Factors Related to Accuracy in Office Cholesterol Testing

Rodney Erickson, MD; Charles Driscoll, MD; Laine Dvorak, MD; Craig Gjerde, PhD; Jolynn Glanzer, MD; Manuel Arteaga; Francis Pisney, MD; and Paul Williamson, MD
Vinton, Iowa City, Cedar Rapids, Humboldt, and Iowa Falls, Iowa

Background. There has been growing interest in the performance of diagnostic testing in physician office laboratories (POLs). Since the measurement of cholesterol is a well-defined and standardized laboratory test, it was selected to assess factors related to test accuracy in POLs.

Methods. One hundred thirty-one family practice offices were eligible to participate in the survey. Each was mailed a cholesterol specimen with a standardized value in October 1988. The laboratory characteristics of those POLs with results that were within 10% of the true specimen value were compared with those with results that were greater than 10% in error.

Results. Of the 131 POLs, 122 returned an answer for the unknown specimen. Ninety-eight (80%) were within 10% of the true value, and 114 (93%) were within 15%. Factors that were related to lower error rates (more likely to be within 10% total error) were whether the laboratory performed more than 25 laboratory tests per day, participated in a proficiency testing program, and ran daily quality controls, as well as the type of instrument the laboratory used.

Conclusions. Overall performance of the POLs compared favorably with reference laboratories; however, running controls and participating in a proficiency testing program may further improve POL test accuracy.

Key Words. Cholesterol; office laboratory testing; family practice. *J Fam Pract 1991; 33:457-461.*

Interest in serum cholesterol increased in the early 1980s when results from the Framingham Study[1,2] and the Lipid Research Clinics Coronary Primary Prevention Trial[3–5] better defined the role of serum cholesterol in the development of coronary artery disease. The National Cholesterol Education Program (NCEP) of the National Institutes of Health began in 1988. The first efforts of the NCEP focused on public and physician awareness of the importance of the recognition and treatment of hypercholesterolemia.[6] The next focus of the NCEP was on establishing appropriate laboratory standards and accuracy for measuring cholesterol.[7] This emphasis on laboratory uniformity and performance came at a time when technology was providing greater availability of in-office cholesterol testing.

Several studies have examined the factors that affect the accuracy of serum cholesterol testing. These studies have shown that laboratory-trained personnel achieve better results than physicians and untrained personnel,[8,9] and that certain instruments perform better than others.[10–12] There has been little study, however, of the factors associated with test accuracy in actual practice settings. In one study, participation in proficiency testing did not improve performance among the physician office laboratories (POLs) involved during a 15-month period[13]; another study has found that those POLs required to participate in proficiency testing as part of an overall quality assurance program showed improved performance.[14]

Governmental concern about the accuracy and error of POLs exists, as evidenced by the proposed regulations of the Clinical Laboratory Improvement Act of 1988 (CLIA '88).[15] Despite these regulations, little is known about which factors relate to POL error, and therefore, which factors could best address the concerns of both physicians and the public. To address these concerns, the Iowa Academy of Family Physicians (IAFP) initiated a study aimed at identifying those factors related to POL error. Cholesterol determination was chosen because it involves a commonly run test with well-defined standards.

Methods

The study was conducted between March and October 1988. Initially the office of each member of the IAFP was

Submitted, revised, July 18, 1991.

From the Iowa Academy of Family Physicians Research Network (Dr Erickson, Vinton; Dr Glanzer, Cedar Rapids; Dr Dvorak, Humboldt; and Dr Pisney, Iowa Falls); and the Department of Family Medicine, University of Iowa, Iowa City (Drs Driscoll, Gjerde, Arteaga, and Williamson). Requests for reprints should be addressed to the Executive Secretary of the Iowa Academy of Family Physicians, 100 East Grand, Suite 170, Des Moines, IA 50309.

ISSN 0094-3509

contacted by phone to: (1) identify which members were associated in a single office and identify which offices had laboratories; (2) identify a contact person for each laboratory; (3) introduce the physicians to the project and determine their willingness to participate; and (4) gather preliminary data about the laboratories including the number of physicians, type of tests performed, estimate of the test volume, and error rates considered acceptable in cholesterol testing (<5%, 5%, 10%, 15%, and 20% were the choices given).

A questionnaire was mailed to each POL; a follow-up questionnaire was sent 1 month later if the first one was not returned. The following information was requested: practice volume (patients per day), laboratory volume (laboratory tests run per day), specific type and number of tests run (urinalysis, streptococcus screens, blood glucose, serum cholesterol, and serum potassium), the training and years of laboratory experience of the person supervising the POL, and quality assurance activities. Possible quality assurance activities included participation in proficiency testing, written safety procedures, procedure manuals, personnel logs, daily quality control sheets, and instrument maintenance logs.

Each POL performing serum cholesterol measurements was sent a single sample for cholesterol level determination. One of three specimens with a known value of either 3.88 mmol (150 mg/dL), 6.15 mmol (238 mg/dL), or 8.71 mmol (337 mg/dL) was randomly assigned and sent to each POL. Specimens were reference material for serum cholesterol obtained from the College of American Pathologists using the values assigned by the National Bureau of Standards (NBS) and were accurate to within ±3.7% of the stated value.

For the purpose of data analysis, an unacceptable error level was defined as a deviation of more than 10% from the NBS assigned value. This level was chosen for two reasons. First, according to the phone survey, it was the most common (mode) level of acceptable error for serum cholesterol used by POLs. Second, this level proved sufficiently sensitive to permit the identification of those factors responsible for laboratory variability. Categorical variabilities were compared using chi-square, $P \leq .05$. Sample sizes were too small to perform multivariate analysis.

Results

The initial phone interview identified 345 offices, representing 676 family physicians. Questionnaires were returned by 251 (73%) offices, representing 528 (78%) family physicians. Of the nonresponders, many had already indicated they performed no or minimal laboratory testing. Of the returned questionnaires, 236 indicated that they did some office laboratory testing, and 131 indicated that they performed serum cholesterol tests. Of these 131 laboratories, 122 (93%) reported the values they obtained for the unknown specimen.

Table 1. Characteristics of Family Physician Office Laboratories (N = 122)

Characteristics	Mean ± SD	Range
Patients per day	74 ± 57	8–380
Laboratory tests per day	47 ± 41	2–300
Cholesterol tests per day	4.3 ± 13.6	<1–63
Years experience of laboratory supervisor	12 ± 8.1	1–29

SD denotes standard deviation.

Of the 122 returns, 64 (52%) were within 5% of the expected value, 98 (80%) were within 10%, and 114 (93%) were within 15% (the accuracy limit defined by the proposed CLIA '88 regulations for serum cholesterol determinations). All samples were run within 3 days of receipt. Values did not vary by the day they were run or the distance they had been shipped.

Basic information about the offices and POLs is provided in Table 1. The average office laboratory that performed serum cholesterol tests saw 74 patients per day, and performed 47 total laboratory tests per day and 4.3 cholesterol tests per day. The principal staff person employed in the laboratory had an average of 12 years of laboratory experience; 38 (31%) had specialized laboratory training (6 months to 4 years), 49 (40%) had 1 year of general patient care training (licensed practical nurse or medical assistant), 20 (16%) were registered nurses, 5 (4%) were physicians, and 10 (8%) were unspecified or self-trained.

For analysis, those POLs with more than 50 patient visits per day were compared with those with 50 or fewer. The POLs performing more than 25 total laboratory tests per day were compared with those performing 25 or fewer, and those that ran three or more cholesterol tests per day were compared with those that ran two or fewer. These results are shown in Table 2. Of these three factors (patients, total tests, and cholesterol tests per day) only for total tests per day did the higher volume POLs have a significantly lower error rate.

POL personnel factors are shown in Table 2. Because of small sample sizes, supervisor training was condensed into three groups: laboratory trained; licensed practical nurses or medical assistants; and other (including physicians, registered nurses, and self-trained). Differences between these three groups did not reach statistical significance, but there was a trend toward lower error rates in those with laboratory training.

Persons performing the test were identified only as

Table 2. Laboratory Variables and Cholesterol Testing Accuracy

Variables	Laboratory Error ≤10% No. (%)	Laboratory Error >10% No. (%)	P Value
Practice characteristics			
Patients per day			
≤50	47 (76)	15 (24)	
>50	51 (85)	9 (10)	NS
Laboratory tests per day			
≤25	37 (70)	16 (30)	<.05
>25	61 (88)	8 (12)	
Cholesterol tests per day			
0–2	46 (77)	14 (23)	
>2	52 (84)	10 (16)	NS
Laboratory personnel			
Supervisor training			
Laboratory trained*	34 (89)	4 (11)	
LPN or medical assistant	40 (82)	9 (18)	NS
Others†	24 (69)	11 (31)	
Person performing sample testing			
Laboratory trained*	50 (85)	9 (15)	NS
Nonlaboratory trained	47 (75)	16 (25)	
Instrument factors			
Method			
Dry chemistry	61 (79)	16 (21)	
Wet chemistry	23 (82)	5 (18)	NS
Not specified	14 (82)	3 (18)	
Cost			
≥$7500	36 (92)	3 (8)	
<$7500	48 (73)	18 (27)	<.02
Not specified	14 (82)	3 (18)	

**Six months to 4 years of training in laboratory methods.*
†Registered nurses, physicians, self-trained, in-office trained, and others.
NS denotes not significant; LPN denotes licensed practical nurse.

having had formal laboratory training or not. Again there was no measurable difference between these two groups. Years of laboratory experience for the person performing the test were divided into two groups: those with 0 to 9 years of laboratory experience and those with 10 years or more. There was no statistically significant difference between these two groups.

A comparison of the instruments is shown in Table 2. An analysis was done comparing both the instrument method (comparing those that used a "dry" chemistry method with those that used a "wet" chemistry method) and instrument cost (comparing those with a retail list price of over $7500 with those listing at a cost of less than $7500). When comparing instrument method, there was no difference between the two groups; instrument cost was found to be a significant variable. Ninety-two percent of laboratories with an instrument costing more than $7500 were within the 10% accuracy limit compared with 73% of those laboratories with instruments costing less than $7500. This difference was significant ($P < .02$).

Quality control factors are listed in Table 3. Forty-

Table 3. Quality Control Factors and Cholesterol Testing Accuracy

Factors	Laboratory Factor ≤10% No. (%)	Laboratory Factor >10% No. (%)	P Value
Participation in proficiency testing			
Yes	57 (89)	7 (11)	
No	41 (71)	17 (29)	<.02
Quality assurance activities			
Written safety procedures			
Yes	45 (76)	14 (24)	
No	53 (83)	10 (17)	NS
Procedure manuals			
Yes	83 (60)	21 (20)	
No	15 (83)	3 (17)	NS
Laboratory personnel records			
Yes	47 (78)	13 (22)	
No	51 (82)	11 (18)	.055
Daily quality control			
Yes	76 (84)	14 (16)	
No	22 (67)	11 (33)	NS
Instrument maintenance log			
Yes	58 (79)	15 (21)	
No	40 (81)	9 (19)	NS

NS denotes not significant.

eight percent of laboratories had established safety procedures; 85% used procedure manuals; 49% kept personnel records; 74% kept a daily quality control log; and 60% kept an instrument maintenance log. While none of these were significantly related to error rates, the use of daily quality controls did approach significance ($P = .055$). As shown in Table 3, participation in a proficiency program was associated with better accuracy. A comparison of the accuracy rate of proficiency program participants (89%) and nonparticipants (71%) was significant ($P < .02$).

Comparing high-volume POLs (over 25 tests per day) to low-volume POLs (25 or fewer), the former group was 1.5 times as likely to have a supervisor with laboratory training (36% to 24%), 2.2 times as likely to use an analyzer costing more than $7500 (42% to 19%), and 1.6 times as likely to participate in proficiency testing (69% to 42%).

Discussion

Overall the laboratories that participated in this study performed quite well. Ninety-three percent of the POLs in this study already met the proposed grading criteria of CLIA '88 for serum cholesterol determination. This compares favorably with reference laboratories already being regulated.[7,16,17] The Iowa POLs in this study actually performed better than some reference laboratories.[7,17] A 1981 study showed that only 25% of POLs

achieved acceptable levels for serum cholesterol measurement when compared with the accuracy of other clinical laboratories.[18]

As only 80% of laboratories were within the 10% error, which was the self-defined acceptable limit by the Iowa physicians participating in the study, there is still room for improvement.

Several of the instruments representing the majority of the POLs in this study have been shown to perform to NCEP standards (5% error at the time of the study and 3% at the present time) when the testing is performed by proper personnel in well-controlled circumstances.[7,10] The number of laboratories surveyed in this study that fall outside this range suggests that these instruments are subject to operator variability under "field" (ie, noninstitutional) conditions. Others studying instrument performance in field conditions have shown that they may not achieve the same level of performance.[11] Performance variability of the various instruments needs to be better understood, and physicians selecting and operating instruments need to regularly check for proper performance. Furthermore, manufacturers and vendors need to provide appropriate information regarding the variance of their instruments in real-world conditions and to provide methods to assure proper performance. This becomes increasingly important as less operator input becomes necessary for instrument operation. The problem of instrument and laboratory variability is not unique to POLs and smaller analyzers. Large analyzers have also shown significant bias that places their accuracy outside the NCEP guidelines. Only 78% of clinical laboratories in a one-state study had results conforming to NCEP guidelines,[16] and another study showed that two commonly used multichannel analyzers may have up to a 20% bias when compared with Lipid Research Clinics methodology.[19]

Several other factors are apparently related to POL error rates. While increased laboratory tests per day resulted in a lower error rate, this may have been due to factors other than test frequency. Higher volume POLs were more likely to have supervisors trained in laboratory methods, to use more accurate (and more expensive) instruments, and to participate in proficiency testing. As these factors were in themselves related to lower error rates, they may have also accounted for the difference between the two groups.

Previous studies have shown that medical technologists perform better on chemistry analyzers than physicians and other office personnel.[9,10] The current study suggests that those POLs that had a laboratory-trained supervisor may have had lower error rates than those that did not, but this result was not significant. Nevertheless, 76% of those without a laboratory-trained supervisor did well, and it did not appear to matter who had actually performed the test. This suggests that there are factors other than personnel training that affect results.

The use of some quality assurance activities was related to lower error rates. The use of daily quality controls might be expected to improve performance, as it assures regular instrument validation. Participation in proficiency testing provides feedback that may help identify recurring problems in technique or equipment. While only 53% of POLs in this study participated in proficiency testing, each of the other quality control activities was used by over 75%, with over 95% (117/122) using at least one of the listed activities. This is in contrast to only 29% of POLs having a formal quality control program in a survey conducted in 1981[18] and to 44% having a quality control program in 1986.[20] The later study also showed that the POLs of residency graduates were more likely to have quality control programs. These changes over time suggest that POL directors are gradually increasing quality control activities in response to improved educational and informational efforts.

The differences between instruments found in this study have been noted in other studies.[10–12] The more expensive instruments are associated with lower error rates and are designed for less manipulation of the samples, hence, decreased operator error. Also, there appears to have been an association between instrument type, laboratory supervisor training, laboratory volume, and utilization of quality assurance factors. The relative role of each could not be defined in the present study.

This study has several limitations. Two selection biases may have been operative. Only POLs with at least one state academy member were enrolled, and participation was voluntary. While these circumstances may have favored participation by physicians with greater interest in POL performance, the high participation rate suggests self-selection was not a major factor. Another limitation was the use of only a single sample per POL. This prevented analysis of intralaboratory variation and may have created an error rate in excess of the true rate due to sample variation. Another potential source of error was a possible matrix effect, which is an error appearing in reconstituted lyophylized specimens, but not seen with fresh patient samples.[10]

Finally, this was an observational study, and the factors identified are associations, and may not be causally related to actual laboratory error.

Conclusions

Office laboratory testing is commonly performed by family physicians. Of the POLs in this study, 93% performed

cholesterol measurements within the proposed CLIA '88 guidelines. Factors relating to higher error rates suggest that testing accuracy can be improved by supervision by persons with training, quality assurance programs, and better instrumentation. This study also suggests that prior to regulation of POLs, most family physicians are voluntarily employing quality assurance programs, participating in proficiency testing, and performing accurate cholesterol testing. As training in the management of POLs increases, POL performance should continue to improve.

Acknowledgment

This was a project of the Research Network of the Iowa Academy of Family Physicians and was supported by grants from the American Academy of Family Physicians Foundation and the Iowa Academy of Family Physicians. We would like to thank Janet Wee for her assistance in the survey distribution and data collection.

References

1. Kannel WB, Castelli WP, Gordon T. Cholesterol in the prediction of atherosclerotic disease: new perspectives in the Framingham Study. Ann Intern Med 1979; 90:85.
2. Castelli WP, Garrison RJ, Wilson PWF, et al. Incidence of coronary artery disease and lipoprotein cholesterol levels: The Framingham Study. JAMA 1986; 256:2835.
3. Lipid Research Clinics Program. The Lipid Research Clinics Coronary Primary Prevention Trial results, I: reduction in incidence of coronary heart disease. JAMA 1984; 251:351.
4. Lipid Research Clinics Program. The Lipid Research Clinics Coronary Primary Prevention Trial results, II: the relationship of reduction in incidence of coronary heart disease to cholesterol lowering. JAMA 1984; 251:365.
5. Lowering blood cholesterol to prevent heart disease [Consensus Conference]. JAMA 1985; 253:2080.
6. The Expert Panel. Report of the National Cholesterol Education Program Expert Panel on detection, evaluation, and treatment of high blood cholesterol in adults. Arch Intern Med 1988; 148:36.
7. Current status of blood cholesterol measurement in clinical laboratories in the United States: a report from the Laboratory Standardization Panel of the National Cholesterol Education Program. Clin Chem 1988; 34:193.
8. Belsey R, Goitein RK, Baer DM. Evaluation of a laboratory system intended for use in physicians' offices I: reliability of results produced by trained laboratory technologists. JAMA 1987; 258: 353.
9. Belsey R, Vandenbark M, Goitein RK, Baer DM. Evaluation of a laboratory system intended for use in physicians' offices II: reliability of results produced by health care workers without formal or professional laboratory training. JAMA 1987; 258:357.
10. Burke JJ, Fischer PM. A clinician's guide to the office measurement of cholesterol. JAMA 1988; 259:3444.
11. Naughton MJ, Luepker RV, Strickland D. The accuracy of portable cholesterol analyzers in public screening programs. JAMA 1990; 263:1213.
12. Kaufman HW, McNamara JR, Anderson KM, et al. How reliably can compact chemistry analyzers measure lipids? JAMA 1990; 263:1245.
13. Bloch MJ, Cembrowski GS, Lembesis GJ. Longitudinal study of error prevalence in Pennsylvania physicians' office laboratories. JAMA 1988; 260:230.
14. Crawley R, Belsey R, Brock D, Baer DM. Regulation of physicians' office laboratories. The Idaho experience. JAMA 1986; 255:374.
15. Clinical Laboratory Improvement Amendments of 1988: HR 5471, October 6, 1988.
16. McManus BM, Toth AB, Engel JA, et al. Progress in lipid reporting practices and reliability of blood cholesterol measurement in clinical laboratories in Nebraska. Efforts to align results with the Centers for Disease Control, and feasibility of meeting National Cholesterol Education Program Guidelines. JAMA 1989; 262:83.
17. Hartman AE, Naito HK, Burnett RW, Welch MS. Accuracy of participant results utilized as target values in the CAP Chemistry Survey Program. Arch Path Lab Med 1985; 109:894.
18. Grayson RT. Effects of regulatory controls on the accuracy of clinical laboratory test. J Med Tech 1984; 1:632.
19. Blank DW, Hoeg JM, Kroll MH, Ruddel ME. The method of determination must be considered in interpreting blood cholesterol levels. JAMA 1986; 256:2867.
20. Wildermann RF, Schneider KA. Regulatory and legal influences on physicians' office laboratories. JAMA 1986; 256:252.

For editorial comment, see page 453.