Need and projected demand for lipid-modifying agents in New Zealand

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Abstract

Objectives
To assess current and projected need (eligible patient numbers), demand (actual user numbers) and costs of providing lipid modifying agents (LMAs) in New Zealand.

Design
Application of guidelines for LMA use to prevalence data, population projections, possible future changes in prevalence of absolute risk of CHD, average daily drug costs, and estimations of programme coverage (cumulative for presentation rates, rates of identification and optimal management, 5% dietary cholesterol reduction on absolute risk, script uplift rates, and historical differences between expected and actual drug unit volumes by LMA type). Sensitivity analyses with varying prevalence and denominator populations, unchanging absolute risk of CHD, differing dietary cholesterol reductions, differing changes in LMA mix, and reducing statin costs.

Setting
New Zealand, 1996 to 2011.

Subjects
Patients aged 35 to 84, stratified by coronary heart disease status (established CHD, genetic lipoprotein disorders, at-risk levels according to Framingham logistic equation) by age by sex.

Main outcome measures
Numbers of patients eligible, numbers of actual users and pharmaceutical spending (NZ dollars) on fibrates and statins.

Results
An estimated 13.7% of people aged 35-84 are eligible for LMAs, some 221,000 for New Zealand in 1995 and costing $174 million at current drug prices (excluding GST). This includes 91,300 aged 35-69 in NHF groups A and B. By year 2011, overall numbers eligible for LMAs would increase by 22% to reach 269,000 (292,000 if unchanged need in the at-risk group). In practice, 20% of all eligible aged 35-84 would currently receive LMAs, ie 43,600 patients costing $43.4 million (including 32,000 LMA users in groups A and B aged 35 to 69 at $30.5 million). Combining ± 1 standard deviation for prevalence data with 10% and 2.5% average reductions in dietary cholesterol would cause demand to vary between 31,000 and 51,600 ($31-$51 million), while decreasing statin costs by one-third would decrease overall pharmaceutical spending on LMAs to $31 million. Assuming 1995 drug prices but improving programme coverage and changing populations, by year 2011 numbers would reach 75,200 (72% increase) at $75 million costs. However, there could be as many as 80,700 users costing $100 million if unchanged need in the at-risk group with 10% annual change in mix towards statins.

Conclusions
Investing in LMAs represents both significant costs to regional health authorities and large potential health gains to their populations. Targeting LMAs to those with greatest need will produce substantial health gains, since many eligible patients do not receive LMAs. But LMA use must also be prioritised, since some groups will receive much less benefit and other cardiovascular prevention and treatment is more cost-effective. Dietary reductions in total cholesterol will substantially reduce numbers of people needing LMAs.

Introduction

Lipid-modifying agents (LMAs) are used to modify serum lipids in order to prevent and at times reverse arteriosclerosis and its impacts upon the cardiovascular system. LMAs include the fibrate and statin (HMG coA-reductase inhibitor) classes of agents, as well as others. Currently in New Zealand $18 million is spent each year on LMAs (year to date June 1996), 26% higher than the previous year.

Much impetuous to the growth in LMA use has been gained from major guidelines recommending their wider use[1] [2], and publication of recent evidence supporting the overall efficacy of statin drugs. The Scandinavian Simvastatin Survival Study (4S)[3], West of Scotland Coronary Prevention Study (WOSCOPS)[4] and CARE[5] have shown respectively that statins can effectively prevent premature all-cause mortality as well as cardiovascular events in patients with established coronary heart disease (CHD), prevent cardiovascular events in high-risk patients without established CHD, and prevent events in CHD patients with lower baseline total cholesterol levels.

New Zealand's National Heart Foundation (NHF) has recently updated its guidelines for lipid management[6]. PHARMAC, which manages subsidised pharmaceuticals on behalf of New Zealand's four regional health authorities, wished to assess the impact of extending LMA use to those populations suggested by these guidelines and other criteria. To achieve this, PHARMAC developed a model to assess both the likely extent of LMA "need" and programme costs of providing LMAs to those in need who are likely to uptake LMAs ("demand"), both for 1996 and projected to year 2011.

Methods

The model uses "need" criteria derived from the NHF 1996 updated guidelines and PHARMAC's Pharmaceutical and Therapeutics Advisory Committee (PTAC) subcommittee on LMA's suggested thresholds for LMA use. The NHF 1996 guidelines describe "need" as various combinations of age; absolute risk of cardiovascular events; serum total cholesterol; total:HDL cholesterol ratios; and impact of dietary and other modification of lipid and other risk factors. "Absolute risk of cardiovascular events" in turn comprises patients with proven cardiovascular disease; genetic lipoprotein disorders; diabetic nephropathy; and patients otherwise at risk of developing cardiovascular (>20%, 15-20%, 10-15% and <10% 5-year absolute risks). The PTAC subcommittee has recommended that, for patients meeting the NHF criteria, fibrates or statins be prescribed according to total cholesterol levels: for manifest cardiovascular disease, statins for total cholesterol >=6.5 mmol/l, fibrates <6.5 mmol/l; statins for familial hyperlipidaemias, fibrates for familial dysbetalipoproteinaemia; statins for established diabetic nephropathy; for "at risk" patients, statins for total cholesterol >= 8.0 mmol/l, fibrates <8.0 mmol/l.[7] Thus the NHF and PTAC subcommittee criteria combine to describe "need" according to: absolute cardiovascular risk; total cholesterol; total:HDL cholesterol ratio; impact of dietary and other modification of lipid and other risk factors; and class of LMA. This is shown in figure 1. [insert figure 1 near here]

For the model, I grouped the NHF guidelines' groups into three populations:
Population 1: patients with proven CHD ± other arteriosclerotic cardiovascular disease (part of group A of the 1996 NHF guidelines);
Population 2: those with asymptomatic genetic lipoprotein disorders without proven CHD yet (part of group A of the 1996 NHF guidelines); and
Population 3: patients with neither proven cardiovascular disease nor genetic lipoprotein disorders with varying degrees of absolute risk of developing cardiovascular disease (part of group A, and groups B, C and D of the 1996 NHF guidelines).

To model both need and demand, I undertook and then combined seven separate analyses:
1. estimated current numbers of patients in New Zealand theoretically eligible for LMAs (need, ie potential numbers of patients)
2. pharmaceutical spending associated with 1
3. predicted future need and costs
4. estimated programme coverage (presentation and screening rates, adherence and dietary intervention effects)
5. adjustments to predicted need for programme coverage (need-based demand, ie expected numbers of actual users)
6. pharmaceutical spending associated with 5 (actual pharmaceutical costs)
7. non-pharmaceutical costs of providing LMAs

Each analysis is described in detail below.

Potential patient numbers, current

For populations 1 and 3, I obtained data from the Fletcher Challenge-University of Auckland Heart and Health Study (FCUAHHS) undertaken in 1993/94 on the prevalence of total cholesterol levels and total:HDL cholesterol ratios according to age, sex, and past history and/or absolute risk of coronary heart disease (according to the Framingham equation[8]) [Source: Rod Jackson and Roy Lay Yee, Auckland School of Medicine]. I further subdivided population 1 according to levels of risk, using total cholesterol levels as a surrogate for absolute risk of cardiovascular events.[9 10 11] I then combined the NHF guideline/PTAC recommendations with these prevalances to calculate the proportions in each subpopulation likely meeting to need LMAs (fibrates or statins). I finally then applied prevalences to projected age/sex-specific NZ populations expected for 1995[12], to produce age/sex/CHD status-specific estimates of the numbers of New Zealanders currently needing LMA (fibrates or statins).

For population 2, I used overseas prevalence rates of 1:500 for familial hyperlipidaemias and 1:5000 for familial dysbetalipoproteinaemia to NZ population projections for those aged 0-64[13]. This is given these groups' higher death rates due to premature CHD, and assuming average life expectancy of 64 years. I assumed all in population 2 were eligible for LMAs (in view of dsyslipidaemia and high absolute risks of CHD).

Table 1 summarises the prevalence of "need" for fibrate and statin classes for each CHD-status group, aggregated into broad age-bands combining both men and women. [insert table 1 near here].

Potential pharmaceutical spending on LMAs, current

I calculated total pharmaceutical spending after deriving current annual pharmaceutical costs per patient, based on data supplied by Health Benefits Limited. For fibrates, using bezafibrate as an indicator drug, I used NZ$348 current annual cost per patient ($0.78 per average daily dose (ADD) x 365¼ days/year). For statins, I used NZ$1311 current annual cost per patient, based on a volume-weighted average of simvastatin and pravastatin ADDs (simvastatin: $2.98 ADD x 3.5 million units for year ending June 1996; pravastatin $2.28 ADD x 233,000 units). I then applied these costs to the above projected patient numbers by LMA class. Note that pharmaceutical costs/patient/year are greater that ex-manufacturer prices, in that they included both wholesale margins (10%) and retail margins (pharmacist dispensing fees of 11.28%), with 22.4% combined margins above ex-manufacturer price. Costs excluded GST, and exclude patient prescription (± part) charges.

Potential patient numbers, future

I anticipated the numbers of those potentially eligible for LMAs will change over time. This is due to two competing factors: underlying population growth, with changes in age-sex distributions; and possible changes in the prevalence of coronary heart disease and absolute risk. To account for these changes, I attempted to predict both growth of source populations and changes in prevalence.

To account for population growth, I applied Statistics NZ age/sex 1995 medium mortality/medium fertility/medium net migration (net emigration of 5,000 each year) population projections to "potential patient numbers, current".

I next attempted to adjust for possible changes over time in the prevalence of coronary heart disease and absolute risk [ie the % of the population who have coronary heart disease at any time, or who have particular levels of absolute risk]. These changes are due to uneven reductions in both the mortality and the incidence of coronary heart diseases, with improved survival times outweighing decreases in new cases; and improvements in patients' absolute risk profiles, due to dietary modifications and other risk factor improvements (eg smoking cessation, improved blood pressure control).

I predicted future prevalence of absolute risk of CHD for population 3, but not for those with established CHD (population 1) nor genetic lipoprotein disorders (population 2). To obtain age/sex-specific projections of the prevalence of absolute CHD risk (<u>for population 3</u>), I combined: ARCOS secular trends in the age-standardised sex-specific incidence of fatal and non-fatal coronary heart disease 1980-92 (ie -4.3% and -3.4% respectively for men, -3.4% and -3.2% respectively for women)[14]; age/sex-specific predictions of annual decline in coronary heart disease mortality for New Zealand[15]; and an estimate of the proportion of decline in coronary heart disease incidence in the ARCOS study which can be attributed to the decline in risk factor prevalence (50-75%).[16] I then combined these to obtain age/sex-specific projections of the prevalence of absolute coronary heart risk:

$$rf_{(as)} = mort_{(as)} \times \frac{nf_{(std)}}{f_{(std)}} \times a\#_{(rf)}$$

where
$rf_{(as)}$ = projected age/sex-specific decline in risk factor prevalence
$mort_{(as)}$ = predicted age/sex-specific annual decline in CHD mortality
$nf_{(std)}$ = average annual change in age-standardised non-fatal CHD events
$f_{(std)}$ = average annual change in age-standardised fatal CHD events
$a\#_{(rf)}$ = mean fraction attributable to decline in risk factor prevalence

For populations 1 and 2, I assumed no change in prevalence.

Extent of programme coverage
Although "potential patient numbers, current" calculated the numbers in theory who need LMAs, not all patients will receive LMAs. This is because of: people not accessing and presenting for medical care and screening; practitioners not identifying dyslipidaemia and absolute cardiovascular risk; practitioners not managing dyslipidaemia and absolute cardiovascular risk to the full extent of guidelines; effective dietary and other cardiovascular risk factor interventions negating the need for LMAs; and patients not uplifting scripts from pharmacies. I therefore adjusted the estimated eligible (theoretical) populations for these factors, ie the expected extent of programme coverage (actual populations) and effects. These adjustments incorporated: Presentation rates (the proportion of eligible patients attending for medical care in a 5-year period); Screening rates (% of pesenting patients screened for cardiovascular risk factors, including lipids); Rates of Appropriate Post-screening Patient Management (% of screened patients managed according to the updated NHF guideline, viz absolute risk identified and treated ± subsequently LMA prescribed if still needed); Effective dietary intervention ± other absolute risk reduction (% of managed patients still requiring LMAs despite 3-6 month dietary and/or other risk factor modifications (eg smoking cessation)); and Patient uplift rates (% of patients prescribed LMAs uplifting scripts from retail pharmacies). Each adjustment is described in detail below.

Adjustment 1 Presentation rates:
For population 3, adjustment 1 used age/sex specific data from the 1992/93 Household Health Survey[17], viz proportion of the population who state they had visited a general practitioner at least once in the previous year (by age/sex group). To obtain prevalence rates of visiting within the previous 5 years, I inflated the 1-year rates to reflect 90% overall 5-year visiting rates compared with 80% overall 1-year visiting rates. For population 1, I assumed 100% 5-year visiting rates. I assumed population 2's rates to be halfway between those of population 1 and 3.

Adjustment 2 Screening rates:
For population 1, I assumed that initially 92% of patients would be screened, increasing to 100% by the year 2005. This is given 92% of New Zealand doctors surveyed in 1991 stated they measured lipid levels in patients with symptomatic coronary heart disease or positive family history[18], and assumes that within 10 years all doctors will know and adhere to guidelines for this high risk group. For population 3, I assumed that initially 60% of patients would be screened, given that in the same 1991 survey 60% of doctors stated they measured lipid levels in smokers. However, given promotion of guidelines etc, I assumed screening would increase to a notional 75% by the year 2011. For population 2, I assumed rates to be halfway between those of population 1 and 3. I incorporated differences in screening rates between older patients and younger patients into age-dependent variations in prescriber adherence, below.

Adjustment 3 Rates of appropriate post-screening patient management:
For population 1 aged <70, I assumed 75% of prescribers will be specialist cardiologists or general physicians and 25% will be general practitioners. Of these, I assumed a notional 95% of specialists will initially manage patients according to recommendations, rising to 100% by 2005 for this high risk group. This was given apparent wide publicity and acceptance of the

4S data, relating to those with pre-existing CHD (let alone WOSCOPS) I expected eventual similarly high rates of appropriate management amongst general practitioners, given: the likely accumulation of evidence of the benefits of LMAs; increasing acceptance amongst the medical profession; and promotion by leading cardiologists and the pharmaceutical industry. I therefore assumed a notional 72% of general practitioners would initially prescribe according to recommendations, rising to 100% by 2005.

For population 3 aged <70, I assumed that initially 50% of prescribers would follow recommendations for treatment. This was given 41% of a sample of general practitioners had read the National Advisory Committee on Core Health and Disability Support Services' ("Core" Committee) report on the treatment of raised blood pressure[19] shortly after its 1992 release, and 50% conformed with those guidelines.[20] However, given promotion of guidelines etc, I assumed prescribing rates would increase to a notional 80% by the year 2011.

For all patients aged 70 years and over, I assumed markedly lower prescribing rates than for patients aged less than 70. This was given anecdotal evidence that prescribers in general are less aggressive with preventive pharmaceutical treatment for older people than younger, particularly with older people's lesser life expectancy and their greater potential for polypharmacy. This was supported by New Zealand practitoners'attitudes reported by Bradley et al, with only 8% of doctors agreeing that older patients aged >75 years should be treated for hypercholesterolaemia with drugs. I directly used Bradley et al's prescriber attitude rates for patients those aged >70 and >75 for prescribing rates, weighted according to attitudes and presumed prescriber prevalence by specialty (similar to population 1 <70 years above). I assumed these prescribing rates remained constant with time.

For population 2, I assumed rates to be halfway between those of population 1 and 3.

Adjustment 4 Effects of dietary intervention
For populations 1 and 3, I again obtained FCUAHHS prevalence data, but this time with each participant's absolute CHD risk recalculated according to different levels of total cholesterol reduction, ie amending the total cholesterol variable in the Framingham logistic equation [source: R Jackson, R Lay Yee]. These were for three scenarios of dietary effects on total cholesterol, viz each individual having a 2.5%, 5%, and 10% reduction in total cholesterol. I then divided each scenario's recalculated prevalence by the original (0% reduction) age/sex/CHD status-absolute risk/total cholesterol prevalence to calculate the relative change in prevalence for each stratum. I finally applied these fractions to the corresponding numbers of eligible patients (component 1), to calculate new numbers for each scenario of dietary cholesterol reduction for each stratum. For the base case, I selected the 5% level for individuals' reductions in total cholesterol with effects on individuals' absolute risk of CHD.

Adjustment 5 Patient uplift
I assumed 91% uplift rates (ie proportions of patients in 4 who will present and uplift their LMA scripts from retail pharmacies). This estimate is based on 1992 data from the RNZCGP computer research group, showing that 8.9% of scripts prescribed for raised blood pressure were not dispensed (and assumes similar dispensing rates for LMAs).[21]

Adjustment 6 Mix effect
The above adjustments presumed that LMAs are prescribed by Rx class according to guidelines/criteria. Current evidence however suggested that fibrates were prescribed at much lower levels than would be expected by the NHF's 1993 guidelines[22] - viz $5.1 million actual (year ending June 1996) rather than $13.1 million predicted. Conversely, statins were prescribed at slightly higher rates than expected ($12.4 million actual versus $11.5 million predicted). I therefore finally adjusted programme coverage to reflect current realities of prescribing by LMA class, in addition to coverage and dietary modification effects common to both fibrates and statins. This meant adjusting numbers receiving fibrates by a factor of

39%, and statins by 107%. Table 2 shows these calculations, from predicted and actual patient numbers and costs of fibrates and statins according to NHF 1993 and 1996 guidelines. [insert table 2 near here]

Actual use (expected populations)

"Extent of programme coverage" adjustments accumulate, so that patients who actually receive LMAs are a fraction of those eligible: actual use (programme coverage) = need x (presentation rate x screening rate x rate of appropriate post-screening patient management x effect of dietary and other risk factor modification x patient uplift) x adjustment for mix effect. Figure 2 shows how, according to the model, these fractions vary widely according to age/sex, CHD status/risk, and class of LMA. [insert figure 2 near here]. To calculate actual populations, I applied "Extent of programme coverage" cumulative adjustments to the theoretical numbers of "Potential patient numbers, current" and "Potential patient numbers, future". Note that because not all patients continue with LMAs[23 24], only a proportion of patients who receive LMAs will gain benefit from prevented death and cardiovascular morbidity, with even less of all those eligible.

Actual pharmaceutical costs

I calculated actual pharmaceutical costs in a similar fashion to "Actual use (expected populations)" calculations, applying "Extent of programme coverage" cumulative adjustments to "Potential patient numbers, current", "Potential patient numbers, future", and costs from "Potential pharmaceutical spending, current".

Sensitivity analyses

Given the sample frames and size used by the Auckland Heart and Health Study, and the number of assumptions inherent in the model, I examined the effects on patient numbers of varying the base case (sensitivity analyses) by:

1. varying prevalence of need (according to age, sex, absolute CHD risk and total cholesterol) from the Auckland Heart and Health Study by ± 1 standard deviation
2. excluding one half of Maori and Pacific Island people from denominator populations
3. assuming NO decrease in prevalence of absolute risk of CHD for population 3, ie prevalence remains constant (as with populations 1 and 2).
4. varying programme coverage according to the effectiveness of dietary interventions (2.5% and 10% reductions in total cholesterol)
5. varying programme coverage according to the effectiveness of dietary interventions (2.5% and 10% reductions in total cholesterol)
6. compounding 5% annual change in the mix of fibrates and statins (currently fibrate:statin ratio of 0.13 , with statins increasing and fibrates decreasing)
7. compounding 10% annual change to fibrate:statin mix
8. combining NO decrease in prevalence of absolute risk of CHD for population 3 with 5% compounded annual change to fibrate:statin mix
9. combining variability in prevalence of need with variability in programme coverage (- 1 standard deviation from need prevalence, with 10% reduction in total cholesterol; +1 standard deviation from need prevalence, with 2.5% reduction in total cholesterol)
10. decreasing statin pharmaceutical costs by one-third

Results

Extent of "need"

According to the model, 13.7% of people aged 35-84 are eligible for LMAs, some 221,000 for New Zealand in 1995. 143,300 eligible are aged 35-69, which is 65% of all eligible and 10.5% of everyone in this age group; 91,300 of these are in NHF groups A and B (ie manifest cardiovascular disease; genetic lipoprotein disorders; diabetic nephropathy; >20% 5-year risk of cardiovascular disease), including 79,900 with pre-existing CHD or other cardiovascular disease. A further 77,200 elderly aged 70-84 have need in terms of their lipid profiles and absolute risk, 35% of all eligible and 31% of all in this age group; 49,700 of these have pre-existing CHD/other cardiovascular disease. Note the NHF guidelines do not expressly recommend LMAs for all eligible over the age of 70, but state treatment is warranted in some, particularly those with established CHD.

If all 221,000 eligible patients were to receive LMAs, annual total costs would be in the region of $174 million (at current fibrate and statin prices).

Overall numbers of people eligible for LMAs would increase by 22% over the 15 years to year 2011, reaching 269,000. Figure 3 shows trends in need over time by subgroup. Overall numbers of eligible 35-69 year olds would increase by 24% over the 15 years to year 2011, reaching 177,000; of these, those with pre-existing CHD would increase by 35%, but those with lowest risk would decrease by -13% (and only 8% growth for all at-risk for this age). Elderly eligible aged 70-84 would grow 19% over the same period, reaching 92,100 . [insert figure 3 near here]

The model is sensitive to prevalence trends, and mildly sensitive to prevalence rates and underlying populations (see figures 4 and 5). Varying need by ± 1 standard deviation means prevalence varies between 12.9% and 14.6%, ie between 207,000 and 235,000 eligible; likewise, 35-69 year olds in groups A & B of the NHF guidelines would number between 85,400 and 97,100 (6.3% to 7.1%). Excluding one half of Maori and Pacific Island people from base populations means numbers decrease to 205,000 (93% of base case), with 85,700 aged 35-69 in NHF groups A & B (94% of base case). Assuming NO decrease in need prevalence for the at-risk group means overall need for LMAs would increase by 32% by year 2011, reaching 292,000; this is 2.24 times larger than the base case increase, and includes 38% growth for all "at-risk" aged 35-69. [insert figures 4 and 5 near here]

Likely demand

According to the model, in practice 20% of all eligible people would receive LMAs, some 43,600 patients. These comprise 39,400 aged 35-69, and 4,250 aged 70-84 (ie 27% and 6% of eligible in each age-group respectively), with 14,300 receiving fibrates and 29,300 receiving statins.

Assuming current simvastatin/pravastatin and bezafibrate prices, annual Rx spending would total some $43.4 million (excluding GST), with $5.0 million for fibrates and $38.5 million for statins. This compares with $18 million currently spent on LMAs (year to June 1996), restricted to a narrower range of people (ostensibly genetic lipoprotein disorders or manifest CHD with total cholesterol >7.0 mmol/l, and "at risk" with total cholesterol >9.0 mmol/l) and hospital pharmacy dispensing.

32,000 LMA users would be in groups A and B of the NHF guidelines aged 35 to 69 years, costing some $30.5 million and including 29,600 with pre-existing CHD. Of these in groups A & B, fibrates would be prescribed for 11,900 patients and statins for 20,100, costing $4.2 million and $26.3 million respectively at current prices.

Assuming drug prices remained at 1995 levels, but accounting for improvements in programme coverage and population changes over time, patient numbers and costs would rise

72% and 73% respectively by year 2011, reaching 75,200 patients and $75 million costs. This would be 28% of eligible patients at that time, a 41% higher proportion of those eligible than for 1996. These trends are shown in figures 6 and 7. [insert figures 6 and 7 near here]

The model is particularly sensitive to combining programme coverage with prevalence and to Rx price, moderately sensitive to trends in prevalence and Rx mix, and mildly sensitive to underlying populations (see figures 8 to 11). Demand could vary anywhere between 14% and 23% of eligibility, according to the effectiveness of dietary interventions (10% and 2.5% reductions in total cholesterol respectively), ie between 33,300 and 48,200 actual users; likewise, 35-69 year old users in groups A & B of the NHF guidelines would number between 26,600 and 35,100 (27% to 42% of eligibility). Combining sampling variability (ie ± 1 standard deviation) with the above programme coverage variability means a wide margin of error, with user numbers ranging between 31,000 and 51,600 (ie +/- 24% variance on the base 43,600 figure), costing between $31 million and $51 million. Excluding one half of Maori and Pacific Island people from base populations means user numbers decrease to 40,600 with 30,000 aged 35-69 in NHF groups A & B, costing $40 million and $29 million respectively. Decreasing statin costs by one-third means overall pharmaceutical spending on LMAs would decrease to $31 million(70% of base case costs). Assuming NO decrease in prevalence for the at-risk group means overall demand for LMAs would increase 85% by year 2011 to reach 80,700 users, costs rising 87% to $81 million; this includes 176% growth for all “at-risk” aged 35-69. Assuming a 5% change each year in the mix of fibrates and statins means overall costs increase 102% by year 2011 to reach $88 million (increasing change to more expensive statins). 10% annual change causes a 116% increase with $94 million. Combining both a 10% annual change in Rx mix with nil decrease in “at-risk” prevalence causes a 131% increase in spending to reach $100 million, 1.8 times the increase seen in the base case. [insert figures 8 to 11 near here]

Results are summarised in tables 3 and 4.

Discussion

There are a number of methodological issues to discuss. Many issues arise from the model's need to make a number of assumptions, summarised in table 5. [insert table 5 near here]

Firstly, the FCUAHHS data were based on a random sample of 2,465 European urban Aucklanders drawn from (non-Maori) general electoral rolls.[25] These included 370 people with evidence of current or past coronary heart disease. The data thus largely exclude Maori and Pacific Island populations. These ethnic groups have higher absolute risks of CHD than NZ Europeans[26], but this effect on need for LMAs is mitigated by both lower cholesterol levels[27] and possible proportionately lesser effects of dyslipidaemia (and grater effects of hypertension) on the absolute risk of CHD than is predicted by the Framingham equation[28]. In addition, these groups might well have lower uptake of LMA programmes (lower rates of presenting for medical care, lower rates of patient adherence), decreasing demand.

Secondly, the prevalence data used for genetic lipoprotein disorders preclude combined familial hyperlipidaemia (FCH). FCH may affect nearly 10% of patients with myocardial infarction[29], but will be manifest in the Auckland data in those with pre-existing CHD with high total cholesterol levels. The prevalence data also exclude rarer forms of genetic lipoprotein disorders, but the effects of these on overall prevalence will be negligible.

Thirdly, I did not explicitly factor diabetic nephropathy into the model (group A3 of the NHF 1996 guidelines). I since estimate perhaps around 6,100 people aged 35 to 84 might have diabetic nephropapthy eligible for statins under the NHF/PTAC subcommittee criteria (ie albumin excretion > 300 mg/day, total cholesterol > 5.5 mmol/l or total:HDL cholesterol > 5.5), being 9% of diabetics of that age[30] (where diabetes prevalence is 4.7% for that age[31]). If 62% were to receive statins, then costs would be a further $5.1 million.

Fourthly, the model assumes the prevalence of both absolute risk of coronary heart disease, and of patients with established coronary heart disease, will change with time. This is since the incidence of both fatal and non-fatal coronary heart disease has declined appreciably in the past two decades. Much of the decline in coronary heart disease mortality is considered due to the decrease in the incidence of new case, largely due to decreases in risk factor levels and thus absolute risk. However, it is difficult to predict the future prevalence of patients with established coronary heart disease (population 1), and the effects of this upon population size. Some of the decline in coronary heart disease mortality is due to improvements in case-fatality rates, with longer survival. Longer survival counteracts any decrease in prevalence due to decreases in new cases. There are insufficient data to confidently adjust for these competing effects. It is however feasible to predict changes in the prevalence of absolute risk, decreasing the size of population 3, given improvements in patients' absolute risk due particularly to decreases in cigarette smoking, with dietary modifications to a lesser extent. However, much depends on continuing falls in levels of cigarette smoking and blood pressure, and the Auckland data suggest that although total cholesterol is declining, so too is HDL cholesterol while total:HDL cholesterol ratios and obesity (BMIs) are increasing.[32] These adverse trends for HDL cholesterol, total:HDL cholesterol ratios and obesity will counter the benefits of declining total cholesterol and hence may negate any decreases in population 3's size.

Fifthly, the model's 5% global reductions in total cholesterol from dietary interventions are based upon estimates of 4% average reductions for patients undergoing GP consultation only, 6% for GP consultations combined with practice nurse education and oversight, and 10% for hospital dietician services.[33] Reduction rates can be as high as 17% in intensive clinical trial settings in high risk patients[34], but tend to be lower in community settings (eg 2.3% in nurse-initiated programmes in general practice populations at lower risk[35]). Using global dietary reductions precludes evidence relating dietary response rates to baseline cholesterol levels (ie

greatest percentage reductions occur in patients with highest baseline total cholesterol levels)[36], but such variable reductions were difficult to model.

Finally, I have not formally calculated non-pharmaceutical programme costs of providing LMAs (personal and public health services) at this stage, for a number of reasons. Non-pharmaceutical costs comprise five components: primary health care costs (screening and other general practice costs to identify those with dyslipidaemias ± other risks warranting further intervention); laboratory costs of screening ± calculating absolute risks; costs of dietetic service / dietary clinic intervention and advice for those identified with dyslipidaemias ± other risks warranting intervention; costs of general population-based health promotion activities to improve diets including hence lipid profiles; and costs of adverse side-effects of LMA drugs (hospitalisations, primary health care costs, etc). There are few data to help quantify the marginal costs of managing patients for dyslipidaemias in general practice, when in addition to managing other cardiovascular risk or established coronary heart disease. Marginal costs of extending non-LMA dietetic services to wider eligible populations are uncertain, given likely variability in current service provision and uncertainty as to what extent demand may increase. However, in areas where service levels are low and/or under-utilised, increased demand may cause logistical and resource difficulties. Marginal costs of health promotion activities are likely to be negligible. I have found few data to date to help quantify the costs of adverse effects of LMAs.

The model suggests that 20% of those eligible under the 1996 NHF guidelines aged 35 to 84 years will actually receive LMAs, according to historical actual versus predicted volumes for statins and fibrates. This usage rate is higher than the 13% calculable from work by North et al[37], who applied the 1993 guidelines to FCUAHHS prevalence data which included participants' actual LMA use. Their data suggest that whereas 10.7% of European New Zealanders aged 35 to 74 met the then treatment criteria, only 1.4% actually received LMAs. Four possible reasons for our higher rate might include: differences in denominator age-groups and ethnic make-up; differences in the prevalence of users (26,000 person-year equivalents of LMA use for all New Zealand for the year ending June 1996 equates to 1.6% of all those aged 35 to 84); some people who receive LMAs do not meet the NHF's eligibility guidelines; and any combination of the above three possibilities.

Dietary interventions have significant impacts on both cholesterol levels (hence need for LMAs) and absolute cardiovascular risk. A 0.6 mmol/l long-term reduction in dietary cholesterol lowers the risk of ischaemic heart disease by 50% at age 40.[38] A 5% reduction in New Zealanders aged 35-69's total cholesterol would cause an estimated 16.5% reduction in total CHD incidence.[39] This is more than the 2.1% which might be achieved through providing LMAs to those eligible of the same age (since only a proportion of events occur in eligible patients, of whom not all receive and continue medication, and many events are not prevented).[40] According to the model, 2.5%, 5% and 10% global reductions in individuals' total cholesterol levels cause 12%, 22% and 45% reductions in numbers of people needing LMAs. Figures 12 and 13 show the relative and absolute impact of these changes on the need for LMAs, which are similar in size to the reductions possible using the 1993 NHF guidelines reported by North et al. Figure 14 shows how reducing total cholesterol levels shifts the distribution of absolute CHD risk in the model so that the prevalence of absolute risk decreases for high-risk groups but increases for lower risk groups. [insert figures 12 to 14 near here]

Given the relative expense of LMAs and the large numbers of patients potentially eligible, investing in LMAs represents both significant costs to regional health authorities and significantly potential health gains to their populations. For instance, treating all those with pre-existing CHD aged 35 to 69 eligible for statins for five years would cost some $189 million (ie 28,800 patients x $1,311/patient/year x 5 years) but might save some 12,300 life

years through preventing premature death alone (ie 28,800 patients x 0.13 life years saved/patient/year[41] x 5 years x 68% continuation rate for statins[42 43]).

LMAs give value for money when compared with other pharmaceuticals preventing cardiovascular disease (eg treating some patients with antihypertensives). There should be substantial health gains from targeting LMAs to those with greatest need, given that many eligible patients do not receive LMAs. For example, if 20% of those with pre-existing CHD aged 35 to 69 eligible for statins predicted by the model did not receive them because of non-presentation/sub-optimal identification and management/non-uplift, then 2,500 life years would be lost needlessly over the 5 years for $47 million not spent (ie 28,000 patients x 77% still requiring statins following 5% dietary cholesterol reduction x (1 - 80%) receiving statins x 68% continuation rate x 0.13 LYS/patient/year x 5 years; 28,000 patients x 77% x 25% x $1311 x 5 years).

But also there is a need to prioritise LMA use for those with greatest need. This is given some groups with lower absolute risk reductions and life expectancy will receive much less benefit (eg a 20-fold difference in statin QALYS between men 35-39 with pre-existing CHD and total cholesterol ≥ 7.5 mmol/l and women aged 80-84 “at risk” with 10-14% 5-year risk[44]), and the gains for these groups are very expensive when compared other cardiovascular prevention and treatment such as dietary cholesterol reduction, tobacco control and CABG.

Table 1: Need for LMAs by CHD-status group

LMA need

population characteristics				need (Auckland H&H Study prevalence data)		
CHD status	gender	age-group	t.cholesterol, or 5-year risk/person	fibrates	statins	combined fibrate/statin programme
past CHD	m&f	35-69	>=7.5 mmol/l	0.0%	0.6%	0.6%
past CHD	m&f	35-69	6.5-7.4 mmol/l	0.0%	1.5%	1.5%
past CHD	m&f	35-69	5.5-6.4 mmol/l	3.2%	0.0%	3.2%
past CHD	m&f	35-69	<5.5 mmol/l	0.5%	0.0%	0.5%
past CHD	*m&f*	*35-69*	*all past CHD*	*3.8%*	*2.1%*	*5.9%*
at risk	m&f	35-69	at risk >=20%	0.5%	0.2%	0.6%
fam.xanth	m&f	35-69	fam.xanth			
at risk	m&f	35-69	at risk15-19%	0.7%	0.1%	0.8%
at risk	m&f	35-69	at risk 10-14%	0.3%	0.7%	1.0%
at risk	m&f	35-69	at risk 5-9%	0.4%	0.7%	1.1%
at risk	m&f	35-69	at risk <5%	0.0%	0.8%	0.8%
total	*m&f*	*35-69*		*5.7%*	*4.9%*	*10.5%*
past CHD	m&f	70-84	>=7.5 mmol/l	0.0%	3.0%	3.0%
past CHD	m&f	70-84	6.5-7.4 mmol/l	0.0%	7.1%	7.1%
past CHD	m&f	70-84	5.5-6.4 mmol/l	8.3%	0.0%	8.3%
past CHD	m&f	70-84	<5.5 mmol/l	1.6%	0.0%	1.6%
past CHD	*m&f*	*70-84*	*all past CHD*	*9.9%*	*10.2%*	*20.1%*
at risk	m&f	70-84	at risk >=20%	4.0%	0.2%	4.2%
fam.xanth	m&f	70-84	fam.xanth			
at risk	m&f	70-84	at risk15-19%	2.7%	0.1%	2.8%
at risk	m&f	70-84	at risk 10-14%	0.7%	1.0%	1.8%
at risk	m&f	70-84	at risk 5-9%	0.0%	1.7%	1.7%
at risk	m&f	70-84	at risk <5%	0.0%	0.7%	0.7%
total	*m&f*	*70-84*		*17.2%*	*13.9%*	*31.2%*
total, all ages		*35-84 m&f*		*7.5%*	*6.3%*	*13.7%*
NHF risk groups, m&f 35-69				*1.9%*	*2.6%*	*4.5%*
NHF groups A&B, m&f 35-69				***4.2%***	***2.5%***	***6.7%***

Table 2: Predicted and actual patient numbers and costs of fibrates and statins, according to NHF 1993 and 1996 guidelines

		NHF 1993 criteria		NHF 1996 criteria	
		no.	cost (millions)	no.	cost
Modelled	fibrates	37,600	$13,100,000	36,500	$12,700,000
(AkH&H prvl of eligibility x prog coverage)	statins	10,800	$ 11,500,000	27,300	$ 35,800,000
(1993 statins hosp pharm only)	*total*	*48,400*	*$ 24,600,000*	*63,800*	*$ 48,500,000*
Actual	fibrates	14,700	$ 5,100,000	14,300	$ 5,000,000
(HBL data for 1993, used to predict for 1996)	statins	11,500	$ 12,400,000	29,300	$ 38,500,000
	total	*26,300*	*$ 17,500,000*	*43,600*	*$ 43,400,000*
% LMA users of 35-84 year old population		1.6%		2.7%	
Actual/Modelled	fibrates	39%	39%		
	statins	107%	107%		
	total	*54%*	*71%*		

(Patient numbers as person-year equivalents. Actual patient numbers for 1993 criteria = 1995 actual costs / average price per patient per year. Modelled patient numbers for 1993 and 1996 based on NHF and PTAC criteria, Auckland Heart and Health Study prevalences, estimated programme coverage, and population projections. Modelled costs for 1993 and 1996 = modelled patient numbers x average price per patient per year. 1996 actuals = 1993 actuals x 1996 modelled / 1993 modelled. % LMA users of 35-84 year old population = total actual patient numbers / NZ population aged 35-84)

Table 3: Need for LMAs

LMA need

population characteristics				need (Auckland H&H Study prevalence data)					
				prevl	potential no.people				potential cost to PHARMAC
CHD status	gender	age-group	t.cholesterol, or 5-year risk/person	NHF 1996 criteria:	all	eligible, NHF 1996 criteria			eligible under NHF 1996 criteria
						fibrates	statins	total	
past CHD	m&f	35-69	>=7.5 mmol/l	0.6%	8,400	-	8,400	8,400	$ 11,010,000
past CHD	m&f	35-69	6.5-7.4 mmol/l	1.5%	20,400	-	20,400	20,400	$ 26,790,000
past CHD	m&f	35-69	5.5-6.4 mmol/l	3.2%	43,600	43,600	-	43,600	$ 15,190,000
past CHD	m&f	35-69	<5.5 mmol/l	0.5%	32,800	7,400	-	7,400	$ 2,580,000
past CHD	*m&f*	*35-69*	*all past CHD*	*5.9%*	105,300	51,000	28,800	79,900	*$ 55,570,000*
at risk	m&f	35-69	at risk >=20%	0.6%	10,800	6,130	2,600	8,730	$ 5,550,000
fam.xanth	m&f	35-69	fam.xanth		2,690	240	2,440	2,690	$ 3,290,000
at risk	m&f	35-69	at risk15-19%	0.8%	21,800	9,620	1,930	11,600	$ 5,890,000
at risk	m&f	35-69	at risk 10-14%	1.0%	68,500	4,690	9,460	14,100	$ 14,030,000
at risk	m&f	35-69	at risk 5-9%	1.1%	218,000	5,260	9,850	15,100	$ 14,740,000
at risk	m&f	35-69	at risk <5%	0.8%	934,000	70	11,200	11,200	$ 14,670,000
total	*m&f*	*35-69*		*10.5%*	1,362,000	77,000	66,300	143,300	*$ 113,730,000*
past CHD	m&f	70-84	>=7.5 mmol/l	3.0%	7,480	-	7,480	7,480	$ 9,810,000
past CHD	m&f	70-84	6.5-7.4 mmol/l	7.1%	17,700	-	17,700	17,700	$ 23,200,000
past CHD	m&f	70-84	5.5-6.4 mmol/l	8.3%	20,600	20,600	-	20,600	$ 7,160,000
past CHD	m&f	70-84	<5.5 mmol/l	1.6%	19,300	3,910	-	3,910	$ 1,360,000
past CHD	*m&f*	*70-84*	*all past CHD*	*20.1%*	*65,100*	*24,500*	*25,200*	*49,700*	*$ 41,540,000*
at risk	m&f	70-84	at risk >=20%	4.2%	13,500	9,790	560	10,400	$ 4,150,000
fam.xanth	m&f	70-84	fam.xanth		-	-	-	-	$ -
at risk	m&f	70-84	at risk15-19%	2.8%	22,600	6,570	240	6,810	$ 2,600,000
at risk	m&f	70-84	at risk 10-14%	1.8%	36,400	1,840	2,590	4,430	$ 4,040,000
at risk	m&f	70-84	at risk 5-9%	1.7%	53,200	-	4,280	4,280	$ 5,610,000
at risk	m&f	70-84	at risk <5%	0.7%	56,800	-	1,660	1,660	$ 2,170,000
total	*m&f*	*70-84*		*31.2%*	*248,000*	*42,700*	*34,500*	*77,200*	*$ 60,110,000*
total, all ages		*35-84 m&f*		*13.7%*	*1,609,000*	*119,700*	*100,800*	*221,000*	*$ 173,840,000*
NHF risk groups, m&f 35-69				*4.5%*	*1,254,000*	*25,800*	*35,000*	*60,800*	*$ 54,870,000*
NHF groups A&B, m&f 35-69				*6.7%*	*118,800*	*57,400*	*33,900*	*91,300*	*$ 64,410,000*

Table 4: LMA actual use and costs

LMA demand and costs

population characteristics				demand (NHF 1996 criteria)							demand/ need	
				actual no.people				actual cost to PHARMAC			no. people	cost
CHD status	gender	age-group	t.cholesterol, or 5-year risk/person	excluding discontinuations			including discontinuations	NHF 1996 criteria, excl discontinuations				
				fibrates	statins	total		fibrates	statins	total		
past CHD	m&f	35-69	>=7.5 mmol/l	-	5,290	5,290	3,660	$ -	$ 6,900,000	$ 6,900,000	63%	63%
past CHD	m&f	35-69	6.5-7.4 mmol/l	-	13,000	13,000	9,000	$ -	$ 17,000,000	$ 17,000,000	64%	63%
past CHD	m&f	35-69	5.5-6.4 mmol/l	9,580	-	9,580	4,250	$ 3,300,000	$ -	$ 3,300,000	22%	22%
past CHD	m&f	35-69	<5.5 mmol/l	1,710	-	1,710	750	$ 600,000	$ -	$ 600,000	23%	23%
past CHD	*m&f*	*35-69*	*all past CHD*	*11,300*	*18,300*	*29,600*	*17,700*	*$ 3,900,000*	*$ 24,000,000*	*$ 27,900,000*	*37%*	*50%*
at risk	m&f	35-69	at risk >=20%	590	610	1,200	590	$ 200,000	$ 800,000	$ 1,000,000	14%	18%
fam.xanth	m&f	35-69	fam.xanth	40	1,170	1,220	750	$ 15,000	$ 1,500,000	$ 1,600,000	45%	49%
at risk	m&f	35-69	at risk15-19%	590	280	860	390	$ 200,000	$ 360,000	$ 570,000	7%	10%
at risk	m&f	35-69	at risk 10-14%	330	1,910	2,230	1,230	$ 110,000	$ 2,500,000	$ 2,600,000	16%	19%
at risk	m&f	35-69	at risk 5-9%	280	1,790	2,070	1,140	$ 98,000	$ 2,300,000	$ 2,400,000	14%	16%
at risk	m&f	35-69	at risk <5%	-	2,220	2,220	1,140	$ -	$ 2,900,000	$ 2,900,000	20%	20%
total	*m&f*	*35-69*		*13,100*	*26,300*	*39,400*	*22,900*	*$ 4,600,000*	*$ 34,400,000*	*$ 39,000,000*	*27%*	*34%*
past CHD	m&f	70-84	>=7.5 mmol/l	-	790	790	580	$ -	$ 1,000,000	$ 1,000,000	11%	10%
past CHD	m&f	70-84	6.5-7.4 mmol/l	-	1,990	1,990	1,480	$ -	$ 2,600,000	$ 2,600,000	11%	11%
past CHD	m&f	70-84	5.5-6.4 mmol/l	730	-	730	350	$ 250,000	$ -	$ 250,000	4%	3%
past CHD	m&f	70-84	<5.5 mmol/l	120	-	120	60	$ 42,000	$ -	$ 42,000	3%	3%
past CHD	*m&f*	*70-84*	*all past CHD*	*850*	*2,780*	*3,630*	*2,470*	*$ 300,000*	*$ 3,600,000*	*$ 3,900,000*	*7%*	*9%*
at risk	m&f	70-84	at risk >=20%	190	10	200	80	$ 67,000	$ 12,000	$ 79,000	2%	2%
fam.xanth	m&f	70-84	fam.xanth	-	-	-	-	$ -	$ -	$ -		
at risk	m&f	70-84	at risk15-19%	120	10	130	50	$ 42,000	$ 7,000	$ 49,000	2%	2%
at risk	m&f	70-84	at risk 10-14%	10	130	150	90	$ 5,000	$ 170,000	$ 180,000	3%	4%
at risk	m&f	70-84	at risk 5-9%	-	120	120	80	$ -	$ 160,000	$ 160,000	3%	3%
at risk	m&f	70-84	at risk <5%	-	10	10	10	$ -	$ 20,000	$ 20,000	1%	1%
total	*m&f*	*70-84*		*1,180*	*3,070*	*4,250*	*2,780*	*$ 410,000*	*$ 4,000,000*	*$ 4,400,000*	*6%*	*7%*
total, all ages		*35-84 m&f*		*14,300*	*29,300*	*43,600*	*25,700*	*$ 5,000,000*	*$ 38,500,000*	*$ 43,400,000*	*20%*	*25%*
NHF risk groups, m&f 35-69				*1,780*	*6,810*	*8,590*	*4,500*	*$ 620,000*	*$ 8,900,000*	*$ 9,500,000*	*14%*	*17%*
NHF groups A&B, m&f 35-69				*11,900*	*20,100*	*32,000*	*19,000*	*$ 4,200,000*	*$ 26,300,000*	*$ 30,500,000*	*35%*	*47%*

Table 5: Model assumptions

Potential patient numbers, current:

1. numbers eligible for LMAs equate to estimates of pre-existing CHD and high absolute risk of CHD
2. FCUAHHS prevalence data relate to the entire New Zealand population
3. absolute risks derived from the Framingham logistic risk equation, used by FCUAHHS, are relevant to New Zealand now
4. FCUAHHS accurately identifies cases of past myocardial infarction and of angina in the community
5. the prevalence of overall genetic lipoprotein disorders is the same as the (1:500 + 1:5000) rates cited for familial hypercholesterolaemia and familial dysbetalipoproteinaemia cited in the international literature, whilst the denominator population for genetic lipoprotein disorder prevalence (to obtain numerators) is those aged 0-64, given this group's stated early mortality due to CHD.

Potential pharmaceutical spending, current:

1. the simvastatin/pravastatin combination represents all costs for HMG-coA reductase inhibitors (statins), and bezafibrate represents all costs for fibrates.
2. an average daily dose for simvastatin of 16 mg/day
3. price and ADD are fixed at 1996 levels.

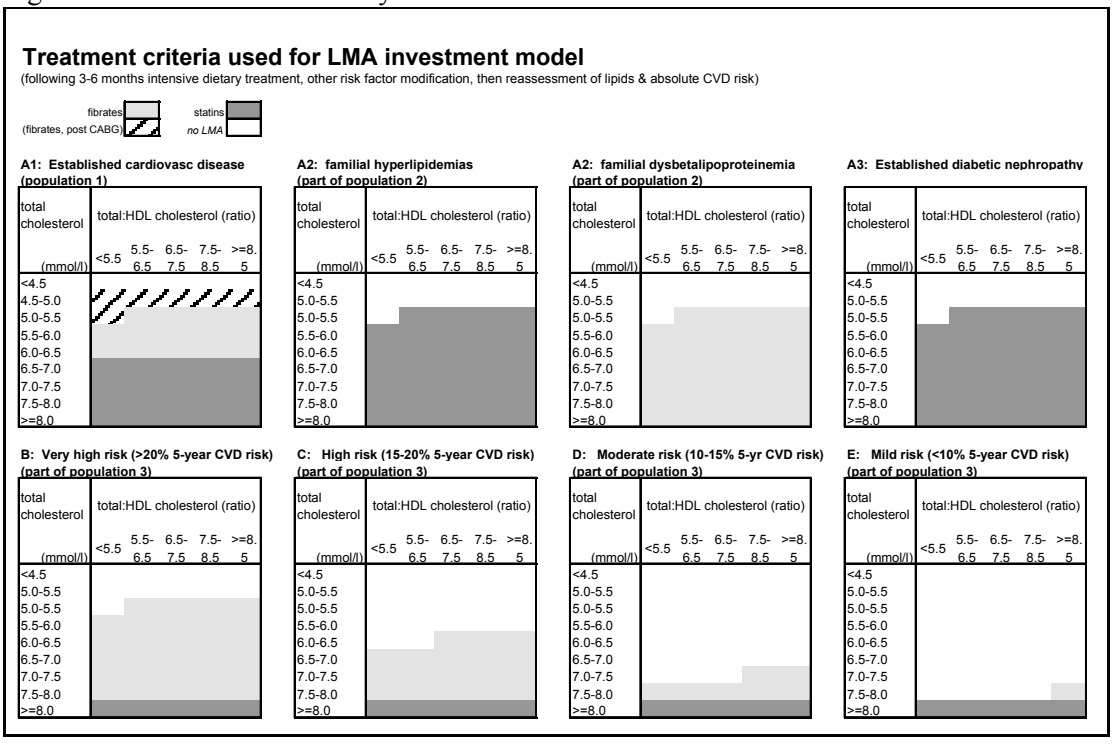
Potential patient numbers, future:

1. medium population growth, based upon medium mortality, medium fertility and medium net migration projections. These in turn are based upon 1991 and previous census data.
2. CHD mortality continues an exponential decline at the same extent as occurred during 1980-92 in Auckland (ARCOS data)
3. trends in the incidence of non-fatal CHD reflect the incidence of all CHD (new cases)
4. CHD incidence continues to decline at the same extent as occurred during 1980-92 in Auckland (ARCOS data)
5. absolute risk of CHD continues to decline at the same extent as occurred during 1980-92 in Auckland (ARCOS data)
6. risk factor declines continue to contribute 50-75% to the overall decline in CHD mortality
7. any age-sex distribution for the decline in CHD incidence follows that of CHD mortality
8. projections based on historical rates account for any cohort effects

Extent of programme coverage

1. presentation, screening and prescriber rates for patients with genetic lipoprotein disorders (population 2) are midway between populations 1 and 3, ie 50% are identified and receive treatment equal to that of population 1, whilst the other half are not identified and are treated "normally" (as with population 3).
2. all patients in population 1 visit a medical practitioner at least once every five years
3. presentation rates for population 3 based on 1992-93 Household Health Survey
4. screening rates based on 1991 survey results
5. prescribing rates based on a 1992 sample of Auckland GPs and 1991 survey results, with assumptions about who treats population 1, their prescribing rates, and lower prescribing rates for older patients
6. dietary interventions will cause 5% reductions in total cholesterol levels for all patients, regardless of age/sex, CHD status/absolute risk, and baseline total cholesterol levels
7. dietary interventions will proportionately affect patients' overall levels of absolute CHD risk, but absolute risk will otherwise remain unchanged (ie no effects from concomitant blood pressure reduction, smoking cessation etc.)
8. 91% of patients uplift LMA scripts from retail pharmacies.
9. subsidy criteria are complied with, without "over-treatment" of "ineligible" patients.

Figure 1: “Need” criteria used by model



(alternative sizing for) Figure 1: “Need” criteria used by model

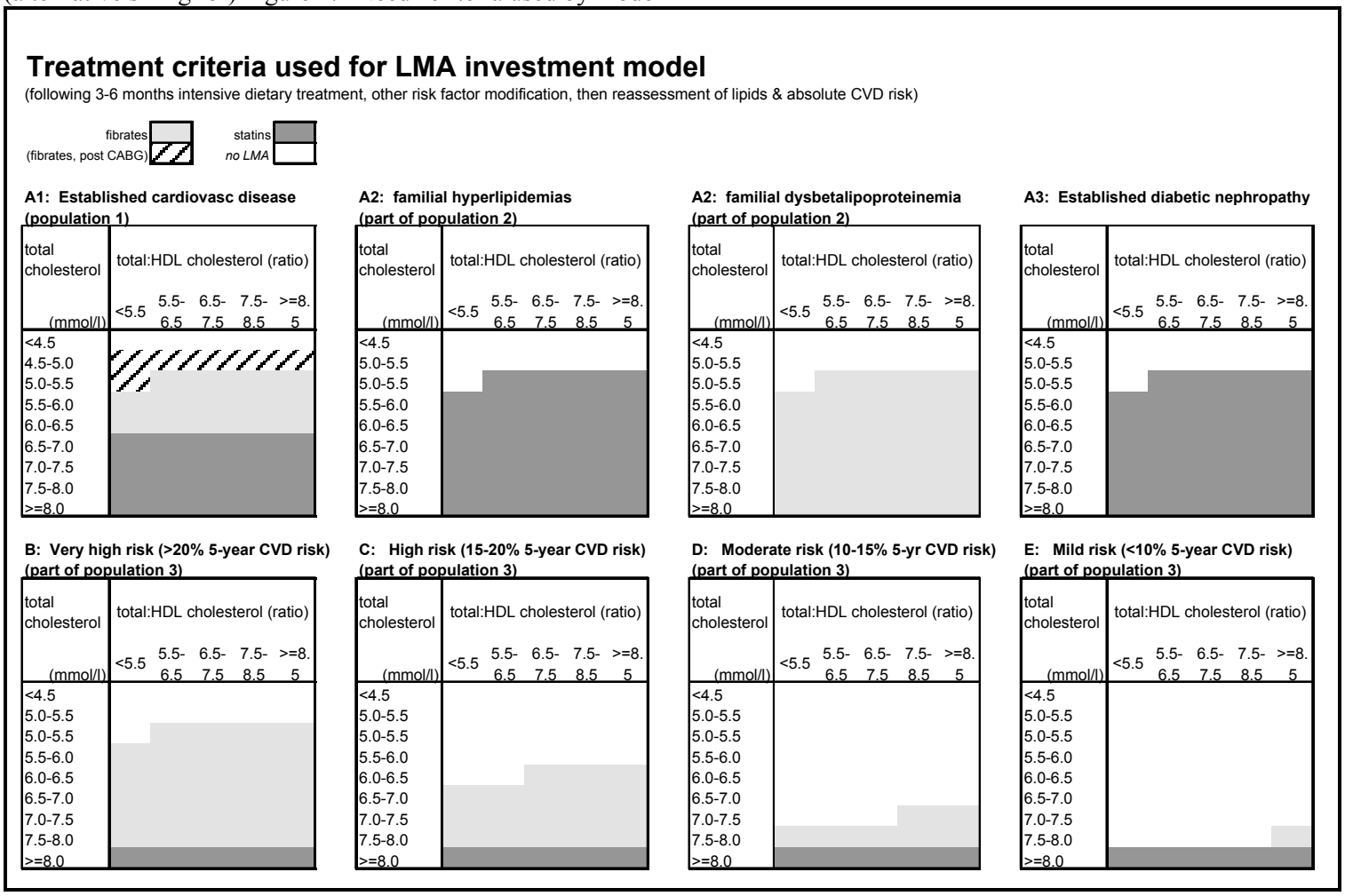


Figure 2: Cumulative effects of programme coverage and dietary interventions on LMA uptake (actual use/"need")

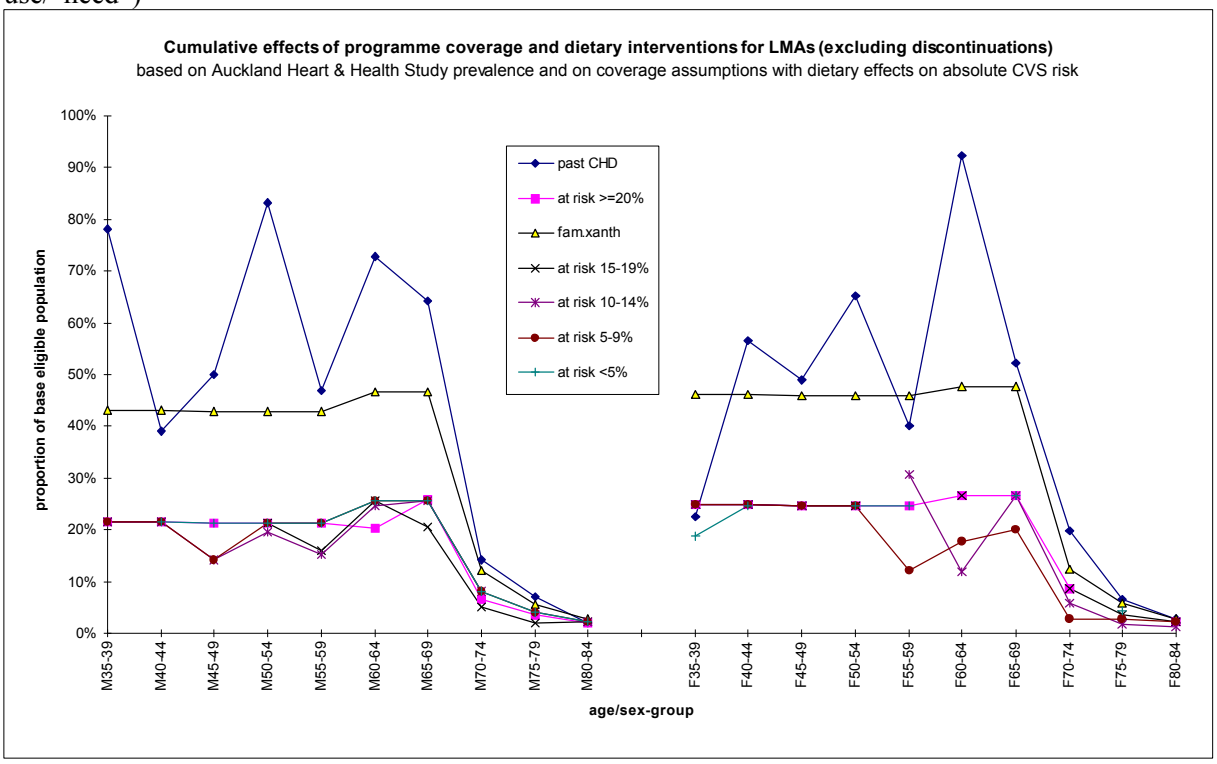


Figure 3: Projected trends in LMA need by subgroup

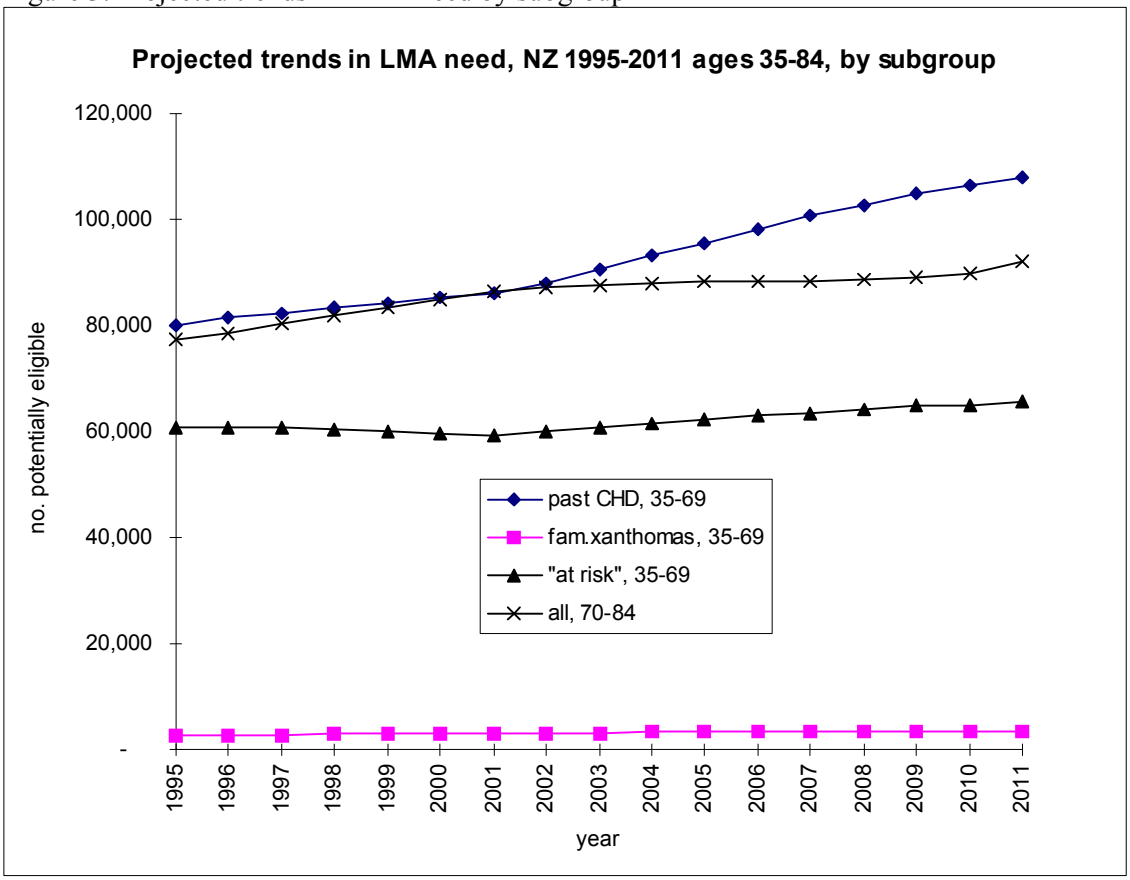


Figure 4: Sensitivity analyses of need for LMAs

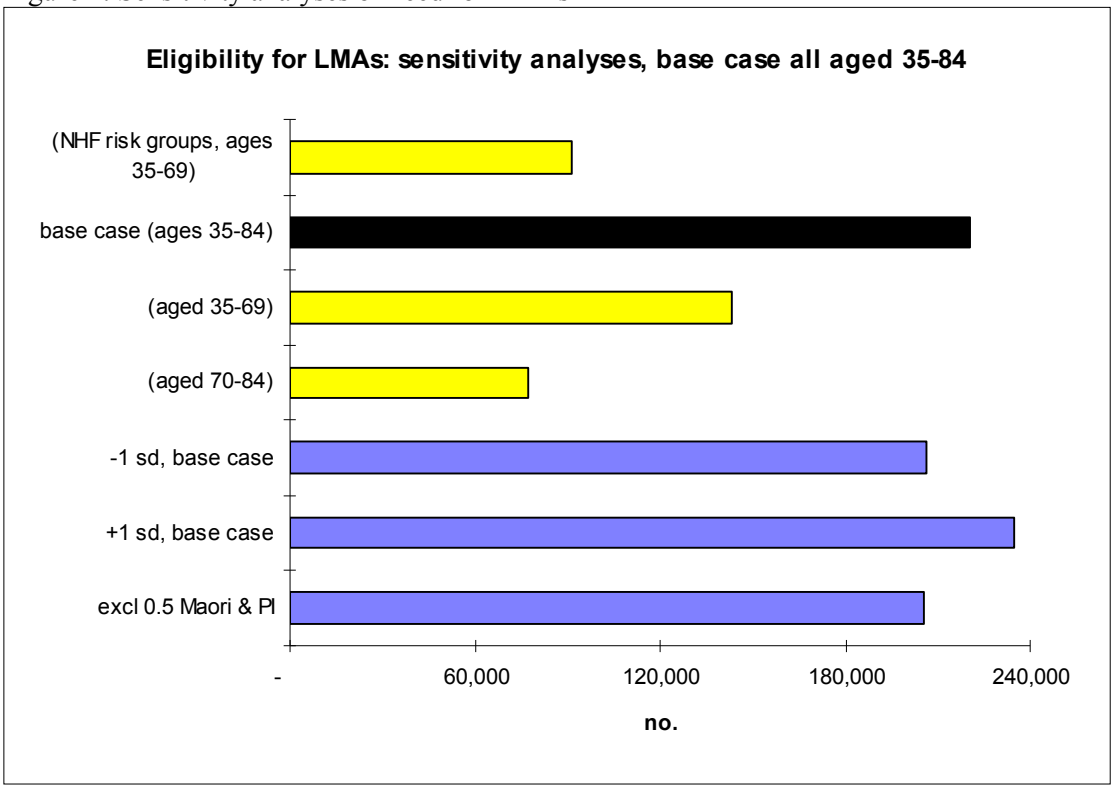


Figure 5: Sensitivity analyses of trends in LMA need

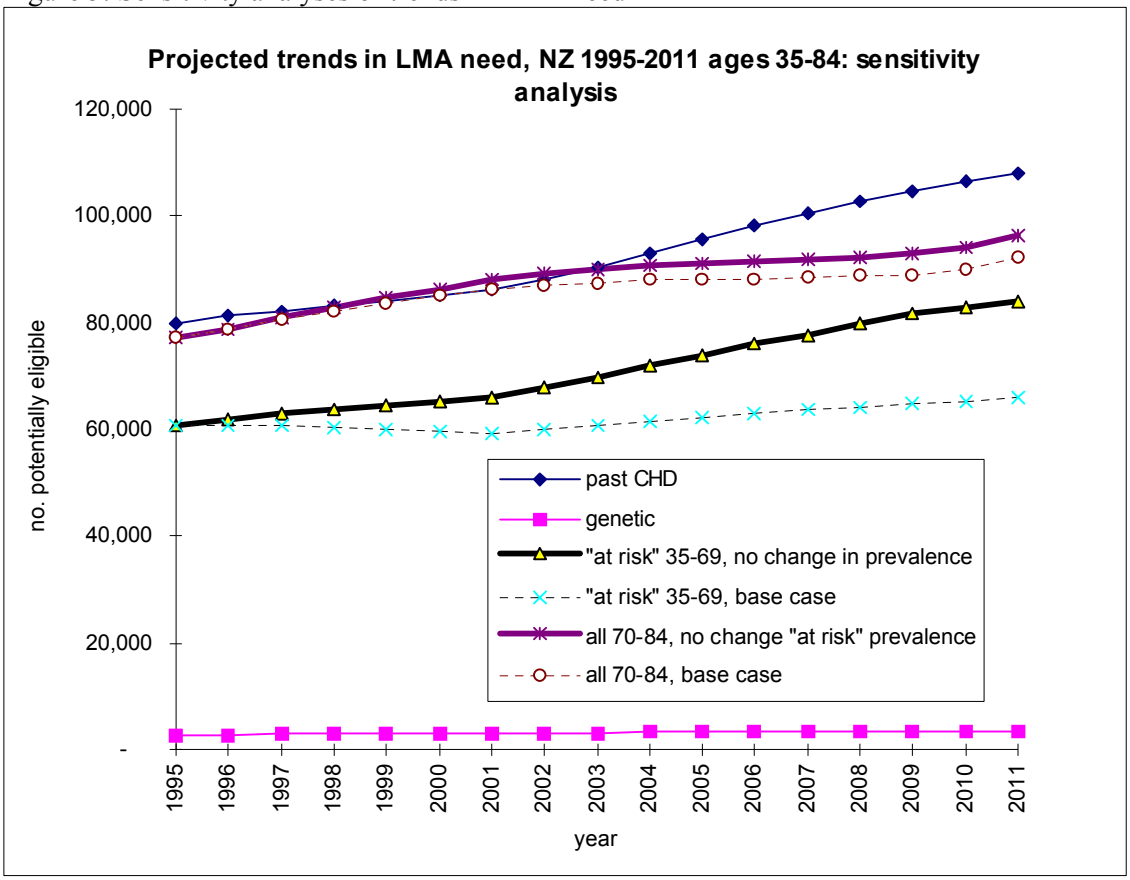


Figure 6: Projected trends in LMA users

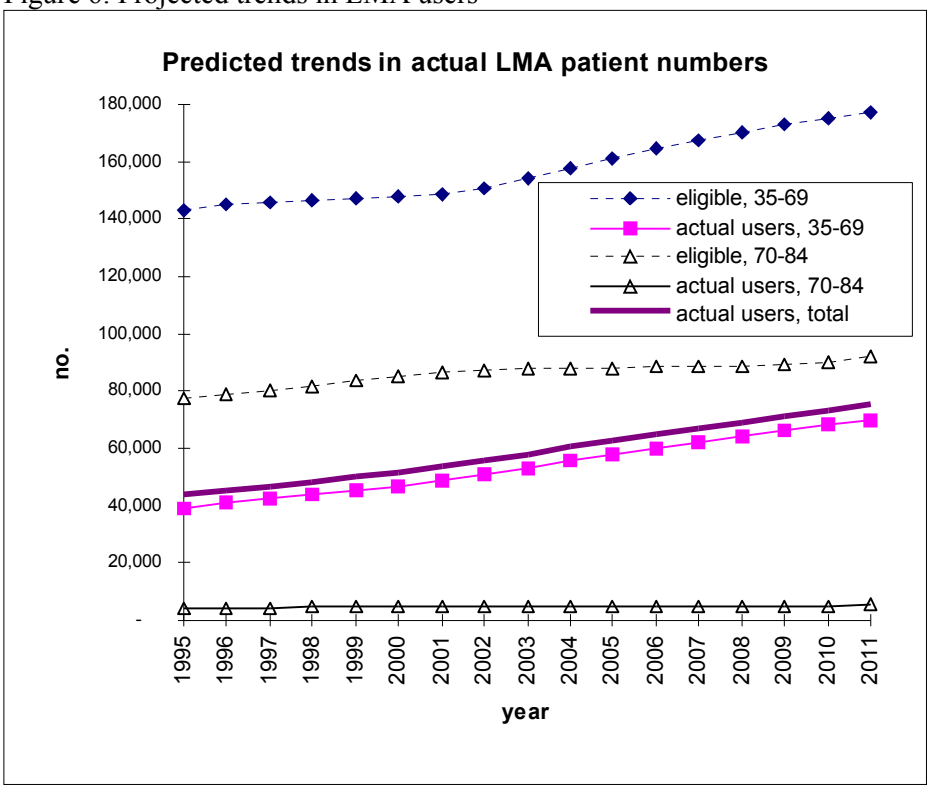


Figure 7: Projected trends in LMA costs

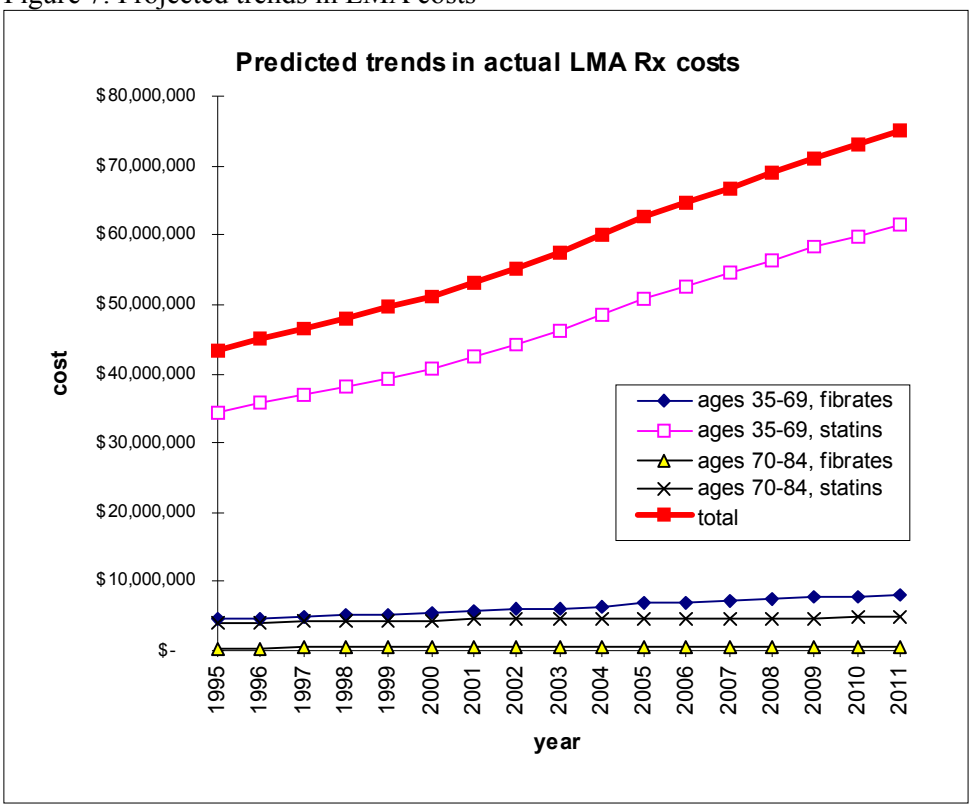


Figure 8: Sensitivity analyses of LMA actual use

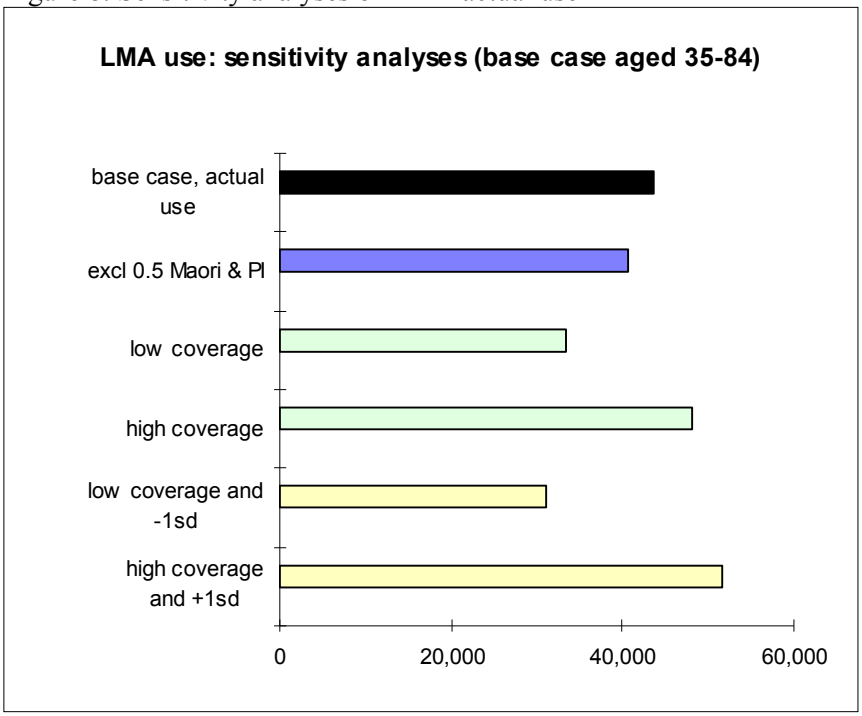


Figure 9: Sensitivity analyses of LMA actual costs

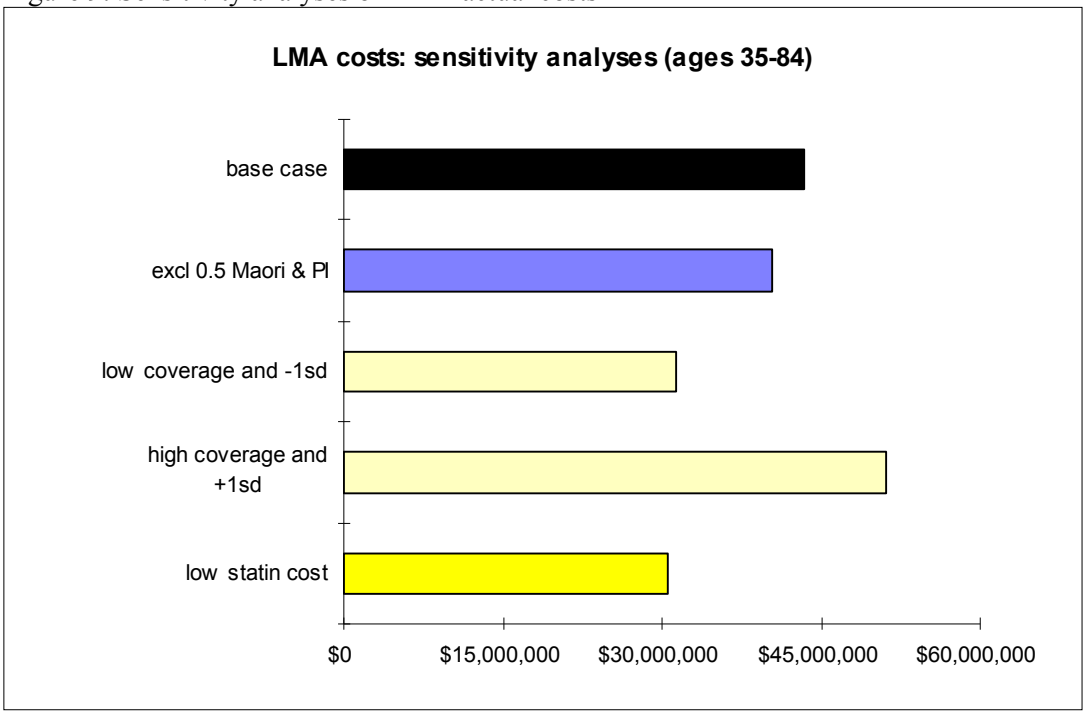


Figure 10: Sensitivity analysis of trends in actual LMA use

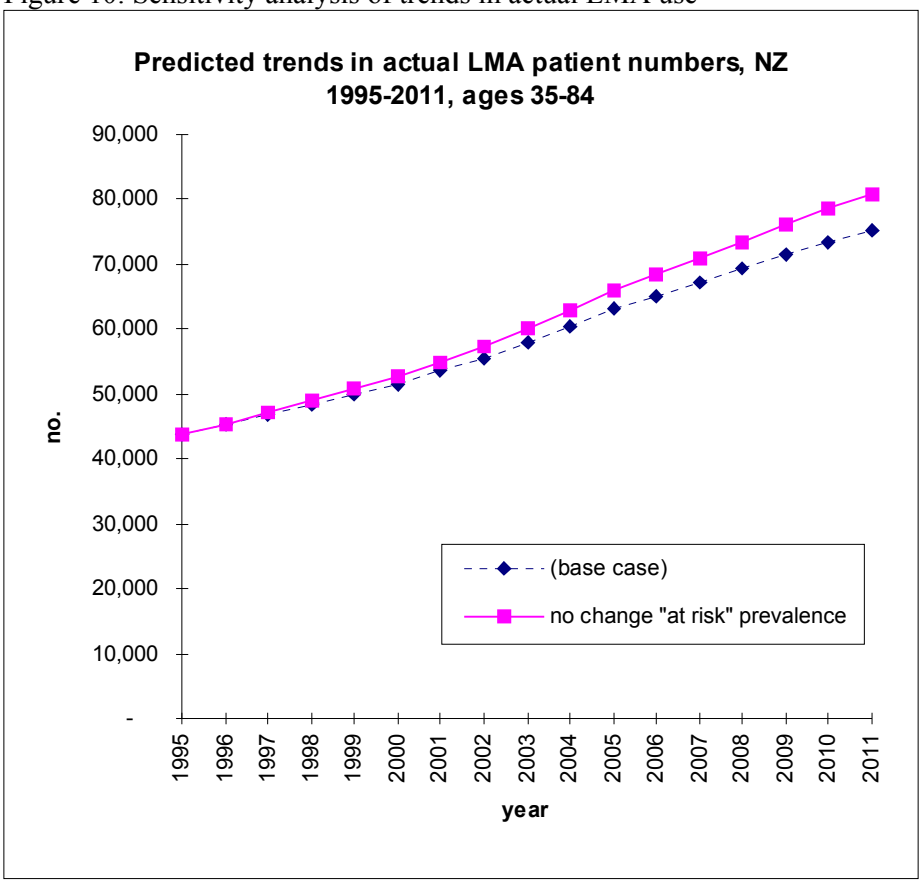


Figure 11: Sensitivity analysis of trends in actual LMA costs

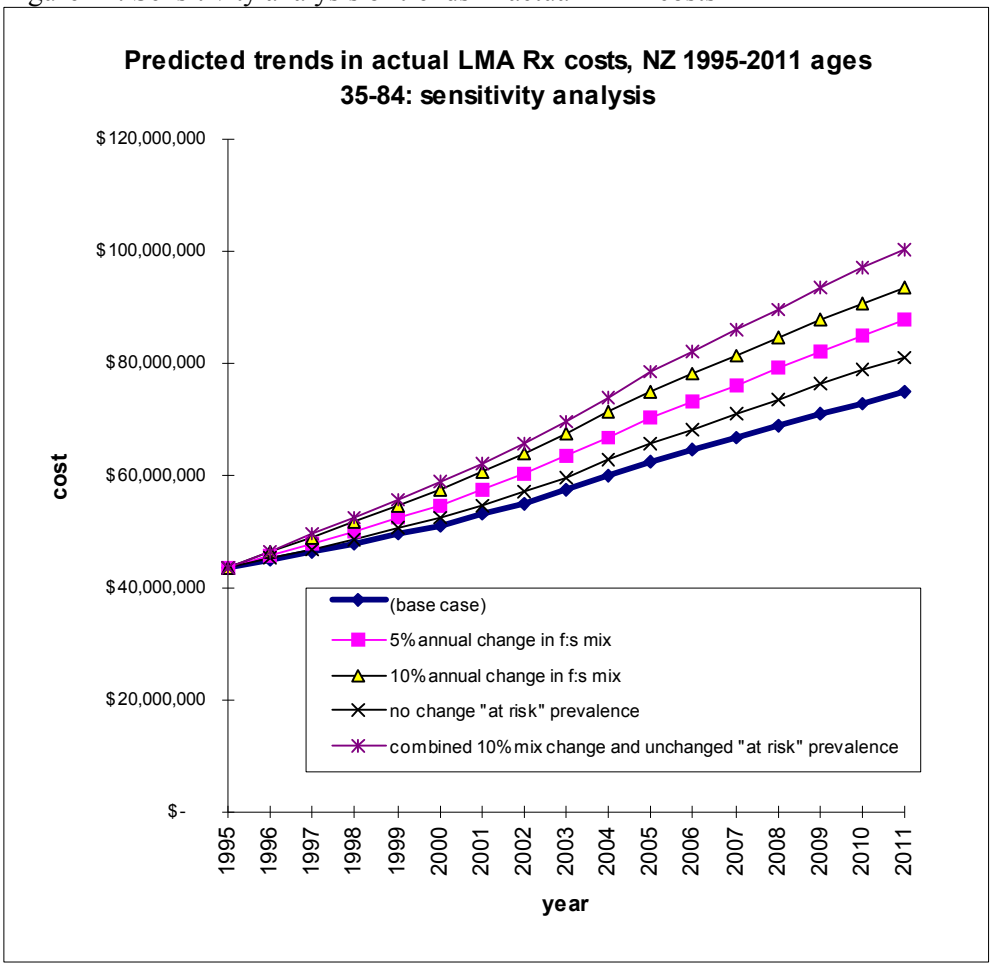


Figure 12: Effects of total cholesterol reductions upon relative need for LMAs

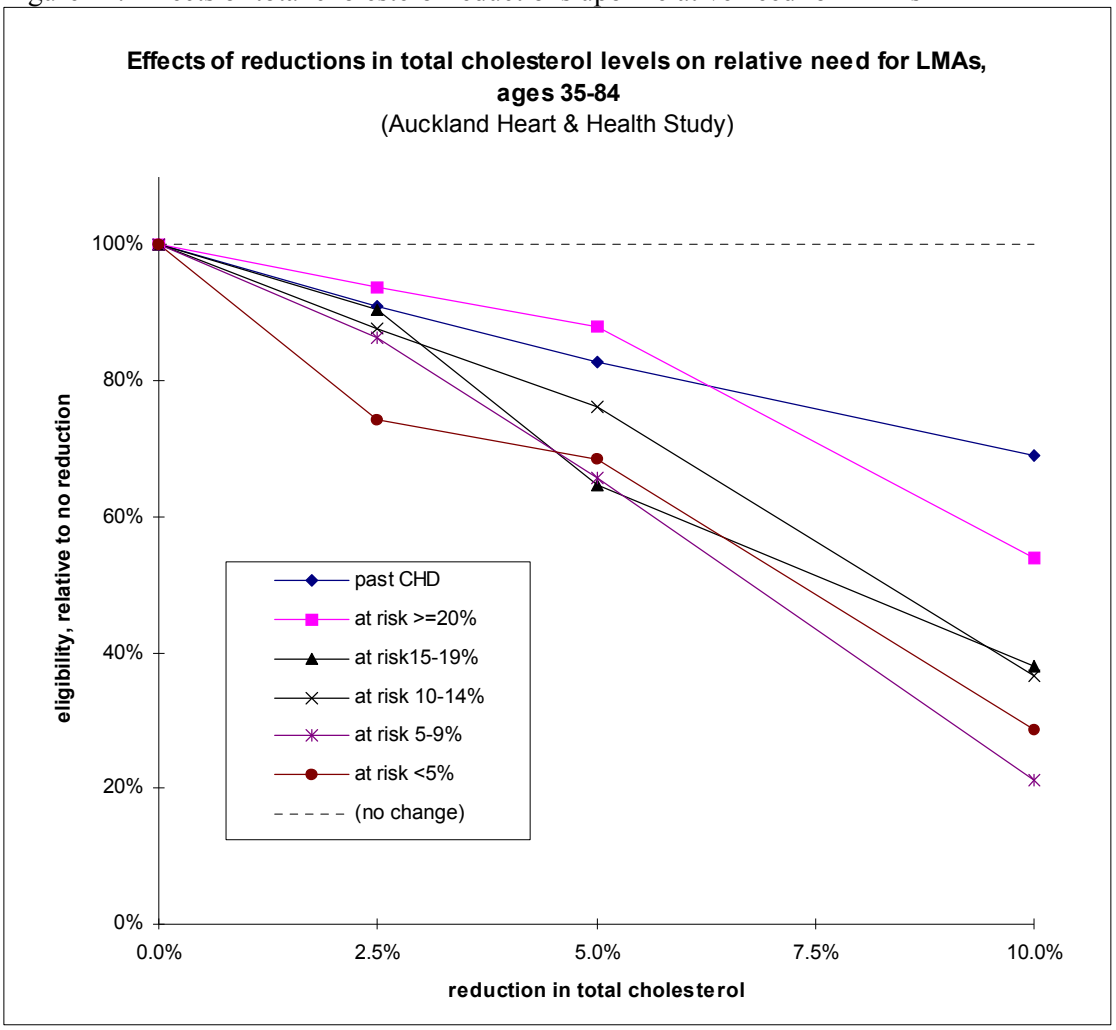


Figure 13: Effects of total cholesterol reductions on numbers of people needing LMAs

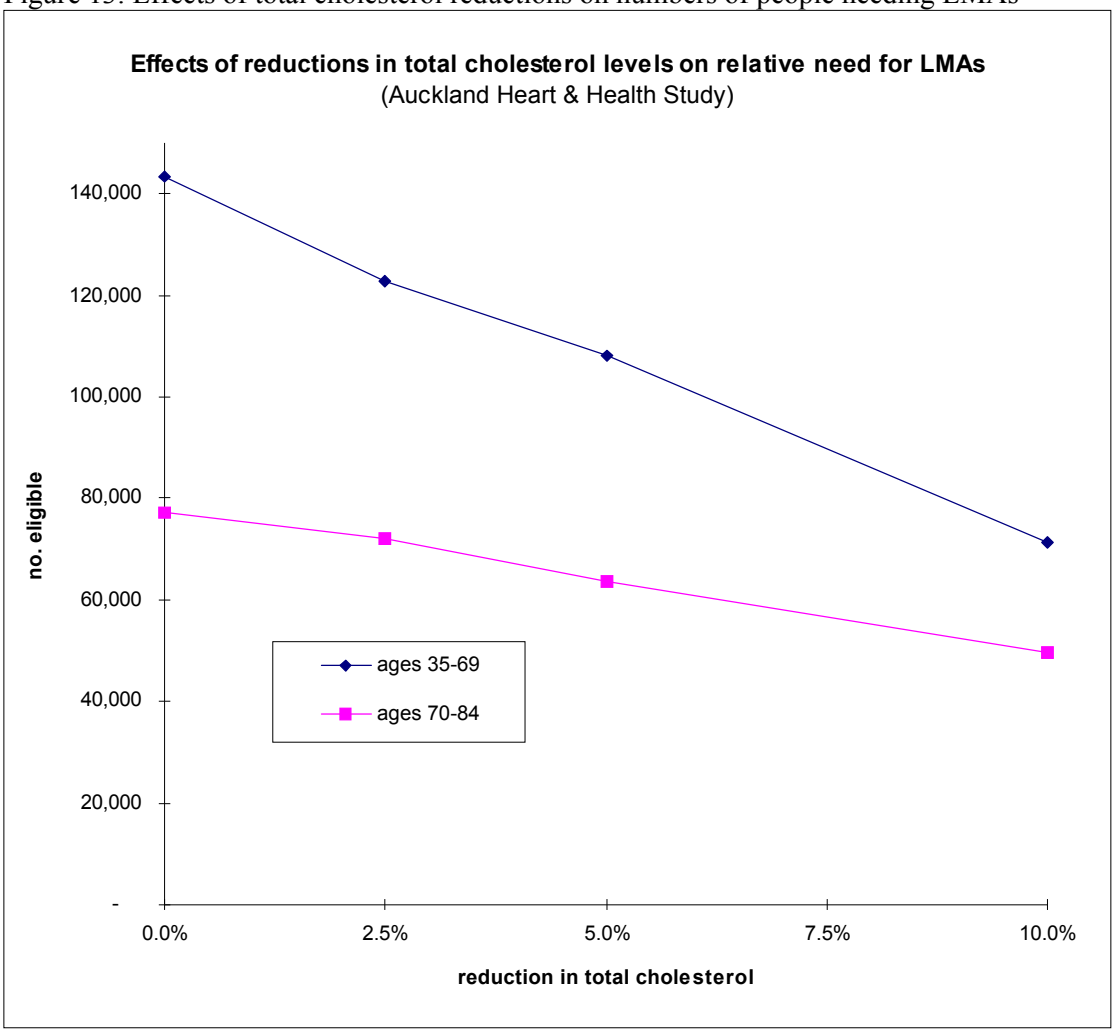
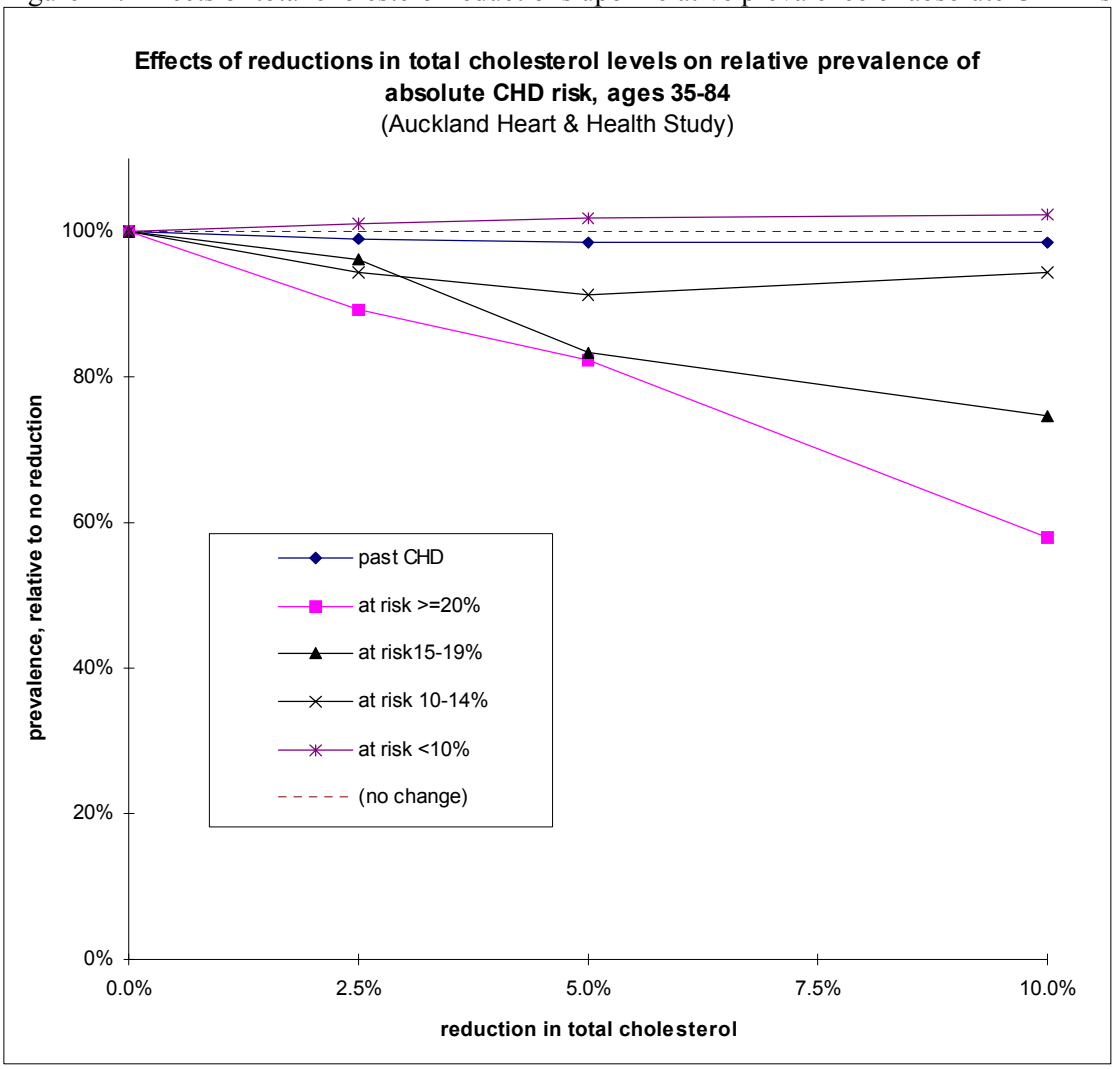


Figure 14: Effects of total cholesterol reductions upon relative prevalence of absolute CHD risk



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