Evaluation of Near Patient Cholesterol Testing Using the Cholestech LDX

August 2001

MSAC application 1026

Assessment report

ISBN
ISSN (Print) 1443-7120
ISSN (Online) 1443-7139

First printed

Electronic copies of the report can be obtained from the Medical Service Advisory Committee's Internet site at:

http://www.msac.gov.au

Hard copies of the report can be obtained from:

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The Medical Services Advisory Committee is an independent committee which has been established to provide advice to the Commonwealth Minister for Health and Ageing (formerly the Commonwealth Minister for Health and Aged Care) on the strength of evidence available on new and existing medical technologies and procedures in terms of their safety, effectiveness and cost-effectiveness. This advice will help to inform Government decisions about which medical services should attract funding under Medicare.

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The report was endorsed by the Commonwealth Minister for Health and Aged Care on 18 September 2001.

Publication approval number:

MSAC recommendations do not necessarily reflect the views of all individuals who participated in the MSAC evaluation.

Table of Contents

EXECUTIVE SUMMARY ..... **VI**

The procedure vi
Medical Services Advisory Committee - role and approach vi
Assessment of the Cholestech LDX vi
Clinical need vii
Safety vii
Effectiveness viii
Cost effectiveness xii
Recommendations xiii

INTRODUCTION **1**

BACKGROUND **2**

Cholestech LDX 2
Clinical need/burden of disease 3
Existing procedures 5
Comparator 6
Marketing status of the device 7
Current reimbursement arrangement 7

APPROACH TO ASSESSMENT **8**

Overview 8
Review of literature 8
Expert advice 10

RESULTS OF ASSESSMENT **11**

Is it safe? 11
Is it effective? 22
What are the economic considerations? 27

CONCLUSIONS **42**

Safety 42
Effectiveness 42
Cost effectiveness 44

RECOMMENDATIONS **45**

APPENDIX A MSAC TERMS OF REFERENCE AND MEMBERSHIP **47**

APPENDIX B SEARCH HISTORY FOR MEDLINE, CURRENT CONTENTS, HEALTHSTAR AND BIOSIS **48**

APPENDIX C SEARCH HISTORY FOR THE COCHRANE LIBRARY **49**

APPENDIX D LIST OF DATABASES SEARCHED 50

APPENDIX E SEARCH HISTORY FOR OTHER SEARCHES 52

APPENDIX F SUPPORTING COMMITTEE 54

APPENDIX G SAMPLE EVALUATION FORM 55

APPENDIX H ACCURACY AND PRECISION DATA 56

APPENDIX I CALCULATION OF OVERALL ESTIMATES FOR CV, %BIAS AND TOTAL ERROR 59

APPENDIX J RECOMMENDATIONS FOR OBTAINING FINGERSTICK SPECIMENS 60

APPENDIX K VARIABLES IN THE MODELLED EVALUATION 61

ABBREVIATIONS 74

REFERENCES 75

TABLES

Table 1 Current guidelines for the initiation of PBS listed lipid-lowering medications 4

Table 2 Number of lipid tests conducted in Australia by year and item number 5

Table 3 Lipid tests performed during general practice consultations in Australia 5

Table 4 Current lipid tests available on the MBS 7

Table 5 NHMRC designation of levels of evidence 10

Table 6 Summary of studies used to examine accuracy & precision of the Cholestech LDX 12

Table 7 Combined estimates of percent bias, co-efficient of variation and total error derived using the Cholestech LDX 15

Table 8 Comparison of site for total cholesterol values on the Cholestech LDX 19

Table 9 Combined estimates of co-efficient of variation, percent bias and total error for total cholesterol categorised by setting 19

Table 10 Summary of the between operator (trained/experienced vs untrained/inexperienced) data for the Cholestech LDX 20

Table 11 Summary of the data comparing fingerstick and venous blood samples for cholesterol analysis. 21

Table 12 Variables and assumptions used by the modelled evaluation to determine total cost of treatment 32

Table 13 Variables and assumptions used by the modelled evaluation to determine additional patients detected with elevated cholesterol 32

Table 14 Variables and assumptions used by the modelled evaluation to determine patients with normal lipid levels....33

Table 15 Variables and assumptions used by the modelled evaluation to determine mortality ..33

Table 16 Variables and assumptions used by the modelled evaluation to determine life years gained 34

Table 17 Costs and outcomes of the modelled evaluation....35

Table 18 Incremental cost-effectiveness of near-patient testing....35

Table 19 Results of the sensitivity analysis....37

FIGURES

Figure 1 Incidence of major CHD events in quintiles of baseline cholesterol from three prospective non-intervened cohorts (from Gunnar and Olov, 1997)....3

Figure 2 Accuracy and precision of total cholesterol estimation using the Cholestech LDX.....16

Figure 3 Accuracy and precision of HDL-cholesterol estimation using the Cholestech LDX...17

Figure 4 Accuracy and precision of triglyceride estimation using the Cholestech LDX. 18

Figure 5 Decision tree used in the modelled evaluation....29

Figure 6 Change in the incremental cost-effectiveness of NPT with the growth in the number of cholesterol tests performed....38

Figure 7 Change in the incremental cost-effectiveness of NPT with the proportion of new tests being performed in patients with normal cholesterol....39

Figure 8 Change in the incremental cost-effectiveness of NPT with changes in the number of follow-up GP consultations associated with laboratory testing....39

Figure 9 Change in the incremental cost-effectiveness of NPT with changes in the proportion of patients discontinuing medication....40

Executive summary

The procedure

The Cholestech LDX® is a small, portable analyser and test cassette system that uses reflectance photometry (the amount of light reflected from a solid surface) to measure the quantity of substances in blood. The Cholestech LDX can measure the level of total cholesterol (TC), high-density lipoprotein associated cholesterol (HDL) and triglycerides (TG) in whole blood (capillary or venous), serum or plasma. The device can also calculate the TC/HDL ratio and derives estimates of low-density lipoprotein (LDL) and very low-density lipoprotein (VLDL) associated cholesterol.

Medical Services Advisory Committee - role and approach

Medical Services Advisory Committee (MSAC) is a key element of a measure taken by the Commonwealth to strengthen the role of evidence in health financing decisions in Australia. MSAC advises the Minister for Health and Ageing (formerly the Minister for Health and Aged Care) on the evidence relating to the safety, effectiveness and cost-effectiveness of new and existing medical technologies and procedures, and under what circumstances public funding should be supported.

A rigorous assessment of the available evidence is thus the basis of decision-making when funding is sought under Medicare. For the Cholestech LDX, a search of the medical literature available on the device was undertaken and the evidence assessed and classified according to the NHMRC hierarchy of evidence. A modelled economic evaluation was also undertaken. A supporting committee with expertise in this area then evaluated the evidence and provided advice to MSAC.

Assessment of the Cholestech LDX

Lipid estimations may not accurately reflect the true lipid level due to measurement error (accuracy and precision) and natural biological variation. These sources of error can cause misclassification of patients, the result being that some patients receive treatment inappropriately whilst others requiring intervention remain untreated. The measurement error associated with the Cholestech device in comparison to currently available accredited laboratory tests was evaluated. This included an assessment of site, operator and blood sample type (fingerstick or venous) on the accuracy and precision of the Cholestech LDX.

The comparator is considered to be the test most likely to be replaced in practice by each of the three tests in the sponsor's submission. Cholesterol, triglyceride and HDL-cholesterol tests are available via Group P2 on the MBS. Such tests must be conducted in an accredited pathology laboratory. It was not possible to fully define the comparator test in terms of specific devices or chemistry, primarily because a large number of laboratory-based devices are available. The comparator was therefore considered to be any laboratory-based test performed in an accredited pathology laboratory.

Clinical need

High blood cholesterol is one of the major modifiable risk factors for coronary heart disease (CHD). Despite declining mortality from CHD, it remains the major cause of premature death in Australia and imposes high personal, social and economic costs. The last national survey to measure blood cholesterol levels in Australia was conducted by the National Heart Foundation in 1989. At that time it was estimated that over 4.5 million adult Australians (aged 20-69 years) had high-risk cholesterol levels. The survey found 47 percent of men and 39 percent of women had cholesterol levels above 5.5 mmol/L. In terms of those at very high risk of cardiovascular disease, over 15 percent of men and women had blood cholesterol levels of 6.5 mmol/L or more.

Although blood cholesterol levels are an important determinant of the risk of CHD in a population, for any single individual blood cholesterol by itself is a relatively poor predictor of their risk of a CHD event. In Australia, a combination of blood lipids and other independent risk factors (eg smoking, high blood pressure, diabetes, reduced physical activity, and obesity) are used to identify individuals at-risk of CHD. In Australia, both the National Heart Foundation and the Royal Australian College of General Practitioners (RACGP) recommend appropriate lipid tests be conducted to better evaluate an individual's risk of CHD. The RACGP, for example, recommends lipid tests be conducted at least once every 5 years.

In 1999/2000, a total of 3,469,490 tests were conducted in Australia that included evaluation of triglyceride and/or cholesterol. Of these, 16 percent evaluated only cholesterol and/or triglyceride while the remainder included the assessment of other blood chemistry. When HDL-cholesterol tests are included, over 4.5 million lipid tests were conducted in Australia in 1999/2000.

Safety

The Cholestech LDX device does not come into contact with the individual undergoing lipid testing and no direct safety concerns were identified with the device in the evaluation. The introduction of near patient testing for lipids may result in increased blood collection in general practice. To ensure that risks associated with blood collection are minimised, appropriate Australian or international guidelines should be followed.

Effectiveness

Accuracy and Precision

Australian guidelines regarding the accuracy and precision of lipid tests have not been developed. This evaluation therefore used guidelines for lipid and lipoprotein measurement developed in the United States by The National Cholesterol Education Program (NCEP). The guidelines specify an acceptable upper limit of %bias, coefficient variation (CV) and total error (TE) for TC, HDL-C, LDL-C and TG. These criteria were used when assessing reported data. Under ideal conditions the evaluation found the Cholestech LDX to be precise and accurate in its measurement of TC, HDL-C and TG. Although the pooled estimates for %bias and CV did not always fall within the NCEP guidelines for TC, HDL-C and TG, the pooled TE for these three measures always met the NCEP criteria.

The evaluation also examined how accuracy and precision of the Cholestech LDX may be influenced by the site where it is used, the type of operator of the device and the sample type (fingerstick blood compared with venous blood) used in the test.

No clear conclusions can be drawn about the influence of site because only a small number of studies were available and those that were available were not designed to assess differences in this parameter. In terms of operator, no relevant articles could be found in the literature reporting the effect of the operator on results obtained by the Cholestech LDX. As a result, another NPT device for cholesterol, the Reflotron, was used as a proxy. When combining all available information, the CV increased by 32.42 percent for TC and by 53.53 percent for TG when a non-technical operator performed the tests. If this same increase could be expected when a non-technical operator performed tests on the Cholestech LDX, then the total error for both TC and TG would fall outside the NCEP guidelines.

The evaluation found that at present there is insufficient evidence to determine whether the Cholestech LDX would meet the NCEP guidelines when used in a setting such as a specialised clinic or office of a general practitioner. If the operator-dependence of similar devices were used, the device would not meet the NCEP guidelines. It should be noted this evaluation aimed to examine the incremental difference in accuracy and precision between tests conducted using the Cholestech LDX and tests conducted in accredited pathology laboratories. For this reason it did not formally examine the accuracy and precision of laboratory tests per se. The estimates of total error were derived using estimates of bias based on split sample analysis, comparing the result from a Cholestech LDX test to that of a laboratory-based test. This approach should provide reasonable incremental estimates of the accuracy and precision of the Cholestech LDX. An earlier Australian study has examined the comparative performance of laboratory and portable analysers directly. The study found that whilst some analysers can perform at acceptable levels in comparison to laboratory tests, performance is highly variable both between different tests conducted on the same analyser and between different analysers. Unfortunately, the study did not include the Cholestech LDX nor did it provide estimates of total error. The evaluation found that lipid determinations derived from either fingerstick-derived or venous blood samples are equivalent. To achieve such results in a near-patient environment, it is likely a combination of clear guidelines regarding fingerstick-derived blood collection and an experienced phlebotomist would be needed.

The evaluation did not formally examine the influence of fasting versus non-fasting samples or biological variation on lipid analysis. Nonetheless, it is recommended that tests for either HDL-cholesterol or triglycerides be conducted on blood samples collected after a 12-hour fast.

Identifying patients suitable for lipid lowering treatment

The primary role of the Cholestech LDX would be to provide lipid tests in a near patient environment with acceptable levels of accuracy and precision. These tests can be used to further evaluate the risk of CHD in an individual and where appropriate, initiate treatment. For patients without established CHD, testing has the potential to identify those with elevated total cholesterol (and other lipid profiles) at sufficient risk of CHD to warrant lipid-lowering treatment. This will apply particularly for patients with other known risk factors for CHD where the cost-effectiveness of lipid lowering treatment is well established. For patients with established CHD, lipid testing is of less importance because lipid-lowering treatment will benefit most patients.

In addition to identifying patients for treatment, near patient testing may also have benefits not directly related to the accuracy and precision of an individual test. These benefits could be viewed as being device-independent and would vary according to the clinical value of the test being conducted and the circumstances of its use (eg the population being tested). In terms of NPT for lipid testing, this evaluation identified a number of potential benefits that may result from its introduction. These were:

- Reductions in the number of patients lost to follow-up;
- Improved compliance to, and reduced discontinuation from, lipid-lowering medication;
- Improved lipid control;
- Alterations in the number of tests conducted; and
- Improved process-of-care and patient quality of life.

Reductions in the number of patients lost to follow-up

Patients who do not return to the GP, or do not arrive at a pathology lab following referral from a GP are effectively lost to follow-up. Some of these patients may actually require intervention because of elevated cholesterol. A literature search failed to find any studies that specifically examined the number of patients lost to follow-up after a laboratory lipid test had been ordered or the possible change in follow-up once NPT had been introduced.

Improved compliance to, and reduced discontinuation from, lipid lowering medication

Hypercholesterolaemia is a chronic, painless condition where there is a long lag-time between an individual's current behaviour and ultimate health consequences. Therapy is likely to be needed long-term, perhaps for a lifetime. This can have important implications on the levels of adherence and compliance to drug therapy.

In Australia, up to 60 percent of patients discontinue use of lipid-lowering medication after one year. The main reasons for discontinuing therapy were patients being unconvinced about the need for therapy (32 percent) and poor efficacy of the treatment (32 percent). Similarly the benefit experienced by those patients who are compliant with their therapy compared with those who are not has been examined in a primary prevention study in Scotland. The relative risk reduction for cardiovascular death amongst the compliant cohort (i.e. patients who took over 75 percent of their prescribed medication) was 37 percent compared with 32 percent for the non-compilers.

Studies in other clinical areas such as diabetes have demonstrated that NPT can improve the process of patient care. If reductions in discontinuation from, and improved compliance to, lipid lowering medication occurred from the introduction of NPT for lipids, substantial benefits in clinical outcomes might be expected. A literature search identified one study that examined compliance issues in relation to NPT. Unfortunately the study did not determine a baseline compliance value nor did it use a control group for comparison. Furthermore, only 70 percent of the initial enrolled trial population were used in the analysis, raising the potential for substantial bias in the study findings. The evaluation found there is insufficient evidence available at present to determine whether NPT would result in improved compliance to, and/or discontinuations from lipid lowering medications.

Improved lipid control

A study of general practice lipid testing in Scotland found that of the people identified as having raised cholesterol, 40 percent were apparently treated (not further described) and 40 percent of these achieved target lipid levels. This study did not examine compliance issues but it does suggest that even in compliant patients only a proportion are achieving target lipid levels. This may be due to inadequate monitoring and dose titration of the lipid lowering medication. A literature search identified only one study that examined the possible impact of NPT on changes to the proportion of patients that achieves target lipid levels. This study did find that at the completion of the 2-year evaluation period, 63 percent of patients were achieving target lipid levels. However, as this study had substantial limitations in both design and analysis (see comments in previous section), the

evaluation found there is insufficient evidence available at present to determine the likely impact of NPT on improving the number of patients achieving target lipid levels.

Alterations in the number of tests conducted

The introduction of NPT for cholesterol has the potential to cause an increase in the number of tests conducted. If these tests are conducted in patients at relatively high risk of CHD, then for each incremental increase in the number of tests a substantial number of at-risk individuals will be identified and stratified to treatment. In contrast, if the extra tests are conducted in low-risk patients, then for each incremental increase in the number of tests only a small number of at-risk individuals will be identified.

A literature search was undertaken to examine whether the introduction of NPT would influence the frequency of lipid testing in general practice and to examine in which population any increase may occur. Four reports were identified in the search, one conducted in Australia. These studies found that following the introduction of NPT, tests for total cholesterol increased by between 82 and 193 percent whilst tests for triglycerides increased by 129 percent. Only one study examined whether the population being tested by NPT differed from that being tested by laboratory analysis. The study found that in comparison to laboratory tests, an NPT for cholesterol was significantly more likely to be used for screening or patient demand and less likely for monitoring or diagnosis.

Therefore, based on the available evidence it is likely the introduction of the Cholestech LDX would result in an increase in tests for total cholesterol. The magnitude of the increase is likely to be between 82 and 193 percent. Although similar increases may occur in tests for triglycerides and HDL-cholesterol, only limited information is available and the magnitude of the increase is at present unclear. In terms of the population that will be tested, the available evidence suggests NPT is more likely to be used for screening rather than monitoring or diagnosis.

Improved process-of-care and patient quality of life

One study using the Cholestech LDX examined the impact on the process-of-care in patients with hypercholesterolaemia. The indicators of process-of-care in this study included the physician's documentation of six points including: referrals to dieticians for assistance in cholesterol management; changes in hyperlipidaemic regimen; and orders for diagnostic tests of cardiovascular status. Although the study had a very small sample size, it found that using a NPT for cholesterol improves the process-of-care in patients with hypercholesterolaemia with respect to cholesterol management. Another study demonstrated near patient testing for cholesterol is both convenient and improves the satisfaction of the patient with their process-of-care. This included improvements in patient satisfaction via reductions in anxiety through having immediate test results. Nearly all patients preferred their own GP to perform the test as they believed their GP understood their needs better than an outside laboratory.

The evaluation found some improvements in the process of care following the introduction of NPT for cholesterol have been observed. Similarly, patient's quality of life is likely to improve because of enhanced perceptions of the process-of-care and the convenience aspects of NPT. However, these benefits have at present not been quantified in a manner suitable for incorporation into an economic evaluation.

Cost effectiveness

As no studies were found that thoroughly examined the cost-effectiveness of NPT for cholesterol in comparison to current laboratory testing, an economic evaluation was conducted. An evaluation based on a decision analytic model was used to determine the costs and effectiveness of NPT for total cholesterol using the Cholestech LDX compared to current laboratory testing. The model included variables for the accuracy of a total cholesterol test, the number of tests conducted, the population tested and the impact of lipid lowering medications on clinical outcomes.

In comparison to laboratory testing, the use of near patient testing resulted in an extra cost of $1.17 per patient presenting for a GP consultation. Overall, in the NPT arm of the model more patients received a total cholesterol test, more patients with elevated cholesterol were detected and fewer patients died. The model predicted that for every 100,000 GP consultations, an additional 298 patients would be detected with elevated cholesterol, an additional 91 patients would achieve target lipid levels and less than one CHD death would be avoided. The model estimated incremental cost-effectiveness ratios for three endpoints. The incremental cost per additional patient detected with elevated cholesterol was $392; per additional patient achieving target lipid levels was $1,287; and per life-year gained was $132,934. Sensitivity analysis indicated these ratios were influenced most by the rate of growth of cholesterol testing due to the presence of NPT and the population in which the new tests were being performed. The ratios remained largely unchanged when the accuracy of the Cholestech test was altered. When the total error of the Cholestech test was reduced to zero in comparison to laboratory-based tests, the incremental cost per life year gained was $101,419.

A study into recommendations made by the Pharmaceutical Benefits Advisory Committee between 1993 and 1996 found that no intervention was accepted with an incremental cost per life year gained greater than $100,000. This suggests the incremental cost per life year gained of $132,934 is outside the range of reasonable cost-effectiveness.

Recommendations

On the strength of evidence pertaining to near patient cholesterol testing using Cholestech LDX:

- The unrestricted use of near patient cholesterol testing using the Cholestech LDX is not recommended;

- The restricted use of near patient cholesterol testing, as an alternative to laboratory testing of lipids, should be considered in settings or circumstances where there is adequate training, accreditation and quality assurance. Interim funding in these circumstances should be considered with monitoring and review of testing (see Recommendation 3) to assess diagnostic performance and to ensure there is not an increase in testing or broadening of indications beyond that currently undertaken; and

- It is strongly recommended that further information be collected on the diagnostic performance of the NPT devices in the community setting and the impact of near patient testing on patient outcomes including changes in lipid management, compliance with lipid lowering therapies and amount of doctor visits.

- The Minister for Health and Aged Care accepted this recommendation on 18 September 2001. -

Introduction

The Medical Services Advisory Committee (MSAC) has evaluated the Cholestech LDX for cholesterol testing in a near patient setting.

MSAC is a key element of a measure taken by the Commonwealth to strengthen the role of evidence in health financing decisions in Australia. MSAC advises the Minister for Health and Ageing on the evidence relating to the safety, effectiveness and cost effectiveness of new and existing medical technologies and procedures, while taking into account other issues such as access and equity. MSAC adopts an evidence-based approach to its assessments, based on reviews of the scientific literature and other information sources, including clinical expertise.

MSAC's terms of reference and membership are shown in Appendix A. MSAC is a multidisciplinary expert body, comprising members drawn from such disciplines as diagnostic imaging, pathology, surgery, internal medicine and general practice, clinical epidemiology, health economics, consumer affairs and health administration.

This report summarises the assessment of the Cholestech LDX for measurement of blood lipids in a near patient setting.

Background

Cholestech LDX

The procedure

The Cholestech LDX® is a small, portable analyser and test cassette system that uses reflectance photometry (the amount of light reflected from a solid surface) to measure the amount of substances in blood. The device employs a single-use, disposable cassette that is composed of a sample well where the blood sample is dispensed and a magnetic strip. The magnetic strip identifies the cassette type, information to enable the device to perform the test and access calibration information. The reagents required for each test are contained within the cassette.

After a blood sample is dispensed in the sample well (a volume of blood between 35 and 60 μL is needed), it moves to the separation system where the red blood cells are separated from the plasma. The plasma is transferred to the reagent pads on the reaction bar for testing. The device then measures the colour change of the reaction bar and calculates the amount of the particular substance being evaluated. The results of the analysis are converted by the device to mg/ml or mmol/L and displayed on a liquid crystal display. The Cholestech LDX takes approximately 2-3 minutes to display results from the time the sample is applied to the cassette.

The Cholestech LDX can measure the level of total cholesterol (TC), high-density lipoprotein associated cholesterol (HDL) and triglycerides (TG) in whole blood (capillary or venous), serum or plasma. The device can also calculate the TC/HDL ratio and derive estimates of low-density lipoprotein cholesterol (LDL) and very low-density lipoprotein (VLDL)-associated cholesterol. Individual cassettes are available for assessment of the following:

i) Total cholesterol (range 100 -500 mg/dL or 2.59 - 12.93 mmol/L);

ii) Total cholesterol (range as above) and HDL-associated cholesterol (range 15-100 mg/dl or 0.39-2.59 mmol/L); and

iii) Total cholesterol, HDL-associated cholesterol (ranges as above) and triglycerides (45-650 mg/dl or 0.51 - 7.34 mmol/L).

Results outside the specified ranges are reported as less than (<) the lower limit or greater than (>) the upper limit by the device.

Intended purpose

The Cholestech LDX was evaluated as a device to analyse blood lipids in a near-patient environment. The tests evaluated by MSAC were total cholesterol, HDL-cholesterol and triglycerides. For the purpose of the evaluation, a near patient environment included offices of a general practitioner, a private clinic or hospital clinic.

Clinical need / burden of disease

The major plasma lipids, including cholesterol (or total cholesterol (TC)) and triglycerides do not circulate freely in plasma but are bound to proteins and transported as complexes called lipoproteins. The major lipoprotein classes are chylomicrons, very low-density lipoproteins (VLDL), low-density lipoprotein (LDL) and high-density lipoprotein (HDL). Elevated levels of cholesterol or hypercholesterolaemia can result from overproduction of VLDL, increased conversion of VLDL to LDL, or defective clearance of LDL. Although elevated levels of both cholesterol and triglycerides can result from genetic disorders or underlying conditions such as diabetes, in most cases elevations are due to dietary excess.

High blood cholesterol is one of the major modifiable risk factors for coronary heart disease (CHD). Despite declining mortality from CHD, it remains the major cause of premature death in Australia and imposes high personal, social and economic costs. In 1996, 23 percent of all deaths in Australia were attributed to CHD. Averaged over 1992 to 1994, CHD accounted for 168 and 62 deaths per 100,000 of the male and female populations, respectively. If estimates of decline are correct, the number of deaths should have decreased to 117 and 43 per 100,000 of the male and female populations respectively, in the year 2000.

The average level of blood cholesterol within a population is an important determinant of the CHD risk (see Figure 1). In countries where the average cholesterol levels of the population are low, CHD tends to be uncommon. The last national survey to measure blood cholesterol levels in Australia was conducted by the National Heart Foundation in 1989 (Risk Factor Prevalence Study Management Committee, 1990). At that time, it was estimated that over 4.5 million adult Australians (aged 20-69 years) had high-risk cholesterol levels with over 15 percent of men and women having blood cholesterol levels of 6.5 mmol/L or more. , The survey found 47 percent of Australian men and 39 percent of women were at increased risk of CHD because their total cholesterol levels were above 5.5 mmol/L. The survey did not examine how many of these high risk individuals had been previously tested for lipids.

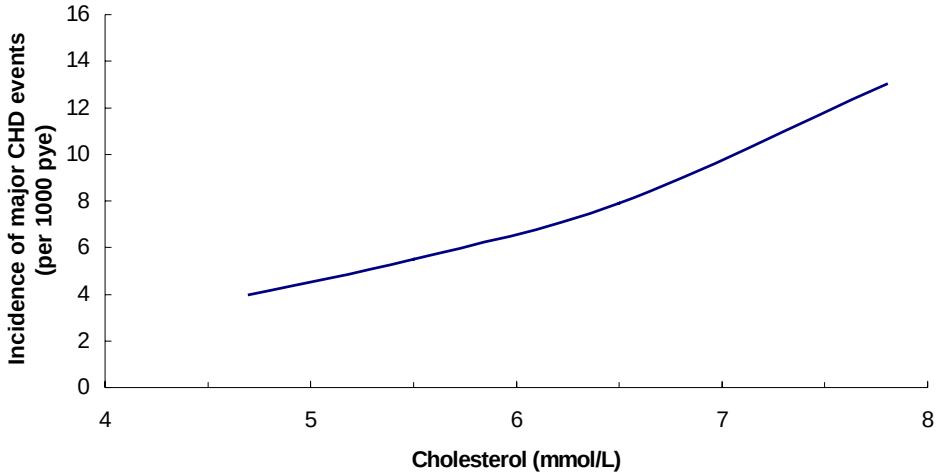


Figure 1 Incidence of major CHD events in quintiles of baseline cholesterol from three prospective non-intervened cohorts (from Gunnar and Olov, 1997)

Although blood cholesterol levels are an important determinant of the risk of CHD in a population, for any single individual blood cholesterol by itself is a relatively poor predictor of their risk of a CHD event. For example, only 42 percent of men who suffered a CHD event over a 15-year period had blood cholesterol over 6.5 mmol/L (Sheldon, Sharp and Boutle 1998). In Australia, a combination of blood lipids and other independent risk factors such as smoking, high blood pressure, diabetes, reduced physical activity and obesity are used to identify individuals at risk of CHD (Sheldon and Song 1993; Tunstall-Pedoe and Smith 1990). Treatment options for at-risk individuals include exercise counselling, alterations in diet or treatment with lipid lowering medication. Dietary changes can result in relatively small but significant reductions in cholesterol levels while lipid-lowering drugs have been shown to significantly reduce both the levels of blood cholesterol and mortality caused by cardiovascular events in high-risk patients (Holme 1995; Katerndahl and Lawler 1999). The Pharmaceutical Benefits Advisory Committee (PBAC) have set criteria including strict lipid levels which need to be determined prior to a patient receiving lipid lowering agents (see Table 1). These guidelines are used later in this evaluation to establish the lipid levels where medication is initiated.

Table 1 Current guidelines for the initiation of PBS listed lipid-lowering medications

Patient category	Lipid levels for subsidy
Patients with existing coronary artery disease	Cholesterol > 4.0 mmol/L
Other patients at high risk with one or more of the following conditions	Cholesterol > 6.5 mmol/L or cholesterol > 5.5 mmol/L and HDL (associated cholesterol) < 1 mmol/L
Diabetes	
Familial hypercholesterolaemia	
Family history of coronary artery disease (first degree relative less than 60 years of age)	
Hypertension	
Peripheral vascular disease	
Patients with HDL (associated cholesterol) < 1 mmol/L	Cholesterol > 6.5 mmol/L
Patients not eligible under the above: men 35 to 75 years; postmenopausal women up to 75 years of age	Cholesterol > 7.5 mmol/L or triglyceride > 4 mmol/L
Other patients not included in the above	Cholesterol > 9 mmol/L or triglyceride > 8 mmol/L

The risk associated with high TC is primarily due to the levels of LDL cholesterol, but there is a strong independent and inverse association between HDL-cholesterol levels and CHD risk. In some studies, measures of HDL or the ratio of TC to HDL are better predictors of CHD risk than is serum cholesterol alone. The higher the ratio, the higher the CHD risk. In Australia both the National Heart Foundation and the Royal Australian College of General Practitioners (RACGP) recommend appropriate lipid tests be conducted to better evaluate an individual's risk of CHD. The RACGP, for example, recommends lipid tests be conducted at least once every 5 years.

In 1999/2000, a total of 3,469,490 tests were conducted in Australia that included evaluation of triglyceride and/or cholesterol (see Table 2). Of these, 16 percent evaluated only cholesterol and/or triglyceride while the remainder included the assessment of other blood chemistry. When HDL-cholesterol tests are included, over 4.5 million lipid tests were conducted in Australia in 1999/ 2000. Between 1997/98 and 1999/2000, the largest increase was observed in the tests where cholesterol and/or triglyceride are evaluated in

combination with four or more other blood chemistry tests (MBS Item No. 66533 see Table 2).

Table 2 Number of lipid tests conducted in Australia by year and item number

Item	Number of tests	
	1997 / 98	1999 / 2000
66521-TC and/ or TG	575,663	568,051
66524- TC and/ or TG +1*	440,877	548,422
66527- TC and/ or TG +2*	40,833	41,560
66530- TC and/ or TG +3*	27,423	23,158
66533- TC and/ or TG + 4* or more	1,684,209	2,288,299
All TC and/ or TG items	2,769,005	3,469,490
66536-HDL	981,125	1,191,220
All items	**3,750,130**	**4,660,710**

*Estimation of cholesterol and/ or triglyceride and one or more non-specified blood chemistry assessments.

The population in which lipid tests are performed can be examined using Australian surveys of general practice (Britt *et al*., 1999a; 1999b; 2000). The surveys reported the proportion of lipid tests conducted based on the main problem examined during a general practitioner (GP) consultation. Although lipid tests were not further defined, it was assumed the majority were estimations of TC, TG or HDL. Currently, for every 100 GP consultations, 2.3 lipid tests are being conducted. Lipid testing rates vary across populations with an elevated risk of CHD; approximately 27 percent of patients with a lipid disorder receive a test whilst for every 100 patients examined in general practice for diabetes, five percent were assessed using a lipid test (see Table 3). The majority of all lipid tests are conducted in a population of patients at relatively low risk of CHD such as those presenting for a general check up or other problems not defined as a risk factor for CHD (see Table 3).

A more recent Australian survey included data on patients attending for lipid lowering medications (Britt *et al*., 2000). The most common reason for patient presentation in this group was a request for prescription (31.6 per 100 encounters) rather than for monitoring of their condition. In this population, pathology for lipid tests was ordered at a rate of 34.5 per 100 encounters.

Table 3 Lipid tests performed during general practice consultations in Australia

Problem managed	% of those given a lipid test	% of total lipid tests
Lipid disorder	27	34
Screening for risk factors	15	2
General check-up & other	10#	42*
Diabetes	5	6
Ischaemic heart disease	5	4
High blood pressure	3	12
Total	**-**	**100**

Only general check-up included; *includes patients without any other reported risk factor for CHD.
Proportions have been calculated using Britt *et al*., 1999a and 1999b.

Existing procedures

At present, cholesterol, triglyceride and HDL-cholesterol tests are available under Pathology Services on the MBS. (Chemical: Group P2 see Table 4). The tests must be

conducted by or on the behalf of an approved pathology practitioner in an accredited pathology laboratory. The proprietor of the laboratory where the test is performed must be an approved pathology authority.

Comparator

The comparator is considered to be the test most likely to be replaced in practice by each of the three tests in the sponsor's submission. As mentioned previously, cholesterol, triglyceride and HDL-cholesterol tests are available via Group P2 on the MBS (see Table 4). Although such tests must be conducted in an accredited pathology laboratory, each test may be performed using a variety of biochemical assays in combination with a measuring device. It was not possible to fully define the comparator test in terms of specific devices or chemistry, primarily because a large number of laboratory-based devices are available. The comparator was therefore considered to be any laboratory-based test performed in an accredited pathology laboratory.

Table 4 Current lipid tests available on the MBS

Test	Item number (MBS Group P2)	Description
Cholesterol/ Triglyceride	66521 (66524, 66527,66530,66533)*	Quantitation (except by reagent strip with or without reflectance meter or electrophoresis) of cholesterol or triglycerides or both in serum, plasma, urine or other body fluid.
HDL-cholesterol	66536	Quantitation of HDL cholesterol or apolipoprotein B/A1 ratio in patient who: has a serum cholesterol level >5.5 mmol/L; or has a fasting serum triglyceride level> 2.0 mmol/L; or is on a lipid lowering drug prescribed by a medical practitioner; or has a serum cholesterol level>4.0 mmol/L and a history of ischaemic heart disease. Each episode to a maximum of 4 episodes in a 12-month period.

* Tests where additional blood chemistry is evaluated in addition to cholesterol or triglyceride.

Marketing status of the device

The Cholestech LDX is exempt from listing (or registration) on the Australian Register of Therapeutic Goods when used by health professionals. The Cholestech LDX has received Clinical Laboratory Improvement Amendments (CLIA) waiver status in the United States. Waiver status is given to tests that are so simple and accurate to perform that the likelihood of erroneous results is negligible. There is no requirement for testing personnel for such tests.

Current reimbursement arrangement

Under current arrangements, a general practitioner would need to apply to become an Approved Pathology Practitioner, an Approved Pathology Authority and an Accredited Pathology Laboratory (Category M: Medical Practice). Category M is allocated to laboratories that provide a specified limited range of tests for the patients of the medical practice at which the laboratory is situated. Once accredited, it would be possible to obtain reimbursement for the lipid tests conducted by the Cholestech LDX. A Category M laboratory is not able to provide tests on patients referred from other medical practices or other medical practitioners other than those medical practitioners of the medical practice at which the laboratory is sited.

Approach to assessment

MSAC reviewed the literature available on the Cholestech LDX and convened a supporting committee to evaluate the evidence regarding the device and provide expert advice.

Overview

This evaluation examined only those tests provided by the Cholestech LDX that are associated with lipid estimation. The tests evaluated were total cholesterol, triglyceride and HDL-cholesterol. As the Cholestech LDX uses the Friedewald formula to estimate LDL from direct measurements of TC, TG and HDL cholesterol (LDL=TC-HDL-VLDL; where VLDL =TG/2.2), the LDL test was not formally included in the evaluation. The supporting committee resolved to omit non-lipid tests because they were not appropriate in the context of the sponsor's submission.

Lipid estimations may not accurately reflect the true lipid level due to measurement error (accuracy and precision) and natural biological variation. These sources of error can cause misclassification of patients, the result being that some patients receive treatment inappropriately whilst others who require intervention remain untreated. The measurement error associated with the Cholestech LDX in comparison to currently available accredited laboratory tests was evaluated. The effectiveness of NPT is likely to vary according to the circumstances of its use (eg the population being tested and the clinical value of the result). In terms of NPT for lipid testing, this evaluation identified a number of potential benefits that may result from its introduction. Evidence supporting these benefits was evaluated.

The applicant has requested that lipid tests offered by the Cholestech LDX be added to the P9 group of simple basic pathology tests in the Medicare Benefits Schedule (MBS). The P9 group contains tests that "may be performed by a medical practitioner in the practitioner's surgery without the need to obtain Approved Pathology Authority, Approved Pathology Practitioner or Accredited Pathology Laboratory status". In this setting additional measurement error may occur. The sources of such error include the setting or site where the device is used, the operator of the device and the type of blood sample used (finger stick rather than venipuncture; fasting versus non-fasting). The evaluation also examined the measurement error associated with these parameters in the context of the Cholestech LDX. A mechanism to ensure ongoing quality control of the device is also discussed.

Review of literature

Search strategy

Accuracy and precision

The medical literature was searched to identify relevant studies published that examined the accuracy and precision of Cholestech LDX or the influence of site, operator or sample type (fingerstick blood compared with venous blood) on the accuracy and precision of the device. Additional searches were performed to identify publications comparing cholesterol levels in fingerstick specimens with conventional venous

specimens using laboratory tests. The sponsor also supplied a number of literature searches; these were reviewed for relevant studies.

Online computer searches were conducted using Medline (1966-2000), EMBASE (1980-2001), Current Contents, HealthSTAR (1975-2000), BIOSIS and PubMed (see Appendix B for search terms used). In addition, a search was performed on The Cochrane Library database (see Appendix C for search terms used).

Searches were also performed on several external databases including the British Columbia Office of Health Technology Assessment (BCOHTA), Canadian Coordinating Office for Health Technology Assessment (CCOHTA), Health Services Utilization and Research Commission (HSURC), International Network of Agencies for Health Technology Assessment (INAHTA), Centre for Health Program Evaluation (CHPE, Monash University), and International Society for Technology Assessment in Health Care (ISTAHC). (See Appendix D for full list of searched databases).

The applicant submitted a number of pieces of evidence including conference abstracts and unpublished results. The search identified one other published article on the Cholestech device.

The key words used in the literature search included:

- Cholesterol; triglycerides; HDL-cholesterol; lipids; blood chemical analysis; serum; whole blood; fingerstick; coronary heart disease; capillary blood;
- Cholestech; Cholestech LDX; desktop lipid analyser;
- Precision; accuracy; quality control; quality assurance; monitoring; biochemical; and
- Near patient; near patient test; point of care; primary care; family practice; general practice; laboratory setting; physicians office testing; clinical study.

The inclusion criteria were:

- Studies comparing the Cholestech LDX to a valid comparator test; and
- Studies where the Cholestech LDX test and its comparator test were measured independently (blind) of each other.

The exclusion criteria were:

- Reviews;
- Studies where the Cholestech LDX machine was not used; and
- Evidence presented in the selected studies which was assessed and classified according to the National Health and Medical Research Council hierarchy of evidence (NHMRC 1999) shown in Table 5.

Table 5 NHMRC designation of levels of evidence

I	Evidence obtained from a systematic review of all relevant randomised controlled trials.
II	Evidence obtained from at least one properly randomised controlled trial.
III-1	Evidence obtained from well-designed pseudo-randomised controlled trials (alternate allocation or some other method).
III-2	Evidence obtained from comparative studies with concurrent controls and allocation not randomised (cohort studies), case-control studies or interrupted time series with control group.
III-3	Evidence obtained from comparative studies with historical control, two and more single arm studies or interrupted time series without a parallel control group.
IV	Evidence obtained from case series, either post-test or pre-test and post-test.

Source: NHMRC 1999

Additional Searches

Additional searches were conducted to examine the following:

- The potential benefits following the introduction of a Near Patient Test (NPT) for cholesterol;
- Economic evaluation of NPT for cholesterol; and
- Information required for the modelled economic evaluation.

The approach used for each search is outlined in the relevant section of this report. Search histories are provided in Appendix E.

Expert advice

A supporting committee with expertise in clinical epidemiology, microbiology, lipid biology, cardiology and general practice was established to evaluate the literature and provide advice to MSAC from a clinical perspective. A consumer representative was also included on the committee. In selecting members for supporting committees, MSAC's practice is to approach the appropriate medical colleges, specialist societies and associations and consumer bodies for nominees. Membership of the supporting committee is provided in Appendix F.

Results of Assessment

Is it safe?

The Cholestech LDX device does not come into contact with the individual undergoing lipid testing and no direct safety concerns were identified with the device in the evaluation. The introduction of near patient testing for lipids may result in increased blood collection in general practice. To ensure that risks associated with blood collection are minimised, appropriate Australian or international guidelines should be followed.

Accuracy and precision of the Cholestech LDX

Available Evidence

Nineteen studies were reviewed in order to provide evidence regarding the accuracy and precision of the Cholestech LDX. As all the reviewed studies were classified as providing Level IV evidence, an additional classification was undertaken. The quality of the included studies was examined by assessing the following criteria:

- Whether the study used a random sample of participants;
- Whether clinical outcomes subsequent to the test results were evaluated;
- Whether the test being evaluated was compared to a valid comparator test;
- Whether the test and its comparator were measured independently (blind) of each other,
- Whether the choice of patients assessed using the comparator test were independent of the test's results; and
- Whether both tests (the one being evaluated and the comparator) were conducted prior to any interventions being started with knowledge of test results.

These criteria are based on those recommended by the Cochrane Methods Group on Systematic Review of Screening and Diagnostic Tests to assess study validity. A score of one was given to each question that could be answered with yes. Thus, the highest score an article could receive would be six. Papers where information was not reported were assigned a zero score. Scores were used to provide guidance on the quality of individual studies; no studies were excluded based on a poor score. A summary of the studies included in the evaluation is provided in Table 6 (see Appendix G for a sample of the evaluation form). As no studies examined clinical outcomes after cholesterol testing (Criteria 2 above), the highest quality score achieved was five (Drimmer, 1995).

Four studies were excluded from the review: one foreign language publication (Norwegian; Ose *et al.*, 1995); two review articles (Warnick, 1994; 1991); and one that examined lot-lot variability of Cholestech LDX lipid cassettes (Misner, 1993).

Table 6 Summary of studies used to examine accuracy and precision of the Cholestech LDX

Reference	Objective	Level of Evidence	Quality Score
Miller *et al*., 1992	Accuracy evaluation of Cholestech LDX	IV	4
Carlson *et al*., 1993	Evaluation of Cholestech LDX using whole blood.	IV	2
Hewett, 1993	Evaluation of within-run and day-to-day precision of Cholestech LDX.	IV	0
Rogers *et al*., 1993	Total cholesterol evaluation using seven different LDX instruments.	IV	4
Cobbaert *et al*., 1994	Evaluate the analytical performance of the Cholestech LDX lipid analyser using heparinized venous blood (2 analysers and 2 reagent cassette lots).	IV	3
Gregory *et al*., 1994	Accuracy of total cholesterol measurements by 8 different desktop analysers.	IV	4
Malkus, 1994	Evaluation of the Cholestech HDL-cholesterol test	IV	3
Cummings *et al*., 1994	To compare TC, TG & HDL-C concentrations measured by LDX & standard (DAX) laboratory analyser	IV	2
Blunt *et al*., 1994	To evaluate the precision of the Cholestech LDX	IV	1
Tan, 1995	To verify the accuracy and precision of the Cholestech LDX analyser compared with the Synchron analyser (reference method).	IV	2
Cholestech Corp., 1995	Precision study: Effect of operator, effect of site	IV	1
Cholestech Corp., 1995	Performance characteristics: within-run, day-to-day, method comparison	IV	3
Cholestech Corp., 1995	Accuracy study: Reference data vs Cholestech data	IV	
Drimmer, 1995	To compare alternate site testing offered by the Cholestech LDX system for accuracy/precision to hospital reference laboratory and NCEP-LSP guidelines.	IV	5
Kafonek *et al*., 1996	To assess the biological variability of total cholesterol, triglycerides, high-density lipoprotein cholesterol and calculated low-density lipoprotein cholesterol in three serial (monthly) capillary and venous specimens.	IV	4
Issa, 1996	To examine whether lipids analyses by the Cholestech-lipid desktop analyser (LDX), were in agreement with the guidelines of the NCEP.	IV	3
Bard *et al*., 1997	To determine analytical performance capability of the LDX	IV	3
Volles *et al*., 1998	To determine the accuracy and precision of the Cholestech LDX. Assess the reliability of capillary samples for cholesterol measurements. Determine the percentage of patients who would be correctly referred for further evaluation.	IV	4
Shephard, 2000	Evaluate precision & accuracy of the Cholestech LDX as well as the correlation between capillary & venous whole blood samples	IV	4

Accuracy and Precision

The primary measurement when determining analytical performance is the total analytical error (TE). This measure takes into account both accuracy (how close a measure it is to its true value) and precision (reproducibility or how closely several results analysed on the same sample agree) when a single estimate is made of a sample. The derivation of TE is outlined below. Total error (TE) = %Bias + (1.96 x %coefficient of variation (CV)) where %Bias represents accuracy and %CV represents precision.

Total error has the advantage that a slightly higher level of inaccuracy is acceptable if the measurements are very precise; conversely, a higher level of imprecision is acceptable if the measurements are accurate. The estimation of TE allows derivation of the 95 percent confidence interval around a sample measurement. For example, if the true cholesterol value of a sample was 4.80 mmol/L and it was being assessed using a device with a TE of 8.9 percent then the 95 percent confidence interval of the cholesterol estimation would be between 4.37 and 5.23 mmol/L.

The evaluation used guidelines for lipid and lipoprotein measurement developed in the United States by The National Cholesterol Education Program (NCEP). The guidelines specify an acceptable upper limit of %bias, CV and TE for TC, HDL-C, LDL-C and TG (see Table 7). These criteria were considered appropriate for the evaluation undertaken and were used when assessing reported data. The Royal College of Pathologists of Australasia and the Australasian Association of Clinical Biochemists (RCPA-AACB) recommend allowable limits of performance (i.e. Total Error) that should be achieved in their local quality assurance program (RCPA-AACB Chemical Pathology Quality Assurance Programs, Information Handbook, September 1997). These are:

- Total Cholesterol
  + or - 0.50 mmol/L for values < 10.0 mmol/L (5.0% for values > 10.0 mmol/L)

- HDL-Cholesterol
  + or - 0.20 mmol/L for values< 2.0 mmol/L (10.0% for values > 2.0 mmol/L)

- Triglycerides
  + or - 0.20 mmol/L for values < 2.0 mmol/L (10.0% for values > 2.0 mmol/L)

The NCEP guidelines were thought to provide a reasonable summary estimate of the TE in relation to the recommendations for performance by Australian pathology laboratories. For example, for total cholesterol measurements at 6.5 mmol/L, the TE by Australian or NCEP guidelines would be 7.7 percent or 8.9 percent, respectively.

This evaluation aimed to examine the incremental difference in accuracy and precision between tests conducted using the Cholestech LDX and tests conducted in accredited pathology laboratories. For this reason, it did not formally examine the accuracy and precision of laboratory tests per se. The estimates of total error were derived using estimates of bias based on split sample analysis, comparing the result from a Cholestech LDX test to that of a laboratory-based test. This approach should provide reasonable incremental estimates of the accuracy and precision of the Cholestech LDX.

The RCPA-AACB Serum Chemistry quality assurance program kindly provided information on the performance of lipid analyses by Australian Laboratories participating in their program. This program estimates the total error of enrolled devices in relation to the true lipid value in a sample provided to participating laboratories. When the median performance is used (i.e. median %CV and %bias), the total error estimated for all Australian laboratories was 8.1 percent. It should be noted that this total error is in relation to the true lipid value in a sample and not the total error between tests on different devices as was determined in this evaluation.

An earlier Australian study has examined the comparative performance of laboratory and portable analysers directly (Non-laboratory Pathology Working Party of the National Health Technology Advisory Panel, 1991). The study found that whilst some analysers can perform at acceptable levels in comparison to laboratory tests, performance is highly variable both between different tests conducted on the same analyser and between different analysers. Unfortunately the study did not include the Cholestech LDX nor did it provide estimates of total error.

The reported results for %CV, %bias and TE for TC, HDL-C and TG using the Cholestech LDX are summarised in Figures 2, 3 and 4, respectively (see also Appendix H). These figures include estimates based on samples derived from either venous blood or fingerstick blood. An overall estimate pooling the data from all studies is also presented in Figures 2, 3 and 4 and in Table 7 (for calculations see Appendix I). It should be noted the pooled estimate was derived by combining studies that only used venous blood samples. The %bias associated with fingerstick versus venous blood is examined in a later section. In determining accuracy and precision of the Cholestech LDX, only TE will be discussed as it incorporates the other measures. The Figures also include the score for each article using the criteria outlined previously.

For analysis of total cholesterol (TC), four out of eight reports produced a TE that met the NCEP criteria (see Figure 2). Of these four, three of the reports were from comparatively good quality studies. The remaining four failed to meet the NCEP criteria. The pooled analysis found the test overall met the NCEP criteria (see Table 7).

In respect of the analysis of HDL-cholesterol (HDL-C), two out of five reports met NCEP guidelines with one of these two complying studies being of good quality (see Figure 3). Three studies failed to meet the NCEP criteria. The pooled analysis found the tests overall met the NCEP criteria (see Table 7).

For analysis of triglycerides, three out of five studies were within the NCEP criteria and two of the three were good quality studies (see Figure 4). The remaining two failed to meet the NCEP criteria. The pooled analysis found the test overall met the NCEP criteria (see Table 7).

In summary, the results of these studies show the Cholestech LDX to be precise and accurate in its measurement of TC, HDL-C and TG. Although the pooled estimates for %bias and CV did not always fall within the NCEP guidelines for TC, HDL-C and TG (see Figures 2, 3 and 4 as well as Table 7), the pooled TE for these three measures always met the NCEP criteria. In contrast to the present evaluation, one study comparing the accuracy and precision of the Cholestech LDX to other devices suitable for cholesterol estimation in a near patient setting, found the Cholestech LDX did not meet NCEP guidelines whereas a number of other devices did meet these criteria (Gregory *et al.*, 1994). Given some uncertainty in the difference in total error between a Cholestech LDX test and a laboratory-based test, the impact of varying the total error is examined in later sections of this report. A modelled economic evaluation is undertaken and the impact of varying the comparative TE between the Cholestech and laboratory-based test examined using sensitivity analysis. For convenience, the model assigns a laboratory-based cholesterol test a total error of zero percent. Sensitivity analysis is then used to examine how changes in total error influence the cost-effectiveness ratios, including the situation where both the Cholestech LDX test and laboratory-based test have an equivalent total error.

Table 7 Combined estimates of percent bias, co-efficient of variation and total error derived using the Cholestech LDX

		CV (%)		Bias (%)		Total Error (%)	
Analyte	**Studies (N)**	**Cholestech LDX**	**NCEP**	**Cholestech LDX**	**NCEP**	**Cholestech LDX**	**NCEP**
Total cholesterol	10	3.36	3	2.05	3	8.64	8.9
HDL-cholesterol	8	5.14	4	1.47	5	11.69	12.8
Triglyceride	7	4.14	5	5.16	5	13.27	14.8

NCEP: National Cholesterol Education Program

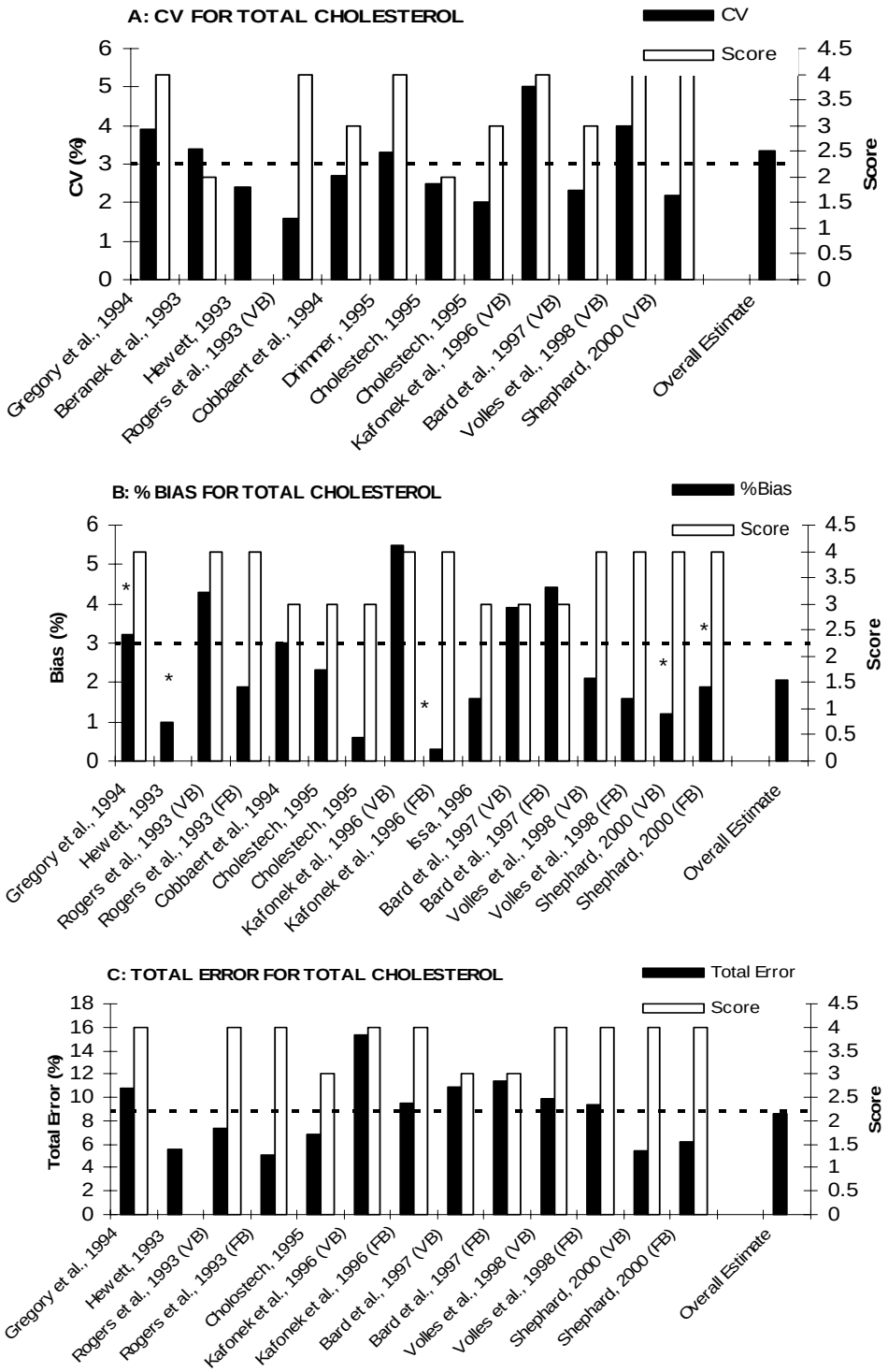


Figure 2 Accuracy and precision of total cholesterol estimation using the Cholestech LDX.

The figure outlines the coefficient of variation (CV; Figure 2A), %bias (Figure 2B) and total error (Figure 2C) for total cholesterol. The estimates derived from individual studies for each variable are provided (■) together with the quality score for that study (□). An overall, pooled estimate is provided for each variable (see Appendix I for details). In some cases, %bias values were negative and this is indicated by an *. The dotted line represents the NCEP cut-off point. FB represents fingerstick samples and VB represents venous samples.

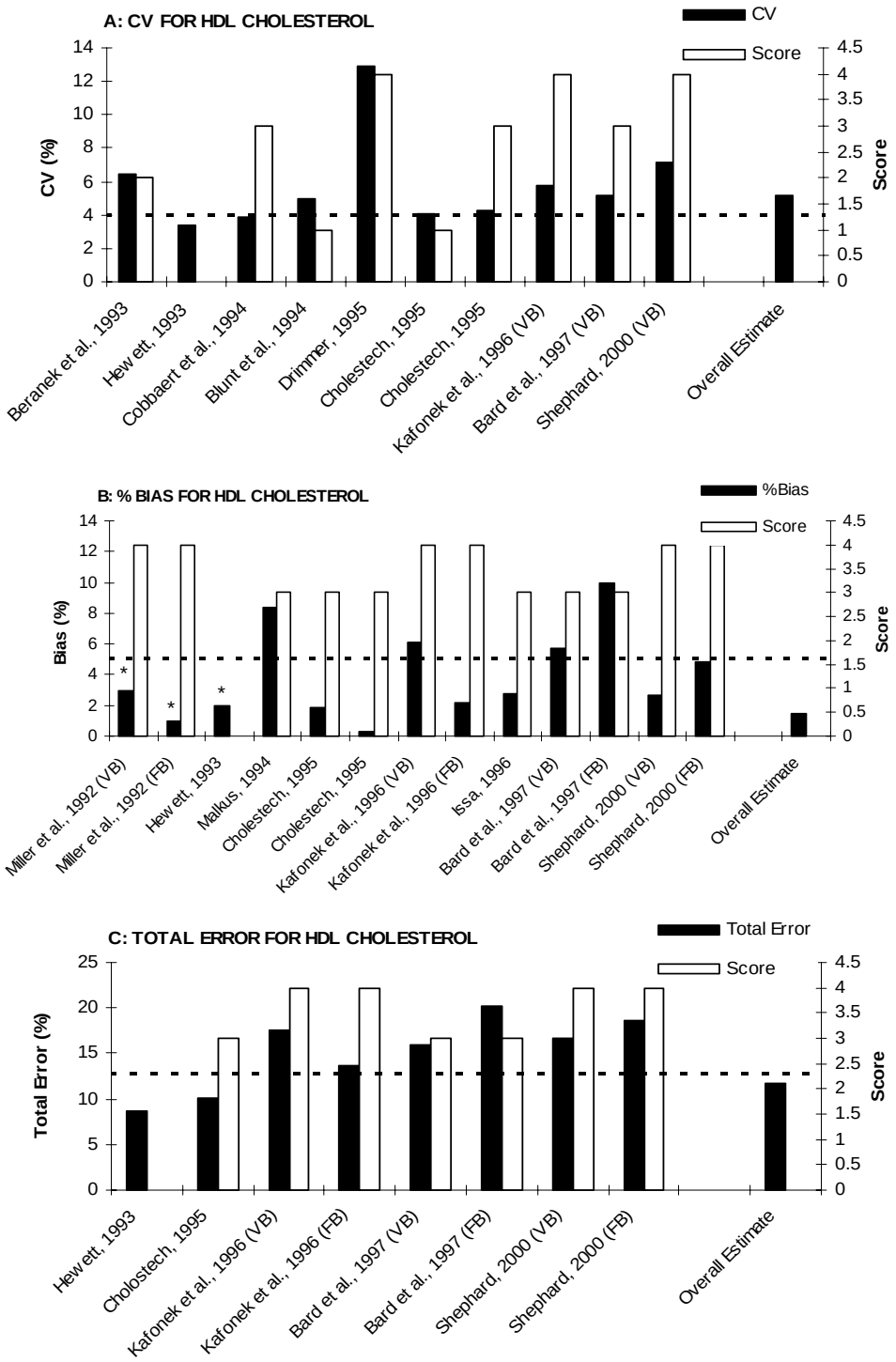


Figure 3 Accuracy and precision of HDL-cholesterol estimation using the Cholestech LDX.

The figure outlines the coefficient of variation (CV; Figure 3A), %bias (Figure 3B) and total error (Figure 3C) for HDL-cholesterol. The estimates derived from individual studies for each variable are provided (■) together with the quality score for that study (□). An overall, pooled estimate is provided for each variable (see Appendix I for details). In some cases, %bias values were negative and this is indicated by an *. The dotted line represents the NCEP cut-off point. FB represents fingerstick samples and VB represents venous samples.

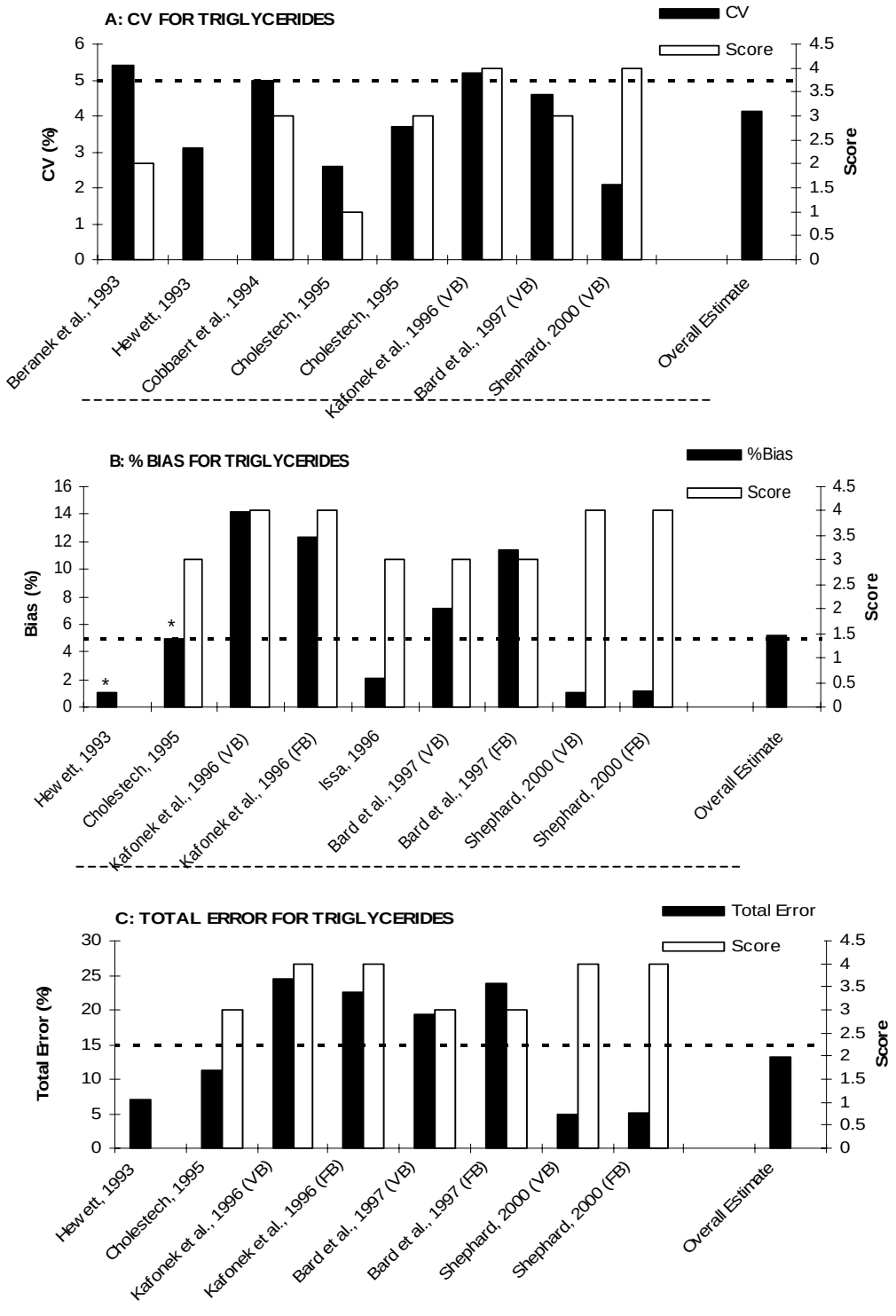


Figure 4 Accuracy and precision of triglyceride estimation using the Cholestech LDX.

The figure outlines the coefficient of variation (CV; Figure 4A), %bias (Figure 4B) and total error (Figure 4C) for triglyceride estimation using the Cholestech LDX. The estimates derived from individual studies for each variable are provided (■) together with the quality score for that study (□). An overall, pooled, estimate is provided for each variable (see Appendix I for details). In some cases, %bias values were negative and this is indicated by an *. The dotted line represents the NCEP cut-off point. FB represents fingerstick samples and VB represents venous samples.

Effect of site

No study directly comparing the effect of site on the performance of the Cholestech LDX was identified in the literature search. To examine the possible influence of site in the accuracy and precision of the Cholestech LDX, studies used in the previous section were reviewed and grouped according to the site of testing. Three studies reported that the tests were conducted in a primary care setting (physician's office, medial centre), one study reported tests from a lipid clinic and two studies reported results conducted in a laboratory setting (see Table 8). These studies were combined for each category of setting in the same manner as previously described (see Table 9 and Appendix I). The combined estimated total error for total cholesterol in the studies performed in a primary care and laboratory setting were similar with both meeting the NCEP guidelines. By contrast, the total cholesterol study performed in the clinic setting had a total error markedly outside the NCEP guidelines. No clear conclusions can be drawn from this comparison because only a small number of studies were available and those were not designed to assess differences in site. It is also likely that trained technicians were operating the Cholestech LDX at all sites.

Table 8 Comparison of site for total cholesterol values on the Cholestech LDX

Reference	Setting	(*n*)	CV	%Bias	Total Error
Hewett, 1993	Primary Care	80	2.4%	-1.0%	5.6
Volles *et al*., 1998	Primary Care	100	4.0%	+2.1%	9.9
Shephard, 2000	Primary Care	50	2.2%	-1.2 %	5.5
Kafonek *et al*., 1996	Clinic	100	5.0%	+5.5%	15.3
Rogers *et al*., 1993	Laboratory	18	1.6%	+4.3%	7.44
Bard *et al*., 1997	Laboratory	40	2.8%	+3.9%	10.9

Table 9 Combined estimates of co-efficient of variation, percent bias and total error for total cholesterol categorised by setting.

Setting	Studies (N)	CV (%) NCEP = 3	Bias (%) NCEP = 3	Total Error NCEP = 8.9
Primary care	3	2.9	0.3	6.0
Clinic	1	5.0	5.5	15.3
Laboratory	2	2.2	4.0	8.3

NCEP: National Cholesterol Education Program

Effect of operator

Possible variation in the accuracy and precision of the Cholestech LDX could be due to differences in the operator of the device (Du Plessis *et al.*, 2000). Only one study could be found reporting the effect of a trained versus an untrained operator using the Cholestech LDX (Table 10). This study was conducted by the manufacturer of the device and found no significant differences between the trained and untrained operators. The 95 percent confidence interval around the %bias point estimate was –3.01 to 1.96 percent.

Table 10 Summary of the between operator (trained/experienced vs untrained/inexperienced) data for the Cholestech LDX

Reference	(*N*)`	%Bias (exp vs inexp)
Cholestech Corporation, 1995	50	-1.7 (-3.01-1.96%)#

#Calculated value

The sponsors provided additional information comparing trained to untrained users, which showed the results are similar in both groups when compared using regression analysis (slope = 0.976, intercept = 1 and r value = 0.996). However, it should be noted the methodology of the study was poor. Of the 60 samples analysed, 60 untrained users tested one blood sample each and three trained professionals tested 20 samples each. Both of these studies examining inexperienced/experienced users were supplied by the sponsor. Neither study is published and no details of the methodology were available, so the value of this evidence should be considered accordingly.

As no other relevant articles could be found in the literature reporting the effect of operator on results obtained by the Cholestech LDX, a search was performed to retrieve articles reporting the effect of operator on results with the Reflotron, another NPT device for cholesterol. For the purposes of the evaluation, it was assumed the two devices were comparable in ease-of-use and the types of untrained operators using the Reflotron would be similar to those operating the Cholestech LDX in a primary care setting. It should be noted that unlike the Cholestech LDX, the Reflotron has not been given CLIA waiver status (see earlier section: Marketing status of the device).

Four studies reported the effect of operator on the precision of the Reflotron. Three of these studies reported operator differences for both TC and TG (Nanji *et al.*, 1988a, b, c), while the other noted differences for TC only (Bhatnagar & Durrington, 1993). No studies reported differences in HDL-C. When combining all publications, the CV increased by 32.42 percent for TC and by 53.53 percent for TG when a non-technical operator performed the tests. If this same increase could be expected when a non-technical operator performed tests on the Cholestech LDX, then the total error for both TC and TG would fall outside the NCEP guidelines. The non-technical operators in these publications consisted of nurses, medical office personnel and physicians. These are the same types of non-technical operators who would be expected to use the Cholestech LDX.

Another article was retrieved investigating the effect of intensified training on the operation of the Reflotron (Rohac *et al.*, 1988). The study found the results obtained by operators given minimal training on the Reflotron correlated very poorly with results obtained by the routine laboratory (correlation coefficient of 0.794). However, if the operator was given intensified training on the operation of the machine, their results correlated very well with those obtained by the routine laboratory (correlation coefficient of 0.981).

At present there is insufficient evidence to determine whether the Cholestech LDX would meet the NCEP guidelines when used in a setting such as a specialised clinic or office of a general practitioner. If the operator-dependence results of similar devices were used, the device would not meet the NCEP guidelines.

Fingerstick-derived blood versus venous blood

The Cholestech LDX is designed to analyse cholesterol levels using blood from fingerstick samples. Since classification of patients is based on guidelines determined

using venous blood, it is important to establish whether results from fingerstick specimens are equivalent to those from venous derived specimens. Seven publications were retrieved where there were direct comparisons of total cholesterol values between fingerstick and venous blood samples (Table 11). These studies appear to be highly contradictory. Of the seven studies, two found fingerstick specimens had cholesterol levels that were between four and nine percent lower than conventional venous specimens. However, two other studies report fingerstick samples to be four to five percent higher than venous samples. There is no difference, however, between fingerstick and venous samples when the overall estimate is examined. It should be noted that only one of the seven studies compares the two specimens using the Cholestech LDX. This study indicates equivalent results (-0.6%) between fingerstick and venous specimens.

Reports of very accurate fingerstick results were found in the two later studies (Table 11) where detailed recommendations for obtaining fingerstick measurements were followed (see Appendix J). One of these studies also found the results were more accurate if the phlebotomist (person who takes blood) is experienced (Warnick *et al.*, 1994). Therefore, provided experienced personnel follow appropriate guidelines, fingerstick derived blood samples should provide equivalent results to venous blood.

Table 11 Summary of the data comparing fingerstick and venous blood samples for cholesterol analysis.

Reference	Range mmol/L	(*n*)	%Bias (FB vs VB)
Ishikawa *et al*., 1974	NR	181	+0.1%#
Kupke *et al*., 1979	NR	40	-8.6%
Alzofon *et al.*, 1985	NR	40	+4.8%#
Greenland *et al*., 1990	~3.6-8.4	108	+3.6%
Dorner & Dorn-Zachertz, 1991	NR	12	-3.9%
Warnick *et al*., 1994	NR	49	-0.2%#
Shephard, 2000*	2.96-8.44	50	-0.6%#
Overall Estimate			0.35%

#Calculated value

*Cholestech LDX

Fasting versus non-fasting samples

Whether or not a patient is in the fasting state is a major biological factor that can affect lipid measurements. A standard fasting period of 12 hours before lipid analysis has long been used for both clinical and research measurements. However, Folsom *et al*. (1983) found that measurement of total cholesterol and HDL-cholesterol were not significantly affected by the fasting state. Wilder *et al*. (1995) found HDL-cholesterol values to be 1.5-4 percent lower in the non-fasting state compared to the fasting state but concluded that non-fasting HDL-cholesterol values are acceptable for screening purposes. In a more recent study, Craig *et al*. (2000) found non-fasting HDL-cholesterol values to be similar to fasting levels. The suggestion that fasting samples may not be necessary is supported by the 1995 NCEP guidelines. These state that a non-fasting sample can be used for cholesterol determination but this should be taken into account when interpreting the values. Although this evaluation did not examine the influence of fasting versus non-fasting samples, in keeping with current guidelines it is recommended tests for triglycerides be conducted on blood samples collected after a 12-hour fast. A repeat

fasting HDL-cholesterol test is desirable following a borderline non-fasting test result. The Cholestech LDX device requires fasting samples for estimates of LDL-cholesterol which are derived using the Friedewald formula.

Biological variability

In any individual, blood-lipid levels are not constant over time. Estimates of the within-person variation show a CV of approximately seven percent over a one-year period (NCEP, 1995; Laboratory Standardisation Panel, 1990). In order to reduce misclassification, several measurements should be made separately over time. In Australia, at least two tests are required before drug treatment commences. If the Cholestech LDX were introduced, the underlying biological variation in each individual would occur equally using either a near patient or a laboratory device. The influence of biological variation in possible misclassification was therefore not examined in this evaluation.

Quality assurance

The applicant suggests the instrument be enrolled in a quality assurance program such as the one currently being conducted by the Royal College of Pathologists of Australia and the Australian Association of Clinical Biochemists (RCPA-AACB). The RCPA-AACB offers quality assurance programs to Chemical Pathology Laboratories in Australia, New Zealand and overseas and already provides a Near Patient Testing Program to general practitioners' offices, health clinics and also a number of branch laboratories of main hospital laboratories. Cholestech LDX devices currently in use are enrolled and reported in this program. To ensure ongoing quality control, it is envisaged that any device used in a near patient environment would be enrolled in the RCPA-AACB program.

Is it effective?

Identifying patients suitable for lipid lowering treatment

The primary role of the Cholestech LDX would be to provide lipid tests in a near patient environment with acceptable levels of accuracy and precision. These tests can be used to further evaluate the risk of CHD in an individual and where appropriate, initiate treatment. For patients without established CHD, testing has the potential to identify those with elevated total cholesterol (and other lipid profiles) at sufficient risk of CHD to warrant lipid-lowering treatment. This will apply particularly for patients with other known risk factors for CHD where the cost-effectiveness of lipid-lowering treatment is well established. For patients with established CHD, lipid testing is of less importance because lipid-lowering treatment is of benefit to almost all patients.

In addition to identifying patients for treatment, near patient testing may also have benefits not directly related to the accuracy and precision of an individual test. These benefits could be viewed as being device independent and would vary according to the clinical value of the test being conducted and the circumstances of its use (eg the population being tested). A number of reviews have examined the broader implications of NPT and the current evidence available to support its potential benefits (Hobbs *et al*., 1997; Delaney *et al*., 1999). In terms of NPT for lipid testing, this evaluation identified a number of potential benefits that may result from its introduction. These were:

- Reductions in the number of patients lost to follow-up;

- Improved compliance to, and reduced discontinuation from, lipid lowering medication;
- Improved lipid control;
- Alterations in the number of tests conducted; and
- Improved process-of-care and patient quality of life.

A literature search, confined to NPT for lipid or cholesterol testing, was conducted to identify studies that examined these issues. The results are discussed in the following sections.

Reductions in the number of patients lost to follow-up

Patients who do not return to the GP, or do not arrive at a pathology lab following referral from a GP are effectively lost to follow-up. Some of these patients may actually require intervention for elevated cholesterol levels. A literature search failed to find any studies that specifically examined the number of patients lost to follow-up after a laboratory lipid test had been ordered or the change in the proportion of patients returning to their GPs for follow-up once NPT had been introduced.

While it is likely fewer patients would be lost to follow-up after the introduction of NPT, the current review found no evidence to quantify the benefit that may occur.

Improved compliance to, and reduced discontinuation from, lipid lowering medication

Hypercholesterolaemia has a long lag-time between an individual's current health status and the ultimate consequences of the condition. Numerous large-scale clinical trials have demonstrated there are effective treatments to substantially lower lipid levels and reduce the risk of CHD mortality (see for example Katrndahl *et al.*, 1999). However, such therapy is likely to be needed long-term, perhaps for a lifetime. The levels of adherence and compliance to drug therapy can suffer because of this necessary commitment.

It has been reported that discontinuation rates for lipid-lowering medications are unusually high. An American study found the one-year probability of drug discontinuation was 46 percent for niacin, 41 percent for sequestrants and 15 percent for statins (Andrade *et al.*, 1995). A more recent study reported discontinuation rates for niacin at one and four years to be 48 percent and 71 percent respectively, for sequestrants 59 percent and 83 percent and for statins 10 percent and 28 percent after one and four years respectively (Hiatt *et al.*, 1999). Similarly, an Australian study reported one-year discontinuation of 60 percent for all lipid-lowering medications combined (Simons *et al.*, 1996). The main reasons for discontinuing therapy were patients being unconvinced about the need for therapy (32 percent) and poor efficacy of the treatment (32 percent).

Similarly, the benefit experienced by those patients who are compliant with their therapy compared with those who are not has been examined in a primary prevention study in Scotland (Shepherd *et al.*, 1995; WOSCOPS). The relative risk reduction for cardiovascular death amongst the compliant cohort (ie patients who took over 75 percent of their prescribed medication) was 37 percent compared with 32 percent for the non-

compilers. This study found that at the end of five years, 26 percent of the patients were non-compliant with therapy. Similarly, a more recent retrospective health management organisation study found after two years only 37 percent of patients remained compliant with their lipid lowering medication (defined as 90 percent of all doses; Sung *et al*., 1998).

Encouraging open discussion between patient and physician regarding their medication, as well as convincing the patient of the long-term benefits of reaching and maintaining target cholesterol levels, can improve compliance (La Rosa & La Rosa, 2000). An integral part of this would be to adequately monitor and inform the patient of their current lipid levels. Studies in other clinic areas such as diabetes have demonstrated that NPT can promote patient compliance (Grieve *et al.*, 1999) and similar improvements may occur if NPT were introduced for lipid testing.

A literature search identified one study that provided Level III evidence of compliance issues in relation to NPT (Bluml *et al.*, 2000). The study was conducted in a US pharmacy environment where the focus on medication usage is likely to be far greater than in Australian general practice. So although the study does examine the possible impact of NPT on compliance to lipid-lowering medication, the results may have limited generalisability to an Australian general practice setting. The study suggests pharmacists, with the aid of the Cholestech LDX, can improve the levels of compliance to lipid-lowering drugs as well as increase the number of patients who reach target lipid goals. The study defined compliance based on an evaluation of the number of missed doses for each lipid-lowering medication and refill timing. The medications reviewed in the study included statins (89 percent of patients), niacin (five percent), fibrates (four percent) and bile acid resins (two percent). Compliance rates reported in the study were 90 percent. Unfortunately the study did not determine a baseline compliance value nor did it use a control group for comparison. Furthermore, only 70 percent of the initial enrolled trial population were used in the analysis, raising the potential for substantial bias in the study findings. There is insufficient evidence available at present to determine whether or not NPT would result in improved compliance with a prescribed regimen of lipid-lowering medications.

Improved lipid control

There is clear evidence cholesterol lowering with statin drugs is both safe and effective in high-risk patients. However, as no studies have specifically examined the optimal goals for lipid-lowering therapy, some uncertainty exists regarding the target lipid levels that should be achieved in primary and secondary prevention (Grundy 1998). Nonetheless, recommendations have been made regarding appropriate target lipids after the initiation of drug therapy (see for example The National Heart Foundation of Australia recommendations). The proportion of patients achieving target levels may prove to be a useful surrogate outcome measure to examine potential reductions in CHD events.

A study of general practice lipid testing in Scotland found that, of the people identified as having raised cholesterol, 40 percent were treated (not further described), and 40 percent of these achieved target lipid levels. This study did not examine compliance issues but it does suggest that even in compliant patients only a minority is achieving target lipid levels. This may be due to inadequate monitoring and dose titration of the lipid-lowering medication. Consistent with this, Australian general practice studies indicate that only one-third of patients on lipid-lowering medication are regularly assessed by lipid tests (Britt *et al*., 2000).

A literature search identified only one study that examined the possible impact of NPT on changes to the proportion of patients who achieve target lipid levels (this was the previously mentioned study by Bluml *et al.*, 2000). This study found that, at the completion of the two-year evaluation period, 63 percent of patients were achieving target lipid levels.

The review found Level III evidence that examined the likely impact of NPT on improving the number of patients achieving target lipid levels. Given the setting and the limitations of this study (see previous section), it is uncertain whether the potential improvements in the proportion of patients achieving target lipid levels would occur following the introduction of NPT for lipids.

Alterations in the number of tests conducted

The introduction of NPT for cholesterol has the potential to cause an increase in the number of tests conducted. If these tests are conducted in patients at relatively high risk of CHD, then for each incremental increase in the number of tests a substantial number of at-risk individuals will be identified and stratified to treatment. By contrast, if the extra tests are conducted in low-risk patients, then for each incremental increase in the number of tests only a small number of at-risk individuals will be identified.

Australian data suggest approximately 15 to 16 percent of the general population have cholesterol levels >6.5 mmol/L. Currently, approximately 40 percent of patients who are lipid tested in general practice have elevated serum cholesterol (>6.5 mmol/l; Smith *et al*., 1999). This suggests lipid testing is currently being conducted in a population at higher risk of elevated cholesterol levels than the general population. Although it is unclear what proportion of the at-risk population (i.e. cholesterol > 6.5 mmol/L) is currently being tested, it is unlikely to be 100 percent. Therefore, the improved availability of testing using a NPT may identify additional at-risk patients.

A literature search was undertaken to examine whether the introduction of NPT would influence the frequency of lipid testing in general practice and to examine in which population any increase may occur. Four reports were identified in the search, one conducted in Australia. The Australian study employed a crossover design to examine the impact of the introduction of desktop analysers in general practice (Non-laboratory Pathology Working Party of the National Health Technology Advisory Panel, 1991). The study found that following the introduction of desktops analysers testing rates increased by 46 percent. The study did not provide information separately for cholesterol tests.

Franks *et al.* (1991) conducted a study investigating the effect of free office cholesterol testing. While this study found an increase in the number of cholesterol tests performed, this could be attributed to their advertisements for free cholesterol testing. This is likely to have substantially biased the results, making them unreliable. Hobbs *et al.* (1992) examined changes that occurred in a variety of tests after the introduction of a desktop analyser. This study found there was a substantial increase in the number of tests overall (168 percent) with substantial increases in tests for either cholesterol (193 percent) or triglycerides (129 percent). A study by Rink *et al.* (1993) assessed the clinical and economic impact of NPT in general practice for six different biochemical and bacteriological tests. The study found testing rates increased by 16.5 percent overall when NPT equipment was made available with the largest increase occurring in cholesterol testing (82.1 percent: a change from 3.2 tests/week to 5.8 tests/week). The study found,

in comparison to laboratory tests, an NPT for cholesterol was significantly more likely to be used for screening or patient demand and less likely for monitoring or diagnosis.

Based on the available evidence, it is likely the introduction of the Cholestech LDX would result in an increase in tests for total cholesterol. The magnitude of the increase is likely to be between 82 and 193 percent. Although similar increases may occur in tests for triglycerides and HDL-cholesterol, limited information was available so the magnitude of the increase is at present unclear. In terms of the population that will be tested, the available evidence suggests NPT is more likely to be used for screening rather than monitoring or diagnosis.

Improved process-of-care and patient quality of life

One study using the Cholestech LDX examined the impact on the process-of-care in patients with hypercholesterolaemia (Ruffin & McKenney, 1997). The indicators of process-of-care in this study included the physician's documentation of six points including referrals to dieticians for assistance in cholesterol management, changes in hyperlipidaemic regimen and orders for diagnostic tests of cardiovascular status. While the study found that using a NPT for cholesterol improves the process-of-care in patients with hypercholesterolaemia with respect to cholesterol management, the differences between groups was not significant. However, the study does highlight the potential benefits of rapid cholesterol results even though a difference in lipid control or compliance between groups was not examined. Two out of the 19 patients randomised to the NPT group had immediate intervention that was directly attributed to the availability of results from the Cholestech LDX. One patient was immediately referred for cardiac catheterisation after obtaining a high LDL cholesterol reading coupled with the patient's presenting symptoms. Another patient, after obtaining an unusually high triglyceride result, was screened for diabetes and subsequently diagnosed with diabetes mellitus. These findings emphasise the possible importance of NPT in providing rapid results for cholesterol testing in a primary care setting.

A report by Cohen *et al.*, 1998 showed near patient testing for cholesterol is both convenient to the patient and improves their process-of-care. To determine the patients' attitude to NPT, a questionnaire was devised consisting of five main scales:
1) convenience; 2) allaying anxiety; 3) personal attention; 4) reliability of results; and 5) costs. The study found NPT eliminated the extra time taken for patients to attend specialist laboratories and reduced the costs associated with travelling and the test itself. The majority of the patients preferred the finger-prick of NPT to the venipuncture associated with laboratory testing. Patient satisfaction was also increased because most felt that having immediate test results relieved the anxiety associated with their condition. Nearly all patients preferred their own GP to perform the test as they believed their GP understood their needs better than an outside laboratory employee.

Based on the available evidence, some improvements in the process-of-care following the introduction of NPT for cholesterol have been observed. Similarly, patient's quality of life is likely to improve because of enhanced perceptions of the process-of-care and the convenience aspects of NPT. However, these benefits have at present not been quantified in a manner suitable for incorporation into an economic evaluation.

What are the economic considerations?

Economic evaluation of new health care technologies is particularly important where the new technology offers health benefits at additional cost. It is clear there will always be a limit to the additional cost which would be paid for a given health gain. Economic evaluation is generally aimed at determining whether such incremental costs represent value for money.

The usual process for an economic evaluation is first to consider the additional benefits accrued with the new device/procedure relative to the comparator (i.e. the incremental effectiveness), and to then proceed with determining cost differences between the new procedure and the comparator (i.e. incremental costs). When both of these quantities are known, then an incremental cost-effectiveness ratio (ICER) can be determined. The calculation of an incremental cost-effectiveness ratio is shown below:

$$\text{ICER} = \frac{Cost_{NEW} - Cost_{COMPARATOR}}{Effectiveness_{NEW} - Effectiveness_{COMPARATOR}}$$

In cases where a new technology offers inferior or equal health benefits at a higher cost it clearly does not provide value for money. This technology is "dominated" by the comparison technology.

Literature search

A literature search was conducted to identify papers that compare the cost-effectiveness of a NPT for cholesterol with the current laboratory test. The databases examined were Medline, EMBASE and the external databases previously outlined in this document (see Accuracy and Precision: Literature Search and Appendix E for search results of the bibliographic databases). A large number of studies have examined the cost-effectiveness of cholesterol testing or screening using laboratory tests; however, these were not reviewed for this evaluation. Three studies were retrieved that included an economic evaluation of NPT; two articles examined NPT in the context of lipid testing (Rink *et al.,* 1993; Cohen *et al.,* 1998), the remaining study conducted an economic analysis of point-of-care versus central laboratory testing (Tsai *et al.,* 1994).

The study by Rink *et al*., (1993) estimated the comparative costs associated with a laboratory and near patient test for cholesterol. The only benefit included in the cost-effectiveness analysis was improved medical recording (not described). The study found the cost per improved record was £36. No further analysis was undertaken. The study by Cohen *et al*. (1998) included a cost analysis of a laboratory and near patient test for cholesterol in Australia. No benefits were included in the analysis and no incremental cost-effectiveness ratios determined. The study by Tsai *et al*. (1994) simply compared NPT and laboratory tests in a hospital environment.

As no studies thoroughly examined the cost-effectiveness of NPT for cholesterol in comparison to current laboratory testing, an economic evaluation was conducted for this report. A decision analytic modelled evaluation was used to determine the costs and effectiveness of NPT for total cholesterol using the Cholestech LDX compared to current laboratory testing. The model was designed to capture the effects of greater recruitment, improved monitoring and poorer accuracy that are associated with NPT using the Cholestech LDX. The model and its results are described in the following sections.

Approach of the modelled evaluation

The modelled evaluation was designed to estimate the costs and health outcomes associated with cholesterol testing. The model incorporated three important features of near-patient cholesterol testing that will impact on patient outcomes and health care costs. These were:

- The effect of the accuracy of the test on the diagnosis and treatment of patients with elevated cholesterol;
- The effect on costs and effectiveness of an increase in the use of cholesterol testing; and
- The effect of near-patient testing in improving compliance and reducing the number of patients who discontinue therapy.

The accuracy and precision of the Cholestech LDX will affect the classification of patients being tested. Reductions in accuracy and precision will probably result in increasing misclassification of patients. Patients requiring treatment may be incorrectly classified as normal whilst other patients with normal blood cholesterol levels may be classified as at-risk and receive treatment. Increasing misclassification has the potential to influence health outcomes (ie some patients are not adequately treated) and costs (ie inappropriate treatment of some patients).

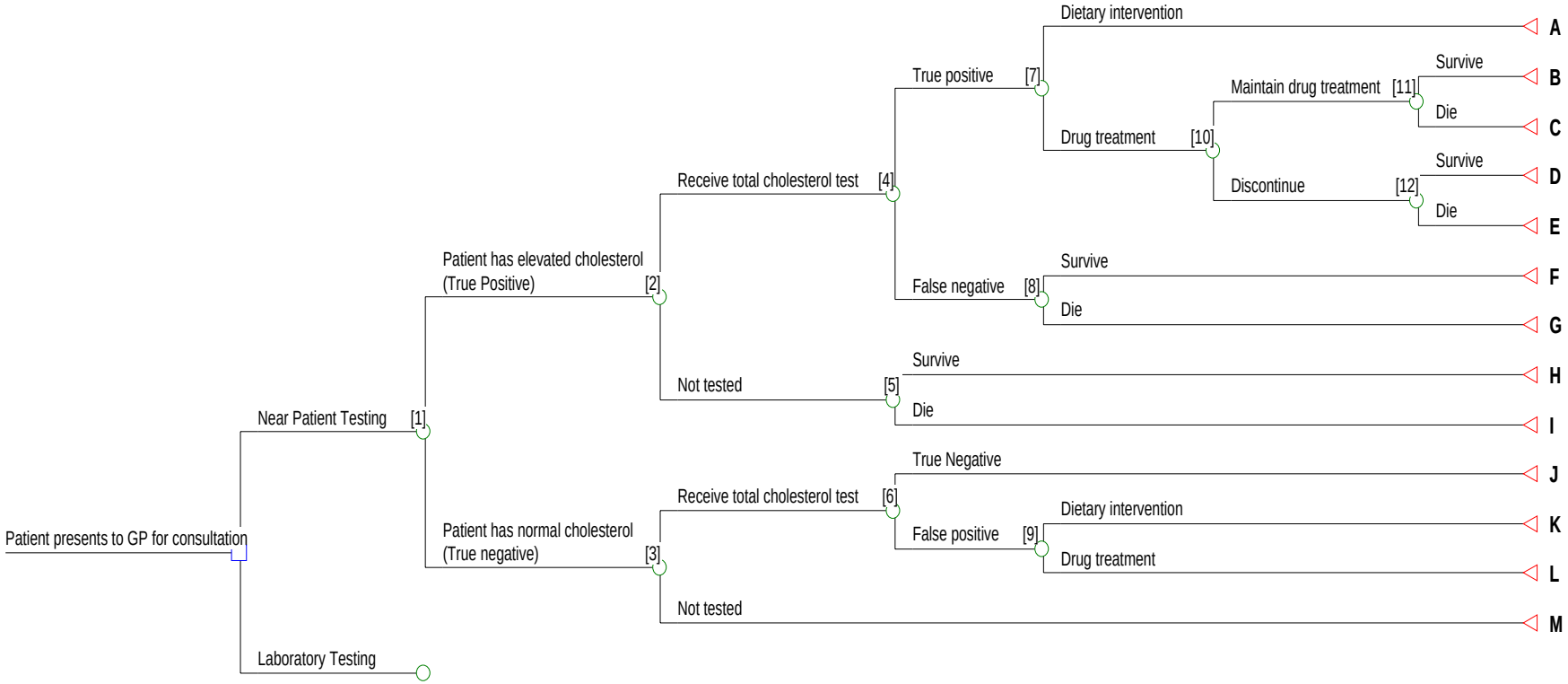
The introduction of NPT may alter the number of tests conducted in general practice. Higher testing rates could result in more patients with elevated cholesterol being detected. For example, testing in populations at increased risk (i.e. with proportionally more patients with elevated cholesterol) will increase the number of cases detected. Although higher testing rates will increase overall health costs, this will be balanced by improved health outcomes for those patients detected. However, this is true only if the testing population still contains patients with elevated cholesterol levels. Once all those with elevated cholesterol levels have been detected, additional tests will no longer impact on health outcomes.

The effectiveness of lipid-lowering medications is at present limited to some extent by poor compliance and high discontinuation rates in the community. One possible benefit of NPT for cholesterol is improved monitoring and compliance with lipid-lowering medication. This would improve the effectiveness of such therapies, thus improving health outcomes. Improved monitoring will also increase total health care costs. The decision analytic model follows patients through different treatment pathways to determine the costs and health outcomes of patients receiving cholesterol tests. The modelled evaluation considered four effectiveness measures. These were:

- Additional patients detected with elevated cholesterol;
- Additional patients with controlled lipid levels;
- Mortality; and
- Life years gained.

The decision tree used to determine costs and the four effectiveness measures described above is presented in Figure 5. Costs and outcomes were calculated over a one-year period. It is important to note that the decision tree is not necessarily a depiction of clinical management after a cholesterol test. Rather, it is a simplified accounting tree used to estimate expected costs and outcomes within a one-year period.

Figure 5 Decision tree used in the modelled evaluation



Points 1 to 12 below explain each node in the decision tree on the previous page. Further information about the derivation of each variable used at each node in the decision tree is provided in Appendix K.

1. The modelled population is representative of the Australian population. The 1989 Risk Factor Prevalence Survey found 16.0 percent of men and 14.2 percent of women had elevated cholesterol (Total Cholesterol ≥ 6.5 mmol/L). Therefore, 15.1 percent of the population in the model have elevated cholesterol.

2. For every 100 GP consultations of patients with elevated cholesterol, it was calculated 6.40 would include a lipid test. When NPT is introduced, it is expected to increase the rate of testing by 82.1 percent (Rink *et al.* 1993). However, it is expected a minority (21 percent) will be performed in patients with elevated cholesterol (Rink *et al.* 1993). The probability of a patient with elevated cholesterol being tested when NPT is available was calculated as 0.090 (9.0 tests conducted per 100 GP consultations involving patients with elevated cholesterol; see Appendix K for details on calculations).

3. For every 100 GP consultations of patients with normal cholesterol presenting for a GP consultation, it was calculated 1.57 would be given a lipid test. When NPT is introduced, it is expected to increase the rate of testing by 82.1 percent (Rink *et al.*). It is anticipated the majority of extra tests will involve patients with normal cholesterol (79 percent; Rink *et al.* 1993). The probability of a patient with normal cholesterol being tested when NPT is available was calculated as 0.033 (Appendix K).

4. The sensitivity of total cholesterol testing with the Cholestech device was estimated as 0.928. This is based on a threshold of 6.5 mmol/L and a total error of eight percent (see Appendix K).

5. The annual probability of CHD death for a patient not detected with elevated cholesterol was estimated as 0.00156 (Appendix K).

6. The specificity of a single total cholesterol test with the Cholestech device was estimated as 0.974. This is based on a threshold of 6.5 mmol/L and a total error of eight percent (Appendix K).

7. The proportion of patients detected with elevated cholesterol who receive lipid lowering medication is 40 percent (Smith *et al.* 1996). The population receiving lipid lowering medication in the modelled evaluation represents a population with co-morbidities and/or risk factors who qualify for lipid-lowering medication through the Schedule of Pharmaceutical Benefits.

8. The annual probability of CHD death for a patient not detected with elevated cholesterol was estimated as 0.00156 (Appendix K).

9. The proportion of patients detected with elevated cholesterol who receive lipid lowering medication is 40 percent (Smith *et al.* 1996). This population receives no benefit from medication since they are not at risk of cholesterol-related mortality.

10. Because 59.8 percent of patients starting lipid-lowering medication discontinue within one year (Simons *et al.* 2000), it has been argued that the use of NPT may

improve compliance with medication (Cohen *et al*., 1998). The effect of improved compliance on the cost-effectiveness of NPT is explored in sensitivity analysis.

11. The annual probability of CHD death for a patient maintained on lipid lowering therapy is 0.0026 (WOSCOPS trial).

12. The annual probability of CHD death for a patient not maintained on lipid lowering therapy is 0.0039 (WOSCOPS trial).

Variables and assumptions in the modelled evaluation

Determining each of the four effectiveness measures required different sets of variables and assumptions. The assumptions and variables used are presented in Tables 12 to 16.

- Table 12 presents the cost variables and assumptions;
- Table 13 presents the variables and assumptions used to determine the number of additional patients detected with elevated cholesterol;
- Table 14 presents the variables and assumptions used to determine the number of patients in the model population achieving normal lipid levels;
- Table 15 presents the variables and assumptions used to estimate mortality; and
- Table 16 presents those used to estimate life years gained.

The data and other evidence underlying these assumptions are provided in Appendix K.

Table 12 Variables and assumptions used by the modelled evaluation to determine total cost of treatment

Assumption	Source
70% of near patient cholesterol tests require a long consultation.	Assumption. This assumption accounts for the value of the extra professional and nurse time required to administer a cholesterol test at the surgery. Also, Cohen *et al*. (1998) found 70% of patients receiving a near patient cholesterol test were offered management advice. The time taken to perform a test, offer advice and conduct the rest of a standard consultation will be greater than 20 minutes meaning a long consultation will be reimbursed.
Total cost per Cholestech total cholesterol test is $57.13	$14.90 test ($12.00 per cartridge + $2.90 for reimbursement of capital expenditure. See Appendix K)
	$8.10 standard consultation (× 30%)
	$34.13 long consultation (× 70%)
Total cost per lab-performed total cholesterol test is $71.63. It is assumed that 70% of patients will require a follow-up consultation to report results and initiate treatment and/or dietary intervention. This is consistent with the 70% of patients requiring a long consultation with a near patient test.	$11.40 test (MBS Item 66521)
	$27.00 consultation (MBS Item 23)
	$14.33 PEI (MBS Items 73907, 73915)
	$18.90 follow-up consultation (× 70%)
Total cost per patient not receiving a cholesterol test is $27.00	$27.00 consultation (MBS Item 23)
1 follow-up consultation and total cholesterol laboratory test per patient with elevated cholesterol is performed per year	Assumption
An average of 1.82 follow-up consultations and near patient cholesterol tests per patient with elevated cholesterol are performed per year	Rink *et al*. report an 82.1% increase in testing due to the availability of a near patient device
Annual cost per patient maintained on lipid-lowering medication is $671	HIC. PBS Item statistics

PEI: Patient Episode Initiation; HIC: Health Insurance Commission; PBS: Pharmaceutical Benefits Schedule; MBS: Medicare Benefits Schedule

Table 13 Variables and assumptions used by the modelled evaluation to determine additional patients detected with elevated cholesterol

Assumption	Source
Sensitivity of the Cholestech device is 0.928	Calculation by Monte Carlo population simulation. Appendix K.
Specificity of single Cholestech test is 0.974	Calculation by Monte Carlo population simulation. Appendix K.
The availability of near patient testing will increase the number of patients tested by 82.1%	Rink *et al*. 1993
Of the additional patients tested due to the availability of near patient testing, 21% will have elevated cholesterol (compared to 42% in laboratory based testing)	Assumption based on evidence suggesting the average cholesterol level is lower in patients tested with NPT compared to laboratory based testing (Rink *et al*. 1993)

The majority of assumptions used to estimate the proportion of patients achieving normal lipid levels were the same as those used to determine additional patients detected with elevated cholesterol (Table 13). Additional assumptions are presented in Table 14.

Table 14 Variables and assumptions used by the modelled evaluation to determine patients with normal lipid levels

Assumption	Source
40% of patients who are correctly diagnosed with high cholesterol and treated achieve target lipid levels	Smith *et al*. 1996

The majority of assumptions used to estimate mortality in the modelled evaluation were also the same as those used to determine additional patients detected with elevated cholesterol (Table 13). Additional assumptions are presented in Table 15.

Table 15 Variables and assumptions used by the modelled evaluation to determine mortality

Assumption	Source
Proportion of patients with elevated cholesterol who receive lipid lowering-medication is 40%	Smith *et al*. 1996
The probability of CHD death for a patient with high cholesterol and who is not treated is 0.0039 per patient year	WOSCOPS trial
The probability of CHD death for a patient with high cholesterol and who is treated is 0.0026 per patient year	WOSCOPS trial
The probability of CHD death for a patient not detected with high cholesterol is 0.00156	$0.0039 \times 40\%$
59.8% of patients discontinue lipid lowering therapy in the current setting	Simons *et al*. (1996)
59.8% of patients discontinue lipid lowering therapy when near patient testing is introduced	Assumption

The model uses the relative efficacy of lipid-lowering medication observed in the WOSCOPS trial. However, since 77 percent of the WOSCOPS population were eligible for drug treatment according to the National Cholesterol Education Program (WOSCOPS group 1997), this model slightly underestimates the true benefit of therapy that a PBS population would receive. Furthermore, the incremental cost-effectiveness ratio of lipid-lowering medication implied by the parameters of the modelled evaluation is $36,622 per life year gained (see Appendix K). This is a similar result to an economic evaluation of the 40 percent of patients at highest risk in the WOSCOPS population which estimated an incremental cost effectiveness ratio of £13,995 per life year gained (A$31,066 using health care sector purchasing power parity of Stl£1 = A$2.22) (Caro *et al*. 1997). The estimate of $36,622 used by the modelled evaluation is therefore reasonable.

Assumptions used to determine life years gained were the same used to determine mortality. In addition, it was assumed each death resulted in a loss of 25 life years. This is based on the average age (56 years) and life expectancy of a typical population receiving a cholesterol test in Australia. Life years gained was discounted at five percent per annum (25 life years is equivalent to 14.1 discounted life years see Table 16).

Table 16 Variables and assumptions used by the modelled evaluation to determine life years gained

Assumption	Source
Average age of patient receiving a total cholesterol test is 56 years	MBS Item Statistics. Item 66521
Average life expectancy of patients receiving a total cholesterol test is 25 years	Australian life tables 1996 (23 years for 56 year old male) (27 years for 56 year old female)
Discount rate of 5% per annum applied to life years gained	PBAC guidelines

MBS: Medicare Benefits Schedule

A number of costs are associated with maintenance and quality assurance of the Cholestech LDX device. These costs include cassette usage for internal and external quality control, fees for provision of an external quality assurance program, maintenance contract or extension of warranty beyond first year, miscellaneous consumables and operator time. However, the fee for the laboratory-based test used in the economic analysis includes associated maintenance and quality assurance costs and the assumption used in the model was that both test fees include all associated costs.

Results of the modelled evaluation

In comparison to laboratory testing, the use of near patient testing resulted in an extra cost of $1.17 per patient presenting for a GP consultation. Overall, in the NPT arm of the model more patients received a total cholesterol test, more patients with elevated cholesterol were detected and fewer patients died. The model predicted that, for every 100,000 GP consultations, an additional 298 patients would be detected with elevated cholesterol, an additional 91 patients would achieve target lipid levels and less than 1 CHD death would be avoided (see Table 17).

The model estimated incremental cost effectiveness ratios for three endpoints. The incremental cost per additional patient detected with elevated cholesterol was $392; per additional patient achieving target lipid levels was $1,287; and per life year gained was $132,934 (see Table 18).

Table 17 Costs and outcomes of the modelled evaluation

Outcome	Near patient testing	Laboratory testing	Incremental
Cost per patient	$31.21	$30.04	$1.17
Patients detected with elevated cholesterol	0.01265	0.00966	0.00298
Patients achieving target lipid levels	0.85285	0.85194	0.00091
CHD deaths	0.00023292	0.00023354	0.00000062
Life years gained	14.090662	14.090653	0.000009

Table 18 Incremental cost-effectiveness of near-patient testing

Outcome	Incremental cost	Incremental outcome	Incremental cost-effectiveness
Incremental cost per additional patient detected with elevated cholesterol	$1.17	0.00298	$ 392
Incremental cost per additional patient achieving target lipid levels	$1.17	0.00091	$ 1,287
Incremental cost per life year gained	$1.17	0.000009	$132,934

Sensitivity analysis of the modelled evaluation

The values of a number of variables were derived with a degree of uncertainty. The effect of changing these variables on the results of the modelled evaluation is considered in the sensitivity analysis. The variables considered in sensitivity analyses were:

- The total error associated with the Cholestech LDX total cholesterol test: eight percent total error was the base case. Sensitivity analysis considered values of eleven, four and zero percent.

- The growth in the number of total cholesterol tests when NPT is introduced: 82.1 percent was the base case value. Sensitivity analysis considered values from zero to 100 percent

- The proportion of extra cholesterol tests that are performed on patients with high cholesterol: 21 percent was the base case value. Sensitivity analysis considered values from 15.1 percent to 42 percent

- The proportion of patients using NPT who discontinue lipid-lowering medication: 59.8 percent was the base case value. Sensitivity analysis considered values from 30.8 percent to 59.8 percent.

- The proportion of follow-up consultations required per lab test performed. 70 percent was the base case value. Sensitivity analysis considered values from zero to 100 percent.

Altering the TE of the test had limited impact on the cost-effectiveness ratios. When the TE for the Cholestech LDX total cholesterol test was reduced to zero percent (i.e. equivalent to the lab test), the incremental cost per life year gained still exceeded $100,000 ($101,419; see Table 19).

The results of the analysis are sensitive to the growth in cholesterol testing due to the availability of NPT (see Table 19). This is because it is only through increasing the

number of tests performed that NPT can provide benefit. An increase in the number of tests means more patients will be detected and more patients will receive cost-effective interventions. However when the same number of near-patient tests and laboratory-based tests are performed, near patient testing is associated with poorer health outcomes and lower costs. The modelled evaluation found that, if there was no growth in the number of tests, 0.000002 life years per patient would be lost and costs would decrease by $0.36 per patient presenting to a GP.

If the additional NPT tests were performed in a general, un-screened population (i.e. 15.1 percent of the new tests are performed in patients with elevated cholesterol), the incremental cost-effectiveness of NPT is $165,657 per life year gained (see Table 19). If the new tests are conducted under the current screening guidelines (i.e. 42.0 percent of the new tests are performed in patients with elevated cholesterol), the incremental cost effectiveness of NPT is $98,850.

If all patients who discontinued medication for reasons other than efficacy and adverse events (i.e. only 30.8 percent of patients on lipid lowering medication discontinue treatment within one year) were kept on prescribed medication, the incremental cost effectiveness ratio of NPT is $48,699 per life year gained(see Table 19). If a cost per life year threshold value of $40,000 is desired, near-patient testing would have to improve compliance to medication from 40.2 percent to greater than 70 percent.

Table 19 Results of the sensitivity analysis

Variable and values	Incremental cost per LYG
The total error associated with the Cholestech total cholesterol test	
11%	$151,378
4%	$115,615
0%	$101,419
The growth in the number of total cholesterol tests when NPT is introduced:	
50%	$117,577
100%	$137,005
The proportion of extra cholesterol tests which are performed on patients with high cholesterol:	$165,657
15.1%	$ 98,850
42.0%	
The proportion of patients using NPT who discontinue lipid lowering medication:	
30.8%	$ 48,699
59.8%	$132,934
The proportion of follow-up consultations required per laboratory test performed:	
0%	$188,189
100%	$109,254

Figures 6 to 9 show the effect of changes in key variables on the incremental cost-effectiveness of near patient testing. Figure 6 shows that a certain amount of growth in NPT tests is required for it to be considered cost-effective (approximately 22-25 percent). Above this level, the incremental cost effectiveness of NPT increases as the number of tests increases. If only limited test growth occurs, then the benefits of NPT are less than those of laboratory testing.

Figure 6 **Change in the incremental cost-effectiveness of NPT with the growth in the number of cholesterol tests performed**

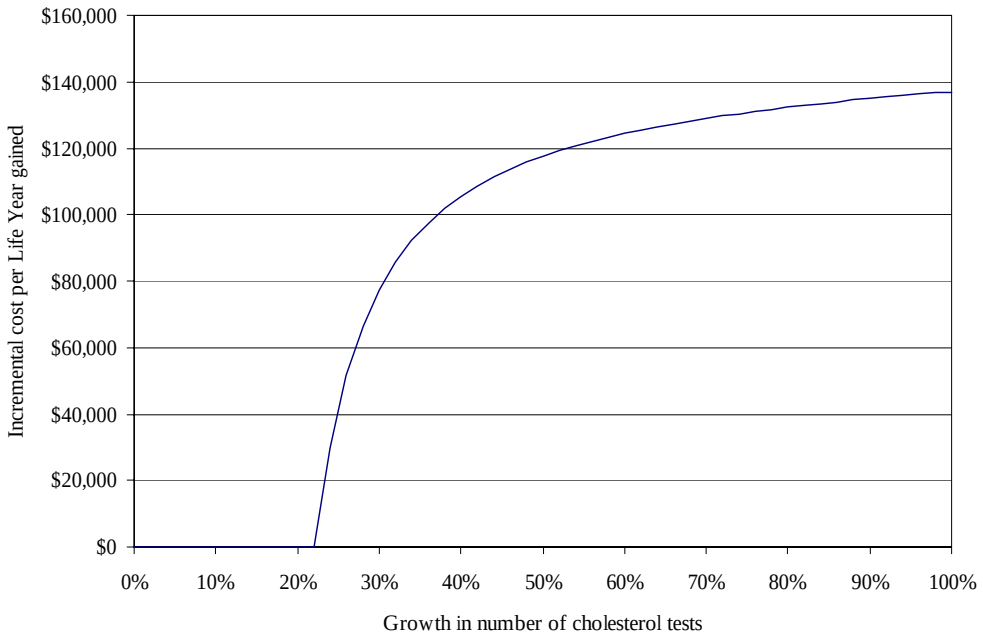
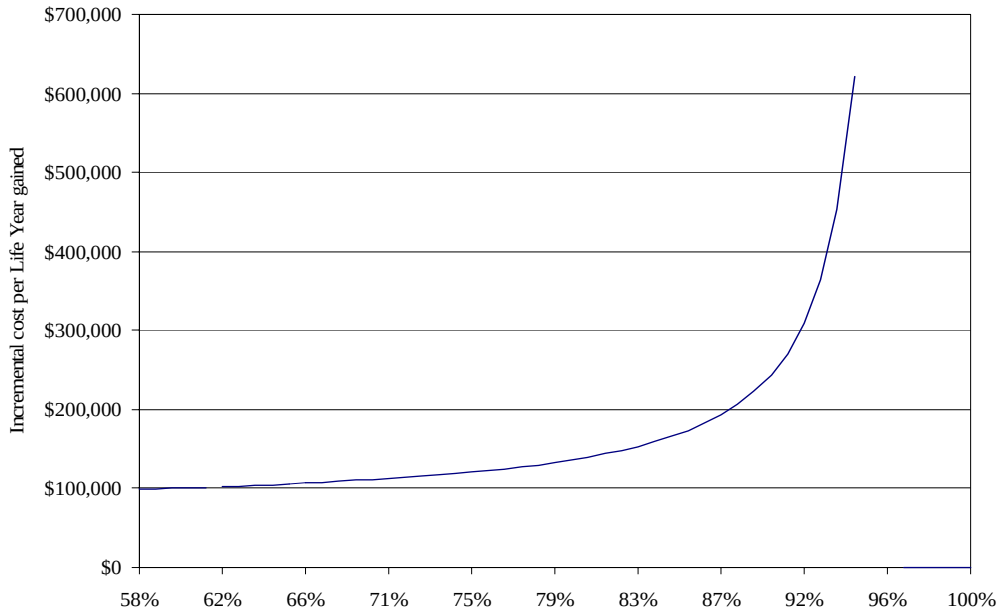


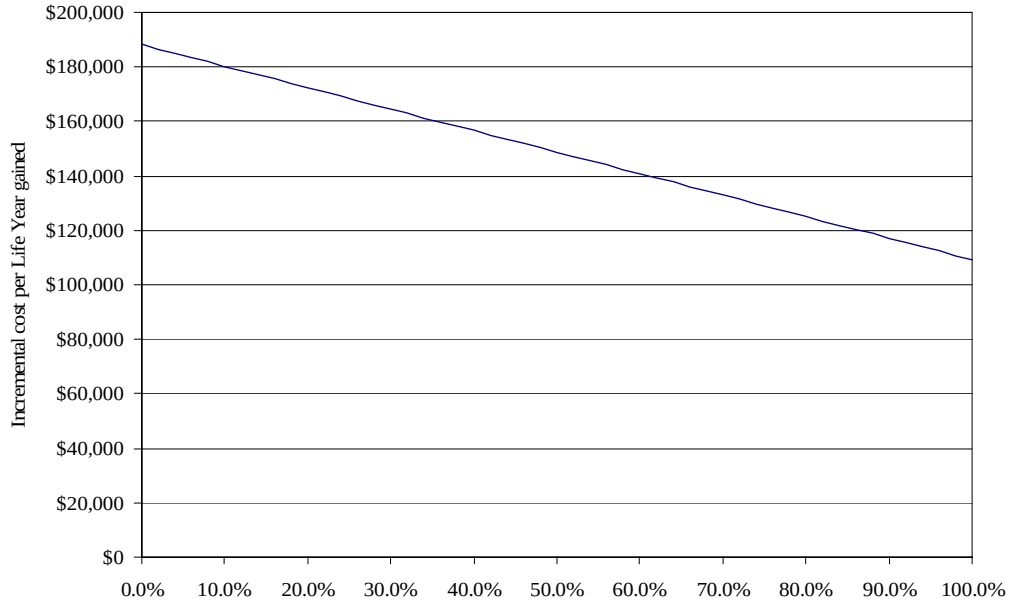
Figure 7 shows that the incremental cost-effectiveness of NPT decreases as the proportion of tests performed on patients with normal cholesterol increases. At present, approximately 60 percent of patients undergoing laboratory tests have normal cholesterol (Smith *et al*., 1991). Following the introduction of NPT for cholesterol, Rink *et al*. (1993) found the cholesterol level of patients receiving cholesterol tests in the near patient setting was significantly lower than the cholesterol levels of patients receiving cholesterol tests in the laboratory setting. This suggests the population being tested contained more patients with normal cholesterol which has implications for the cost-effectiveness of near patient testing. As more tests are performed on patients with normal cholesterol, costs increase without any improvement in health outcomes. Therefore, the cost-effectiveness of near-patient testing worsens.

Figure 7 **Change in the incremental cost-effectiveness of NPT with the proportion of new tests being performed in patients with normal cholesterol**



As expected, the incremental cost-effectiveness of NPT improves when the number of follow-up GP consultations associated with laboratory testing increases (see Figure 8).

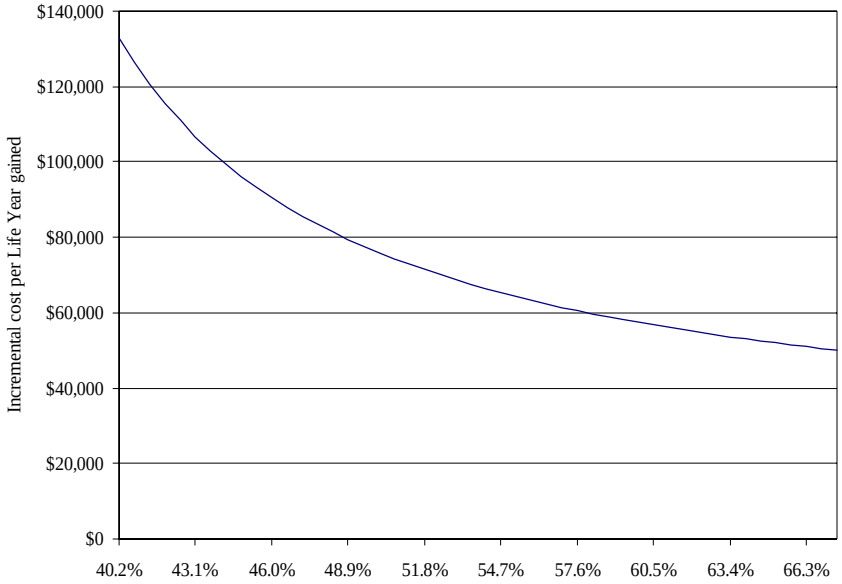
Figure 8 **Change in the incremental cost-effectiveness of NPT with changes in the number of follow-up GP consultations associated with laboratory testing**



In the base case analysis, it was assumed the proportion of patients completing one year of lipid lowering medication was the same in the laboratory and near patient settings (40.2 percent; see Figure 9). It has been argued that near patient testing may improve compliance to medication through better monitoring. If a cost-per-life-year threshold

value of $40,000 is desired, near patient testing would have to improve compliance to medication from 40.2 percent to greater than 70 percent.

Figure 9 Change in the incremental cost-effectiveness of NPT with changes in the proportion of patients discontinuing medication



Summary

A decision analytic modelled evaluation was used to determine the costs and effectiveness of NPT for total cholesterol using the Cholestech LDX compared to current laboratory testing. The model was designed to capture the effects of greater recruitment, improved monitoring and poorer accuracy that are associated with NPT using the Cholestech LDX.

The model provided information on a number of incremental cost-effectiveness ratios. These included the incremental cost per additional patient detected with elevated cholesterol ($392), the incremental cost per additional patient achieving target lipid levels ($1,287) and the incremental cost per life year gained ($132,934). Sensitivity analysis indicated these ratios were influenced most by the rate of growth of cholesterol testing due to the presence of NPT and the nature of the population in which the new tests were being performed. The ratios remained largely unchanged when the accuracy of the Cholestech LDX test was altered. When the total error of the test was reduced to zero in comparison to laboratory-based tests, the incremental cost per life year gained was $101,419.

The incremental cost-effectiveness ratio estimated for NPT is high. A study into recommendations made by the Pharmaceutical Benefits Advisory Committee between 1993 and 1996 found that no interventions were accepted with an incremental cost per life year gained greater than $100,000 (George *et al.*, 1998). This suggests the incremental cost per life year gained of $132,934 is outside the range of reasonable cost-effectiveness.

When interpreting the results of the modelled economic evaluation, a number of factors need to be considered. They include:

- Uncertainty around the parameters of the modelled evaluation and the very small incremental benefit of near patient cholesterol testing; and

- The population(s) in which the near patient and laboratory tests are performed and ultimately where lipid-lowering medication are used.

There is a degree of uncertainty around many of the modelled parameters. Although much of this uncertainty was tested in sensitivity analysis, the level of uncertainty should be interpreted in the context of the incremental benefit estimated in the modelled evaluation. The extremely low incremental benefit (0.000009 life years) is a result of combining a low rate of cholesterol testing, the efficacy of treatment and the annual risk of death. It is unlikely that the individual model parameters are reliable enough to accurately predict the life years gained with the precision required to estimate an incremental benefit of only 0.000009 life years.

Current evidence suggests near patient tests for cholesterol are being conducted in a population with proportionally fewer at-risk individuals (i.e. those with total cholesterol > 6.5 mmol/L) than the population currently being laboratory tested. As a result, a greater number of tests that offer no benefit would be performed after the introduction of near patient testing for cholesterol. The cost-effectiveness ratio for near patient testing is therefore weighted on the side of cost because a large number of the additional tests performed do not stratify patients into therapy. Without changing clinical management, the test offers no benefit (in terms of life years gained). For example, if a patient with normal cholesterol is tested, no treatment or advice will be offered. Therefore, the additional cost of the test has accrued without any corresponding benefit.

Conclusions

High blood cholesterol is one of the major modifiable risk factors for coronary heart disease (CHD). Currently, a substantial number of Australians have elevated cholesterol levels that may place them at increased risk of CHD. The last national survey to measure blood cholesterol levels in Australia was conducted by the National Heart Foundation in 1989. At that time it was estimated that over 4.5 million adult Australians (aged 20-69 years) had high-risk cholesterol levels. The survey found that 47 percent of men and 39 percent of women had cholesterol levels above 5.5 mmol/L. In terms of those at very high risk of cardiovascular disease, over 15 percent of men and women had blood cholesterol levels of 6.5 mmol/L or more.

A combination of blood lipid analysis and determination of other independent risk factors (eg smoking, high blood pressure, diabetes, reduced physical activity, and obesity) is current best practice to identify individuals at-risk of CHD. In Australia both the National Heart Foundation and the Royal Australian College of General Practitioners (RACGP) recommend appropriate lipid tests be conducted to better evaluate an individual's risk of CHD. The RACGP, for example, recommend lipid tests be conducted at least once every 5 years.

Under present arrangements, cholesterol, triglyceride and HDL-cholesterol tests are available under Pathology Services on the MBS. Introduction of the Cholestech LDX would allow these tests to be performed in an office or clinic setting, although no changes would occur in the type of tests currently available.

Safety

The Cholestech LDX device does not come into contact with the individual undergoing lipid testing and no safety concerns related to the device were identified in the evaluation

Effectiveness

Accuracy and Precision

At present there is insufficient evidence to determine whether the Cholestech LDX would meet the NCEP guidelines when used in a setting such as a specialised clinic or office of a general practitioner. If the operator-dependence of similar devices is used, the device does not meet the NCEP guidelines.

Effectiveness

Identifying patients suitable for lipid lowering treatment

The primary role of the Cholestech LDX would be to provide lipid tests in a near patient environment with acceptable levels of accuracy and precision. These tests can be used to further evaluate the risk of CHD in an individual and where appropriate, initiate treatment.

In addition to identifying patients for treatment, near patient testing may also have benefits not directly related to the accuracy and precision of an individual test. These

benefits could be viewed as being device independent and would vary according to the clinical value of the test being conducted and the circumstances of its use (eg the population being tested). In terms of NPT for lipid testing, this evaluation identified a number of potential benefits that may result from its introduction. These were:

- Reductions in the number of patients lost to follow-up;
- Improved compliance to, and reduced discontinuation from, lipid lowering medication;
- Improved lipid control;
- Alterations in the number of tests conducted; and
- Improved process-of-care and patient quality of life

The following conclusions were made following a review of the available evidence.

Reductions in the number of patients lost to follow-up

While it is likely that fewer patients would be lost to follow-up after the introduction of NPT, the current review found no evidence as the extent of the benefit that may occur.

Improved compliance to, and reduced discontinuation from, lipid lowering medication

There is insufficient evidence available at present to determine whether NPT would result in improved compliance to, and/or discontinuations from lipid lowering medications.

Improved lipid control

The review found Level III evidence that examined the likely impact of NPT on improving the number of patients achieving target lipid levels. Given the setting and the limitations of this study, the evaluation found there is insufficient evidence to determine whether the introduction of NPT for lipids would improve the proportion of patients achieving target lipid levels.

Alterations in the number of tests conducted

Based on the available evidence, it is likely that the introduction of the Cholestech LDX would result in an increase in tests for total cholesterol. The magnitude of the increase is likely to be between 82 percent and 193 percent. Although similar increases may occur in tests for triglycerides and HDL-cholesterol, only limited information was available and the magnitude of the increase is at present unclear. In terms of the population that will be tested, the available evidence suggests NPT is more likely to be used for screening rather than monitoring or diagnosis.

Improved process-of-care and patient quality of life

Based on the available evidence, some improvements in the process-of-care following the introduction of NPT for cholesterol have been observed. Similarly, patient's quality

of life is likely to improve because of enhanced perceptions of the process-of-care and the convenience aspects of NPT. However, none of these benefits have at present been quantified in a manner suitable for incorporation into an economic evaluation.

Cost effectiveness

The cost-effectiveness of near patient testing for cholesterol does not compare favourably with a range of other common health care interventions.

Recommendations

On the strength of evidence pertaining to near patient cholesterol testing using Cholestech LDX:

1. The unrestricted use of near patient cholesterol testing using the Cholestech LDX is not recommended.

2. The restricted use of near patient cholesterol testing, as an alternative to laboratory testing of lipids, should be considered in settings or circumstances where there is adequate training, accreditation and quality assurance. Interim funding in these circumstances should be considered with monitoring and review of testing (see Recommendation 3) to assess diagnostic performance and to ensure there is not an increase in testing or broadening of indications beyond that currently undertaken.

3. It is strongly recommended that further information be collected on the diagnostic performance of the NPT devices in the community setting and the impact of near patient testing on patient outcomes including changes in lipid management, compliance with lipid lowering therapies and amount of doctor visits.

- The Minister for Health and Aged Care accepted this recommendation on 18 September 2001. -

Appendix A MSAC terms of reference and membership

MSAC's terms of reference are to:

- advise the Minister for Health and Ageing on the strength of evidence pertaining to new and emerging medical technologies and procedures in relation to their safety, effectiveness and cost-effectiveness and under what circumstances public funding should be supported;
- advise the Minister for Health and Ageing on which new medical technologies and procedures should be funded on an interim basis to allow data to be assembled to determine their safety, effectiveness and cost-effectiveness;
- advise the Minister for Health and Ageing on references related either to new and/or existing medical technologies and procedures; and
- undertake health technology assessment work referred by the Australian Health Ministers' Advisory Council (AHMAC), and report its findings to AHMAC.

The membership of MSAC comprises a mix of clinical expertise covering pathology, nuclear medicine, surgery, specialist medicine and general practice, plus clinical epidemiology and clinical trials, health economics, consumers, and health administration and planning:

Member	Expertise
Professor David Weedon (Chair)	pathology
Ms Hilda Bastian	consumer health issues
Dr Ross Blair	vascular surgery (New Zealand)
Mr Stephen Blamey	general surgery
Dr Paul Hemming	general practice
Dr Terri Jackson	health economics
Professor Brendon Kearney	health administration and planning
Mr Alan Keith	Assistant Secretary, Diagnostics and Technology Branch, Commonwealth Department of Health and Ageing
Dr Richard King	gastroenterology
Dr Michael Kitchener	nuclear medicine
Professor Peter Phelan	paediatrics
Dr David Robinson	plastic surgery
Associate Professor John Simes	clinical epidemiology and clinical trials
Dr Bryant Stokes	neurological surgery, representing the Australian Health Ministers' Advisory Council

Appendix B Search History for Medline, Current Contents, HealthSTAR and BIOSIS

	Search History	Results			
		Medline	Current Contents	Health STAR	BIOSIS
1	Cholesterol	104640	36938	32176	55415
2	Lipoproteins	14535	11971	7777	59369
3	Triglycerides	43859	8576	13354	12587
4	Lipids	103105	26162	18360	32424
5	1 or 2 or 3 or 4	189682	61267	46191	82661
6	Blood chemical analysis	8836	15	3029	36
7	Serum	414966	150708	115638	209661
8	Blood/ or plasma/ or whole blood	51563	268620	225652	41351
9	Fingerstick	130	71	115	113
10	Capillary blood	2868	866	1231	1296
11	6 or 7 or 8 or 9 or 10	465019	536578	362724	247740
12	5 and 11	34692	31196	26539	18802
13	Cholestech	7	2	13	7
14	Cholestech LDX	5	1	5	4
15	Desktop lipid analyser	0	0	0	0
16	13 or 14	7	2	13	7
17	12 and 16	7	0	0	5
18	Near patient	163	140	166	135
19	Near patient test	12	14	12	16
20	Point of care	361	337	512	321
21	Primary care	17394	10900	18822	5655
22	Family practice	34800	1279	29619	453
23	General practice	13076	5774	10308	2456
24	Laboratory setting	545	387	373	325
25	Physicians office testing	6	0	6	1
26	18 or 19 or 20 or 21 or 22 or 23 or 24 or 25	53758	16467	48777	8619
27	12 and 26	208	253	398	103
28	Precision	20840	29510	12713	15108
29	Accuracy	59642	81180	43812	37226
30	Quality control	20353	7636	18631	7006
31	Quality assurance	7270	5024	8576	3628
32	28 or 29 or 30 or 31	98784	114231	76348	57126

Appendix C Search History for the Cochrane Library

Search term: (((((CHOLESTEROL or LIPOPROTEINS) or TRIGLYCERIDES) or LIPIDS) and ((((((BLOOD next (CHEMICAL next ANALYSIS)) or SERUM) or BLOOD) or PLASMA) or FINGERSTICK) or (CAPILLARY next BLOOD))) and ((((PATIENT or (POINT next (OF next CARE))) or (PRIMARY next CARE)) or (FAMILY next PRACTICE)) or (GENERAL next PRACTICE))) [No restrictions]

DATABASE	HITS [Total]
The Cochrane Database of Systemic Reviews	
Complete reviews	
Protocols	49 [923]
Database of Abstracts of Reviews of Effectiveness	19 [827]
Abstracts of quality assessed systematic reviews	
Other reviews: bibliographic details only	25 [1899]
The Cochrane Controlled Trials Register	0 [799]
(CENTRAL/CCTR)	
References	
Medical Editors Trial Amnesty	970 [290256]
The Cochrane Methodology Register	0 [2]
References	
About the Cochrane Collaboration	1 [1349]
The Cochrane collaboration	
Collaborative review groups – CRGs	0 [1]
Fields	8 [50]
Methods groups	1 [10]
Networks	1 [16]
Centres	0 [1]
Sources of support	0 [15]
Health Technology Assessment Database (HTA)	0 [1]
Abstracts by INAHTA and other health care technology agencies	
NHS Economic Evaluation Database (NHS EED)	2 [1978]
Abstracts of economic evaluations of health care interventions	38 [5656]

Appendix D List of Databases Searched

- Medline (see Appendix A for search terms used) Extensive search produced a number of interesting articles.
- Current Contents (see Appendix A for search terms used) Extensive search produced papers with a large overlap with Medline.
- HealthSTAR (see Appendix A for search terms used) Extensive search produced a few articles previously not found with other searches.
- Pubmed - Limited search produced six new articles.
- EMBASE - Limited searches retrieved articles generally identified elsewhere.
- Cochrane Library (see Appendix B for search history) Extensive search produced three new articles.
- NLM Locator Plus - Limited search produced two new articles.
- BIOSIS (see Appendix A for search terms used) - Extensive search produced one new article.
- British Columbia Office of Health Technology Assessment (BCOHTA) - Limited search produced one new article.
- Canadian Coordinating Office for Health Technology Assessment (CCOHTA) - Limited search produced no new articles.
- Alberta Heritage Foundation for Medical Research - no relevant articles found.
- Health Services Utilization and Research Commission (HSURC) - Search produced no relevant articles.
- Institute for Clinical and Evaluative Sciences in Ontario (ICES) Search produced no relevant articles.
- Manitoba Centre for Health Policy Evaluation (MCHPE) - Search produced no relevant articles.
- International Network of Agencies for Health Technology Assessment (INAHTA) – Search produced no new articles.
- Centre for Health Program Evaluation (CHPE, Monash University) - no relevant articles found.
- Australian Institute of Health and Welfare - no relevant articles found.
- Swedish Council on Technology Assessment in Health Care (SBU) - no relevant articles found.

- World Health Organisation (WHO) - no relevant articles found.
- Health Canada - no relevant articles found.
- Health Economics Research Group (Brunel University)
- International Society for Technology Assessment in Health Care (ISTAHC) - Search produced three new articles.
- NHMRC Publication List - no relevant articles found.
- National Health Service (NHS) - no relevant articles found.
- US Office of Technology Assessment (OTA) - no relevant articles found.
- National Coordinating Centre for Health Technology Assessment (NCCHTA) - no relevant articles found.

Appendix E Search History for Other Searches

Fingerstick vs venous blood

	Search History	EMBASE
1	Fingerstick	71
2	Capillary blood	869
3	1 or 2	922
4	Venous blood	3697
5	Whole blood/ serum/ plasma	7983
6	4 or 5	159
7	Cholesterol	37069
8	Lipids/ lipoproteins	26224
9	7 or 8	55073
10	3 and 6 and 9	7

Cost-effectiveness

	Search History EMBASE 1980 to 2001 Week 11	Results
1	Cost effectiveness analysis/	21276
2	Cost benefit analysis/	11968
3	Cost minimisation analysis/ or cost minimisation.mp.	334
4	Cost utility analysis/	439
5	1 or 2 or 3 or 4	32184
6	NEAR PATIENT TEST$.mp.	105
7	POINT OF CARE TEST$.mp.	162
8	OFFICE TEST$.mp.	95
9	6 or 7 or 8	358
10	5 and 9	48
11	Cholesterol/ or cholesterol.mp.	78338
12	10 and 11	2
13	from 12 keep 2	1

Cost-effectiveness (cont.)

	Search History MEDLINE 1966 to December Week 4 2000	Results
1	Cost-benefit analysis/ or cost effectiveness.mp.	23268
2	COST MINIMISATION.mp.	31
3	COST UTILITY.mp.	340
4	Economics, medical/ or economic evaluation.mp.	5037
5	Economics, medical/ or Technology assessment, biomedical/ or economic evaluation.mp.	7247
6	2 or 3 or 4 or 5 or 6	29570
7	Point-of-care systems/ or near patient test.mp.	719
8	OFFICE TEST.mp.	32
9	8 or 9	751
10	Cholesterol/ or cholesterol.mp.	104640
11	7 and 10 and 11	1
12	10 and 11	5
13	7 and 10	44
14	from 14 keep 44	1

Near Patient Testing

	Search History	Results	
		CINAHL	Embase
1	near patient test$.tw.	9	87
2	Point-of care testing/	195	-
3	point of care test$.tw.	78	145
4	office test$.tw.	9	38
5	1 or 2 or 3 or 4	221	266
6	limit 5 to human	-	222
7	limit 6 to English language	-	211
8	6 not 7	-	11
9	limit 7 to abstracts	-	10
10	7 or 9	-	221
11	cholestech.tw.	1	-
12	5 or 11	222	-

Appendix F Supporting Committee

Supporting committee MSAC application 1026 Cholestech LDX

Associate Professor John Simes (Chair) BSc(Med), MBBS, MD, FRACP NHMRC Clincal Trials Centre	Member of MSAC
Professor Philip Barter MBBS, MRACP, PhD, FRACP Cardiovascular Investigation Unit Royal Adelaide Hospital	Nominated by the National Heart Foundation
Associate Professor Sydney Bell MBBS, FRCPA, MD Area Director of Microbiology South East Sydney Area Health Service	Nominated by the Pathology Services Table Committee
Dr Jonathan Cohen MBBS, FRACGP, MFamMed General Practitioner	Nominated by the Royal Australian College of General Practitioners
Dr Jane Cook MBBS, FRACGP Medical Officer, Medicare Benefits Branch Department of Health and Ageing	Medical Advisor to the Department of Health and Ageing
Professor Brendon Kearney FFPHM, FACHSE, MBBS, MRACP, FRACP, FRACMA Executive Director Statewide Department of Human Services	Member of MSAC
Dr John Primrose MBBS, FRACR, MRACR Medical Officer, Diagnostics and Technology Branch Department of Health and Ageing	Medical Advisor to MSAC
Associate Professor David Sullivan MBBS, FRACP,FRCPA Department of Clinical Biochemistry Royal Prince Alfred Hospital	Nominated by the National Heart Foundation
Professor David Thomas BMedSc, MBBS,MRACP, MAACB, FRACP, FRCPA Division of Laboratory Medicine Women's and Children's Hospital	Nominated by the Royal College of Pathologists of Australia
Mr Cyril Wyndham Consumer Representative	Nominated by the Consumers' Health Forum of Australia

Appendix G Sample evaluation form

Reference Details							
Objectives							
Quality			Yes		No		NR
1. Did the study use a random sample of participants?							
2. Were clinical outcomes subsequent to the test results evaluated?							
3. Was the test being evaluated compared to a valid comparator test?							
4. Was the test and its comparator measured independently (blind) of each other?							
5. Was the choice of patients who were assessed by the comparator test independent of the test's results?							
6. Were both tests (ie that being evaluated and its comparator) conducted prior to any interventions being started with knowledge of test results?							
Publication Type	Journal		Abstract		Other		
Year of study	1991						
Sample size	N/A						
Study design	Prospective				Retrospective		
Comparator test							
Cholestech Test	Cholesterol		Triglyceride		HDL-cholesterol		
Setting	Primary care		Hospital		Not reported		
Test material used	Capillary blood (fingerstick)			plasma	venous		
Raw data	yes			No			
Results by: patient subgroups sample type by operator	 yes yes yes			 No No No			
Patient spectrum contribution (age, sex, disease severity)	NR						
Co-morbid conditions.	NR						
% excluded because test was infeasible or result indeterminate	NR						
Primary estimates (means and standard deviations)	Cholesterol (mmol/L) Range: Mean: SD:		Triglyceride Range: Mean: SD:		HDL-cholesterol Range: Mean: SD:		
Secondary estimates (% bias/ error, Coefficient of variation etc).	Cholesterol		Triglyceride		HDL-cholesterol		

Appendix H Accuracy and Precision Data

Summary of the accuracy and precision data for the Cholestech LDX in whole blood/plasma/serum

Reference	Test	Range (mmol/L)	(*n*)	CV	%Bias (CI)	Total Error	N Replicates	Score
Miller *et al.*, 1992	HDL	0.44-2.72	100	NR	-3.0 (-17.6-11.6%)		1	4
Carlson *et al.*, 1993	TC	NR	50	3.1-3.6%	NR		2 levels control material for CV	2
	HDL	NR	50	4.4-8.6%	NR			
	TG	NR	41	5.1-5.7%	NR			
Hewett, 1993	TC	NR	80	1.6-3.1%	-1%	4.1-7.1	NR	0
	HDL	NR	78	1.9-4.9%	-2%	5.7-11.6		
	TG	NR	79	2.1-4.0%	-1%	5.1-8.8		
Rogers *et al.*, 1993	TC	3.89-6.37	18	1.6%*	+4.3%	7.44	1	4
Gregory *et al.*, 1994	TC	3.24-9.32	20-21	3.9%	-3.2%	10.8	NR	4
Cobbaert *et al.*, 1994	TC	NR	43	2.5-2.9%	<3%		2	3
	HDL	NR	43	3.5-4.3%				
	TG	NR	37	3.9-6.0%				
Malkus, 1994	HDL	0.54-2.43	20	NR	+8.4 (-22.2-66.0%)#		NR	3
Cummings *et al.*, 1994	TC	3.4-8.7	40	NR	LR		NR	2
	HDL	0.5-1.9	40	NR	LR			
	TG	0.5-5.2	40	NR	LR			
Blunt *et al.*, 1994	HDL	15-100	31	<5.0%	LR			1

Summary of the accuracy and precision data for the Cholestech LDX in whole blood/plasma/serum (cont.)

Reference	Test	Range (mmol/L)	(*n*)	CV	%Bias (CI)	Total Error	N Replicates	Score
Tan, >1995	TC	4.0-8.8	24	NR	+6.3 (-1.4-20.8%)#		2	2
	HDL	0.4-2.5	24	NR	+3.7 (-14.3-23.1%)#			
Cholestech Corporation, 1995	TC	NR	NR	2.5%	NR		NR	1
	HDL	NR		4.1%	NR			
	TG	NR		2.6%	NR			
Cholestech Corporation, 1995	TC	NR	10	2.0%	NR		NR	3
	HDL	NR	10	4.3%	NR			
	TG	NR	10	3.7%	NR			
Kafonek *et al.*, 1996	TC	NR	100	5.0%	+5.5%	15.3	3 serial	4
	HDL	NR	100	5.8%	+6.1%	17.5		
	TG	NR	100	5.2%	+14.2%	24.4		
Issa, 1996	TC	NR	45	NR	+1.6%		NR	3
	HDL	NR		NR	-2.74%			
	TG	NR		NR	+2.11%			
Bard *et al.*, 1997	TC	3.5-8.8	40	1.4-4.1%	+3.6-4.2%	6.3-15.4	4	3
	HDL	0.65-2.33	40	4.6-5.8%	+4.6-6.7%	11.5-20.4	2 different machines; 2 operators	
	TG	0.60->7.35	37	3.5-5.6%	+6.2-8.0%	14.8-23.9		
Volles *et al.*, '98	TC	~3.0-8.4	100	4.0%	+2.1%	9.9	NR	4
Shephard, 2000	TC	3.1-8.5	50	0.9-3.5%	-1.2 (-15.9-14.9%)#	5.5	1	4
	HDL	1.6-5.6	49	6.3-7.9%	+2.7 (-16.4-31.7%)#	16.6		
	TG	0.5-7.8	50	1.6-2.5%	+1.0 (-17.1-11.7%)#	5.0		

*Quality control sera used, not whole blood; #Calculated value

Summary of the accuracy and precision data for the Cholestech LDX in capillary blood

Reference	Test	Range (mmol/L)	(*n*)	CV	%Bias	Total Error	N Replicates	Score
Miller *et al*., 1992	HDL	0.44-2.72	100	NR	-1.0% (-21.2-19.2%)		1	4
Rogers *et al*., 1993	TC	3.9-6.4	18	as above	+1.92%	5.1	1	4
Drimmer, 1995	TC	~3.1-6.8	47	2.3-4.2%**	LR		1	5
	HDL	~0.4-2.1	45	13.8 11.9%**	LR			
Cholestech Corporation, 1995	TC	<2.6-8.8	60	NR	+2.3%		NR	3
	HDL	0.5->2.6	60	NR	+1.9%			
	TG	<0.5-4.0	60	NR	-5.0%			
Cholestech Corp., 1995	TC	4.1-7.0	17	NR	+0.6 (-6.5-8.9%)		NR	3
	HDL	0.5-2.0	17	NR	+0.3 (-9.3-12.5%)			
Kafonek *et al*., 1996	TC	NR	100	as above	-0.3%	9.5	3 serial	4
	HDL	NR	100		+2.2%	13.6		
	TG	NR	100		+12.3%	22.5		
Bard *et al*., 1997	TC	3.5-8.8	40	as above	+3.8-5.0%	6.5-16.2	4	3
	HDL	0.6-2.3	40		+6.8-13.1%	13.7-26.8	2-different machines	
	TG	0.6->7.3	37		+8.4-14.4%	17-30.8	2-different operators	
Volles *et al*., 1998	TC	~3.0-8.4	100	as above	+1.6%	9.4	NR	4
Shephard, 2000	TC	3.1-8.5	50	0.9-3.5%	-1.9 (-7.7-7.4)#	6.2	1	4
	HDL	1.6-5.6	49	6.3-7.9%	+4.8 (-16.5-25%)#	18.7		
	TG	0.5-7.8	50	1.6-2.5%	+1.1 (-13.1-29.2%)#	5.1		

**Day to day precision #Calculated value

Appendix I Calculation of overall estimates for CV, %bias and total error

In order to evaluate how the studies compared with the NCEP guidelines when all results were combines, an overall estimate of the CV, %bias and hence an overall measure of total error were calculated.

A weighted average of the CV's was deemed to be most appropriate. The weight was chosen from the following candidates (a) weights all equal to 1, (b) the square roots of the sample size and (c) the sample size. In the absence of any measures of the variability (or statistical "information") of estimates, these were thought to be the most appropriate. Note that (a) leads to the arithmetic mean and (c) is the result if the weight is the inverse of the variance of each estimate when the variances are assumed to be the same.

Percent bias was assumed to have been calculated by averaging the %bias over all individuals. The overall %bias was calculated by summing the total (not average) %bias and averaging the result.

The overall total error (TE) was calculated as TE=overall %bias + 1.96 x overall CV.

The results for the weights described above are tabulated below:

Reading Type	Estimates of CV	Number of studies	Estimates of %bias	Estimates of total error
TC	3.36	10	2.05	8.64
HDL	5.14	8	1.47	11.69
TG	4.14	7	5.16	13.27
TC	3.18	10	2.05	8.29
HDL	5.2	8	1.47	11.67
TG	4.13	7	5.16	13.25
TC	2.99	10	2.05	7.9
HDL	5.15	8	1.47	11.56
TG	4.11	7	5.16	13.22

The results are similar for all weights, suggesting any method is appropriate. Therefore, the results for method (a) have been graphed and referred to in the main body of the text.

Appendix J Recommendations for obtaining fingerstick specimens

Phlebotomist preparation:

Assemble the necessary supplies (gloves, antiseptic pads, lancets, capillaries, band-aids). A phlebotomy chair with arm support is convenient. Wear gloves and change them between patients.

Patient preparation:

Have patients sit quietly for at least five minutes before blood collection. Values change with standing or reclining. This is a good time to have the patient complete enrolment forms or read relevant literature. If patients must move a short distance from waiting area, have them walk quietly to the phlebotomy area.

Check hands:

Warm hands bleed better. If the hands are cold, ask the patient to rub them together or shake vigorously for several minutes. Massaging by the phlebotomist can help to relax the hand, straighten fingers and stimulate blood flow.

Select finger:

The non-dominant hand is recommended. The ring finger is usually preferred because of fewer calluses. The middle finger may be better on women and children with small hands. Squeeze and release the chosen fingertip a few times. The "flushing of colour" into the area is an indicator of good blood flow.

Cleansing:

Cleanse end of finger with alcohol or antiseptic pad. With a sterile gauze pad or cotton ball, thoroughly dry the site.

Fingerstick:

Pinch end of finger from the side opposite the puncture site to distract patient and keep skin taut at the puncture site. Use a spring-loaded device with a chisel or blade type lancet and enough force to give a good puncture or incision. Holding the arm palm up, puncture or cut on the upper side corner of the chosen finger up away from the nail bed. Orient the lancet blade to cut across the fingerprint. Hold the lancet tightly against the skin, activate and do not release pressure during the puncture.

Blood collection:

Remove lancet and with sterile gauze wipe away the first drop of blood that can be contaminated with tissue fluid or alcohol. With palm turned down, allow drops to form and touch into capillary or droplet. When collection is complete, place a sterile pad over the puncture site and have the subject maintain pressure. When blood flow has stopped, a band-aid, preferably the spot type can be placed over the site.

Stimulating blood flow:

If blood flow is slow, the following may help:

Lower hand.

Express blood down from the hand toward the finger by progressively squeezing gently and releasing downward across the hand and finger in a "milking" motion. Avoid squeezing the puncture site directly; this can cause dilution with tissue fluid.

Wiping the puncture site with gauze can clear a developing clot and promote flow.

Try pulling cut open carefully with the fingers to restore flow. If flow is still inadequate, sticking another finger may be necessary.

Precautions:

Avoid leaving blood more than 2 or 3 minutes in a capillary tube before analysis. Heparin can be unevenly distributed in the tube allowing clotting to occur in some portions.

Contaminated materials should be safely discarded according to accepted guidelines.

Source: Warnick *et al.*, 1994

Appendix K Variables in the modelled evaluation

Sensitivity and specificity of the Cholestech LDX test (Monte Carlo simulation)

- The Monte Carlo simulation assigns a patient entering the simulation a true cholesterol level. This cholesterol level is selected from the distribution of cholesterol levels in the Australian population (RFPS 1989).

- The model then generates two tests results for the patient. The test results are based on a total error with a 95 percent confidence interval of ±8 percent. A diagnosis/classification is made on the basis of the average of the two results. A patient is classified with elevated cholesterol if the average of the two results is ≥6.5 mmol/L. A patient is classified with normal cholesterol if the average of the two results is <6.5 mmol/L. The classification was then compared with the patient's true cholesterol.

- This process was simulated 10,000 times for each cholesterol level between 2.5 mmol/L and 9.4 mmol/L. In each simulation, the number of incorrect classifications were counted. The probability of an incorrect classification is thus determined for each true cholesterol level.

- A total probability of error for the negative population (1 - specificity) is calculated as a weighted average of all the probabilities of error across the range of true negative cholesterol levels.

- A total probability of error for the positive population (1 - sensitivity) is calculated as a weighted average of all the probabilities of error across the range of true positive cholesterol levels.

- The calculated sensitivity and specificity of the Cholestech LDX test at a threshold cholesterol level of 6.5 mmol/L were 0.928 and 0.974 respectively. The data below show the calculation of the specificity and sensitivity of the Cholestech LDX test with ±8 percent total error.

Calculating probability of misclassification in a true negative population

True cholesterol	Proportion of total population with this cholesterol level	NEGATIVE population with this cholesterol level	Prob of incorrect classification
A	B	C	D
2.5	0.1%	0.2%	0.00000
2.6	0.1%	0.2%	0.00000
2.7	0.1%	0.2%	0.00000
2.8	0.1%	0.2%	0.00000
2.9	0.1%	0.2%	0.00000
3.0	0.8%	1.0%	0.00000
3.1	0.8%	1.0%	0.00000
3.2	0.8%	1.0%	0.00000
3.3	0.8%	1.0%	0.00000
3.4	0.8%	1.0%	0.00000
3.5	0.8%	1.0%	0.00000
3.6	0.8%	1.0%	0.00000
3.7	0.8%	1.0%	0.00000
3.8	0.8%	1.0%	0.00000
3.9	0.8%	1.0%	0.00000
4.0	2.6%	3.2%	0.00000
4.1	2.6%	3.2%	0.00000
4.2	2.6%	3.2%	0.00000
4.3	2.6%	3.2%	0.00000
4.4	2.6%	3.2%	0.00000
4.5	2.6%	3.2%	0.00000
4.6	2.6%	3.2%	0.00000
4.7	2.6%	3.2%	0.00000
4.8	2.6%	3.2%	0.00000
4.9	2.6%	3.2%	0.00000
5.0	3.6%	4.2%	0.00000
5.1	3.6%	4.2%	0.00000
5.2	3.6%	4.2%	0.00000
5.3	3.6%	4.2%	0.00000
5.4	3.6%	4.2%	0.00000
5.5	3.6%	4.2%	0.00000
5.6	3.6%	4.2%	0.00000
5.7	3.6%	4.2%	0.00000
5.8	3.6%	4.2%	0.00000
5.9	3.6%	4.2%	0.00050
6.0	2.2%	2.6%	0.00210
6.1	2.2%	2.6%	0.01190
6.2	2.2%	2.6%	0.04870
6.3	2.2%	2.6%	0.13910
6.4	2.2%	2.6%	0.29160
6.5	2.2%	2.6%	0.50000
TOTALS	**83.8%**	**100%**	**0.026**

Monte Carlo True cholesterol level; B Risk Factor Prevalence Survey 1989 (p60)
C divided by SUM(B); D simulation. Total is sum of the products of columns C and D

Calculating expected probability of misclassification in a true positive population

True cholesterol	Proportion of total population with this cholesterol level	POSITIVE population with this cholesterol level	Prob. of incorrect classification (Monte Carlo Simulation)
A	B	C	D
6.6	2.2%	13.5%	0.30660
6.7	2.2%	13.5%	0.14790
6.8	2.2%	13.5%	0.05860
6.9	2.2%	13.5%	0.02090
7.0	0.6%	3.9%	0.00610
7.1	0.6%	3.9%	0.00150
7.2	0.6%	3.9%	0.00060
7.3	0.6%	3.9%	0.00010
7.4	0.6%	3.9%	0.00000
7.5	0.6%	3.9%	0.00000
7.6	0.6%	3.9%	0.00000
7.7	0.6%	3.9%	0.00000
7.8	0.6%	3.9%	0.00000
7.9	0.6%	3.9%	0.00000
8.0	0.1%	0.6%	0.00000
8.1	0.1%	0.6%	0.00000
8.2	0.1%	0.6%	0.00000
8.3	0.1%	0.6%	0.00000
8.4	0.1%	0.6%	0.00000
8.5	0.1%	0.6%	0.00000
8.6	0.1%	0.6%	0.00000
8.7	0.1%	0.6%	0.00000
8.8	0.1%	0.6%	0.00000
8.9	0.1%	0.6%	0.00000
9.0	0.1%	0.4%	0.00000
9.1	0.1%	0.4%	0.00000
9.2	0.1%	0.4%	0.00000
9.3	0.1%	0.4%	0.00000
9.4	0.1%	0.4%	0.00000
TOTALS	16.2%	100.0%	0.072

A **True cholesterol level**

B **Risk Factor Prevalence Survey 1989 (p60)**

C **B divided by SUM(B)**

D **Monte Carlo simulation. Total is sum of the products of columns C and D**

Calculating the testing rates in patients with normal and elevated cholesterol - For laboratory based testing

A	Cohort (Number of GP consultations)	1,000
B	Number of GP consultations which include a cholesterol test	23
C	Proportion of all cholesterol tests which show elevated cholesterol	42%
D	Number of cholesterol tests being performed in patients with elevated cholesterol	9.7
E	Number of cholesterol tests being performed in patients with normal cholesterol	13.3
F	Proportion of Australian population with elevated cholesterol (≥6.5 mmol/L)	15.10%
G	Number of GP consultations performed on patients with elevated cholesterol	151
H	Number of GP consultations performed on patients with elevated cholesterol	849
I	Proportion of GP consultations performed on patients with elevated cholesterol which include a cholesterol test	0.0640
J	Proportion of GP consultations performed on patients with normal cholesterol which include a cholesterol test	0.0157

The calculations are presented for a cohort of 1,000 GP consultations.

General Practice Activity in Australia 1999-2000 p88

Smith *et al.* 1996

B × C

B × (1-C)

Risk Factor Prevalence Survey 1989

A × F

A × (1 - F)

D / G

E / H

Calculating the testing rates in patients with normal and elevated cholesterol - For near patient based testing

K	Cohort (Number of GP consultations)	1,000
L	Growth in cholesterol testing due to availability of NPT	82.10%
M	Number of GP consultations which include a cholesterol test	42
N	Number of new tests due to NPT	19
O	Number of tests being performed in patients with elevated cholesterol (before NPT)	9.7
P	Proportion of new tests being performed in patients with elevated cholesterol	21.0%
Q	Number of new tests being performed in patients with elevated cholesterol	4.0
R	Total number of tests being performed in patients with elevated cholesterol	13.6
S	Number of tests being performed in patients with normal cholesterol (before NPT)	13.3
T	Proportion of new tests being performed in patients with normal cholesterol	79.0%
U	Number of new tests being performed in patients with normal cholesterol	14.9
V	Total number of tests being performed in patients with normal cholesterol	28.3
W	Proportion of GP consultations performed on patients with elevated cholesterol which include a cholesterol test	0.0902
X	Proportion of GP consultations performed on patients with normal cholesterol which include a cholesterol test	0.0333

The calculations are presented for a cohort of 1,000 GP consultations.

Rink *et al.* 1993

B × (1+ L)

M - B

D

Assumption

N × P

O+ Q

E

1 - P

N × T

S + U

U / G

V / H

Total medical resource cost per Cholestech test

Medical resource	Unit Cost	Reference
Initial GP consultation (standard) - 30% of tests	$\$27.00 \times 30\%$	MBS Item 23
Initial GP consultation (long) - 70% of tests	$\$48.75 \times 70\%$	MBS Item 36
Cholesterol test (Cholestech)	$14.90	Appendix L (below)
Total cost per test	$57.13	

Total medical resource cost per laboratory performed cholesterol test

Medical resource	Unit Cost	Reference
Initial GP consultation (standard)	$27.00	MBS Item 23
Specimen collection	$14.33	MBS Items 73907 (60%), 73915 (40%)
Cholesterol test (pathology lab)	$11.40	MBS Item 66521
Follow-up GP consultation - 70% of tests	$\$27.00 \times 30\%$	MBS Item 23
Total cost per test	$71.63	

Expected item fee per near patient cholesterol test performed

The appropriate cost per near-patient cholesterol test was conservatively estimated. The costing assumes a general practice will recoup capital expenditure over a seven-year period with a risk free rate of return of five percent per annum (compounded monthly). It is likely that the capital expenditure will become superseded over less than seven years and that a higher rate of return would be expected. This would imply that the fee charged per test would be greater than the $14.90 used in the economic evaluation.

GP costs related to near patient cholesterol testing

	Parameter	Value	Reference
A	Capital cost of Cholestech equipment	$3,900	Applicant
B	Annual return on investment	5.0%	RBA cash target rate (April 2001)
C	Life time of Cholestech equipment	7 years	Assumption
D	Scrap value of capital equipment	$ 0	Assumption
E	Capital cost to be recuperated over life time of machine	$5,530	$3,900 compounded monthly at 5% for 7 years
F	GP consultations per surgery per year	6,500	Department of Health and Aged Care
G	Cholesterol tests per 100 consultations	4.19	Britt *et al.* (2000) plus 82.1% growth
H	Cholesterol tests per year	272	F / 100 × G
I	Cholesterol tests over lifetime of machine	1,906	H × C
J	Capital costs to be recuperated per test	$2.90	E × I
K	Consumable (cartridge) costs per test	$12.00	Applicant
	Total cost per test performed	$14.90	J + K

RBA: Reserve Bank of Australia

Annual cost of lipid lowering medications

Medication	PBS Code	Number of scripts (PBS 2000)	Proportion of total scripts (PBS 2000)	Dispense price per script	Dispense price per year
A	**B**	**C**	**D**	**E**	**F**
atorvastatin 10 mg	8213G	1,739,057	17%	$42.87	$514.44
atorvastatin 20 mg	8214H	1,601,980	15%	$59.35	$712.20
atorvastatin 40 mg	8215J	794,504	8%	$83.17	$998.04
cerivastatin 200 mcg	8303B	45,179	0%	$36.21	$434.52
cerivastatin 300 mcg	8304C	177,195	2%	$42.46	$509.52
cerivastatin 400 mcg	8419D	372	0%	$50.60	$607.20
fluvastatin 20 mg	8023G	127,696	1%	$28.77	$345.24
fluvastatin 40 mg	8024H	112,435	1%	$33.87	$406.44
pravastatin 10 mg	2833D	226,148	2%	$34.86	$418.32
pravastatin 20 mg	2834E	664,032	6%	$52.31	$627.72
pravastatin 40 mg	8197K	467,351	5%	$78.44	$941.28
simvastatin 10 mg	2011W	1,446,555	14%	$42.12	$505.44
simvastatin 20 mg	2012X	2,197,935	21%	$58.18	$698.16
simvastatin 40 mg	8173E	716,583	7%	$81.36	$976.32
simvastatin 5 mg	2013Y	66,496	1%	$30.80	$369.60
simvastatin 80 mg	8313M	2,007	0%	$114.53	$1,374.36
TOTALS	NA	10,385,525	100%	NA	$671

A. Serum lipid reducing agent Schedule of Pharmaceutical Benefits 2001

B. Health Insurance Commission item statistics (January to December 2000)

C. C / SUM(C)

D. Schedule of Pharmaceutical Benefits (February 2001)

E. E × 12. Total F is the sum of the products of Columns D and F.

Cost-effectiveness of lipid lowering medication in the modelled evaluation

Cost-effectiveness parameter	Value	Reference
Incremental cost of lipid lowering medication	$671	Appendix L
Annual probability of CHD death with treatment	0.0026	WOSCOPS trial
Annual probability of CHD death without treatment	0.0038	WOSCOPS trial
Life expectancy of treated patient	25 years	Australian life tables (age 56 years)
Discounted life expectancy	14.1 years	D discounted by 5% per annum
Discounted life years gained with treatment	14.057 years	$(1 - B) \times E$
Discounted life years gained without treatment	14.039 years	$(1 - C) \times E$
Incremental life years gained with treatment	0.018 years	F - G
Incremental cost per life year gained of treatment	$36,622	A / H

Disaggregated results of the decision tree

Proportion of patients reaching each endpoint of the decision tree

In the NPT arm more patients received a total cholesterol test (Endpoints A to G, J to L), more patients with elevated cholesterol were detected (Endpoints A to E) and fewer patients died (Endpoints C, E, G, I).

Endpoint	Description of endpoint	Patients reaching this endpoint - percent	
		NPT Testing	Lab Testing
A	The patient was correctly detected with elevated cholesterol. The patient WAS NOT prescribed medication. The patient was alive after one year.	0.007589	0.005798
B	The patient was correctly detected with elevated cholesterol. The patient WAS prescribed medication. The patient continued medication for one year and was alive after one year.	0.002029	0.001550
C	The patient was correctly detected with elevated cholesterol. The patient WAS prescribed medication. The patient continued medication for one year. The patient suffered a CHD death.	0.000005	0.000004
D	The patient was correctly detected with elevated cholesterol. The patient was prescribed medication. The patient discontinued medication and was alive after one year.	0.003014	0.002303
E	The patient was correctly detected with elevated cholesterol. The patient WAS prescribed medication. The patient discontinued medication and suffered a CHD death.	0.000012	0.000009
F	The patient was incorrectly assessed as having normal cholesterol. The patient received no treatment. The patient was alive after one year.	0.000980	0.000000
G	The patient was incorrectly assessed as having normal cholesterol. The patient received no treatment and suffered a CHD death.	0.000002	0.000000
H	The patient was not tested and received no treatment. The patient was alive after one year.	0.137156	0.141116
I	The patient was not tested and received no treatment. The patient suffered a CHD death.	0.000214	0.000220

J	The patient was correctly assessed with normal cholesterol	0.027512	0.013329
K	The patient was incorrectly assessed as having elevated cholesterol. The patient did not receive any treatment. The patient wads alive after one year.	0.000441	0.000000
L	The patient was incorrectly assessed as having elevated cholesterol and was prescribed lipid lowering medication. The patient was alive after one year.	0.000294	0.000000
M	The patient was not tested and was alive after one year	0.820753	0.835671
TOTAL		**1.000000**	**1.00000**

Medical resource utilisation and costs at each endpoint of the decision tree

Endpoint	Near patient testing		Laboratory testing	
	Medical resources	**Cost**	**Medical resources**	**Cost**
A	30% standard GP consultation	$ 8.10	Standard GP consultation	$ 27.00
	70% long GP consultation	$ 34.13	Specimen collection	$ 14.33
	Cholesterol test	$ 14.90	Cholesterol test	$ 11.40
	Total	$ 57.13	70% follow-up consultation	$ 18.90
			Total	$ 71.63
B	GP consultation and test	$ 57.13	GP consultation and test	$ 71.63
	1.821 follow-up cholesterol tests	$104.03	1 follow-up cholesterol test	$ 71.63
	Lipid lowering medication	$671.00	Lipid lowering medication	$ 671.00
	Total	$832.15	Total	$814.26
C	GP consultation and test	$ 57.13	GP consultation and test	$ 71.63
	1.821 follow-up cholesterol tests	$104.03	1 follow-up cholesterol test	$ 71.63
	Lipid lowering medication	$671.00	Lipid lowering medication	$671.00
	Total	$832.15	Total	$814.26
D	GP consultation and test	$ 57.13	GP consultation and test	$ 71.63
	0.911 follow-up cholesterol tests	$ 52.01	0.5 follow-up cholesterol tests	$ 35.82
	Lipid lowering medication (half year)	$335.50	Lipid lowering medication (half year)	$335.50
	Total	$444.64	Total	$442.95
E	GP consultation and test	$ 57.13	GP consultation and test	$ 71.63
	0.911 follow-up cholesterol tests	$ 52.01	0.5 follow-up cholesterol tests	$ 35.82
	Lipid lowering medication (half year)	$335.50	Lipid lowering medication (half year)	$335.50
	Total	$444.64	Total	$442.95
F	GP consultation and test	$ 57.13	GP consultation and test	$ 71.63
	Total	$ 57.13	Total	$ 71.63
G	GP consultation and test	$ 57.13	GP consultation and test	$ 71.63
	Total	$ 57.13	Total	$ 71.63
H	GP consultation	$ 27.00	GP consultation	$ 27.00
	Total	$ 27.00	Total	$ 27.00

I	GP consultation	$ 27.00	GP consultation	$ 27.00
	Total	$ 27.00	Total	$ 27.00
J	GP consultation and test	$ 57.13	GP consultation and test	$ 71.63
	Total	$ 57.13	Total	$ 71.63
K	GP consultation and test	$ 57.13	GP consultation and test	$ 71.63
	Total	$ 57.13	Total	$ 71.63
L	GP consultation and test	$ 57.13	GP consultation and test	$ 71.63
	Lipid lowering medication	$671.00	Lipid lowering medication	$671.00
	Total	$728.13	Total	$742.63
M	GP consultation	$ 27.00	GP consultation	$ 27.00
	Total	$ 27.00	Total	$ 27.00

Abbreviations

CHD	Coronary heart disease
CV	Co-efficient of variation
GP	General Practitioner
HDL-C	High-density lipoprotein-cholesterol
LDL-C	Low-density lipoprotein-cholesterol
MBS	Medicare Benefits Scheme
NCEP	National Cholesterol Education Program
NHMRC	National Health & Medical Research Council
NPT	Near patient test
RCPA-AACB	Royal College of Pathologists of Australasia - Australasian Association of Clinical Biochemists
TC	Total cholesterol
TE	Total error
TG	Triglyceride
VLDL-C	Very low-density lipoprotein cholesterol
WOSCOPS	West of Scotland Coronary Prevention Study

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