National Institute for Health and Clinical Excellence

Economic analysis of interventions to improve the use of statins interventions in the general population

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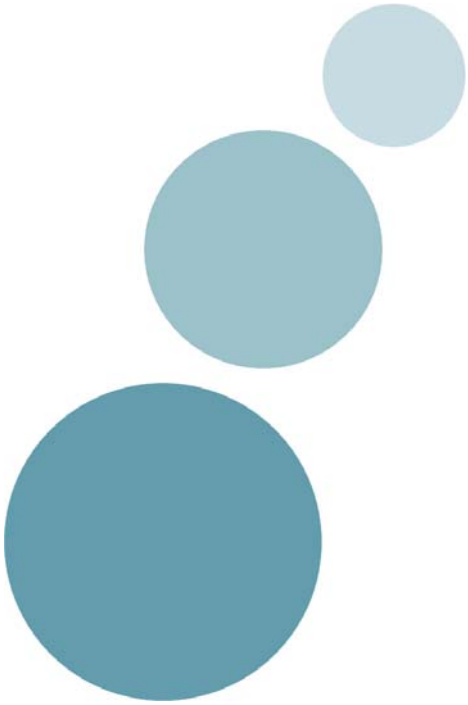

Contents

1.0 Executive summary

Introduction

The National Institute for Health and Clinical Excellence (NICE) has been asked by the Department of Health to develop 'guidance for reducing health inequalities in the short, medium and long term'. Specifically, the guidance will focus on interventions that reduce the rates of premature death in the most disadvantaged and with particular reference to proactive case finding, retention and improving access to services. In particular, the guidance will focus on interventions that identify disadvantaged groups in need of statins and smoking cessation interventions, that improve disadvantaged groups' use of statins and smoking cessation interventions, and that improve the retention of disadvantaged groups within statins and smoking cessation interventions.

The economic analysis takes as its starting point the evidence on effectiveness of interventions to improve the reach, use and retention of smoking cessation interventions and statins identified by Bath University (Bauld et al, 2007) and the University of Cardiff (Turley et al, 2007). The effectiveness evidence identified was of two types: studies that measured the effectiveness of interventions for disadvantaged groups; and studies that measured the effectiveness of interventions for the general population. It was decided that two types of economic analysis would be run. First, an analysis of the cost per QALY gained of interventions targeted at disadvantaged groups. Second, an analysis of the cost per QALY gained of interventions targeted at the general population, as well as an analysis of how the costs and effects of the interventions could vary when applied to disadvantaged groups without causing the cost per QALY gained estimate to exceed £30,000.

As each of these analyses was undertaken for smoking cessation interventions and statins interventions, The Matrix Knowledge Group produced four sets of economic analysis to inform the development of NICE guidance in this area:

1. An economic analysis of interventions to improve the reach, use and retention of ***statins*** interventions in ***disadvantaged groups***.
2. An economic analysis of interventions to improve the reach, use and retention of ***statins*** interventions in the ***general population***.
3. An economic analysis of interventions to improve the reach, use and retention of ***smoking cessation*** interventions in ***disadvantaged groups***.
4. An economic analysis of interventions to improve the reach, use and retention of ***smoking cessation*** interventions in the ***general population***.

This report presents the economic analysis of interventions to improve the reach, use and retention of statins in general population that might be extended to disadvantaged groups.

Method

The following steps are undertaken to estimate the cost per QALY gained associated with interventions to improve the reach, use and retention of statins among the general population:

1. Effect studies identified in the review undertaken by Cardiff University (Turley et al, 2007) were included if they measured the impact of interventions on the general population.
2. Cost and effect data was extracted from the effect studies.
3. Economic models were constructed to transform these cost and effect data into estimates of the cost per QALY gained from interventions.
4. For those interventions with a cost per QALY gained estimate lower than the £30,000 threshold, the parameters in the models were varied to determine the extra cost and reduced effect the interventions could be allowed if they were still to be considered cost-effective when applied to disadvantaged groups.

Findings

From the effectiveness review, 6 studies of pharmacist-based interventions to improve compliance with statins among general population were identified and included in the economic analysis.

The three interventions targeted at primary prevention have a cost per QALY gained of c£3,000 (Blumi et al, 2000; Guthrie, 2001; and Ali, 2003). The three interventions targeted at secondary prevention have a cost per QALY gained of c£20,500 (Gonzalez et al, 2005; Lopez-Cabezas et al, 2006; Faulkner et al, 2000).

The analysis is subject to a number of caveats. First, the studies of primary prevention interventions on which the analysis draws employ poor research designs suggesting that the estimates of the effect of the intervention may be overestimated. Second, the estimates of the cost of the interventions are based on descriptions of the interventions within the effectiveness studies. It is likely that these estimates therefore exclude some of the costs of the intervention, resulting in an overestimation of the cost-effectiveness of the intervention.

The sensitivity analysis suggests that the conclusion that interventions are cost effective is not sensitive to these caveats. Even if intervention costs are increased by 900%, all the interventions have a cost per QALY gained of less than £30,000, and a reduction in effect of c99% is required before the cost per QALY gained of primary prevention interventions exceed £30,000.

The above analysis determines the cost effectiveness of statins interventions when they are targeted at the general population. However, the NICE guidance that the analysis is designed to inform is interested in the cost-effectiveness of interventions when applied to disadvantaged groups. The sensitivity analysis demonstrates that costs would have to increase by very large

amounts or effects would have to reduce by very large amounts before the interventions would have a cost per QALY gained of greater than £30,000. For instance, the lowest increase in costs required to cause the cost per QALY gained to be greater than £30,000 is 1,900 percent (Faulkner et al, 2000). However, most of the interventions require increases in cost in the magnitude of many thousands of percent before the cost per QALY gained exceeds £30,000. A similar story is told for changes in effect. All the interventions require a reduction in effect of c99% before the cost per QALY gained becomes greater than £30,000.

Discussion

Pharmacist-based interventions to improve compliance with statins for primary prevention are cost-effective, with a cost per QALY gained of c£3,000, lower than the £20,000-£30,000 threshold. Similar interventions for secondary prevention are less cost-effective, with a cost per QALY gained of c£20,500, between the £20,000 and £30,000 thresholds.

As with any analysis, the result are subject to a number of caveats, but the analysis demonstrates that the conclusion regarding the cost-effectiveness of the interventions are not sensitive to these caveats.

Furthermore, while this analysis is based on the effectiveness of the interventions for the general population, the cost of the interventions would have to be considerably larger (at least 1,900% larger) or the effect of the interventions considerable smaller (99% lower) when applied to disadvantaged groups before the cost per QALY gained of the interventions exceeds £30,000.

While the above analysis measures the impact of the interventions on health outcomes, as the target population for the guidance belong to disadvantaged groups, the impact is both to increase health outcomes and reduce health inequalities. One way to account for this is to adjust the £30,000 per QALY threshold against which interventions are assessed to include the value of reducing health inequalities. Work on equity adjustments to the cost-effectiveness threshold is in its very early days and only provides very indicative estimates of possible equity-efficiency weights. Work by Professor Dolan and colleagues suggest that interventions that reduce health inequalities should be assessed against a cost-effectiveness threshold of £120,000. This higher cost-effectiveness threshold would reinforce the conclusion that the interventions included in the analysis would be cost-effective when applied to disadvantaged groups. However, this threshold should be treated with caution. Professor Dolan will be presenting fresh empirical evidence, from much larger samples, shortly.

2.0 Introduction

The National Institute for Health and Clinical Excellence (NICE) has been asked by the Department of Health to develop 'guidance for reducing health inequalities in the short, medium and long term', on interventions that reduce the rates of premature death in the most disadvantaged with particular reference to proactive case finding, retention and improving access to services. The focus of this guidance is on interventions that identify disadvantaged groups in need of statins and smoking cessation interventions, that improve disadvantaged groups' use of statins and smoking cessation interventions, and that improve the retention of disadvantaged groups within statins and smoking cessation interventions.

The economic analysis takes as its starting point the evidence on effectiveness of interventions to improve the reach, use and retention of smoking cessation interventions and statins identified by Bath University (Bauld et al, 2007) and the University of Cardiff (Turley et al, 2007). The effectiveness evidence identified was of two types: studies that measured the effectiveness of interventions for disadvantaged groups; and studies that measured the effectiveness of interventions for the general population. It was decided that two types of economic analysis would be run. First, an analysis of the cost per QALY gained of interventions targeted at disadvantaged groups. Second, an analysis of the cost per QALY gained of interventions targeted at the general population, as well as an analysis of how the costs and effects of the interventions could vary when applied to disadvantaged groups without causing the cost per QALY gained estimate to exceed £30,000.

As each of these analyses was undertaken for smoking cessation interventions and statins interventions, The Matrix Knowledge Group produced four sets of economic analysis to inform the development of NICE guidance in this area:

1. An economic analysis of interventions to improve the reach, use and retention of ***statins*** interventions in ***disadvantaged groups***.
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3. An economic analysis of interventions to improve the reach, use and retention of ***smoking cessation*** interventions in ***disadvantaged groups***.
4. An economic analysis of interventions to improve the reach, use and retention of ***smoking cessation*** interventions in the ***general population***.

This report presents the economic analysis of interventions to improve the reach, use and retention of statins in general population that might be extended to disadvantaged groups. The analysis seeks to answer two questions. First, what is the cost per QALY gained for the intervention when applied to the general population? Second, assuming interventions are more costly for disadvantaged groups and/or less effective for disadvantaged groups, for those interventions that are cost-effective for the general population, what is the extra cost and/or

reduced effect the interventions could be allowed if they were still to be considered cost-effective when applied to disadvantaged groups.

The remainder of this section outlines the need for guidance in this policy area and the precise scope of the review. Section 3.0 outlines the methods employed in the economic analysis. Section 4.0 outlines the results of the analysis, and section 5.0 draws conclusions from the analysis.

2.1 The need for guidance: background and policy context

Coronary heart disease (CHD) is the largest single cause of death, claiming 37% of the UK total[1]. The burden of CHD is directly linked to the increasing inequalities health in the UK. The death rate due to CHD among men from manual classes is 40% higher than for non-manual workers. Men of working age in social class V are 50% more likely to die from CHD than men in the population as a whole. The wives of manual workers have nearly twice the risk compared to wives of non-manual workers. There are also ethnic variations. For people born in the Indian sub-continent, the death rate from heart disease is 38% higher for men and 43% higher for women than rates for the country as a whole.

Improving the primary and secondary prevention of cardiovascular diseases in disadvantaged groups will be a significant driver in tackling health inequalities. Primary prevention of cardiovascular diseases requires identification of patients at high risk and treatment of eligible patients. Secondary prevention also requires identification and treatment of those with established CHD.

The National Service Framework for Coronary Heart Disease set standards for general practitioners and primary care to identify all people with established cardiovascular disease and people at significant risk and offer comprehensive advice and appropriate treatment. The use of statin therapy is recommended for adults with clinical evidence of cardiovascular disease and as part of the management strategy for the primary prevention of CVD for adults who have a 20% or greater 10-year risk of developing CVD[2].

2.2 Scope of the modelling exercise

The interventions and participants included in the modelling exercise were driven by the evidence provided by the statins effectiveness review (Turley et al, 2007). These were undertaken in correspondence with the parameters set out for the review, and include:

- ***Participants***
  - Including: patients at increased risk of developing CHD (primary prevention); and patients with established CHD (secondary prevention).
  - Including: disadvantaged, defined as individuals with mental health problems; people who are institutionalised including those serving a custodial sentence; some black and minority ethnic groups; homeless people; people on low incomes; lone parents and poor families; and people on benefits and living in public housing.
  - Excluding: patients not at increased risk of developing, or with established CHD.

[1] Department of Health. National Service Framework for Coronary Heart Disease. March 2000

[2] NICE. Statins for the prevention of cardiovascular events. 2006

- ***Interventions***.
    - Including: NHS interventions aimed at finding and then supporting adults at increased risk of developing, or with established, CHD. These activities will cover both primary and secondary prevention.
    - Including: NHS interventions aimed at providing – and improving access to – services for adults at increased risk of developing, or with established CHD. These activities will cover both primary and secondary prevention.
    - Excluding: interventions and activities not aimed at reducing and/or eliminating premature death from coronary heart disease.
    - Excluding: interventions and activities aimed at reducing and/or eliminating infant mortality.
    - Excluding: the wider determinants of health inequalities such as macro level policies aimed at tackling poverty and economic disadvantage.

- ***Comparators***. Interventions will be examined, where possible, against relevant comparators and/or no intervention.

The review identified studies of a number of interventions for non-disadvantaged groups that could be employed to improve the reach, use and retention of statins for disadvantaged groups. This paper therefore relaxes the criteria that participants have to be from disadvantaged groups.

The economic model diverges from the effectiveness review in the outcomes of interest. The review identified studies with the following ***outcomes***:

- How services identify and reach patients at increased risk of developing, or with established CHD.
- Service use, accessibility and availability among patients at increased risk of developing, or with established CHD.

The economic model extrapolates from these outcomes to, where possible, estimate the cost per Quality Adjusted Life Year (QALY) associated with the intervention. Further detail on the method employed to undertake this extrapolation is available in section 3.0.

3.0 Method

The following four steps are undertaken to estimate the cost per QALY gained associated with interventions to improve the reach, use and retention of statins among the general population:

1. Effect studies identified in the review undertaken by Cardiff University (Turley et al, 2007) were included if they measured the impact of interventions on the general population.
2. Cost and effect data was extracted from the effect studies.
3. Economic models were constructed to transform these cost and effect data into estimate of the cost per QALY gained from interventions.
4. For those interventions with a cost per QALY gained estimate lower than the £30,000 threshold, the parameters in the models were varied to determine the extra cost and reduced effect the interventions could be allowed if they were still to be considered cost-effective when applied to disadvantaged groups.

The remainder of this section provides more detail on each of these steps.

3.1 Selection of effect studies for modelling

The economic model is built on the evidence employed by the review team at Cardiff University to conclude about the effectiveness of interventions (Turley et al, 2007). The effectiveness studies had to fulfil two criteria before they were included in the economic model:

1. Studies had to measure effect of an intervention for the general population. A number of the effect studies measured the impact of interventions to improve the reach, use and retention of statins for disadvantaged groups. These studies were excluded from the analysis presented in this report. Economic analysis for these studies are presented in Matrix Evidence (2007).
2. Studies had to measure reach, use or retention. Studies that did not provide a measure of reach, use or retention were excluded from the modelling. For instance, a number of studies identified participants perceptions of the barriers to accessing statins or practitioners perceptions of the effect of interventions.

Once the criteria had been applied, data on 6 interventions were included in the economic analysis. Appendix one summarises the studies that were included and excluded, and the reasons for any exclusions.

3.2 Extraction of data from effect studies

Data on the cost and effect of the intervention were extracted from the studies included in the modelling:

1. Effect data. Where a choice of effect data was available, the effect 'closest to statins use' was selected. As the objective of the economic analysis was to estimate the cost per QALY gained associated with the interventions, and the objective of the analysis is to assess the cost effectiveness of interventions to increase the reach, use and retention of statins interventions, the economic analysis estimated the cost per QALY gained for the interventions as a result of their impact on statins use. Therefore, while the aim of an intervention may be to identify CHD risk among general population, the QALY gained associated with this intervention results not just from knowing that someone is at risk of CHD, but from the impact that this subsequently has on the likelihood of using statins. In this instance, if the study reported the impact of the intervention on both the likelihood that an intervention identified someone as at risk of CHD, as well as the impact on statins use, the latter data was extracted. The economic analysis then converted the chance of statins use into an estimate of QALY gains. However, if the study only reported the impact of the intervention on the chance that an individual was identified as being at risk of CHD, this data was extracted and the economic analysis extrapolated from being identified as having CHD risk to QALY gains.
2. Cost data[3]. A number of the studies reported the cost of implementing the intervention. Where this was the case, implementation costs were extracted from the study. Where this was not the case, a description of the resources employed by the intervention was constructed from the intervention description in the study, and standard UK-based unit costs applied to this resource use to estimate the cost of the intervention. In a small number of instances, the intervention description was not sufficient to determine the resources used to implement the intervention. In this case, the study is excluded from the modelling. All intervention costs are presented at 2007 prices.

Appendix two summarises the cost and effect data extracted from the studies, any assumptions necessary to calculate resource use from intervention descriptions, as well as the unit cost data used to transform resource use into cost estimates. Assessment of the quality of the effectiveness studies employed in the economic analysis were taken from the effectiveness review undertaken by the University of Cardiff which identified the studies (Turley et al, 2007).

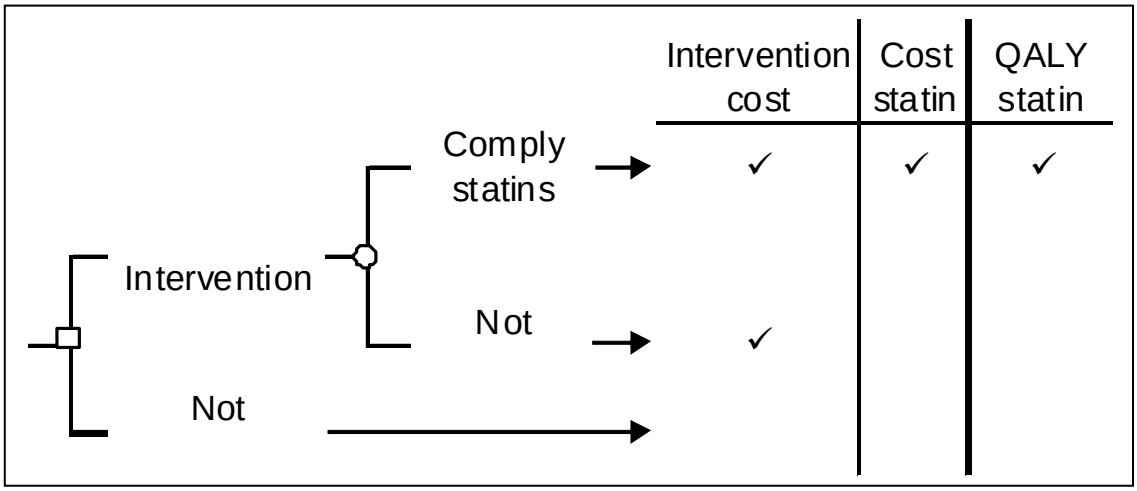
3.3 Economic model

Models were built to transform the effect and resource use measurements taken from the effectiveness studies into estimates of the cost per QALY gained associated with the interventions. The result of the effect data extraction process described in section 3.2 was that studies measured the effect of interventions on participants' compliance with statins

[3] The model assumes that those participants who receive the intervention but who would have experienced a positive outcome even in the absence of the intervention still incur the cost of the intervention. For instance, if an effect study suggests that some participants would have complied with statins even if they had not participated in a motivational interview with their GP, we assume that the GP delivers the same intervention to this group as to those who only comply having received the intervention, as well as to those who do not comply with or without the intervention. An alternative approach would have been to assume that participants who would have achieved a positive outcome in the absence of the intervention incur none of the intervention costs. In reality it is likely that these participants incur some intervention costs but less than other participants. The approach adopted will cause the model to overestimate the cost per QALY gained associated with the intervention.

prescriptions. Figure one summarises the hypothesised pathways post statins use, and the cost and benefits associated with each pathway included in the model.

Figure 1: Economic model of interventions that improve statin compliance for those with CHD risk



The probability of compliance with statins as a result of the intervention was drawn from the effect studies.

The costs and values attached to these pathways were as follows:

1. ***Intervention costs***: Intervention costs were extracted from the individual effect studies (see appendix two for more detail).
2. ***Costs and QALY gains associated with statins***: A review was undertaken to identify estimates of the costs and effects of statins. Individual study interventions and populations were matched to the data identified through this review to determine the most appropriate cost and effect data in each instance. Further detail of this review and matching exercise are available in section 3.4.

Hypothetical example of the calculation of cost per QALY for interventions to improve compliance with statins

An intervention involves a GP delivering a motivational interview aimed at improving compliance with a statins prescription. From the effectiveness study we know that the GP spends 20 mins on the motivational interview and that the intervention causes 50% of participants to comply with their statins prescription when only 25% would have done so in the absence of the GP-based intervention. A review of other studies tells us that 20 minutes of GP time costs £50, and that a course of statins costs £1,000 and results in a gain of 2 QALYs.

Costs: As every participant receives the intervention, the average GP cost per participant is £50 (100% * £50). As 25% of participants now comply with their statins prescription when they would not have done so previously, the average statins cost per participant is £250 (25% * £1,000). Thus, the overall average cost of the intervention per participant is £300 (£50 + £250).

Benefit: As 25% of participants now comply with their statins prescriptions when they would not have done so previously, the average benefit per participant is 0.5 QALYs (25% * 2 QALYs).

Cost per QALY gained: combining the estimates of the cost and benefit of the interventions, we can say that the cost per QALY gained of the GP-based intervention is £600 (£300/0.5 QALYs).

It is likely that participants who do not comply with their statins prescriptions still take part of their prescription. However, we do not know the extent to which the prescription is complied with. In this situation, the modelling team considered the following two assumptions. First, that those participants who do not comply with their statins prescription incur none of the costs of statins. Second, that those participants who do not comply with their statins prescriptions incur all the costs of statins. The models run make the former assumption – that non-compliance results in no statins cost. As this assumption underestimates the cost of the counterfactual, and thus overestimates the extra cost of the intervention, the approach adopted produces an estimate of the maximum cost per QALY of the intervention.

3.4 Review of economic analyses of statins

A review was undertaken to identify estimates of the costs and effects of statins. Incremental Cost Effectiveness Ratios (ICERs) for statins were extracted from existing NICE Health Technology Appraisals (Ebrahim, 1999; and Ward, 2005). 57 ICERs were collected. The following data was extracted to allow the appropriate ICERs to be incorporated into the model:

1. The type of statin studied.
2. The counterfactual against which its cost-effectiveness is measured.
3. The age, gender and CHD risk of the study population.
4. Details of the method employed to calculate the ICER: source of effect data, models employed, length of follow-up, discount rate and perspective employed.

Appendix four summarises the statins ICER data collected.

The following criteria were used to determine which ICERs to employ in the models:

1. Where different types of ICERs were available, ICERs were chosen for the models by applying the following hierarchy: (i) cost per QALY gained, including avoided public sector costs; (ii) cost per QALY gained, excluding avoided public sector costs; (iii) cost per life year gained, including avoided public sector costs; and (iv) cost per life year gained, excluding avoided public sector costs.
2. A ‘do nothing’ counterfactual was adopted.

3. The ICER study and the effect study were matched according to whether they were concerned with primary or secondary prevention.
4. Where possible the gender and age of the ICER study population and the effect study population were matched.

If the above matching process identified more than one statin ICER, the average of those ICERs meeting the criteria was employed in the model Appendix 5 summarises the ICERs included in the model of each effect study.

Employing the results of this review in the models outlined above requires the assumption that the cost per QALY estimates for statins identified in the literature relate to compliance with a statins prescription rather than just being prescribed statins. In the event that this assumption does not hold, and the estimates extracted from the literature are for the cost per QALY gained associated with being prescribed statins, then the cost per QALY gained for complying with statins would be higher than that used in the model. In this case, the model is underestimating the cost per QALY gained for interventions to improve compliance with statins.

It is also important to note that the cost per QALY gained estimates derived from the literature, while being the most recent available, will have been estimated prior to the expiry of the patent on statins. It is understood that the expiry of the patent has resulted in a fall in the price of statins. Consequently, the model overestimates the cost of statins and thus overestimate the cost per QALY gained of interventions to improve compliance with statins

3.5 Sensitivity analysis

Sensitivity analysis was undertaken to test the impact of the following caveats on the results of the economic analysis:

1. Effect size: two questions were raised about the accuracy of the effect data extracted from the studies. First, while the sample of studies modelled includes a number of good quality RCTs, it also includes a poor quality observational study and a number of poor quality before-after designs. The potentially poor measurement of the counterfactual means that there is a possibility that the model overestimates the effect and cost-effectiveness of the intervention. Second, 5 of the 6 studies are non-UK-based, while the other is unknown, raising questions about the transferability of the effect data to the UK context.
2. Intervention costs: In the majority of cases, the estimates of the cost of the interventions were based on descriptions of the interventions within the effectiveness studies. It is likely that these estimates therefore exclude some of the costs of the intervention, resulting in an overestimation of the cost-effectiveness of the intervention.

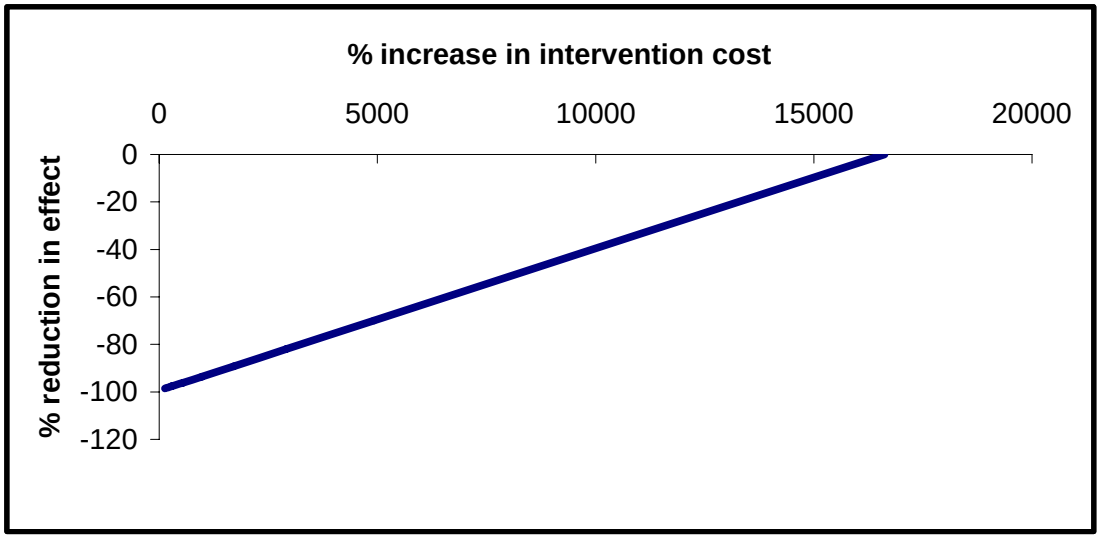
More detail on the sensitivity analysis conducted is available in appendix 6.

3.6 Cost-effectiveness when applied to disadvantaged groups

The above analysis produces an estimate of the cost per QALY gained for interventions when applied to the general population. Assuming that the interventions would be less cost-effective for disadvantaged groups, the final part of the analysis estimates how much more costly or less effective the interventions could be for a disadvantaged group while still being cost-effective compared to a £30,000 per QALY gained threshold. This is performed by calculating the cost-effect combinations for each study which would cause the intervention to have a cost per QALY threshold of £30,000.

An example of the output from this analysis is shown in figure 2. This shows the combination of increases in cost and reductions in effect that would cause the intervention to have a cost per QALY gained of £30,000. The origin of the graphs represents the cost-effect for the intervention when applied to the general population. The axes represent changes in cost and effect from this starting point. The line on the graph represents the changes in costs and effect that would produce a cost per QALY gained of £30,000. In this instance, the intervention would have a cost per QALY gained of £30,000 if costs were increased by c16500% compared to the cost of providing the intervention for a general population, keeping effect estimates constant. Or, the intervention would have a cost per QALY gained of £30,000 if the effect size was reduced by c99% compared to the effect achieved when the intervention is applied to the general population, keeping cost estimates constant. These estimates reflect the range of changes in costs and effect possible if the intervention was applied to disadvantaged groups, while still ensuring the intervention is cost-effective.

Figure 2: Example of analysis of the changes in cost and effect that produce a cost per QALY gained of £30,000



4.0 Findings

From the effectiveness review, 6 studies of pharmacist-based interventions to improve the compliance of statins among general population were identified and included in the economic analysis.

Figure 3 summarises the cost per QALY gained estimates for the interventions included in the model. It demonstrates that pharmacist-based interventions for primary prevention have a cost per QALY gained of £3,053-£3,167. This is lower than the £20,000-£30,000 threshold traditionally implied by NICE decisions. Pharmacist-based interventions for secondary prevention have a cost per QALY gained of £20,469-£20,580. This sits between the £20,000 and £30,000 cost-effectiveness thresholds used by NICE. The unit cost of the pharmacist-based interventions are similar for both primary and secondary prevention. Instead, the differences in cost per QALY gained between the two groups reflects the difference in the ICERs associated with statins use between the two types of patients.

Figure 3: The cost per QALY gained for interventions to improve the reach, use and retention of statins in the general population (interventions to improve compliance)

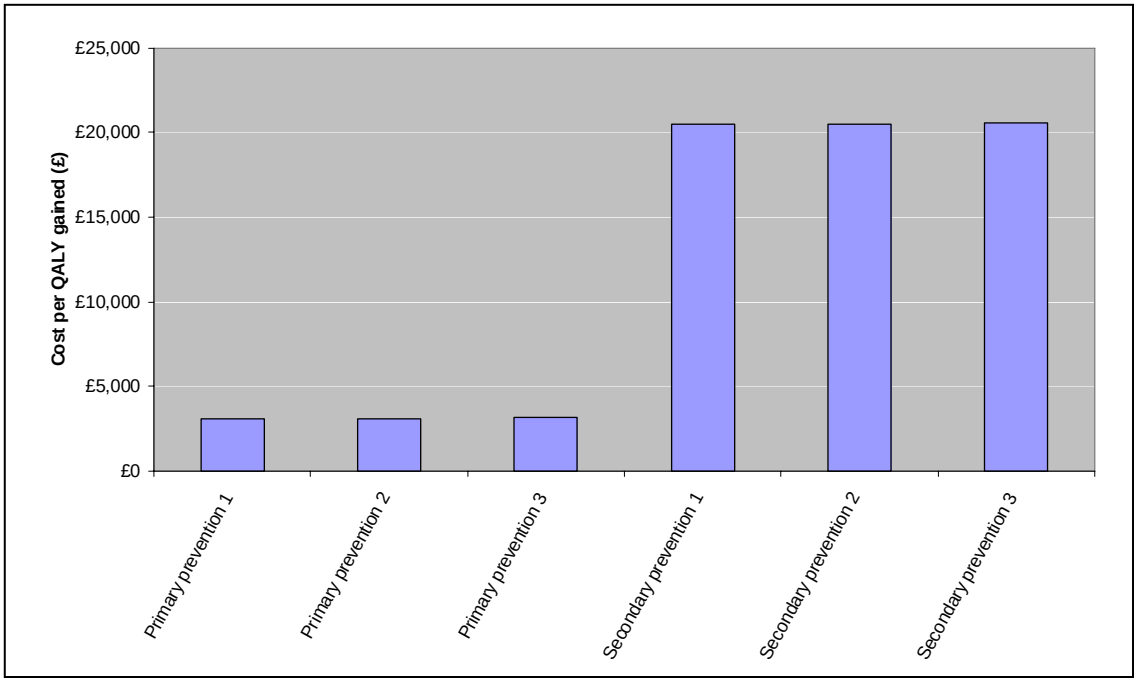


Figure 4 provides a more detailed summary of the result of the economic modelling. This serves to highlight two important caveats to the analysis. First, the quality of the methods employed in the effect studies. The studies of interventions to improve the use of statins for secondary prevention employ better research designs (RCTs), and the effect estimates therefore have a good level of validity. The studies of interventions to improve the use of statins for primary

prevention are based on before-after studies and observation studies. These study designs have less internal validity than RCTs and may result in inaccurate measurement of the effect of the intervention. However, the analysis undertaken on variation in effect size (appendix 6) suggest that the estimate of cost per QALY gained is not sensitive to the effect size employed in the model, and that effect sizes would have to be reduced c99% before the cost per QALY of the three primary prevention interventions passed above the £30,000 threshold.

Figure 4: Estimates of the cost per QALY gained (2007 prices)

Intervention type	Intervention	Authors	Method (quality)	Location	Intervention cost	Cost per QALY
Supporting patients once identified	Pharmacist interventions	Ali, 2003	BA (-)	Canada	£56.72	£3,167
		Bluml et al, 2000	Ob Study (-)	-	£230.15	£3,053
		Gonzalez et al, 2005	RCT (+)	US	£155.67	£20,469
		Guthrie, 2001	BA (+)	Spain	£6.78	£3,093
		Faulkner et al, 2000	RCT (-)	US	£95.88	£20,580
		Lopez-Cabezas et al, 2006	RCT (+)	Spain	£22.19	£20,492

A second caveat is the location of the studies included in the model. Five of the six studies are non-UK-based, while the other is unknown, raising questions about the transferability of the effect data to the UK context. However, the test of the impact of effect size on the conclusion that the intervention are cost-effective reported above also provides some comfort about the transferability of these effects to the UK context. As long as the interventions achieve 1% of the effect in the UK as they did in the US, Canada and Spain, they will still be considered cost-effective.

One other caveat should be noted. In the majority of cases the estimates of the cost of the interventions are based on descriptions of the interventions within the effectiveness studies. It is likely that these estimates therefore exclude some of the costs of the intervention, resulting in an overestimatation of the cost-effectiveness of the intervention. However, the analysis undertaken in appendix six demonstrates that conclusions regarding the cost-effectiveness of interventions are not sensitive to the estimate of intervention cost included in the model. Even when costs are increased 900%, all the interventions still have a cost per QALY gained of less then £30,000.

The above analysis determines the cost effectiveness of statins interventions when they are targeted at the general population. However, the NICE guidance that the analysis is designed to inform is interested in the cost-effectiveness of interventions when applied to disadvantaged groups. In order to inform this guidance, appendix seven presents an analysis of the change in cost and/or effect required before the cost per QALY gained for an intervention becomes £30,000. As the majority of the interventions prove cost-effective for the general population, this analysis assumed that interventions are less cost-effective for disadvantaged groups and thus calculates the increase in cost and/or the reduction in effect required before the cost per QALY gained for an intervention becomes £30,000. It demonstrates that costs would have to increase by very large amounts or effects would have to reduce by very large amounts before the

interventions would have a cost per QALY gained of greater than £30,000. For instance, the lowest increase in costs required to cause the cost per QALY gained to be greater than £30,000 is 1,900 percent (Faulkner et al, 2000). However, most of the interventions require increases in cost in the magnitude of many thousands of percent before they become cost-ineffective. A similar story is told for changes in effect. All the interventions require a reduction in effect of 99% before the cost per QALY gained becomes greater than £30,000.

5.0 Discussion

The analysis demonstrates that pharmacist-based interventions to improve compliance with statins for primary prevention among the general population are cost-effective, with a cost per QALY gained of c£3,000. Interventions that improve statin compliance for secondary prevention are less cost-effective, with a cost per QALY gained of c£20,500, sitting between the £20,000 and £30,000 per QALY thresholds used by NICE.

As with any analysis, the result are subject to a number of caveats. The caveats can be divided into two types. First, those assumptions that cause the analysis to overestimate the cost per QALY gained associated with the intervention. As the estimates of cost per QALY gained emerging from the model are lower than the NICE threshold, these caveats will not change the conclusion of the analysis. Second, those assumptions that cause the analysis to underestimate the cost per QALY gained associated with the intervention. The sensitivity analysis was designed to test the impact of this second type of caveat on the outcome of the analysis and suggests that the conclusion regarding the cost-effectiveness of the interventions are not sensitive to these assumptions.

The above analysis determines the cost effectiveness of statins interventions when they are targeted at the general population. However, the analysis suggests that intervention costs would have to increase by very large amounts or intervention effects would have to reduce by very large amounts when the interventions are applied to disadvantaged groups before the interventions would have a cost per QALY gained of greater than £30,000. For instance, most of the interventions require increases in cost in the magnitude of many thousands of percent or a reduction in effect of c99% before the cost per QALY gained becomes greater than £30,000. Thus it is likely that the intervention would be cost-effective when applied to disadvantaged groups.

While the above analysis measures the impact of the interventions on health outcomes, as the target population for the guidance belong to disadvantaged groups, the impact is both to increase health outcomes and reduce health inequalities. One way to account for this is to adjust the £30,000 per QALY threshold against which interventions are assessed to include the value of reducing health inequalities. Work on equity adjustments to the cost-effectiveness threshold is in its very early days and only provides very indicative estimates of possible equity-efficiency weights. Professor Dolan and colleagues are engaged in on-going research into public preferences over various efficiency-equity trade-offs in health. In one small study of 66 respondents, Dolan and Tsuchiya (forthcoming, a) have estimated the weight given to a unit health gain to the lowest social class compared to a unit health gain for the highest social class. When differences in health are expressed in terms of life expectancy, the average respondent weights a marginal gain in life expectancy to the lowest social class about seven times more highly than the same gain to the highest social class. When differences are expressed in terms of rates of limiting long-term illness, the corresponding weight is four. The lower of these estimates would suggest that an intervention that reduces health inequalities should be

assessed against a cost-effectiveness threshold of £120,000. This higher cost-effectiveness threshold would reinforce the conclusion that the interventions included in the analysis would be cost-effective when applied to disadvantaged groups. However, this threshold should be treated with caution. Professor Dolan will be presenting fresh empirical evidence, from much larger samples, shortly.

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7.0 Appendix 1: Effect review studies included and excluded from the model

Study	Included/excluded
Ahktar et al 2001	Excluded – not general population
Ali 2003	Included
Bader et al 2006	Excluded – not general population
Beswick et al 2004	Excluded - not report relevant outcome data
Biswas et al 1997	Excluded – not general population
Blumi et al 2000	Included
Byers et al 1999	Excluded – not general population
Chatterjee 1997	Excluded – not general population
Clark 2002 et al	Excluded - not report relevant outcome data
Davis et al 1996	Excluded – not general population
East et al 2004	Excluded - not report relevant outcome data
Faulkner et al 2000	Included
Feder et al 1999	Excluded – not general population
Gonzalez et al 2005	Included
Guthrie 2001	Included
Hamilton et al 1997	Excluded – not general population
Haw et al 2004	Excluded – not general population
Higginbottom 2006	Excluded - not report relevant outcome data
Huckerby et al 2006	Excluded – not general population
Kirkpatrick 2004	Excluded – not general population
Krieger et al 1999	Excluded – not general population
Lacey 2004	Excluded – not general population
Lindesey 1997	Excluded - not report relevant outcome data
Lopez-Cabezas et al 2006	Included
Macintosh 2003	Excluded - not report relevant outcome data
Macnee et al 1996	Excluded – not general population
Manson-Siddle et al 1999	Excluded – not general population
Margolis et al 2003	Excluded – not general population
Molokhia 2000	Excluded – not general population
Muhlestein et al 2001	Excluded - not report relevant outcome data
Naqvi 2003	Excluded - not report relevant outcome data
Netto et al 2007	Excluded - not report relevant outcome data
O'Loughlin et al 1996	Excluded – not general population
Oexmann et al 2001	Excluded – not general population
Osborne et al 2003	Excluded – not general population
Richards et al 2003	Excluded - not report relevant outcome data
Tod et al 2001	Excluded - not report relevant outcome data
Tod et al 2002	Excluded - not report relevant outcome data
Vishram et al 2007	Excluded - not report relevant outcome data
Will et al 2004	Excluded – not general population
Williams et al 2001	Excluded – not general population

Study	Included/excluded
Wright et al 2006	Excluded - not report relevant outcome data

8.0 Appendix 2: Data extraction tables

Author And Year	Intervention	Incremental Cost per participant	Effect Data	Comment
Ali et al, 2003	Pharmacist led consultations and telephone calls	£56.72	Within the treatment group 40.7% (51/91) complied with their prescription. Within the control group 56.0% (37/91) complied with their prescription (P<0.05)	Resource use: ➢ Invitation. Assume equivalent to a single issue leaflet. ➢ Pharmacist led educational forum. Assumes one forum given by one pharmacist per 25 patients and that each forum lasts 2 hours. ➢ Educational booklet. Assume each participant receives one. ➢ 30 minute pharmacist consultation. ➢ 2 bi-monthly phone calls from a pharmacist. Assume each phone calls lasts 10 minutes. Cost data: ➢ Pharmacist: £48.55 per hour - Source: N & C (2006) ➢ Booklet: £5.95 - Source: MIDRIS (2007) ➢ Singe issue leaflet: £2.95 - Source: MIDRIS (2007)

Author And Year	Intervention	Incremental Cost per participant	Effect Data	Comment
Blumi et al, 2000	Project ImPACT - A community based pharmacist project	£230.15	Within the treatment group (345/574) 60.1% complied with their prescription. No control groups reported.	Resource use: ➢ 2.5 days of pharmacist training. Assumes that each of the 32 pharmacies employs 2 pharmacists, that training was conducted by the equivalent of two social work team leader and that each day consisted of 8 hours of training. ➢ Initial pharmacist consultation. Length of consultation varies from 30-60 minutes, with a mean of 45 minutes. ➢ Pharmacy consultations. Monthly visits for 3 months, quarterly thereafter. Average length 22 mins. ➢ L-D-X system Cost data: ➢ Pharmacist: £48.55 per hour - Source: N & C (2006) ➢ Pharmacist: £38.22 per hour of non patient related contact, eg training - Source: N & C (2006) ➢ Social work team leader: £25.83 per hour of non patient contact, eg training - Source: N & C (2006) ➢ L-D-X system £1,000 (http://unimedinc.com/cholesterol.html)

Author And Year	Intervention	Incremental Cost per participant	Effect Data	Comment
Faulkner et al, 2000	Pharmacist counselling to improve lipid-lowering therapy compliance	£95.88	Within the treatment group 60.0% (9/15) complied with their statins prescription. Within the control group 26.7% (4/15) complied with their statins prescription	Resource use: ➢ 12 pharmacist phone calls. Assume each phone call lasts 10 mins. Cost data: ➢ Pharmacist: £48.55 per hour - Source: Netten & Curtis (2006)

Author And Year	Intervention	Incremental Cost per participant	Effect Data	Comment
Gonzalez et al, 2005	Nurse education amongst an outpatient heart failure population	£155.67	At 1 year 88.3% complied with their prescription. No control group reported.	Resource use: ➢ Five nurse consultations. Assume each lasts 20 mins. ➢ Three GP consultations ➢ One brochure at each consultation Cost data: ➢ Cost of a nurse £29.73 per hour. Source: Netten & Curtis (2006). ➢ Cost of a GP consultation £25.63. Source: Netten & Curtis (2006). ➢ Cost of a brochure £5.95. Source: MIDRIS (2007)

Author And Year	Intervention	Incremental Cost per participant	Effect Data	Comment
Guthrie 2001	Postal and telephone reminders	£6.78	Within the treatment group 79.7% (2,897/3,635) complied with their Pravastatin prescription. Within the control group 77.4% (707/913) complied with their Pravastatin prescription.	Resource use: ➢ Two telephone reminders. Assume each call takes 10 minutes and is undertaken by the equivalent of a social work assistant. ➢ Postcard. Cost data: ➢ Social work assistant cost £22.55 per hour. Source: Netten & Curtis (2006). ➢ Postcard cost £2.95. Source: MIDRIS (2007)

Author And Year	Intervention	Incremental Cost per participant	Effect Data	Comment
Lopez Cabezas, 2006	Pharmacist led active information programme	£22.19	Within the treatment group 85.0% complied with their prescriptions. Within the control group 73.9% complied with their prescriptions	Incremental cost of 2,170 Euros (2006) taken from article

9.0 Appendix 3: Summary of models employed with each effect study

Study	Economic model applied
Ali 2003	Intervention to improve compliance
Blumi et al 2000	Intervention to improve compliance
Faulkner et al 2000	Intervention to improve compliance
Gonzalez et al 2005	Intervention to improve compliance
Guthrie 2001	Intervention to improve compliance
Lopez-Cabezas et al 2006	Intervention to improve compliance

10.0 Appendix 4: ICER statins

Source	Treatment	Counterfactual	Population: other	Method	ICER
Ebrahim (1999)	Statins (low cost)	Do nothing	Secondary prevention, total mortality pa 3%	Based on meta-analysis of 23 statins trials. Decline in CHD mortality rates of 5% per year assumed throughout; Cost per LYG represents an average across the 23 papers analysed, 6% discount rate, NHS perspective, base-year 1999	£ / LYG: £3785. £ / LYG (included avoided health treatment costs): £2188.
Ebrahim (1999)	Statins	Do nothing	Baseline annual mortality rate: 6%	Based on meta-analysis of 23 statins trials. Decline in CHD mortality rates of 5% per year assumed throughout; Cost per LYG represents an average across the 23 papers analysed, 6% discount rate, NHS perspective, base-year 2000	£ / LYG: £4802. £ / LYG (included avoided health treatment costs): £2480.
Ebrahim (1999)	Statins	Do nothing	Baseline annual mortality rate: 3%	Based on meta-analysis of 23 statins trials. Decline in CHD mortality rates of 5% per year assumed throughout; Cost per LYG represents an average across the 23 papers analysed, 6% discount rate, NHS perspective, base-year 2001	£ / LYG: £6228. £ / LYG (included avoided health treatment costs): £4727

Source	Treatment	Counterfactual	Population: other	Method	ICER
Ebrahim (1999)	Statins (low cost)	Do nothing	Primary prevention, total mortality pa 0.5%	Based on meta-analysis of 23 statins trials. Decline in CHD mortality rates of 5% per year assumed throughout; Cost per LYG represents an average across the 23 papers analysed, 6% discount rate, NHS perspective, base-year 2002	£/ LYG: £5389. £ / LYG (included avoided health treatment costs): £4889.
Ebrahim (1999)	Statins (intermediate cost)	Do nothing	Secondary prevention, total mortality pa 3%	Based on meta-analysis of 23 statins trials. Decline in CHD mortality rates of 5% per year assumed throughout; Cost per LYG represents an average across the 23 papers analysed, 6% discount rate, NHS perspective, base-year 2003	£/ LYG: £7692. £ / LYG (included avoided health treatment costs): £6096.
Ebrahim (1999)	Statins	Do nothing	Baseline annual mortality rate: 1.86% (from trial data)	Based on meta-analysis of 23 statins trials. Decline in CHD mortality rates of 5% per year assumed throughout; Cost per LYG represents an average across the 23 papers analysed, 6% discount rate, NHS perspective, base-year 2004	£ / LYG: £7515. £ / LYG (included avoided health treatment costs): £6391.

Source	Treatment	Counterfactual	Population: other	Method	ICER
Ebrahim (1999)	Statins	Do nothing	Baseline annual mortality rate: 1.5%	Based on meta-analysis of 23 statins trials. Decline in CHD mortality rates of 5% per year assumed throughout; Cost per LYG represents an average across the 23 papers analysed, 6% discount rate, NHS perspective, base-year 2005	£ / LYG: £8239. £ / LYG (included avoided health treatment costs): £7242.
Ebrahim (1999)	Statins (high cost)	Do nothing	Secondary prevention, total mortality pa 3%	Based on meta-analysis of 23 statins trials. Decline in CHD mortality rates of 5% per year assumed throughout; Cost per LYG represents an average across the 23 papers analysed, 6% discount rate, NHS perspective, base-year 2006	£ / LYG: £9318. £ / LYG (included avoided health treatment costs): £7721.
Ebrahim (1999)	Statins	Do nothing	Baseline annual mortality rate: 1%	Based on meta-analysis of 23 statins trials. Decline in CHD mortality rates of 5% per year assumed throughout; Cost per LYG represents an average across the 23 papers analysed, 6% discount rate, NHS perspective, base-year 2007	£ / LYG: £9780. £ / LYG (included avoided health treatment costs): £8992.

Source	Treatment	Counterfactual	Population: other	Method	ICER
Ebrahim (1999)	Statins (intermediate cost)	Do nothing	Primary prevention, total mortality pa 0.5%	Based on meta-analysis of 23 statins trials. Decline in CHD mortality rates of 5% per year assumed throughout; Cost per LYG represents an average across the 23 papers analysed, 6% discount rate, NHS perspective, base-year 2008	£ / LYG: £10952. £ / LYG (included avoided health treatment costs): £10452
Ebrahim (1999)	Statins	Do nothing	Baseline annual mortality rate: 0.5%	Based on meta-analysis of 23 statins trials. Decline in CHD mortality rates of 5% per year assumed throughout; Cost per LYG represents an average across the 23 papers analysed, 6% discount rate, NHS perspective, base-year 2009	£ / LYG: £13260 (£9998-£18184). £ / LYG (included avoided health treatment costs): £12727 (£9596-£17453)
Ebrahim (1999)	Statins (high cost)	Do nothing	Primary prevention, total mortality pa 0.5%	Based on meta-analysis of 23 statins trials. Decline in CHD mortality rates of 5% per year assumed throughout; Cost per LYG represents an average across the 23 papers analysed, 6% discount rate, NHS perspective, base-year 2010	£ / LYG: £13767. £ / LYG (included avoided health treatment costs): £12767
Ward (2005)	Pravastatin (40mg daily) + diet and exercise	Diet and exercise	Primary prevention, 30% 10 yr CHD risk	Individual patient level model, 3.5% discount rate, NHS perspective, follow-up 3 years	£ / LYG: £61000

Source	Treatment	Counterfactual	Population: other	Method	ICER
Ward (2005)	Pravastatin (40mg daily) + diet and exercise	Diet and exercise	Primary prevention, 4% 10 yr CHD risk	Individual patient level model, 3.5% discount rate, NHS perspective, follow-up 3 years	£ / LYG: £120000
Ward (2005)	Pravastatin (40mg daily) + diet and exercise	Diet and exercise	Secondary treatment, 30% 10 yr CHD risk	Individual patient level model, 3.5% discount rate, NHS perspective, follow-up 3 years	£ / LYG: £67000
Ward (2005)	Pravastatin (40mg daily) + diet and exercise	Diet and exercise	Secondary treatment, 4% 10 yr CHD risk	Individual patient level model, 3.5% discount rate, NHS perspective, follow-up 3 years	£ / LYG: 3121000
Ward (2005)	Unknown dosage of Pravastatin	Do nothing	Primary prevention, CHD risk: 1.5%, Male, Average age 55	Markov model utilised, 6% discount rate, NHS perspective, base-year 2004	£ / LYG: £23737
Ward (2005)	20mg daily Simvastatin	Do nothing	Primary prevention, High CHD risk (risk not defined)	28% reduction in cholesterol level modelled on data from the Lipid Research Clinics primary prevention trial; Life expectancies, loss in life expectancy following unset of CHD and treatments costs referenced from unpublished data - Drummond & McGuire, 1998, discount rate 5%, NHS perspective, base-year 2004, follow-up 25 years	£ / LYG: £12745

Source	Treatment	Counterfactual	Population: other	Method	ICER
Ward (2005)	20mg daily Simvastatin	Do nothing	Primary prevention, Low CHD risk (risk not defined)	28% reduction in cholesterol level modelled on data from the Lipid Research Clinics primary prevention trial; Life expectancies, loss in life expectancy following unset of CHD and treatments costs referenced from unpublished data - Drummond & McGuire, 1998, discount rate 5%, NHS perspective, base-year 2004, follow-up 25 years	£ / LYG: £30402
Ward (2005)	2/3 of patients on 20mg daily and 1/3 of patients on 40mg daily of unknown Statin	Do nothing	Pre-existing risk of CHD (not defined) & Cholesterol concentration > 5.4 mmol/L, Average age 55	Costs for myocardial infarction and revascularisation procedures were based on published evidence; Markov model utilised, discount rate 5%, NHS perspective, base-year 2004, follow-up 10 years	£ / LYG: £42483
Ward (2005)	2/3 of patients on 20mg daily and 1/3 of patients on 40mg daily of unknown Statin	Do nothing	No history of CHD & Cholesterol concentration > 6.5mmol/L, Average age 55	Costs for myocardial infarction and revascularisation procedures were based on published evidence; Markov model utilised, discount rate 5%, NHS perspective, base-year 2004, follow-up 10 years	£ / LYG: £180554

Source	Treatment	Counterfactual	Population: other	Method	ICER
Ward (2005)	27mg daily Simvastin	Do nothing	Primary prevention, CHD risk: 4.5%, Average age 55, Male	Study based on a Trent Institute Working Group on Acute Purchasing Study; Lifetable model utilised, discount rate 6%, NHS perspective, base-year 2004	£ / LYG: £8154
Ward (2005)	27mg daily Simvastin	Do nothing	Primary prevention, CHD risk: 1.5%, average age 55, male	Study based on a Trent Institute Working Group on Acute Purchasing Study; Lifetable model utilised, discount rate 6%, NHS perspective, base-year 2004	£ / LYG: £20053
Ward (2005)	40mg daily Pravastatin	Do nothing	Secondary prevention, CHD risk: 4.5%, average age 58, male	Study based on a Trent Institute Working Group on Acute Purchasing Study; Lifetable model utilised, discount rate 6%, NHS perspective, base-year 2004	£ / LYG: £5619
Ward (2005)	40mg daily Pravastatin	Do nothing	Secondary prevention, CHD risk: 1.5%, average age 59, male	Study based on a Trent Institute Working Group on Acute Purchasing Study; Lifetable model utilised, discount rate 6%, NHS perspective, base-year 2004	£ / LYG: £13773
Ward (2005)	Atorvastatin	Placebo	Secondary prevention, non-diabetic population, male	Markov model employed, lifetime costs and benefits, discount rate 6%, NHS perspective, base-year 2004	£ / QALY gained: £3200 - £5000
Ward (2005)	Atorvastatin	Placebo	Secondary prevention, non-diabetic population, female	Markov model employed, lifetime costs and benefits, discount rate 6%, NHS perspective, base-year 2004	£ / QALY gained: £4500 - £5900

Source	Treatment	Counterfactual	Population: other	Method	ICER
Ward (2005)	Atorvastatin	Placebo	Primary prevention	Markov model employed, lifetime costs and benefits, discount rate 6%, NHS perspective, base-year 2004	£ / QALY gained: £1200 - £7300
Ward (2005)	Atorvastatin	Simvastatin	Secondary prevention, non-diabetic population	Markov model employed, lifetime costs and benefits, discount rate 6%, NHS perspective, base-year 2004	£ / QALY gained: £17000
Ward (2005)	Atorvastatin	Simvastatin	Secondary prevention, diabetic population	Markov model employed, lifetime costs and benefits, discount rate 6%, NHS perspective, base-year 2004	£ / QALY gained: £11000
Ward (2005)	Atorvastatin	Simvastatin	Primary prevention	Markov model employed, lifetime costs and benefits, discount rate 6%, NHS perspective, base-year 2004	£ / QALY gained: £4200 - £23100
Ward (2005)	Fluvastatin IR (40mg twice daily) + diet and lifestyle counselling	Diet and Lifestyle counselling	Secondary prevention (patients following percutaneous coronary intervention)	Markov model, use data from the LIPS trial of effectiveness, NHS perspective, follow-up 10 years	£ / QALY gained: £3200
Ward (2005)	Fluvastatin IR (40mg twice daily) + diet and lifestyle counselling	Diet and Lifestyle counselling	Secondary prevention (patients following percutaneous coronary intervention), with diabetes	Markov model, use data from the LIPS trial of effectiveness, NHS perspective, follow-up 10 years	£ / QALY gained: £1900
Ward (2005)	Rosuvastatin	Do nothing	Primary prevention, male	NHS perspective, base-year 2004, follow-up 20 years	£ / QALY gained: £2784. £ / LYG: £4088
Ward (2005)	Rosuvastatin	Do nothing	Primary prevention, female	NHS perspective, base-year 2004, follow-up 20 years	£ / QALY gained: £4730. £ / LYG: £7367
Ward (2005)	Rosuvastatin	Do nothing	Secondary prevention, male	NHS perspective, base-year 2004, follow-up 20 years	£ / QALY gained: £13373. £ / LYG: £7611

Source	Treatment	Counterfactual	Population: other	Method	ICER
Ward (2005)	Rosuvastatin	Do nothing	Secondary prevention, female	NHS perspective, base-year 2004, follow-up 20 years	£ / QALY gained: £31373. £ / LYG: £10775
Ward (2005)	Fluvastatin	Do nothing	Primary prevention, male	NHS perspective, base-year 2004, follow-up 20 years	£ / QALY gained: £2164. £ / LYG: £3174
Ward (2005)	Fluvastatin	Do nothing	Primary prevention, female	NHS perspective, base-year 2004, follow-up 20 years	£ / QALY gained: £3668. £ / LYG: £5725
Ward (2005)	Fluvastatin	Do nothing	Secondary prevention, male	NHS perspective, base-year 2004, follow-up 20 years	£ / QALY gained: £11520. £ / LYG: £6596
Ward (2005)	Fluvastatin	Do nothing	Secondary prevention, female	NHS perspective, base-year 2004, follow-up 20 years	£ / QALY gained: £25903. £ / LYG: £9021
Ward (2005)	Rosuvastatin	Fluvastatin	Primary prevention, male	NHS perspective, base-year 2004, follow-up 20 years	£ / QALY gained: £5214. £ / LYG: £7685
Ward (2005)	Rosuvastatin	Fluvastatin	Primary prevention, female	NHS perspective, base-year 2004, follow-up 20 years	£ / QALY gained: £9165. £ / LYG: £14156
Ward (2005)	Rosuvastatin	Fluvastatin	Secondary prevention, male	NHS perspective, base-year 2004, follow-up 20 years	£ / QALY gained: £19728. £ / LYG: £11001
Ward (2005)	Rosuvastatin	Fluvastatin	Secondary prevention, female	NHS perspective, base-year 2004, follow-up 20 years	£ / QALY gained: £54023. £ / LYG: £17550
Ward (2005)	Rosuvastatin	Do nothing	Primary prevention, male	NHS perspective, base-year 2004, follow-up 20 years	£ / QALY gained: £2023. £ / LYG: £3140
Ward (2005)	Rosuvastatin	Do nothing	Primary prevention, female	NHS perspective, base-year 2004, follow-up 20 years	£ / QALY gained: £3060. £ / LYG: £4843
Ward (2005)	Rosuvastatin	Do nothing	Secondary prevention, male	NHS perspective, base-year 2004, follow-up 20 years	£ / QALY gained: £19001. £ / LYG: £10515
Ward (2005)	Rosuvastatin	Do nothing	Secondary prevention, female	NHS perspective, base-year 2004, follow-up 20 years	£ / QALY gained: £24412. £ / LYG: £9751
Ward (2005)	Fluvastatin	Do nothing	Primary prevention, male	NHS perspective, base-year 2004, follow-up 20 years	£ / QALY gained: £1573. £ / LYG: £2441
Ward (2005)	Fluvastatin	Do nothing	Primary prevention, female	NHS perspective, base-year 2004, follow-up 20 years	£ / QALY gained: £2368. £ / LYG: £3754

Source	Treatment	Counterfactual	Population: other	Method	ICER
Ward (2005)	Fluvastatin	Do nothing	Secondary prevention, male	NHS perspective, base-year 2004, follow-up 20 years	£ / QALY gained: £16579. £ / LYG: £9208
Ward (2005)	Fluvastatin	Do nothing	Secondary prevention, female	NHS perspective, base-year 2004, follow-up 20 years	£ / QALY gained: £20279. £ / LYG: £8231
Ward (2005)	Rosuvastatin	Fluvastatin	Primary prevention, male	NHS perspective, base-year 2004, follow-up 20 years	£ / QALY gained: £3631. £ / LYG: £5632
Ward (2005)	Rosuvastatin	Fluvastatin	Primary prevention, female	NHS perspective, base-year 2004, follow-up 20 years	£ / QALY gained: £5712. £ / LYG: £8988
Ward (2005)	Rosuvastatin	Fluvastatin	Secondary prevention, male	NHS perspective, base-year 2004, follow-up 20 years	£ / QALY gained: £27061. £ / LYG: £14796
Ward (2005)	Rosuvastatin	Fluvastatin	Secondary prevention, female	NHS perspective, base-year 2004, follow-up 20 years	£ / QALY gained: £40280. £ / LYG: £15169

11.0 Appendix 5: Selection of statin ICERs for inclusion in model

Author	Year	Population characteristics	ICER (quality grades in parentheses if given in source document)
Ali	2003	Primary prevention; Age, mean: 50; Gender: Males and Females	Seven ICER £/QALY were identified: £4,730 , £2164, £3668 , £2023, £3060 , £1573 , £2368 Source: Astra Zeneca, Ward (2005)
Blumi et al	2000	Primary prevention; Compliance with lipid lowering therapy; Age, mean: 55; Gender: Males and Females	Seven ICER £/QALY were identified: £4,730, £2164 , £3668, £2023 , £3060 £1573 , £2368 Source: Astra Zeneca, Ward (2005)
Faulkner et al	2000	High risk population receiving lipid lowering lowering therapy; Mean age: 64 yrs; Gender: Males and Females; Secondary prevention	Eight ICER £/QALYs were identified: £19,001, £24,412 , £16,579 , £20,279 , £13,272 , £31,373 , £11,520, and £25,903. Source: Astra Zeneca, Ward (2005).
Gonzalez et al	2005	Secondary prevention; Age, mean: 65; Gender: Males and Females.	Eight ICER £/QALYs were identified: £19,001, £24,412 , £16,579, £20,279 , £13,272 , £31,373 , £11,520, and £25,903. Source: Astra Zeneca, Ward (2005).
Guthrie	2001	Primary prevention; Compliance with pravastatin treatment; Gender: Males and Females; Age: 50	Seven ICER £/QALY were identified: £4,730 , £2164, £3668 , £2023 , £3060 , £1573 , £2368 ; Source: Astra Zeneca, Ward (2005)
Lopez-Cabezas et al	2006	Secondary prevention; Age, mean: 76; Gender: Males and Females.	Eight ICER £/QALYs identified: £19,001, £24,412 , £16,579 , £20,279 , £13,272 , £31,373 , £11,520, and £25,903. Source: Astra Zeneca, Ward (2005).

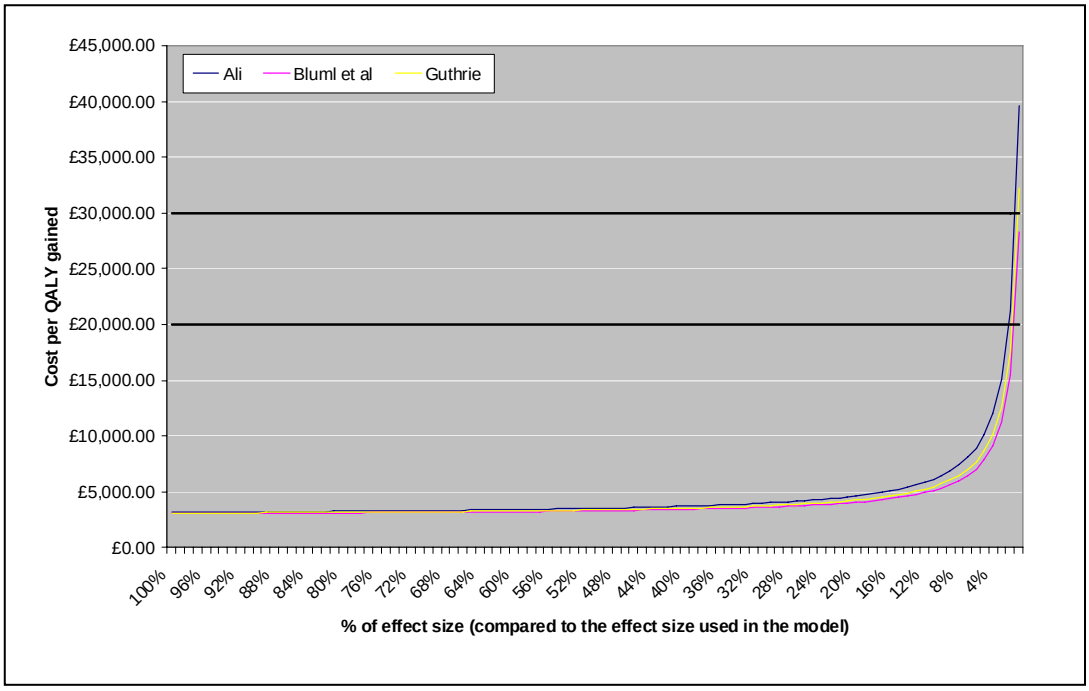
12.0 Appendix 6: Sensitivity analysis 1

This appendix shows the results of a sensitivity analysis undertaken to test the impact of the caveats to the analysis discussed in section 4.0. A number of cost-effectiveness thresholds are included on the figures in this section: the £20,000 and £30,000 threshold traditionally applied by NICE, and the £82,400 and £123,600 equity-weighted threshold calculated by applying the equity-efficiency weights calculated by Dolan and Tsuchiya (forthcoming) to the non-weighted threshold (see section 5.0 for further discussion).

12.1 Testing the impact of intervention effect

Figure 5 tests the impact of intervention effect size on the estimate of the cost per QALY gained from the interventions for which there are question marks over the quality of the research design employed (see section 4 for further detail). It demonstrates that the effect size would have to be reduced by c99% before the cost per QALY gained estimate passes above the £30,000 per QALY threshold.

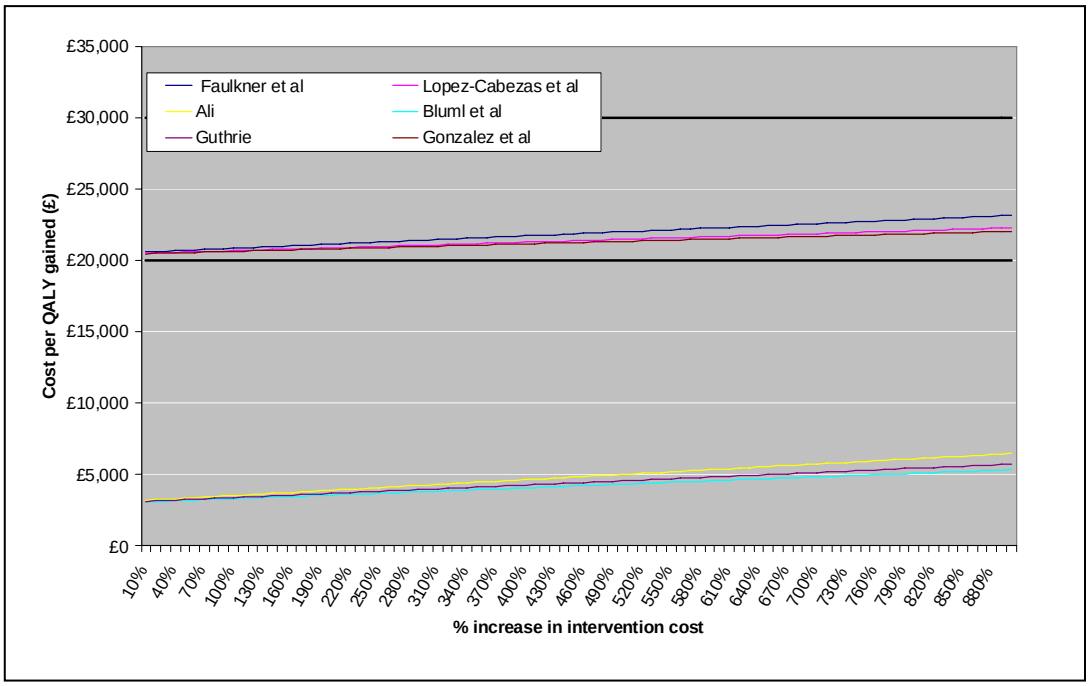
Figure 5: Test of the impact of variation in effect data on estimates of cost per QALY gained.



12.2 Testing the impact of intervention cost

Figure 6 tests the impact of intervention cost on the estimate of the cost per QALY gained. It demonstrates that cost estimates, even when increase by 900%, do not influence the estimates of the cost effectiveness of the intervention.

Figure 6: Test of the impact of increasing intervention cost on estimates of cost per QALY gained.



13.0 Appendix 7: Sensitivity analysis 2

Each of the interventions analysed in this report was evaluated based on its effect on the general population. However, the NICE guidance that the analysis is designed to inform is interested in the cost-effectiveness of interventions when applied to disadvantaged groups. As the interventions prove cost-effective for the general population, assuming that interventions are less cost-effective for disadvantaged groups, this section presents the results of a sensitivity analysis to determine the increase in cost and/or the reduction in effect required for each intervention to have a cost per QALY gained of £30,000. This estimate provides a sense of the reduction in the cost-effectiveness of the intervention allowed when it is applied to disadvantaged groups while still justifying investment in the intervention.

Figure 7 summarizes the increase in cost and reduction in effect possible when the interventions are applied to disadvantaged groups, while still ensuring the intervention is cost-effective compared to a £30,000 per QALY threshold. It demonstrates that costs would have to increase by very large amounts or effects would have to reduce by very large amounts before the interventions would have a cost per QALY gained of greater than £30,000. For instance, the lowest increase in costs require to cause the cost per QALY gained to be greater than £30,000 is 1,900 percent (Faulkner et al, 2000). However, most of the interventions require increases in cost in the magnitude of many thousands of percent before they become cost-ineffective. A similar story is told for changes in effect. All the interventions require a reduction in effect of 99% before the cost per QALY gained becomes greater than £30,000.

Figure 7: Changes in cost or effect required for £30,000 per QALY gained.

Intervention type	Authors	Location	% increase in cost of the intervention	% reduction in effect
Complying with statins	Ali, 2003	Canada	11,000	99
	Bluml et al, 2000	-	6,200	99
	Gonzalez et al, 2005	US	3,200	99
	Guthrie, 2001	Spain	183,000	99
	Faulkner et al, 2000	US	1,900	99
	Lopez-Cabezas et al, 2006	Spain	22,000	99