

# CARDIOVASCULAR RISK SCREENING AND LIPID-LOWERING TREATMENT IN THEIR ECONOMIC CONTEXT

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## EXECUTIVE SUMMARY

This report sets decision-making about cardiovascular risk screening and clinical management into an economic context. It focuses on risk screening and lipid-lowering therapy for individuals without known cardiovascular disease, because a risk screening programme is recommended in these cardiovascular guidelines and lipid-lowering statin therapy has recently been made available for primary prevention of cardiovascular disease in New Zealand. We assess the economic impact for New Zealand of a 'screen and treat' strategy that is recommended by the NZGG Guideline Development Team for the assessment and management of cardiovascular risk, guided partly by these economic analyses. Therapy is maintained for 5 years and benefits are evaluated over the lifetime of the treated cohort. The comparator is clinical practice prior to April 2002, when access to statins was largely restricted to persons with cardiovascular disease.

The guideline recommends comprehensive global cardiovascular risk screening of men aged 45 years or over and women aged 55 years or over without known cardiovascular disease; known smokers and Māori, Pacific peoples and people from the Indian subcontinent are to be screened 10 years earlier. People with diabetes are to be screened at diagnosis. We report the benefits and costs of a 5-year screening programme coupled with 5 years of lipid-lowering therapy for all eligible men and women. We assume that equal numbers of individuals are identified each year over the 5-year period following introduction of the guideline. We also assume that the results of previous lipid tests (if any) will need to be confirmed under the new guideline.

The analysis takes a health care perspective and includes costs to the Ministry of Health as the major third party funder plus private expenditure on health. It excludes non-medical costs such as patient time and transportation and indirect costs including loss of income and/or productivity.

Cardiovascular risk is estimated using a Framingham Heart Study risk equation that predicts the risk of 'any incident cardiovascular event' including myocardial infarction, stroke, angina, transient ischaemic attack, peripheral vascular disease or congestive heart failure. This equation, which is the basis of the previous and the revised guidelines, predicts first cardiovascular admissions and deaths reasonably accurately at a population level. The analysis of receiver operator characteristics of the Framingham Heart Study risk equation indicates that at clinically useful treatment thresholds, its specificity is over 90% but its sensitivity is poor. This highlights the need to complement targeted therapy with population risk reduction strategies.

A risk screening and treatment programme is assumed to be implemented gradually over 5 years and we assume that equal numbers of individuals are screened over years 1 to 5. We also assume that risk screening requires 5 minutes of general practitioner (GP) time and/or practice nurse time plus a full lipid profile in duplicate and one blood glucose test. Individuals who are identified by the screening programme as having 5-year cardiovascular risk greater than 15% are treated for 5 years with simvastatin\* at a starting dose of 20 mg per day titrated to 40 mg per day for one-third of these individuals. Individuals with 'extreme' lipid profiles defined as TC:HDL greater than 8 mmol and/or total cholesterol greater than 8 mmol/L are offered atorvastatin 40 mg per day, regardless of their estimated risk. Drug acquisition costs comprise contracted prices# plus pharmacy mark-up and dispensing fees.

Liver function (alanine amino-transferase) and creatine kinase tests are utilised before and after initiation of statin therapy. After therapy is instigated, full lipid profiles are obtained quarterly in year 1, then biannually for 4 more years. We assume that monitoring of drug therapy entails 20 minutes of GP time in year 1 then 10 minutes per annum in years 2 to 4.

Over 5 years, this strategy would screen 570,000 men and 350,000 women at a (discounted) 5-year cost of \$25.8m. This includes \$15.3m in laboratory tests plus \$10.5m in GP consultation fees, representing a case load equivalent of 12 additional full-time GPs.

Therapy to prevent or delay cardiovascular events can be multifactorial (ie, lifestyle measures, blood pressure lowering and lipid modifying drugs can be utilised concurrently). We assume that lifestyle modification such as smoking cessation and weight reduction therapy has been attempted and that blood pressure lowering therapy is utilised for high risk individuals with TC:HDL less than 4.5 but with elevated blood pressure. In the base case analysis, individuals are offered lipid-lowering therapy if their 5-year risk is at least 15% and TC:HDL greater than or equal to 4.5 or they have 'extreme' lipid values (total serum cholesterol or cholesterol ratio (TC:HDL) greater than 8.0).

Prevention of cardiovascular events with lipid-lowering therapy avoids hospital admissions and community costs of ongoing medical treatment including quarterly GP consultations and medications such as aspirin, beta-blockers and ACE-inhibitors. The cost of 5 years of hospital admissions with a primary cardiovascular diagnosis following a non-fatal first admission over a 5-year period were obtained from routine statistics, based on WEIS5A, medical and surgical plus assessment, treatment and rehabilitation costs. Case fatality at 30 days, 1 year and 5 years beyond a first cardiovascular admission or death was also obtained from routine statistics. The costs of medication for secondary prevention, excluding simvastatin, were obtained from the Pharmaceutical Schedule and the cost of simvastatin was obtained from PHARMAC. Life expectancy was obtained from period life tables and utility (a single index measure of quality of life) for specified cardiovascular endpoints was obtained from the published literature. All costs and benefits were discounted to present value at 5% per annum.

The summary table shows the 5-year costs, lifetime health benefits and cost utility of the proposed 'screen and treat' strategy compared with clinical practice prior to April 2002. For comparison, it also shows the average and incremental benefits, costs and cost utility of broadening the treatment target to include individuals with risk in the range 10 to 15%.

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\*Nothing in this document is intended to imply that simvastatin and atorvastatin are the only appropriate lipid modifying agents, however these agents are fully reimbursed by PHARMAC and widely prescribed. Fibrates were not evaluated because they are not widely utilised.

\*\*Supplier rebates on simvastatin are excluded

## Summary Table

Benefits, costs and cost-effectiveness of a 'screen and treat' strategy at 15% and 10% treatment thresholds (age 35 – 84, threshold lipid ratio 4.5, discount rate 5% per annum, 2003 dollars) from a health care perspective.

Numbers	Men	Women	Total	NNS (events)
Screened	573,758	347,281	921,039	
Treated (>15% risk)	106,937	48,106	155,043	137
Treated (>10% risk)	179,038	101,004	280,043	106
Treated (10 – 15% risk)	72,101	52,898	124,999	

Benefits	Events averted	Deaths delayed	LYG	QALYs gained	NNT (events)
>15% risk	6716	1885	17,205	21,317	23
>10% risk	8716	2312	21,969	28,107	32
10 – 15% risk	2000	427	4763	6789	

5-year Costs (\$m)	Pharms	Labs	GMS	Co-payments	Hospital cost offset	Net cost
>15% risk	\$63	\$15	\$4	\$29	-\$40	\$70
>10% risk	\$108	\$26	\$6	\$55	-\$53	\$142
10 – 15% risk	\$45	\$12	\$2	\$25	-\$13	\$72

Cost-effectiveness	Cost per event averted	Cost per premature death averted	Cost per life year gained	Cost per QALY
>15% risk	\$10,459	\$37,269	\$4083	\$3295
>10% risk	\$16,263	\$61,303	\$6452	\$5043
10 – 15% risk	\$35,753	\$167,276	\$15,011	\$10,532

Abbreviations: **Co-payments** = patient payments; **GMS** = General Medical Services benefit; **Labs** = laboratory tests; **LYG** = life years gained over a lifetime; **NNS** = number of persons screened and treated to prevent one event in 5 years; **NNT** = number of persons treated to prevent one event in 5 years; **Pharms** = pharmaceuticals; **QALY** = quality adjusted life year.

Compared with no systematic screening and lipid-lowering programme, the recommended 'screen and treat' strategy (at a treatment threshold of 15% absolute risk) would prevent 6716 incident cardiovascular events and 1885 premature deaths. Over the lifetime of the cohort this provides 17,205 life years and 21,317 QALYs. The net 5-year cost of the strategy is \$70m including pharmaceuticals, GP consultations and laboratory tests. Hospital costs avoided over 5 years (including incident and recurrent medical and surgical cardiovascular admissions, AT&R and rural admissions) offset about two-thirds of the net cost of pharmaceuticals.

The cost-effectiveness ratios of \$4083 per life year gained and \$3295 per QALY gained are well within the range of those that have been accepted in reimbursing novel drug therapies in New Zealand. Enlarging the pool of individuals who are eligible for statin treatment by reducing the treatment threshold from 15 to 10% absolute risk increases the QALY benefits by about one-third but doubles the total cost of the strategy.

These analyses assume that adherence to therapy is 80% of that achieved in the *Heart Protection Study*, in which 85% of individuals took at least 80% of the tablets over a 5-year period. In practice, adherence may be even lower, with proportionally lower costs and benefits and slightly higher cost effectiveness ratios. Targetting Māori people at a threshold age 10 years lower than non Māori is likely to be at least as cost effective as targetting non Māori people, but insufficient information is available to estimate cost effectiveness ratios. Even less information is available for peoples from the Pacific or Asia

The cost-effectiveness ratio is very sensitive to the screening age threshold but only moderately sensitive to the treatment thresholds (absolute risk 15% or 10% and lipid ratio TC:HDL 4.5 – 6.5), the 5-year case fatality following an incident cardiovascular event, hospital costs, adherence to treatment and long-term health utilities following an event. The incremental cost per QALY remains less than \$NZ10,000 over a wide range of these values, indicating that a 'screen and treat' strategy is very cost-effective compared to no such strategy. Further work is required to analyse the effects of lifestyle modifications, antiplatelet and blood pressure lowering therapy in conjunction with lipid-lowering therapy in primary prevention of cardiovascular disease.

In conclusion, global screening for cardiovascular risk, coupled with lipid-lowering therapy at a 5-year risk threshold of either 15% or 10% and a lipid ratio TC:HDL greater than 4.5, is as cost-effective as recently funded novel drug therapies in New Zealand and highly cost-effective by international criteria. However, the analysis raises questions about resourcing of statins and laboratory tests and also about GP case loads, especially if the current risk threshold of 10% is maintained. It may also raise equity issues because of differential willingness to accept co-payments on both statins and GP consultations.