Canadian Agency for Drugs and Technologies in Health

HTA

HEALTH TECHNOLOGY INQUIRY SERVICE (HTIS)

Title: Cholesterol Testing Devices: Clinical and Cost-Effectiveness

Date: 19 February 2008

Context and policy issues:

Cardiovascular disease accounted for 74, 626 deaths, approximately 33% of all deaths, in 2002.[1] Risk factors, including elevated serum cholesterol concentrations, are present in 80% to 90% of patients who develop coronary artery disease (CAD).[2] The absence of risk factors by 50 years of age is associated with low lifetime risk of CAD and longer survival.[2] The ratio of total cholesterol to high-density lipoprotein cholesterol (TC/HDL-C) is used to predict long-term risk of CAD.[2] When TC/HDL-C reaches a ratio of 6.0, lipid lowering therapy is initiated in most low-risk individuals.[2] The Canadian Cardiovascular Society recommends regular assessment of risk factors, including plasma lipids, every one to three years for all men 40 years or older and all postmenopausal women,.[2] In addition, adults with diabetes mellitus, hypertension, abdominal obesity, chronic kidney disease, atherosclerosis or family history of CAD, may be screened at any age.

While serum fasting lipid levels (TC, triglycerides [TG], low-density lipoprotein cholesterol [LDL-C], and HDL-C) are typically measured in a clinical laboratory, several point of care (POC) cholesterol testing devices have been developed for use in a clinic, office or home setting.[3] Most POC devices use similar technology based on the Trinder reaction to quantify cholesterol but they may not provide a full lipid profile (Table 1).[3] Cholesterol esterase hydrolyzes cholesterol ester, and cholesterol oxidase oxidizes cholesterol producing hydrogen peroxide.[3] Hydrogen peroxide reacts with a substrate in the presence of peroxidase to produce a colored product.[3] Results are based on the instrument reading light reflected off of the test strip that changes color due to this reaction.[3] Some community pharmacists offer cholesterol testing as a patient service in an effort to quickly identify individuals at risk of cardiovascular disease, monitor response to medication, and adjust doses without delay.[4-6]

Table 1: POC Cholesterol Testing Devices

Device	Sample	Measuring Time	Measured Lipids	Health Canada License Date
Reflotron® System HDL-C (Roche Diagnostics GMBH, DE)	Capillary (fingerstick) or venous blood	3 minutes	HDL-C	Device class 3 1999[7]
Accutrend® GCT System (Roche, Canada)	Capillary	3 minutes	TC, TG, glucose	Device class 3 1999[8]
Cholestech LDX® System (Cholestech Corporation, USA)	Capillary	5 minutes	Lipid Profile: TC, HDL-C, non-HDL-C, TG, LDL-C, TC/HDL ratio, glucose Various analyzer cassettes (box of 10: approx. $42-120 US) Monitor: $2100 US Training video Prints results[3]	Device class 3 2000[9]
Venture ™ Home Cholesterol Test (Syntron Bioresearch Inc, USA)	Capillary	10 minutes	Cholesterol	Device class 2 2002[10]
Cholesquick Cholesterol Test (Innovatek, Canada)	NR	NR	Cholesterol	Device class 2 2002[11]

NR: not reported; HDL-C: high-density lipoprotein cholesterol; TC: total cholesterol; TG: triglycerides; non-HDL-C: non high density lipoprotein cholesterol

Despite the evidence of efficacy for lowering cholesterol, individuals at highest risk of cardiovascular disease are least likely to achieve their cholesterol targets.[12] Evidence is sought to support the use of POC cholesterol testing devices in a rural community setting.

Research questions:

1. What is the clinical effectiveness of cholesterol testing devices in adults?

2. What is the cost-effectiveness of cholesterol testing devices in adults?

Methods:

A limited literature search was conducted on key health technology assessment resources, including Pre-Medline, Medline, Embase, Biosis, Pubmed, the Cochrane Library (Issue 1, 2008), University of York Centre for Reviews and Dissemination (CRD) databases, ECRI, EuroScan,

international HTA agencies, and a focused Internet search. Results include articles published between 2002 and the January 2008, and are limited to English language publications only. Filters were applied to limit the retrieval to systematic reviews/HTA, guideline, economic, randomized controlled trial (RCT) studies and observational studies.

Summary of findings:

The literature search yielded two clinical practice guidelines,[13,14] two randomized controlled trials (RCTs),[5,6] and seven observational studies on clinical effectiveness.[15-20] No studies of cost-effectiveness were identified. Studies were prospective in design, conducted between 2001 and 2006, with test and comparator measured simultaneously or immediately after one another. Outcomes range from TC measurements only to full lipid profiles. Study details are provided in appendix A.

Health technology assessments, systematic reviews, meta-analyses

No health technology assessment reports, systematic reviews, or meta-analyses, were identified that specifically addressed the use of POC cholesterol testing devices in a rural community setting.

Clinical guidelines

A clinical practice guideline by the Practice Division of the Royal Pharmaceutical Society of Great Britain was identified regarding POC cholesterol testing by community pharmacies.[13] These guidelines recommended choosing a device evaluated by the Medicines and Healthcare Products Regulatory Agency. The guidelines considered the ease by which the test can be performed, time required for results, level of analytical accuracy, training requirements, manual versus automatic calibration, and whether visual display or printed results are preferred.[13] Two or more cholesterol measurements are required to establish a diagnosis of high cholesterol, noting that readings can vary from day to day, and at different times of day.[13] Clients should be provided with written results and lifestyle advice should be supported by written information. If cholesterol levels are not within the desired range, consent must be obtained before sending this information to their general practitioner.[13]

The US Preventive Services Task Force Guide to Screening for High Blood Cholesterol and Other Lipid Abnormalities reference the accuracy of POC cholesterol testing.[14] Ninety three percent of clinical laboratory test measurements are within nine percent of a reference standard.[14] Desktop analyzers produce reliable results but some devices may not meet standards for accuracy. Variation in training and operating techniques may introduce error when instruments are used outside clinical laboratories. The average bias for measurements based on capillary (fingerstick) samples compared to venous samples was +4-7.[14] A single measure of serum cholesterol could vary as much as 14% from an individual's average value under acceptable laboratory conditions.[14] Patients may be advised of their cholesterol range rather than a single value. An average of at least two measurements on two occasions is recommended, and a third if the first two values differ by more than 16%.[14]

Clinical effectiveness - Randomized controlled trials

Between 1998 and 2000, an RCT was conducted in 54 community pharmacies in Alberta and Saskatchewan to determine the effect of community pharmacist intervention on cholesterol risk management.[5] Patients randomized to pharmacist intervention received education, a brochure

on risk factors, POC cholesterol measurement (Accutrend®, Roche, Quebec), referral to their physician, and 16 weeks of follow-up. Usual care patients received the same brochure, general advice, and minimal follow-up at eight and 16 weeks. The primary end point was a composite of performance of a fasting cholesterol panel by the physician or addition or increase in dose of cholesterol-lowering medication. The study was terminated early due to benefit of the effect of community pharmacist intervention involving POC cholesterol testing. Of the 675 patients enrolled, approximately 40% were women with an average age of 64 years. The primary end point was reached in 196 (57% of) intervention patients versus 102 (31%) of usual care patients [OR: 3.0; 95% CI 2.2, 4.1; p<0.001].[5] The measurement of a fasting cholesterol panel was conducted in 53% of intervention patients versus 29% of usual care patients [OR: 2.8, 95% CI 2.0, 3.7; p<0.001]. New prescription for medication was attained in 10% of intervention patients versus 4% of usual care patients [OR: 2.5, 95% CI 1.3, 4.6; p<0.003]. Increased dose was attained in 3% of intervention patients versus 1% of usual care patients [OR: 3.0, o5% CI 0.99, 8.8; p=0.07]. The effect of the intervention was greater in women than men, with fewer end points reached in the usual care group (27% in women versus 33% in men). The intervention was twice as efficacious in diabetic patients compared to non-diabetic patients. The authors concluded that community-based intervention improves the process of cholesterol management in high-risk patients.[5]

The impact of pharmacist-conducted home visits on the outcomes of lipid-lowering drug therapy was evaluated in a prospective RCT involving 94 Australians recruited between April and October 2001. [6] Participants randomized to pharmacist home visits received monthly visits with education, and POC cholesterol testing (Accutrend®, Roche, NSW) with a follow-up of 6 months. Usual care patients received an initial visit by a pharmacist, followed by POC cholesterol testing at 6 months. The main outcome measure was TC after 6 months and an evaluation of patient and practitioner satisfaction with the program. No significant difference in baseline TC was noted between groups. The reduction in TC levels in the intervention group was statistically significant over the course of study (4.9±0.6, p<0.005), while no change was observed in controls (p=0.26). [6] At 6 months, 44% of intervention patients and 24% of control patients had TC levels below 4.0 mmol/L (p=0.06).[6] The reduction in TC in the intervention group is expected to result in a 21% reduction in cardiovascular mortality risk and a 16% reduction in total mortality risk. Patients surveyed said they would pay between CAN$1.00 to $5.00 for this service and 88% thought it would be best performed at home**.** Authors cited the sensitivity of the Accutrend® GC monitor as a limitation. The minimum measurable level for TC was 3.88 mmol/L. This does not provide great scope for measuring levels below 4.0 mmol/L, which is the current recommended goal. Despite a significant reduction in TC levels, 56% of intervention patients and 76% of control patients had cholesterol levels above the target of 4.0 mmol/L, despite 6 months of lipid-lowering therapy.[6] These results are consistent with other studies showing that despite evidence that reductions in LDL-C reduces cardiovascular risk, targets are achieved in fewer than 50% of patients who receive lipid-lowering therapy. The authors concluded that a pharmacist-conducted educational and monitoring intervention improved outcomes of lipid-lowering drug therapy.[6]

Observational studies

The suitability of Cholestech LDX® (Point of Care Diagnostics, Artarmon, NSW) for the Aboriginal health care setting was evaluated in a prospective observational study involving 51 Australian volunteers.[16] Participants provided capillary and venous blood samples for analysis by Cholestech LDX® and certified laboratory testing. The correlation between Cholestech LDX® and laboratory devices for both capillary and venous whole blood samples was ≥0.96 for TC, ≥0.99 for TG, and ≥0.92 for HDL- and LDL-C.[16] The mean percentage difference between

results was less than 2% for TC and TG analyses and less than 5% for HDL- and LDL-C.[16] A positive bias of 6% was observed on Cholestech LDX® at HDL-C concentrations >1.2 mmol/L.[16] Within-day precision ranged from 0.9 to 3.5% for TC, 1.6 to 2.5% for TG, and 6.3 to 2.9% for HDL-C. No significant difference was noted between capillary and venous whole blood lipid measurements performed on Cholestech LDX®. The authors concluded that Cholestech LDX® would be suitable for the Aboriginal health care setting based on its simple operation, sound analytical performance and ability to produce a full lipid profile in under five minutes.[16]

Cholestech LDX® (Cholestech Corporation, USA) use in remote Australian communities was evaluated in another observational study.[17] Risk factor screening offered to Aboriginal communities in North East Arnhem Land from 2001 to 2003 resulted in 76 to 118 blood samples from a subset of 779 participants. On-site Cholestech LDX® measurements were compared to routine laboratory measurements to assess the agreement of POC testing as an alternative to laboratory testing for population-based risk factor screening. Agreements (with 95% CI) between methods for categorizing results ranged from 88% (77 to 94%) for HDL-C, 99% (92-100%) for glucose, and the degree of agreement noted as kappa coefficients ranged from 0.668 for TC to 0.945 for glucose. Differences in median values were not clinically meaningful, but were statistically significant ($p<0.05$) for HDL-C: 1.05 [0.95, 1.25] versus 1.00 [0.81, 1.20] mmol/L; TG: 1.65 [1.12, 2.19] versus 1.49 [1.07, 2.36] mmol/L and glucose: 5.2 [4.5, 6.0] versus 5.2 [4.7, 5.8] mmol/L, respectively for POC and laboratory methods.[17] Median TC values were not significantly different, 4.4 [3.8, 5.0] versus 4.4 [3.8, 5.1] mmol/L, respectively for POC and laboratory testing.[17] The authors concluded that POC testing provides a reliable alternative to laboratory testing for risk factor screening in remote locations.[17]

Lipid profile measurements of Cholestech LDX® were compared with those from a hospital reference laboratory in a prospective, observational study of 100 patients attending the Cardiac Risk Factor Clinic in Ireland.[19] A fingerstick sample and part of a venous sample was subjected to Cholestech LDX® testing while the remaining venous sample underwent laboratory analysis. Cholestech LDX® overestimated TG by 0.25 mmol/L (95% CI 0.17, 0.24) and underestimated HDL-C by 0.11 mmol/L (95% CI -0.143, -0.078). There were significant correlations between methods for TC ($r=0.92$), TG ($r=0.93$), HDL-C ($r=0.92$) and LDL-c ($r=0.86$) (all $p<0.0001$). [19] The authors concluded that these results validate the use of Cholestech LDX® for POC lipid measurements in clinical practice provided well trained operators are supported by a laboratory delivering quality assurance support.[19]

A prospective observational study of 63 hyperlipidemic adults was conducted in Wisconsin to evaluate the inaccuracy of lipid measurements with Cholestech LDX® in older individuals.[15] Participants were ≥70 years of age with fasting serum LDL-C levels >1.40 g/L. Fasting fingerstick samples were analyzed using the Cholestech LDX® and antecubital venous samples were analyzed in a proficiency-certified clinical laboratory. Cholestech LDX® measurements overestimated TG (0.296 g/L; $p<0.001$) and HDL-C (0.015 g/L; $p=0.026$), and underestimated LDL-C (0.043 g/L; $p=0.046$). Total and non-HDL-C measurements were unbiased but widely variable. The two standard deviations of the mean bias between laboratory and Cholestech LDX® measurements of LDL-C and non-HDL-C exceeded the 0.30 g/L targets in current lipid guidelines. The authors concluded that lipid values obtained by portable analyzers may be useful for screening, but not for individual diagnosis or management.[15]

The performance of CardioChek™ (Polymer Technology Systems, Indianapolis, USA) and Cholestech LDX® (Cholestech Corporation, Hayward, USA) POC devices were compared to laboratory measurement of lipids in a prospective, observational study involving 100 South

Africans from a lipid clinic at Johannesburg Hospital.[18] Results were grouped as low, middle, and high similar to those defined by the National Cholesterol Education Program (NCEP), except in the high range where TC and HDL-C levels were under-read by both analyzers. TC, TG, HDL-C and LDL-C measured by both analyzers correlated significantly with laboratory measures ($p<0.0001$). With the exception of LDL-C, both devices showed reasonable compliance with NCEP goals for coefficients of variation and bias measurements but neither conformed completely to the Guidelines. The authors concluded that compared to National Health Laboratory Service methods, the performance of CardioChek™ PA and Cholestech LDX® are acceptable and offer rapid measurement of lipids.[18]

The bias, precision and utility of the Bioscanner 2000 (Polymer Technology Systems Inc., Indianapolis, USA) for POC TC testing was assessed in a prospective, observational study conducted in the United Kingdom.[20] A single investigator prospectively studied 100 consecutively sampled non-fasting patients attending a hospital-based clinic with symptomatic peripheral artery disease (PAD) over a four month period. Fingerstick samples were analyzed for TC using the Bioscanner 2000 and antecubital venous samples were analyzed in a proficiency-certified clinical laboratory. The Bioscanner 2000 was precise with a coefficient of variation of 1.8 to 3.8%.[20] However, POC TC testing was significantly lower than laboratory TC testing (mean: 4.67, SD: 1.1 versus mean: 5.12, SD: 1.2 mmol/L; $p\leq0.01$) showing a 1.5% negative bias for the Bioscanner 2000. Forty-six percent of TC readings differed by $>$0.5 mmol/L, 16% by $>$1.0 mmol/L, and 3% by $>$2 mmol/L.[20] If the cut-off for statin therapy (lipid lowering drug) were taken as a TC of 5.0 or 3.5 mmol/L, then based on POC testing alone, 18% and 6% of patients, respectively, would not have received a statin. The authors concluded while POC testing with BioScanner 2000 significantly underestimated TC compared to laboratory testing, this would not have affected the decision to prescribe a statin in the majority of cases.[20] The authors questioned whether TC testing is required as the majority of patients with PAD have TC$>$3.5 mmol/L so virtually all PAD patients should be treated with a statin.[20]

The precision of the Reflotron® (Boeringer-Mannheim, Mannheim, Germany), a dry-chemistry analyzer for POC TC testing was assessed in a prospective, observational study involving 100 employees at a university in southern USA.[21] Fasting fingerstick samples were analyzed for TC using the Reflotron® and antecubital venous samples were analyzed in a proficiency-certified clinical laboratory. Reflotron® TC measurements averaged 213.27 mg/dL (SD=44.66 mg/dL) and laboratory measures for TC averaged 228.86 mg/dL (SD=40.50 mg/dL).[21] The mean coefficient of variation showed a 3.3% error rate that is greater than the 3% allowable by the NCEP Guidelines. There was a -7.45% (SD=2.65%) bias and the percentage of participants with TC misclassified was 16.85%.[21] The authors concluded that while Reflotron® met most of the NCEP guidelines for accuracy, the device provided clinically relevant underestimations of TC. Lipid values may be useful for screening, but Reflotron® should not be used as a diagnostic or management tool.[21]

Cost-effectiveness

No evidence was identified that addressed the cost-effectiveness POC cholesterol testing devices.

Limitations

The first RCT regarding the effect of pharmacy intervention programs involving POC cholesterol testing is limited in that results focused on process rather than clinical outcomes.[5] Patient selection was biased in that pharmacists selected patients for study based on their knowledge

of the patient's medical history.[5] The sensitivity of the device was a limitation to researchers in the other RCT regarding pharmacist POC cholesterol testing home visits.[6] Accutrend® has a sensitivity of 3.88 mmol/L for TC, while 4.0 mmol/L is recommended.[6] Study populations in the observational studies were small and may differ from the Canadian context of interest.[15-19,21] The study by Shemesh involved Australian aboriginals with lower TC levels relative to North Americans.[17] Little information is given regarding patient characteristics and how patients were sampled in some observational studies lending uncertainty to the generalizability of results.[15,18,19] The CardioChek™ and Bioscanner 3000 POC cholesterol testing devices are not licensed for use in Canada, limiting the generalizability of the studies conducted in South Africa and the United Kingdom.[18,20]

Conclusions and implications for decision or policy making:

Two randomized controlled trials suggested that pharmacist-based interventions involving TC testing improve the process of cholesterol management in high-risk patients.[5,6] However, methodological issues regarding how patients were selected for study, lack of clinical outcome measurement and blinding should be considered in interpreting these results. Seven observational studies suggested that lipid values obtained by portable analyzers may be useful for screening, but not for individual diagnosis or management.[15-21] A limitation of POC cholesterol testing devices is that some do not offer a full lipid profile making them suitable for screening purposes only. The Cholestech LDX® provides a full lipid profile and printed copy of the results for clinicians who do not have routine access to laboratory services. A full lipid profile may be generated within minutes allowing immediate management, whereas laboratory testing may take a couple of days for the clinician to review the test results and advise the patient. False negative screening results occurred in 16.85% of participants using the Reflotron®. Screening programs are typically used as a means of referral, so false negative results are more damaging than false positive results in this setting. Health professionals should be familiar with the biases of devices and may adjust their screening and education methods accordingly.[21] While no evidence was identified to address the cost or cost-effectiveness of POC cholesterol testing devices, there are likely resource considerations in setting up screening program in a rural setting. Based on the RCTs on pharmacist-based POC cholesterol testing, user training, follow-up, and quality control are important aspects of care.

Prepared by:

Lynda McGahan, MSc., Research Officer
Emmanuel Nkansah, MLS, MA, Information Specialist
Health Technology Inquiry Service
Email: htis@cadth.ca
Tel: 1-866-989-8439

References:

1. Statistics - Incidence of Cardiovascular Disease. In: *HeartandStroke*. Ottawa: Heart and Stroke Foundation; 2002. Available: http://ww2.heartandstroke.ca/Page.asp?PageID=33&ArticleID=1077&Src=news&From=SubCategory (accessed 2008 Feb 8).

2. McPherson R, Frohlich J, Fodor G, Genest J, Canadian Cardiovascular Society. Canadian Cardiovascular Society position statement--recommendations for the diagnosis and treatment of dyslipidemia and prevention of cardiovascular disease. *Can J Cardiol* 2006;22(11):913-27.

3. Taylor JR, Lopez LM. Cholesterol: point-of-care testing. *Ann Pharmacother* 2004;38(7-8):1252-7.

4. McKenney JM, Bradberry JC, Talbert RL, Cahill E, Brown WV. National survey of pharmacists about coronary heart disease, hypercholesterolemia, nonprescription statintherapy, and pharmacists' services. *J Am Pharm Assoc (Wash DC)* 2004;44(5):562-8.

5. Tsuyuki RT, Johnson JA, Teo KK, Simpson SH, Ackman ML, Biggs RS, et al. A randomized trial of the effect of community pharmacist intervention on cholesterol risk management: the Study of Cardiovascular Risk Intervention by Pharmacists (SCRIP). *Arch Intern Med* 2002;162(10):1149-55 (accessed 2008 Jan 31).

6. Peterson GM, Fitzmaurice KD, Naunton M, Vial JH, Stewart K, Krum H. Impact of pharmacist-conducted home visits on the outcomes of lipid-lowering drug therapy. *Journal of Clinical Pharmacy & Therapeutics* 2004;29(1):23-30.

7. Reflotron® System - HDL Cholesterol (Roche Diagnostics GMBH, DE). In: *Medical Devices Active Licence Listing(MDALL) [online database]*. Ottawa: Medical Devices Bureau, Therapeutic Products Directorate, Health Canada; 1999. Licence No.: 3890. Available: http://www.hc-sc.gc.ca/dhp-mps/md-im/licen/mdlic_e.html (accessed 2008 Feb 15).

8. Accutrend® GCT System (Roche Diagnostics GMBH, DE). In: *Medical Devices Active Licence Listing(MDALL) [online database]*. Ottawa: Medical Devices Bureau, Therapeutic Products Directorate, Health Canada; 1999. Licence No.: 1036. Available: http://www.hc-sc.gc.ca/dhp-mps/md-im/licen/mdlic_e.html (accessed 2008 Feb 15).

9. Cholestech LDX® System. In: *Medical Devices Active Licence Listing (MDALL) [online database]*. Ottawa: Medical Devices Bureau, Therapeutic Products Directorate, Health Canada; 2000. Licence No.: 17940. Available: http://www.hc-sc.gc.ca/dhp-mps/md-im/licen/mdlic_e.html (accessed 2008 Feb 15).

10. Venturetm™ Home Cholesterol Test (Syntron Bioresearch Inc, USA). In: *Medical Devices Active Licence Listing(MDALL) [online database]*. Ottawa: Medical Devices Bureau, Therapeutic Products Directorate, Health Canada; 2002. Licence No.: 35813 . Available: http://www.hc-sc.gc.ca/dhp-mps/md-im/licen/mdlic_e.html (accessed 2008 Feb 15).

11. Cholesquick Cholesterol Test (Innovatek Medical Inc., Canada). In: *Medical Devices Active Licence Listing(MDALL) [online database]*. Ottawa: Medical Devices Bureau, Therapeutic Products Directorate, Health Canada; 2002. Licence No.: 39084 . Available: http://www.hc-sc.gc.ca/dhp-mps/md-im/licen/mdlic_e.html (accessed 2008 Feb 15).

12. Olson KL, Tsuyuki RT. Patients' achievement of cholesterol targets: a cross-sectional evaluation. *Am J Prev Med* 2003;25(4):339-42.

13. *Practice Guideline: cholesterol testing*. London (UK): Royal Pharmaceutical Society of Great Britain; 2005. Available: http://www.rpsgb.org.uk/pdfs/choltestguid.pdf (accessed 2008 Feb 8).

14. U.S. Preventive Services Task Force. Chapter 2: Screening for High Blood Cholesterol and Other Lipid Abnormalities. In: *Guide to Clinical Preventive Services*. Second Edition. Rockville (MD): Agency for Healthcare Research and Quality (AHRQ); 2001. Available: http://www.ahrq.gov/clinic/2ndcps/lipid.pdf (accessed 2008 Feb 8).

15. Stein JH, Carlsson CM, Papcke-Benson K, Einerson JA, McBride PE, Wiebe DA. I Inaccuracy of lipid measurements with the portable Cholestech L.D.X analyzer in patients with hypercholesterolemia. *Clin Chem* 2002;48(2):284-90.

16. Shephard M, Tallis G. Assessment of the point-of-care Cholestech lipid analyser for lipid screening in Aboriginal communities. *Aust J Med Sci* 2002;23(1):4-10.

17. Shemesh T, Rowley KG, Shephard M, Piers LS, O'Dea K. Agreement between laboratory results and on-site pathology testing using Bayer DCA2000+ and Cholestech LDX point-of-care methods in remote Australian Aboriginal communities. *Clin Chim Acta* 2006;367(1-2):69-76.

18. Panz VR, Raal FJ, Paiker J, Immelman R, Miles H. Performance of the CardioChek® PA and Cholestech LDX® point-of-care analysers compared to clinical diagnostic laboratory methods for the measurement of lipids. *Cardiovascular Journal of South Africa* 2005;16(2):112-7.

19. Carey M, Markham C, Gaffney P, Boran G, Maher V. Validation of a point of care lipid analyser using a hospital based reference laboratory. *Ir J Med Sci* 2006;175(4):30-5.

20. Hobbs SD, Jones A, Wilmink ABM, Bradbury AW. Near patient cholesterol testing in patients with peripheral arterial disease. *Eur J Vasc Endovasc Surg* 2003;26(3):267-71.

21. Bowden RG, Kingery PM, Long L. Precision of a dry-chemistry method of lipid screening. *Public Health* 2006;120(6):572-6.

Appendix A: Clinical Effectiveness of Cholesterol Testing Devices

Author, Year, Country	Study Design	Participants	Intervention versus Comparator	Outcomes	Results	Conclusions and Limitations
Clinical Effectiveness						
Ross et al., 2002 Canada[5]	RCT Multi-centre Study period: 1998-2000 Follow-up: 16 weeks for intervention; minimal for usual care Intent to treat analysis	n=675 patients with atherosclerosis or diabetes mellitus with another risk factor Males: 410 Females: 265	Pharmacist Intervention: education, brochure, POC cholesterol measurement (Accutrend®, Roche, Canada), referral and 16 weeks follow-up Versus Usual care: brochure, advice, phone call at 8 weeks and closing visit at 16 weeks	Primary end point: composite of performance of a fasting cholesterol panel by the physician or addition or increase in dose of cholesterol-lowering medication	196 intervention patients versus 102 usual care patients achieved the primary end point. [OR: 3.0; 95%CI 2.2, 4.1; p<0.001] Measurement of a fasting cholesterol panel was conducted in 53% of intervention patients versus 29% of usual care patients [OR: 2.8, 95% CI 2.0, 3.7; p<0.001] New prescription for medication was attained in 10% of intervention versus 4% of usual care patients [OR: 2.5, 95% CI 1.3, 4.6; p<0.003] Increased dose was attained in 3% of intervention versus 1% of usual care patients [OR: 3.0, o5% CI 0.99, 8.8; p=0.07]	A community-based intervention program improves the process of cholesterol management in high-risk patients. Possible selection bias: patients were selected community pharmacists with knowledge of medical history Outcome assessors were not blinded to intervention Reasons for 18 withdrawals and loss to follow-up not given

Author, Year, Country	Study Design	Participants	Intervention versus Comparator	Outcomes	Results	Conclusions and Limitations
						Measured process rather than clinical outcomes
Peterson et al., 2004 Australia[6]	Prospective RCT Study period: 2001 Follow-up: 6 months	n=94 patients, 81 completed study n=39 intervention n=42 control Patients discharged from hospital with cardiovascular disease.	Pharmacist intervention: pharmacist home visits received monthly visits with education, and POC cholesterol testing (Accutrend®, Roche, NSW) with a follow-up of 6 months Versus Initial visit by a pharmacist, followed by POC cholesterol testing at 6 months	TC at 6 months	At 6 months, 44% of intervention patients and 24% of control patients had TC levels below 4.0 mmol/L (p=0.06) 56% of intervention patients and 76% of control patients had TC levels above the target of 4.0 mmol/L, despite 6 months of lipid-lowering therapy. Patients surveyed said they would pay between $1.00 to $5.00 CAN for this service and 88% thought it would be best performed at home.	A pharmacist-conducted educational and monitoring intervention improves outcomes of lipid-lowering drug therapy. Accutrend® sensitivity, minimum measurable level for TC is 3.88 mmol/L while 4.0 mmol/L is recommended.
Observational Studies						
Shephard and Tallis., 2001 Austraila[16]	Prospective Observational Study period:	N=51 volunteers Males: NR Females: NR	Cholestech LDX® (fingerstick and venous samples) versus proficiency-	TC HDL-C Triglycerides	Correlation between devices was ≥0.96 for TC, ≥0.99 for TG, and ≥0.92 for HDL- and LDL-C.	Cholestech LDX® is suitable for the Aboriginal health care

Author, Year, Country	Study Design	Participants	Intervention versus Comparator	Outcomes	Results	Conclusions and Limitations
	NR Time between test and control: < 5 minutes	Mean age: NR Sampling: NR	certified clinical laboratory (antecubital venous sample)	LDL-C Non-HDL-C	The mean percentage difference between results was< 2% for TC and TG and < 5% for HDL- and LDL-C. Positive bias of 6% on Cholestech LDX® at HDL-C concentrations >1.2 mmol/L. Within-day precision ranged from 0.9 to 3.5% for TC, 1.6 to 2.5% for TG, and 6.3 to 2.9% for HDL-C.	setting based on its simple operation, sound analytical performance and ability to produce a full lipid profile in under five minutes.[16] Little information given regarding participants, uncertainty regarding generalizability of findings to population of interest.
Shemesh et al., 2006 Australia[17]	Observational Study period: 2001-2003 Time between tests: maximum of 4 hours	76 to 118 blood samples from a subset of 779 participants involved in a larger study. Age: 15 to 72 years	Cholestech LDX® (fasting fingerstick sample) versus proficiency-certified clinical laboratory (antecubital venous sample)	TC HDL-C Triglycerides LDL-C Non-HDL-C Glucose	Agreements (95% CI) ranged from 88% (77 to 94%) for HDL-C, 99% (92-100%) for glucose. Kappa coefficients ranged from 0.668 for TC to 0.945 for glucose. Differences in median values (p<0.05) for HDL-C: 1.05 [0.95, 1.25] versus 1.00 [0.81, 1.20] mmol/L;	POC testing provides a reliable alternative to laboratory testing for risk factor screening in remote locations. North Americans have

Author, Year, Country	Study Design	Participants	Intervention versus Comparator	Outcomes	Results	Conclusions and Limitations
		Sampling: NR			TG: 1.65 [1.12, 2.19] versus 1.49 [1.07, 2.36] mmol/L and glucose: 5.2 [4.5, 6.0] versus 5.2 [4.7, 5.8] mmol/L, respectively for POC and laboratory methods. Median TC values were not significantly different, 4.4 [3.8, 5.0] versus 4.4 [3.8, 5.1] mmol/L, respectively for POC and laboratory testing.[17]	higher TC levels relative to Aboriginal Australians. This may limit generalizability of these results.[17] Authors did not have access to follow-up testing of participants identified as high risk so it was not possible to confirm final clinical outcomes.
Carey et al., 2006 Ireland[19]	Prospective Observational Study period: NR Time between tests: immediately after each other.	n=100 subjects either attending the Cardiac Risk Factor Clinic due to heart disease or hospital staff volunteers 80% fasting; 20% non-	Cholestech LDX® (capillary and venous) versus proficiency-certified clinical laboratory (antecubital venous sample)	TC HDL-C Triglycerides LDL-C Non-HDL-C Glucose	Cholestech LDX® over estimated TG 0.25 mmol/L (95% CI 0.17, 0.24) and under estimated HDL-C -0.11 mmol/L (95% CI -0.143, -0.078). Significant correlations between methods for TC r=0.92, TG r=0.93, HDL-C r=0.92 and LDL-c r=0.86 (all p<0.0001).	These results validate Cholestech LDX® for POC lipid measurements in clinical practice provided trained operators are supported by laboratory quality

Author, Year, Country	Study Design	Participants	Intervention versus Comparator	Outcomes	Results	Conclusions and Limitations
		fasting Males: 30 Females: 70 100 samples for lipid and 40 samples for glucose analysis				assurance. Little information given as to how patients were selected or sampled may limit generalizability.
Stein et al., 2002 USA[15]	Prospective Observational Study period: participants refrained from lipid-lowering agents for 4 weeks; and fasted 12 hours before testing Time between test and control: immediately after each other.	n=63 patients with hyperlipidemia LDL-C: >1.40 g/L TG: <4.00 g/L Males: NR Females: NR Mean age: 75.4±4.2 years Sampling: NR	Cholestech LDX® (fasting fingerstick sample) versus proficiency-certified clinical laboratory (antecubital venous sample)	TC HDL-C Triglycerides LDL-C Non-HDL-C	Device overestimated TG (0.296 g/L; p<0.001) and HDL-C (0.015 g/L; p=0.026); underestimated LDL-C (0.043 g/L; p=0.046) TC and non-HDL-C estimates from device were unbiased, but widely variable -2 SD of the mean bias between lab and device determinations of LDL-C and non-HDL-C exceeded 0.3 g/L guidelines	Lipid values from portable devices are useful for screening, but not for individual clinical decisions for diagnosis or management. Small sample size, few patient characteristics. Entry and exit dates for study are not provided Uncertain how patients were sampled.

Author, Year, Country	Study Design	Participants	Intervention versus Comparator	Outcomes	Results	Conclusions and Limitations
Pranz et al, 2005 Africa[18]	Prospective Observational Study period: NR Time between tests: simultaneously for devices, immediately after for laboratory	n=100 patients hypercholesterolaema is prevalent among South African populations Males: NR Females: NR Mean age: NR Sampling: NR	CardioChek™ and Cholestech LDX® POC devices versus certified clinical laboratory (antecubital venous sample)	TC HDL-C Triglycerides LDL-C Non-HDL-C	In the high range TC and HDL-C levels were under-read by both analyzers (0.5 mmol/L for Cholestech LDX® and 1.3 mmol/L for CardioChek™ PA ($p<0.001$)) TC, TG, HDL-C and LDL-C measured by both analyzers correlated significantly with laboratory measures ($p<0.0001$). With the exception of LDL-C, both devices showed compliance with NCEP goals for coefficients of variation and bias measurements but neither conformed completely to the Guidelines.	Compared to National Health Laboratory Service methods, the performance of CardioChek™ PA and Cholestech LDX® are acceptable and offer rapid measurement of lipids. Little information provided regarding study population. This may limit generalizability of results. CardioChek™ PA is not licensed for use in Canada.
Hobbs et al., 2003 United Kingdom[20]	Prospective Observational Study period: 4 months	n=100 patients with peripheral artery disease M:F ratio:	Bioscanner 2000 (capillary) versus certified clinical laboratory (antecubital venous sample)	TC	Bioscanner 2000 had a coefficient of variation of 1.8 to 3.8%. POC TC testing was significantly lower than	While POC testing with BioScanner 2000 significantly underestimated

Author, Year, Country	Study Design	Participants	Intervention versus Comparator	Outcomes	Results	Conclusions and Limitations
		1.6:1 Mean age: 69± 10.3 Sampling: consecutively			laboratory TC testing (mean: 4.67, SD: 1.1 versus mean: 5.12, SD: 1.2 mmol/L; p≤0.01) 46% of TC readings differed by >0.5 mmol/L, 16% by >1.0 mmol/L, and 3% by >2 mmol/L.	TC compared to laboratory testing, this would not have affected the decision to prescribe a statin in the majority of cases. Bioscanner 2000 is not licensed in Canada.
Bowden et al. 2006 USA[21]	Prospective Observational Study period: NR Time between tests: immediately following each other	n=285 employee volunteers from a southern US university Male: 195 Female: 90 Mean age: 47±9.57	Reflotron® versus certified clinical laboratory (antecubital venous sample)	TC	Reflotron® TC measurements averaged 213.27 mg/dL (SD=44.66 mg/dL). Laboratory TC measures averaged 228.86 mg/dL (SD=40.50 mg/dL). Mean coefficient of variation: 3.3% error rate -7.45% (SD=2.65%) bias False negative screening in 16.85% of participants.	While Reflotron® met most of the NCEP guidelines for accuracy, the device provided clinically relevant underestimations of TC. Lipid values may be useful for screening, but Reflotron® should not be used as a

Author, Year, Country	Study Design	Participants	Intervention versus Comparator	Outcomes	Results	Conclusions and Limitations
						diagnostic or management tool. Participants were volunteers and results may not be generalizable.