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Diagnostic Technology: Point of Care test for the analysis of lipid panels

Clinical Question: Does a point of care test for lipids improve the risk stratification and management of cardiovascular disease compared to standard practice.

Advantages over Existing Technology:
Tests for cholesterol and triglycerides can be performed during consultation, as they require less than 5 minutes to perform. Patients can be informed of their results immediately, providing more accurate categorisation in the QRISK (1) or Framingham Risk Scores (2) and appropriate action, such as starting cholesterol lowering therapy, can be taken.

Details of Technology:
Plasma lipids are comprised of triglycerides and cholesterols (high density lipoprotein [HDL], low density lipoprotein [LDL] and very low density lipoprotein [VLDL]) and levels of these lipids in serum are highly correlated with risk of vascular and cardiac events. Framingham and QRISK calculators require both total and HDL cholesterol measurements. Two small point-of-care CRMLN (Cholesterol Reference Method Laboratory Network) (3) certified devices are on the UK market to measure total and HDL cholesterol:

1. Cholestech LDX® System (Inverness Medical, UK). The device measures a range of values from a fingerstick blood sample. Several test cassettes are available, measuring the following: total cholesterol; total cholesterol and glucose; total cholesterol and HDL; total cholesterol, HDL, and glucose; A lipid panel consisting of total cholesterol (2.6-12.9 mmol/l), HDL (0.4-2.6 mmol/l), triglycerides (0.5-7.3 mmol/l), total cholesterol/HDL ratio, estimate of LDL and VLDL, and an all-inclusive panel consisting of total cholesterol, HDL, triglycerides, glucose, total cholesterol/HDL ratio, estimate of LDL and VLDL.
2. Professional CardioChek P.A. (Polymer Technology Systems, Inc., Indiana, USA; UK: BHR Pharmaceuticals Ltd.). Handheld device using test strips which perform a range of tests from a fingerstick blood sample, depending on the test trip selected: lipid panel and single testing for glucose, ketone, total cholesterol (2.6-10.3 mmol/l), HDL cholesterol (0.6-2.2 mmol/l), triglycerides (1.3-12.8 mmol/l) and calculated LDL cholesterol.

Patient Group and Use:

- Patients requiring primary prevention of cardiovascular disease.
- Management of patients diagnosed with cardiovascular disease.
- NHS Health Check for adults aged 40 to 74.

Importance:
Cardiovascular disease (CVD) is the main cause of death in the UK, accounting for almost 198 000 deaths per year (9). One in three deaths is caused by CVD. Estimates on the prevalence of all coronary heart disease in the UK report 970 000 men and 439 000 women aged 35 and over have had a heart attack and just over 1.1 million men and 850 000 women have had angina. An estimated 1.5 million men and 1 million women aged 35 and over are living in the UK with coronary heart disease. Lipid lowering therapy (usually a statin) is used in all patients with a history of cardiovascular disease. Lipid tests are monitored on a regular (yearly) basis in such patients. Assessment of cardiovascular risk for primary prevention is recommended by NICE for all patients over the age of 40 and includes body mass index, blood pressure, screening for diabetes mellitus and lipid measurement.

Previous Research:

Accuracy compared to existing technology

An evaluation was carried out by the UK NHS Purchasing and Supply Agency in 2005 on 106 samples comparing the CardioChek device with laboratory results (13). Correlations between the laboratory and CardioChek were 0.86 (total cholesterol), 0.74 (HDL cholesterol) and 0.98 (triglyceride). Imprecision was approximately 12% (total cholesterol), 22% (HDL cholesterol) and 14% (triglyceride). Overall the study showed that sensitivity and specificity for detection of risk of coronary heart disease were 85% and 80%, respectively, using total cholesterol results; and 75% and 79%, respectively, using HDL cholesterol. Another study comparing the accuracy of CardioCheck PA with reference methods in 109 patient samples showed that CardioChek classified 48% of patients with normal lipids as having hypercholesterolemia (10).

The accuracy of Cholestech LDX measurements of abnormal blood levels of total cholesterol (TC), calculated low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C) and triglycerides (TG) was compared to laboratory analyses (7). The reported correlations for TC, LDL-C, HDL-C and TG were 0.91, 0.88, 0.77 and 0.93, respectively (all $p< 0.01$) and the sensitivity and specificity of the fingerstick method to identify abnormal lipids and hsCRP was > or = 75%. Fingerstick screening was therefore accurate and showed good clinical utility. A study of point-of-care testing (POCT) in Ireland using Cholestech LDX validated the use of this device (6). However one study of the accuracy of Cholestech in hyperlipidemic individuals over the age of 70 showed that the portable measurements systematically overestimated triglycerides and HDL-C, while LDL-C concentrations were underestimated (12). An evaluation report carried was out by the UK Medical Devices Agency in 1995 comparing 119 samples using the Cholestech with laboratory results. The correlation was 0.97 for total cholesterol and 0.95 for HDL cholesterol. Imprecision was therefore ~5% for total cholesterol and 5-10% for HDL cholesterol (14).

A study comparing CardioChek PA and Cholestech LDX with a standard venous blood sample tested in a laboratory, showed that the Cholestech LDX analyser demonstrated slightly better reproducibility than the CardioChek PA analyser when compared with laboratory gold standard analysis; however, the study was limited by the small sample size (n = 34) with no known risk factors (4) and did not prove superior accuracy of either device. In a comparative study of 100 samples, correlation coefficients between the POCT and laboratory methods were >0.9 for Cholestech and >0.84 CardioChek (5). This translates into machines that are fairly accurate. However, at levels near decision thresholds of diagnosis and treatment, the machines may overestimate triglycerides and HDL, and underestimate LDL.

Impact compared to existing technology

A multi-centre cluster randomised controlled trial of point-of-care testing in GP practices of patients with established hyperlipidaemia, established type 1 or type 2 diabetes, or taking anticoagulant therapy was recently conducted in Australia. The study showed that for all tests except INR and HDL cholesterol, the POCT approach demonstrated the same clinical effectiveness as pathology laboratory testing (8). The same study also showed that access to POCT was associated with the same or better medication adherence (19). A descriptive survey of general practitioners and patients showed that cholesterol POCT was strongly supported by both, citing factors such as convenience, issues of patient care and efficiency (11). A randomised trial of pharmacy-based cholesterol risk management involving 54 community pharmacies and 675 patients at high risk for cardiovascular events showed that in 57% of intervention patients versus 31% in usual care (20), the primary endpoint of a complete fasting cholesterol panel by the GP, or prescription of new cholesterol-lowering medication or an increase in dosage was reached.

Guidelines:

1. The NHS Health Check: Vascular Risk Assessment and Management Best Practice Guidance recommends the use of Framingham and QRISK calculators to ascertain the individual's 10-year risk of developing cardiovascular disease (15).
2. Lipid modification: Cardiovascular risk assessment and the modification of blood lipids for the primary and secondary prevention of cardiovascular disease. NICE clinical guideline 67 (16).

Health Economics:
The provision of POCT for the analysis of lipids could lead to timely and enhanced clinical management, better health outcomes, increased patient and GP satisfaction, greater convenience and cost savings in terms of time. It might however lead to inappropriate testing, increased numbers of consultations and increased patient anxiety due to inaccurate results.

There is only one cost-effectiveness analysis of POCT for lipids in general practice compared to pathology laboratory testing, based on a RCT with 4,698 patients in 53 general practices across Australia (17). The authors found a non-significant increase in per-patient direct costs for the POCT group, although there were also found to be cost savings in terms of patients and family incurred costs (travel and time seeking health care). The main cost contributors were due to increased hospitalisations and significantly increased pharmaceutical costs in the POCT group. The study is limited by the fact that it reports its measure of effectiveness in terms of 'proportion of patients within the therapeutic range', rather than life-years or QALY's hence limiting the application of the results to decision makers – the implementation of this type of testing would be dependent on the value society would place on maintaining a patient within the therapeutic range. In this study POCT is more effective than standard laboratory testing but also more costly; the base case incremental cost-effectiveness ratio (in terms of incremental cost per patient maintained within therapeutic range) is reported to be $AUS 10,082 (£4,567), requiring a decision as to whether this cost is justified in terms of the value placed on the measure of effectiveness used in this analysis.

One further study provides a review of POC cholesterol monitors and describes their possible role in pharmacy based practice in the USA (18). They summarise their review by arguing that POC cholesterol monitors offer several potential advantages compared with standard laboratory testing including ease of use, portability, increased patient access, low cost of monitors, physician or laboratory visits not required and instant results. They argue that provision of the POCT should be administered alongside appropriate patient education and referral.
There is still substantial uncertainty around the economic impact and cost-effectiveness of POCT for lipids, further research is required to determine whether it provides a cost-effective alternative to standard laboratory practice in a UK setting.

Research Questions:
1. Has the device accuracy been sufficiently tested in practice?
2. In the UK Primary Health Care setting, what is the acceptability of and satisfaction with POC cholesterol testing?
3. Is the use of point of care lipid testing cost effective?
4. What is the impact of POCT on clinical decision making?
5. POCT versus laboratory testing for the NHS Health Check
6. POCT versus laboratory testing for treatment compliance

Suggested next step:
Systematic review of point-of-care cholesterol testing in primary care.

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Comments:

This report was prepared by the Primary Care Diagnostic Horizon Scanning Centre Oxford
Contact details: Dr. Annette Plüddemann ; Email: horizonscanning@phc.ox.ac.uk