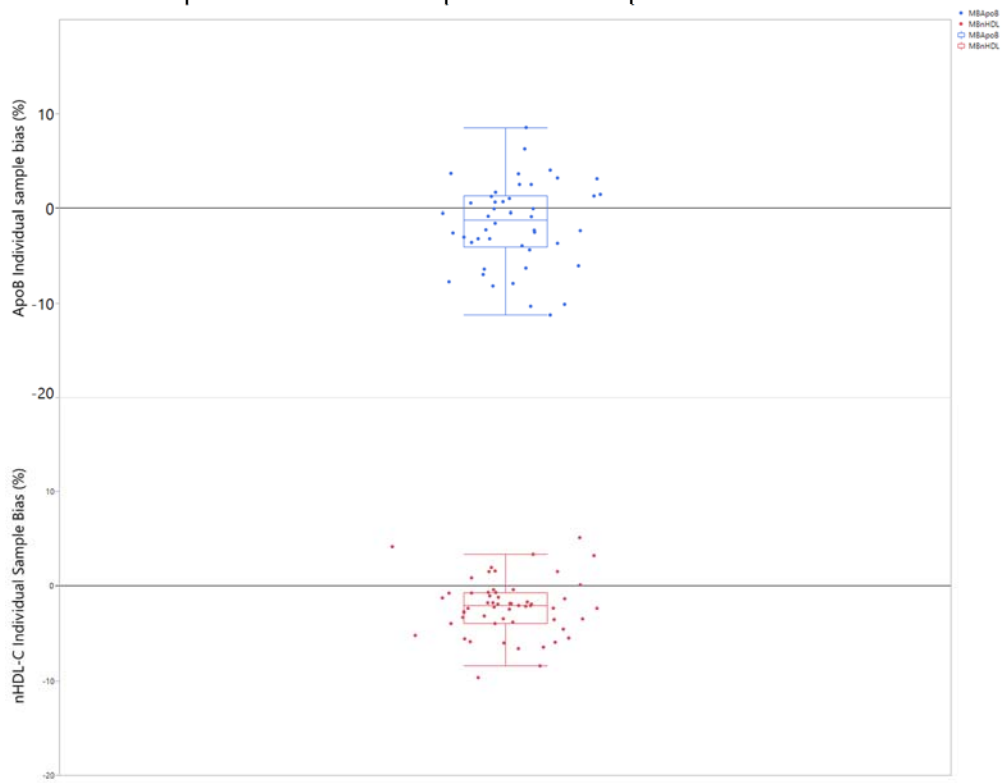
The mean bias to the reference method, calculated using the all method means and averaged across samples, are all within the NCEP requirements, except for mean bias of measured LDL-C and mean imprecision for HDL-C where values are notably higher. The bias and imprecision are not consistent across the three samples. Consistent with observations in the previous ABL Survey, the bias for measured LDL-C (mLDL-C) is outside the NCEP criteria in samples with elevated TG concentrations (ABL-01: 177.8 mg/dL and ABL-03 234.8 mg/dL). Also, in line with the previous ABL Survey, calculated LDL-C (cLDL-C) appear to provide more accurate results in samples with elevated TG values than the measured LDL-C results. This seems noteworthy, as use of direct LDL-C assays has been suggested in situation where TG levels are elevated to the extent where the Friedewald equation cannot be used to calculate LDL-C (Table 2).

Table 2: Mean bias of TC, HDL-C, calculated LDL-C (cLDL-C), measured LDL-C (mLDL-C), TG, apoliporoptein B (ApoB), and non-HDL-C by sample

Sample	TC mean bias	HDL-C mean bias	cLDL-C mean bias	mLDL-C mean bias	TG mean bias	ApoB mean bias	Non-HDL-C mean bias
ABL-01	-1.6%	-1.5%	-3.3%	7.0%	2.5%	-0.4%	-1.8%
ABL-02	0.4%	0.0%	-5.3%	-1.4	-0.4%	-1.6%	-2.9%
ABL-03	-1.3%	2.5%	3.3%	9.0%	-0.5%	0.0%	-2.0%

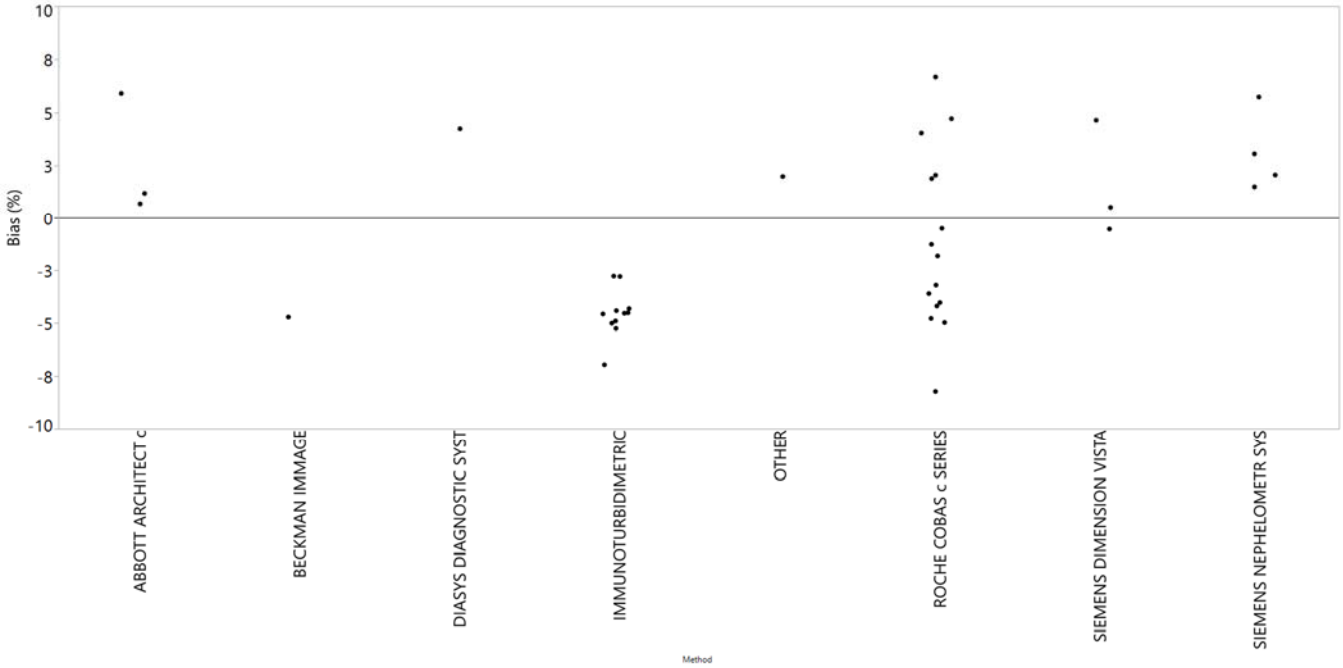
Some guidelines suggest the use of apolipoprotein B or non-HDL-C in situations where measurement or calculation of LDL-C may be compromised. As indicated by the mean bias, measurement results for these analytes indeed appear more accurate and independent of TG concentrations than LDL-C results. While ApoB measurements show a small average bias, the accuracy of individual measurement results show notable variation (Figure 1) with non-HDL-C individual measurements being slightly less variable.

Figure 1: Box-Whisker plot for Individual sample results for ApoB and non-HDL-C



The higher variability in measurement bias with ApoB can be explained with variability in accuracy among as well as within assays (Figure 2), suggesting the need for standardizing these measurements.

Figure 2: Percent bias of individual ApoB measurement results by assay



Recent clinical guidelines rely on accurate determination of LDL-C concentrations for treatment decision, and to assess efficacy of treatments. Thus, it is important to know what factors affect the accuracy and reliability of LDL-C determinations. Elevated TG concentrations appear to affect the accuracy of direct LDL-C assays, while calculated LDL-C using the Friedewald equation appears less affected. However, the use of the Friedewald equation is not recommended at TG concentrations greater than 400 mg/dL. Alternate analytes, such as ApoB and non-HDL-C have been suggested in situations where LDL-C measurements or calculations are compromised. Both measurements appear to be independent of TG concentration and are on average more accurate than direct LDL-C measurements. However, ApoB measurements show notable variability among assays making comparison of results among assays difficult and thus limits the use of common clinical decision points. Non-HDL-C has the advantage that it can be calculated using traditional lipid panel measurements and, because it does not require TG concentrations, can be used with non-fasting samples.

The findings in this Accuracy-Based Survey are limited by the small number of samples. However, most findings in this Survey are consistent with those of previous ABL Surveys using different samples. This Survey uses pooled serum that can be considered commutable and have reference values assigned by generally recognized reference methods. Therefore, this Survey provides unique and reliable information about the accuracy and reliability of lipids and lipoprotein measurements performed in patient care.

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Accuracy Based Programs Committee