An Evaluation of Two Compact Analyzers Used for Lipid Analysis

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Background. A number of relatively inexpensive compact analyzers are available for use in physician offices and outpatient clinics to measure total cholesterol and, more recently, high-density lipoprotein (HDL) cholesterol and triglycerides. This study was designed to document the analytical performance of two of them, the Abbott Vision and the Kodak Ektachem DT60, for assays of total cholesterol, HDL cholesterol, triglycerides, and calculated low-density lipoprotein (LDL) cholesterol.

Methods. Lipid profiles were measured from venous blood samples of 70 subjects with each test device, and results were compared with those from a laboratory standardized to the Centers for Disease Control. Coefficient of variation (CV) of multiple measurements from three pools of human serum (ie, precision), mean percent difference between device and standard laboratory results (ie, accuracy or bias), and 95% tolerance intervals (total error) were determined. The correct classification of patients into risk categories with device results was compared with the standardized laboratory results.

Results. The average CVs for total cholesterol, triglycerides, and HDL cholesterol with the Vision analyzer were 3.6%, 4.4%, and 10.5%, respectively, and with the DT60, 5.0%, 4.1%, and 6.8%, respectively. The average percent biases for the same analytes with the Vision analyzer were 0.2%, 4.0%, and −2.3%, respectively, and with the DT60, −2.1%, 12.1%, and 0.1%, respectively. Total error assessments indicated that total and HDL cholesterol measurements in individual patients met the guidelines of the National Cholesterol Education Program with both devices, but that triglycerides and LDL cholesterol measurements did not. Classification of subjects into risk groups based on total or LDL cholesterol gave clinically satisfactory results with either device.

Conclusions. More precise measurement technology for LDL cholesterol is needed. Physicians and others who rely on compact analyzer results for diagnosis and treatment decisions should consider the degree of inaccuracy and imprecision in these values.

Key words. Cholesterol; clinical protocols; laboratories; evaluation studies. (*J Fam Pract 1993; 36:526-533*)

The relationship between high blood cholesterol and coronary heart disease (CHD) has been established by extensive genetic, animal, epidemiologic, and clinical intervention studies.[1] Recent clinical trials have demonstrated that lowering blood cholesterol levels reduces the incidence of CHD in asymptomatic hypercholesterolemic men and decreases the progression of atherosclerosis in men with established coronary vessel disease.[2–6]

The National Cholesterol Education Program (NCEP) has issued guidelines for the detection, evaluation, and treatment of adults with elevated blood cholesterol levels.[7] This evaluation includes the determination of the low-density lipoprotein (LDL) cholesterol level,

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which is the criterion on which the decision to initiate lipid-altering diet and drug therapy is based, and is used to monitor progress once treatment begins.

The NCEP has also issued guidelines for the measurement of total cholesterol.[8] These specify that total cholesterol measurements should be within 3% of a standard measurement (ie, the definition of accuracy or bias) and that variability in measurements be less than 3% coefficient of variation (CV), ie, the definition of precision. These performance guidelines are intended to ensure that individual measurements be ±8.9% of the true value (ie, 3% maximum bias ±3% CV × 1.96 to include 95% of observations).

Similar accuracy and precision guidelines for other lipid and lipoprotein measurements are being developed by the NCEP Working Group on Lipoprotein Measurement.[9] This group has announced that 5% accuracy and precision should be sought for triglycerides, 10% accuracy and 6% precision should be sought for high-density lipoprotein (HDL) cholesterol, and 4% accuracy and precision should be sought for LDL cholesterol.

A number of relatively inexpensive compact analyzers have become available for use in physician offices and outpatient clinics to measure total cholesterol and, more recently, HDL cholesterol and triglycerides. Few studies have assessed the accuracy and precision of the measurements generated by these instruments.[10,11] Therefore, this study was designed to determine the precision and accuracy of the Abbott Vision and the Kodak Ektachem DT60 for assays of total cholesterol, HDL cholesterol, triglycerides, and calculated LDL cholesterol, and the classification of patients into CHD risk categories based on these values.

Methods

The study's research protocol was approved by the institutional review board, and consent forms were signed by each subject before participation. Subjects included in the study gave a history of high blood cholesterol and were not receiving cholesterol-lowering therapy with diet or drugs. Seventy persons, selected from clinic patients, hospital employees, and students, participated in the study. One half had fasted for at least 12 hours before the evaluation. The study consisted of 16 men and 54 women ranging in age from 23 to 69 years.

The study design was based on guidelines from the National Committee for Clinical Laboratory Standards.[12] The test devices, the Abbott Vision (Abbott Laboratories, Chicago, Ill) and the Kodak Ektachem DT60 (Eastman Kodak, Rochester, NY), were donated by the manufacturers. A company representative calibrated each device and trained two individuals in their proper use. The operators were pharmacists; each operator completed approximately 30 lipid profiles on control solutions, serum pools, and patient samples to familiarize themselves with the technique before the initiation of the study. Every attempt was made to operate the devices as specified by the manufacturer.

The Abbott Vision produces total cholesterol and triglyceride results from a sample of whole blood that is injected directly into a test pack before the test run. The Kodak Ektachem DT60 requires that a whole blood sample be centrifuged first; the plasma is subsequently pipetted onto a reagent slide. For the determination of HDL cholesterol, both devices require that the sample be pretreated with magnesium/dextran sulfate and centrifuged to isolate HDL cholesterol; the sample is then introduced into the test pack or reagent slide for the test run. Subsequent chemical reactions generate a color change that is measured either by spectrophotometry (Abbott Vision) or by reflectance photometry (Kodak Ektachem DT60). The Abbott Vision can analyze up to 10 test packs simultaneously during a 12-minute cycle (maximum of 50 test packs per hour). The Kodak Ektachem DT60 produces a result approximately 5 minutes after pipetting (maximum about 65 results per hour). The Kodak device displays and prints test results; the Abbott device prints test results.

The laboratory used for the accuracy comparison was standardized by participation in the Centers for Disease Control Lipid Standardization Program. Total cholesterol was measured enzymatically with Boehringer Mannheim Diagnostics (Indianapolis, Ind) reagents (No. 692905) and calibrators (No. 125512) using a Cobas-Bio analyzer (Roche Diagnostics, Nutley, NJ). Triglycerides were measured enzymatically with Behring Diagnostics (Somerville, NJ) reagents (No. 869263) using a Cobas-Bio analyzer with a correction for free glycerol, and the molar absorptivity of NADH was used for quantitation. For the HDL cholesterol determination, plasma was fractionated with 92 mmol/L manganese chloride plus 183 μ/L heparin solution followed by centrifugation. The HDL-containing supernatant fraction was assayed for cholesterol as described above. The reference laboratory precision was CV of 2.2% for cholesterol, 3.3% for HDL cholesterol, 3.3% for triglycerides, and 4.0% for calculated LDL cholesterol, with all analytes meeting CDC requirements for accuracy.

Precision is defined as the repeatability of a test procedure and is expressed as the CV. In this study, the total precision of total cholesterol, triglycerides, and HDL cholesterol measurements was determined by duplicate assays with each test device on 20 test days from three pooled samples of human serum that had been

aliquoted and frozen at −70°C until analysis (ie, total of 40 determinations of the lipid and lipoprotein values from each pool sample). Operators made sure that test samples were at room temperature, had been inspected for particulate matter, and were inverted 20 times before use. Within-run precision was evaluated by determining the variance in the duplicate measures of each lipid and lipoprotein value in each subject during the accuracy evaluation (see below) by repeated measures ANOVA.

Accuracy (or bias) is defined as the agreement between a measurement obtained with a test device and the measurement obtained by a standardized laboratory and is expressed as the percent difference in results. In this study accuracy was determined by comparing total cholesterol, triglycerides, HDL cholesterol, and calculated LDL cholesterol measurements obtained with each device from each of the 70 enrolled subjects with results determined by the standardized laboratory. All measurements were made in duplicate from venous blood; the means of these duplicate measures were determined and used in comparisons of device and standardized laboratory data. Low-density lipoprotein cholesterol values were calculated using the method of Friedewald et al[13]; two patients with triglyceride levels over 400 mg/dL (4.52 mmol/L) were excluded from this calculation. Testing was completed on the 70 subjects over a period of 9 days (an average of 8 patients per day, ranging from 3 to 13).

Before the sample collection, each subject was allowed to sit for at least 5 minutes. Approximately 10 mL of venous blood was collected into EDTA-treated tubes. Aliquots of venous samples were analyzed within 6 hours of collection with both desktop devices for total cholesterol, triglycerides, and HDL cholesterol. The remaining venous samples were sent to the standardized laboratory where they were centrifuged, stored under refrigeration at 4°C, and analyzed within 24 hours of collection.

Only measurements that were made in duplicate were used in the determination of accuracy for each lipid and lipoprotein. Duplicate samples were not available for all measurements because of results above or below the analyzer range or hemolysis of specimens. Duplicate measurements of the three lipid values were available for 60 to 70 of the 70 subjects as indicated in the relevant tables. For each subject in whom duplicate results were generated, the mean result from the standardized laboratory was subtracted from the mean result from each test device for each lipid and lipoprotein. This difference was expressed as a percent as follows:

$$[(\text{device result} - \text{standardized laboratory result})/\text{standardized lab result}] \times 100$$

Table 1. Total Precision of Desktop Lipid Analyzers: Coefficient of Variation* on Repeated Measurements from Sample Pool

	Human Serum		
Lipids/Analyzer	Pool 1	Pool 2	Pool 3
Total cholesterol (mg/dL)	189	243	267
Abbott Vision (%)	2.5	4.1	4.1
Kodak DT60 (%)	3.7	5.2	6.0
Triglycerides (mg/dL)	206	322	324
Abbott Vision (%)	5.8	—†	2.9
Kodak DT60 (%)	4.7	4.7	2.8
HDL cholesterol (mg/dL)	56	86	69
Abbott Vision (%)	7.4	11.9	12.1
Kodak DT60 (%)	5.7	7.9	24.4‡

**The coefficient of variation was calculated as (standard deviation/mean) × 100 from 30 to 40 duplicate measurements of each lipid and lipoprotein derived over 20 days from aliquots of three frozen pools of human serum. The following extreme values were excluded from these CV calculations: (1) for the Vision HDL, a value of 101 mg/dL in pool 1, which was 9.0 mg/dL SD from the mean; (2) for the DT60 total cholesterol, values in pool 1 of 229 mg/dL, which was a 6.3 mg/dL SD from the mean, and 147 mg/dL, which was a 5.7 mg/dL SD from the mean, and in pool 2, a value of 324 mg/dL, which was a 7.5 mg/dL SD from the mean; (3) for DT60 triglycerides, values of 246 and 146 mg/dL, which were 11 and 21 mg/dL SD from the mean, respectively, and were likely transcription errors.*

†No results are available because samples were identified as lipemic by the Abbott Vision.

‡Values for this pool ranged in an almost continuous progression from 20 to 105 mg/dL, which strongly suggests that there was a significant matrix effect with this pool that caused an analytical interference with the DT60 assay system.

The mean percent difference for the population was determined by averaging the percent differences for individual patients.

The total analytical error of the lipid and lipoprotein measurements with each device was determined from 95% tolerance intervals of the ratio of intrasubject mean values with the test compared with the comparison method.[14] The tolerance interval describes the performance range within which individual subject values will fall 95% of the time. The acceptable limits for the tolerance interval include contributions from the accuracy and precision of the method being evaluated and from the precision of the comparison method. The ratio of test to reference results will have a value of 1.00 if the two results agree perfectly. Using the ratio allows evaluation of each test measurement on a scale that is independent of the numerical range of concentrations.

Results

The total precision (CV) for 30 to 40 measurements of total cholesterol, triglycerides, and HDL cholesterol made with each test device from three pools of human serum over 20 days are presented in Table 1. A few outlier values were excluded from this determination (see footnote in Table 1). The coefficients of variation were consistently highest for HDL cholesterol and similar for

Table 2. Within-Run Precision of Desktop Lipid Analyzers: Coefficient of Variation* on Duplicate Measurements in Individual Subjects

Lipids	Abbott Vision mg/dL (%CV)	Kodak DT60 mg/dL (%CV)
Total cholesterol	203 (1.4)	200 (2.1)
Triglyceride	97 (2.9)	103 (2.7)
HDL cholesterol	56 (4.3)	58 (4.4)
LDL cholesterol	625 (3.2)	119 (3.8)

**The coefficient of variation was calculated as (standard deviation/mean) × 100 from within subject variance using a repeated measures analysis of variance procedure.*

Table 3. Mean Percent Difference* and Standard Deviation Between Desktop Lipid Analyzers and Standardized Laboratory Results

Lipids	Abbott Vision Bias, % (SD)	Kodak Ektachem DT60 Bias, % (SD)
Total cholesterol	0.2 (±3.6)	−2.1 (±4.9)
Triglycerides	4.0 (±9.4)	12.1 (±14.7)
HDL cholesterol	−2.3 (±11.6)	0.1 (±8.6)
LDL cholesterol†	1.5 (±8.2)	−4.9 (±9.0)

**Mean percent difference was calculated as [(device result − standardized laboratory result)/standardized lab result] × 100 for 9 days of testing sample populations of 70 patients for each lipid and lipoprotein. All measurements were in duplicate and the mean was used in the accuracy calculation.*
†LDL cholesterol was calculated by the method of Friedewald et al.[13]

total cholesterol and triglyceride measurements with both devices. Neither device had CVs of total cholesterol measurements that consistently met the NCEP guideline of 3%. Imprecision in the measurement of triglycerides was generally within the acceptable range of 5% CV, while imprecision in HDL cholesterol measurement was far greater than 6% CV in both devices. The Vision and DT60 had similar precision performance except for HDL cholesterol measurement of pool 3 in which the DT60 had an apparent CV of 24.4% vs 12.1% for the Vision. However, the DT60 values for this pool ranged in an almost continuous progression from 20 to 105 mg/dL (0.5 to 2.72 mmol/L). This strongly suggests that there was a significant matrix effect with this pool that caused an analytical interference with the DT60 assay system.

Coefficients of variation determined as within-subject variance based on the duplicate measures made in individual patients during the accuracy portion of this study are presented in Table 2. These data reflect within-run precision, which is typically better than total precision. Differences between repeat measurements from the same subject sample were small. The within-run CVs for all tests with each device met the NCEP guidelines.

Average accuracy results for the test devices are presented in Table 3. Both devices measured total and HDL cholesterol more accurately than triglycerides. However, the standardized method for triglycerides used a correction for endogenous free glycerol, whereas both test methods did not. Thus, the positive bias for triglycerides is partially due to differences in measurement technique. The mean percent differences for total cholesterol, HDL cholesterol, and triglycerides with the Vision, and total and HDL cholesterol with the DT60 met the NCEP goals for average accuracy. Both devices measured LDL cholesterol within an average of 5% of the true value.

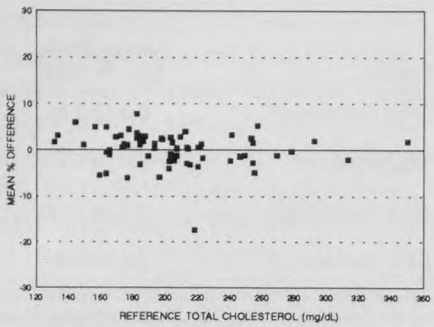
The percent differences between the test device and standardized laboratory measurements of total cholesterol, triglycerides, HDL cholesterol, and LDL cholesterol for individual subjects are given in the Figure. Each point represents the mean of duplicate measurements in each patient. These figures reflect the range of values encountered in the study (ie, total cholesterol values between 130 and 350 mg/dL [3.36 and 9.05 mmol/L]). These plots reveal that compact analyzer values for some patients varied greatly from the standardized laboratory values. Measurements obtained with the Kodak Ektachem DT60 appear to be more scattered than comparable measurements obtained with the Abbott Vision.

The total error of individual measurements includes the combined effects of both accuracy and precision of the measurement system. The performance range, which includes 95% of individual results, is evaluated by the tolerance interval. The 95% tolerance intervals for individual subjects' results are presented in Table 4. The tolerance intervals for total and HDL cholesterol measured with both the Vision and DT60 meet the NCEP guidelines. Neither test device had satisfactory total error performance for triglycerides, which may be partially caused by lack of a free glycerol correction in the measurements. The LDL cholesterol with both devices also failed to meet NCEP guidelines based on 4% bias with 4% CV, although the Vision was close.

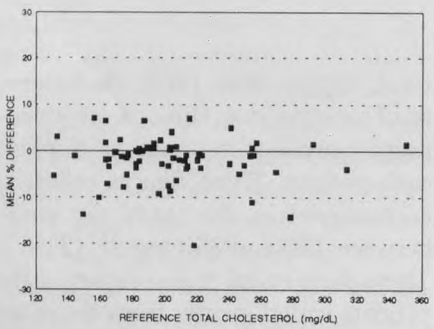
The ability of the Abbott Vision and the Kodak Ektachem DT60 to correctly classify subjects into risk categories based on total and LDL cholesterol is summarized in Table 5. The classification based on total cholesterol values identifies subjects requiring further testing, whereas the classification based on LDL cholesterol identifies subjects for lipid-lowering therapy. The false-positive group reflects subjects whose test device measurement placed them in a higher risk group than the standardized laboratory measurement; the false-negative classification reflects subjects whose test device measure-

PANEL 1

ABBOTT VISION

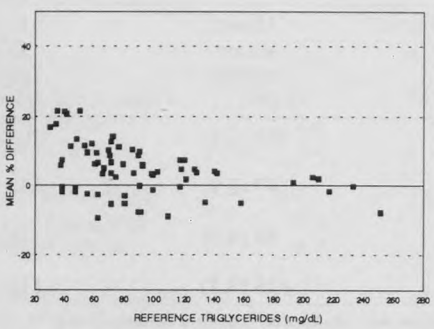


KODAK EKTACHEM DT 60



PANEL 2

ABBOTT VISION



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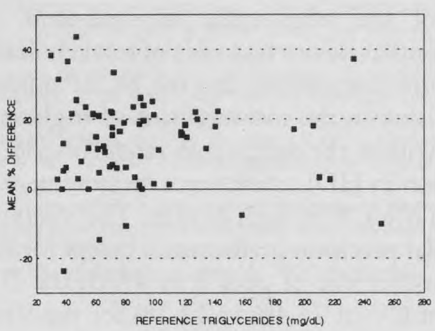
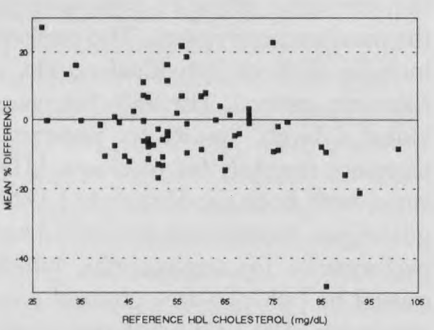


PANEL 3

ABBOTT VISION



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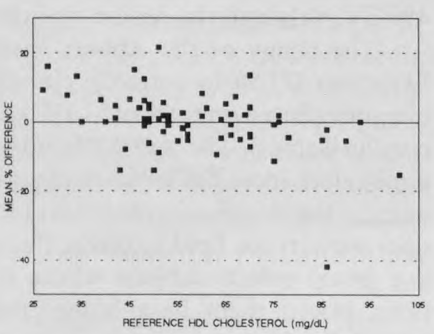
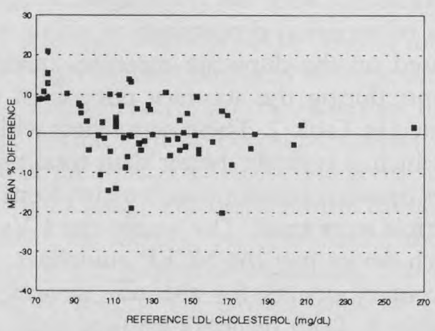
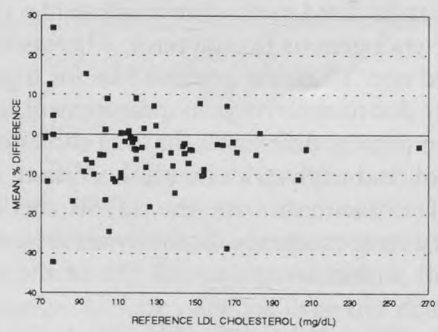


PANEL 4

ABBOTT VISION



KODAK EKTACHEM DT 60



Mean percent differences of test device measurements compared with the standardized laboratory values for total cholesterol (panel 1), triglycerides (panel 2), HDL cholesterol (panel 3), and LDL cholesterol (panel 4).

Table 4. Total Error of Desktop Lipid Analyzers: 95% Tolerance Intervals for 95% of Intrasubject Mean Value Ratios

Lipids	Abbott Vision	Kodak DT60	Acceptable Limits as Defined by NCEP Goals*
Total cholesterol	0.92–1.08	0.87–1.09	0.87–1.13
Triglycerides	0.77–1.32	0.72–1.53	0.79–1.21
HDL cholesterol	0.70–1.26	0.79–1.22	0.62–1.38
LDL cholesterol	0.82–1.21	0.68–1.23	0.82–1.18

**For total cholesterol, performance goals of accuracy ±3%, CV 3% and 2.2% for test and comparison methods, respectively; for triglycerides, goals of accuracy ±5%, CV 5% and 3.3%, respectively; for HDL cholesterol, goals of accuracy ±10%, CV 6% and 3.3%, respectively; and for LDL cholesterol, goals of accuracy ±4%, CV 4% and 4%, respectively.*
NCEP denotes National Cholesterol Education Program.

ment placed them in a lower risk group than the standardized laboratory measurement. False classifications were encountered as frequently for total cholesterol measurements as for LDL cholesterol measurements. More false classifications were encountered with the Kodak DT60 than the Abbott Vision. The classification of subjects with both devices tended to underestimate subjects requiring further testing or treatment. False classifications with both devices were particularly prevalent around classification cutpoints: 200 and 240 mg/dL (5.17 and 6.21 mmol/L) for total cholesterol and 130 and 160 mg/dL (3.36 and 4.14 mmol/L) for LDL cholesterol. When results near the cutpoints were adjusted for imprecision (Table 5), the number of misclassifications was more than cut in half.

Discussion

The performance guidelines from the NCEP specify that total cholesterol should be measured for an individual subject with no more than 3% inaccuracy and no more than 3% CV as a measure of imprecision. However, the inaccuracy and imprecision are not independent for an individual measurement but combine to form a total error for cholesterol measurements. Thus, the 3% accuracy and 3% CV specifications result in an overall allowable error of ±8.9% for an individual cholesterol measurement to meet the NCEP guidelines. In a similar manner, the Working Group on Lipoprotein Measurement is expected to specify performance goals as total allowable error as well as typical specifications for accuracy and precision that would satisfy those goals. The expected total allowable error for triglycerides is 14.8%, for HDL cholesterol, 22%, and for LDL cholesterol, 11.8%.[9] Accuracy and precision specifications that meet these goals would be 5% bias with a 5% CV for triglycerides, 10% bias with 6% CV for HDL cholesterol, and 4% bias with 4% CV for LDL cholesterol.

To further describe the total error or total uncertainty in the group of individual subjects' measurements, we have used the tolerance interval as a statistical tool to assess total error resulting from the combination of inaccuracy and imprecision present in individual measurements. The tolerance interval describes the performance range within which individual subjects' results are expected to fall 95% of the time.

If we consider the average inaccuracy derived from our data set of approximately 70 subjects, we see that for total and HDL cholesterol, both analytical systems produced acceptable results. Other investigators have reported similarly good average accuracy for total cholesterol.[10,11,15–23] Kaufman et al,[10] for example, reported mean percent differences of 1% with the Vision and 1.5% with the DT60. Both measurement devices had very good within-run precision, which means that repli-

Table 5. Percentage of Patients Misclassified by Desktop Lipid Analyzers Compared with Standardized Laboratory

	No. of Subjects	Unadjusted, %		Adjusted* to NCEP Goals, %	
		False Positive	False Negative	False Positive	False Negative
Abbott Vision					
Total cholesterol	70	2.9	5.7	0	1.5
LDL cholesterol	68	7.6	4.5	0	1.5
Kodak DT60					
Total cholesterol	70	1.4	11.4	0	6.1
LDL cholesterol	70	4.3	10.0	0	4.3

**False-positive and false-negative classifications for total cholesterol were adjusted by identifying patient values outside of the cutpoint ±5.1%. The allowance of 5.1% is derived from*

$$1.96 \cdot \sqrt{\frac{(3\%\ CV)^2 + (2.2\%\ CV)^2}{2}}$$

where 3% CV and 2.2% CV are the recommendations from the NCEP and the measured CV of the comparison method respectively, 2 reduces the imprecision for duplicate measurements, and 1.96 gives the one-tail 95% confidence limit for the imprecision. The adjustment for LDL cholesterol was cutpoints ±7.8% based on the 4% CV NCEP recommendation and 4.0% CV for the comparison method.
NCEP denotes National Cholesterol Education Program.

cate measurements of the patient's sample at the same visit or testing event were very similar. If we then consider total imprecision as measured by replicate analyses of frozen serum pools, we see that for total and HDL cholesterol, neither analytical system performs within the current NCEP limitations for imprecision. The total error as measured by the tolerance interval, however, gives acceptable performance for both total and HDL cholesterol measured with these analytical systems. This overall good performance was achieved because the poor between-run precision is compensated for by good accuracy such that, overall, 95% of the individual subjects tested had values that fell in the acceptable performance range. An appreciation for the total error of measurement can be obtained by examining the scatter plots for the various lipid values. For example, 29% of total cholesterol measurements with the Abbott Vision and 37% of these measurements with the Kodak Ektachem DT60 were more than ±3% different from the standardized cholesterol measurement. In spite of this, both devices easily met the ±3% guidelines for average accuracy based on group results and also fell within the acceptable limit based on the tolerance interval assessment of total error. When interpreting test results for total and HDL cholesterol, it is important to remember that individual measurements would satisfy the NCEP recommendations with as much as ±8.9% uncertainty for total cholesterol and as much as ±22% uncertainty for HDL cholesterol measurements.

Our results for triglycerides measurements unfortunately did not meet the proposed guidelines for the NCEP. The total imprecision was generally within the 5% CV guidelines, and the within-run precision was quite good. The average accuracy was within the 5% guidelines for Abbott Vision but substantially exceeded the 5% recommendation with the Kodak Ektachem DT60. The tolerance interval analysis showed, however, that neither analytical system met the combined accuracy and imprecision total error specifications. The Abbott Vision came closer to meeting the total error specifications than did the DT60 because of the better average accuracy obtained with that device. Some of the inaccuracy seen with these devices can be attributed to the comparison method, which was corrected for endogenous free glycerol in each sample. This correction would result in a high tolerance interval ratio. However, both devices also failed to meet the lower acceptable limits of the tolerance interval, which indicates that the scatter in the results was large enough to cause them to fail to meet the total error specifications.

Neither testing device met the total error guidelines of the NCEP for calculated LDL cholesterol, primarily because the calculations included the triglyceride values. However, the Vision average accuracy was acceptable, and total error was only slightly greater than the guidelines. The DT60 performance was poorer for both average accuracy and total error. The scatter in individual results was substantial for either assay system and underscores the need for more precise measurement technology for lipid testing.

There have been a limited number of evaluations of triglyceride and lipoprotein measurements with desktop analyzers. Bachorik et al,[11] studying only the Abbott Vision, reported that mean percent differences between device and laboratory results for HDL cholesterol and triglycerides levels were approximately −11% and −10%, respectively. Kaufman et al[10] reported mean percent differences of 19% and −8% for HDL cholesterol and triglycerides, respectively, with the Abbott Vision, and 6% and −3.8%, respectively, with the Kodak Ektachem DT60.

A number of factors may account for variability in cholesterol measurements. There is variability caused by measurement factors such as differences in performance between the same or different devices,[23] operator technique (which is strongly influenced by training and experience), reagents, instrument calibration, and the setting (ie, field settings generally produce poorer results than laboratory settings).[15,16,22] There is also variability caused by biologic factors[24] such as diet, changes in body position, and season of the year. Further, differences of 3% to 5% are observed between EDTA anticoagulated venous plasma and serum caused by the osmotic dilution of cholesterol in the sample by EDTA.[25,26] These factors were controlled as much as possible in the current study. Because of the effect of these factors on testing results, clinicians should adopt standardized sampling procedures and measurement methods to enhance consistent interpretation of lipid measurements.

In spite of the relative degree of inaccuracy and imprecision found in this study, the classification of subjects into desirable, borderline, and high-risk categories for referral and treatment decisions was acceptable. On average, both devices misclassified less than 12% of subjects. Nearly half of this misclassification occurred within ±5.1% or 7.8% of the cutpoint for total and LDL cholesterol, respectively, a range that reflects the measurement uncertainty. When this degree of measurement uncertainty near the cutpoints was taken into account, false-positive misclassifications were eliminated and false-negative misclassifications were reduced substantially.

The practical lesson of this experience is that, for patients whose cholesterol levels are clearly above or below a cutpoint, classification and treatment decisions can be made with relative confidence. If measurement results fall within the range of analytical uncertainty,

however, repeating the measurement is advised. If measurements remain within this range even after repeat measures, the decision to diagnose and treat a patient for hypercholesterolemia would be left to clinical judgment based on relative degrees of CHD risk and treatment benefit.

Physicians and others who base diagnosis and treatment decisions on cholesterol levels may use the following guidelines to improve the reliability of these measurements. If a contract laboratory is used, it is advisable to periodically inquire about accuracy and precision data and the methods by which these were assessed. If measurements are performed in the office, daily quality control and regular external proficiency testing are necessary to ensure reliable measurements. Also, performing replicate measurements on the same patient improves precision. Regardless of the laboratory used, it is important to base clinical decisions on an analysis of multiple lipid measurements rather than on a single measurement in patients whose cholesterol levels are near cutpoints. It is also recommended that patients be taught about the variability of cholesterol measurements so that they will not be confused when cholesterol measurements obtained in different settings vary. Although the total variability in laboratory results may be ±8.9% to ±22%, the physiological variability over time is approximately double that and must be considered when interpreting results measured at different times.[8]

Acknowledgment

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