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Discussion

The current recommendations for grading the accuracy for lipid and lipoprotein tests are based on the National Cholesterol Education Program (NCEP)[1]. Figure 1 and Table 1 describe the analysis of an alternative voluntary grading criteria for the ABL Survey for total cholesterol. For total cholesterol, total error (Bias + 2 x CV) should be ≤9%. The two components of total error, bias and imprecision, should individually each be ≤3%. As can be seen by Figure 1A, almost all of the tests for total cholesterol in this Survey met the NCEP imprecision goal. In order to pass, at least 95% of participants for any individual assay must report a value less than +/- 9% away from the assigned reference value. Analysis of the participant summary data in this manner incorporates error from both imprecision and bias.

Table 1 shows the expected % of patients that would be misclassified into a different total cholesterol interval based on the following recommended NCEP cutpoints for total cholesterol (Desirable <200 mg/dL, Borderline high 200-239 mg/dL and High ≥240 mg/dL), using the National Health and Nutrition Examination Survey (NHANES) population distribution data for total cholesterol in the United States from 1979. For example, as can be seen for a total cholesterol assay with no imprecision but a bias of 9%, approximately 34% would be misclassified into a wrong cardiovascular risk category based on total cholesterol (Table 1). The multiple number of cutpoints for total cholesterol and the fact that they fall near the middle of the population distribution for total cholesterol accounts for the relatively large number of subjects misclassified with an assay with only modest error. For an assay with an imprecision of 3% but a smaller bias of 3%, which would be more typical of most assays, less subjects would be expected to be misclassified. Nevertheless, such an assay, which would be acceptable with the current NCEP criteria, would still misclassify about 13% of subjects. For those participants that are interested in more carefully evaluating their performance on the ABL Survey, we recommend that following voluntary grading criteria for total error for total cholesterol: >9% not acceptable, 6-9% acceptable, 3-6% good, and <3% excellent. Table 1 shows the % of subjects that would be misclassified for assays with total errors in this range, using total cholesterol. For example, those assays that meet the excellent criteria (total error<3%) would misclassify only 4% of subjects, whereas an assay that is just “acceptable” (total error = 6) would misclassify between 9-22%, depending on the distribution of the total error between bias and imprecision.

In addition, the % of participants with each assay that pass the current NCEP criteria of ≤9% for total error, the alternative voluntary criteria are also applied in Figure 1. Most of the assays for total cholesterol would fall into the “good” criteria (total error = 3-6%) but none would reach the excellent criteria (total error ≤3%), although two tests were close. From this Survey, several of the assays for total cholesterol appear to be inferior in terms of accuracy compared to the other assays, although this should be more carefully assessed on more samples. It is well known, particularly for lipoprotein assays, that individual assays can have a specific bias on a particular sample due to the unique lipid and lipoprotein composition of any given patient sample[2].

In the future, we will provide other voluntary grading criteria for the accuracy of the remaining lipid and lipoprotein tests, along with the impact of the new accuracy criteria on the expected rate of misclassification. This will enable participants to more carefully assess the quality of their assays and how inaccuracy may affect their clinical utility as a cardiovascular biomarker. Such information should also provide an incentive for the further improvement of the accuracy of diagnostic tests for lipid and lipoproteins.

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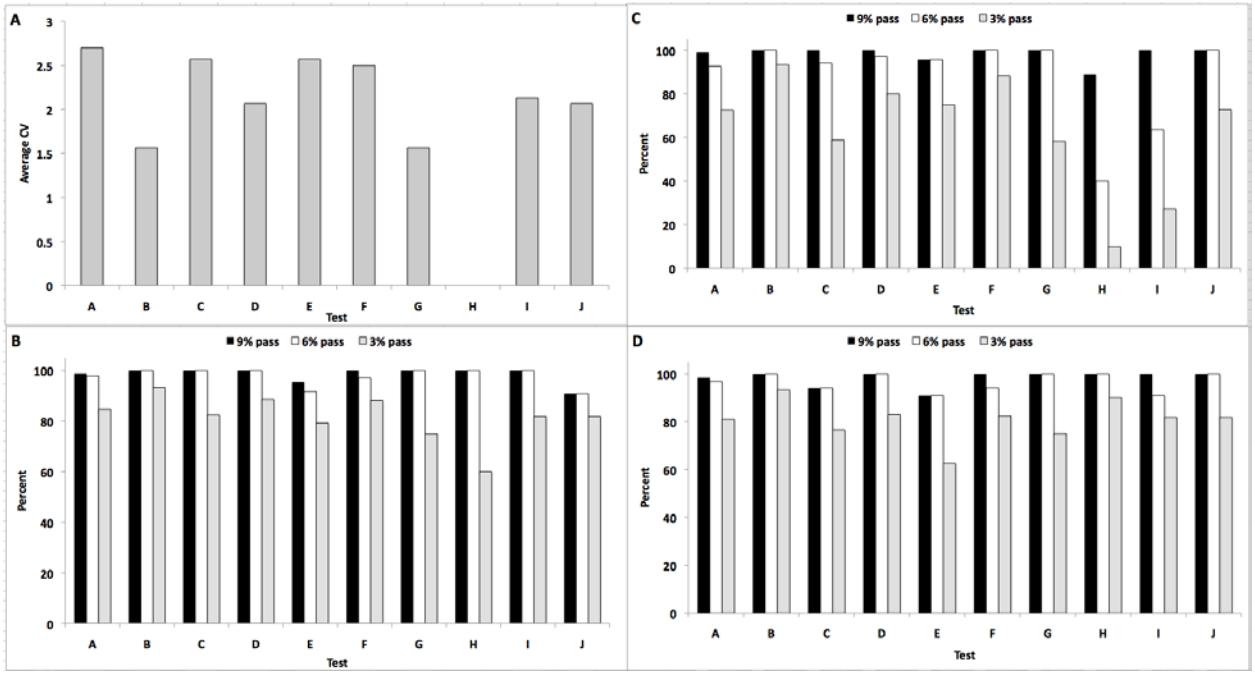

Figure 1: Grading of ABL survey results for total cholesterol using NCEP criteria and alternative voluntary accuracy criteria. Mean precision of assays (Panel A), % of participants that report results within specified criteria of either 9%, 6% or 3% from assigned reference value of total cholesterol for ABL-04 (Panel B), ABL-05 (Panel C), and ABL-06 (Panel D). Test Code: A: Abbott Arch c System, B: Beckman Au series, C: Beckman UniCel DxC Synchron Systems, D: Roche Cobas c500/700 series, E: Roche Modular, F: Siemens Diagnostics ADVIA Chem Syst, G: Siemens Diagnostics Dimension, H: Siemens Diagnostics Dimension Vista, I: Vitros 5,1 Fs,4600/5600 Chemistry Systems

Table 1: Contribution of different types of error in total cholesterol assay to the probability of correct classification.

Bias (%)	Precision (CV) (%)	TE (Bias + 2 x CV) (%)	Percent Misclassified
9	0	9	34 %
3	3	9	13 %
6	0	6	22 %
2	2	6	9%
3	0	3	11 %
1	1	3	4%

References:

1. Warnick GR, Kimberly MM, Waymack PP, Leary ET, Myers GM. Standardization of measurements for cholesterol, triglycerides and major lipoproteins. *Lab Med*. 2008;39:481-490.

2. Miller WG, Myers GL, Sakurabayashi I, et al. Seven direct methods for measuring HDL and LDL cholesterol compared with ultracentrifugation reference measurement procedures. *Clin Chem*. 2010; 56:977-86.