Document 1

Prevention of cardiovascular disease at population level [Question 1; cost-effectiveness]

Report (13th January 2009)

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Prevention of cardiovascular disease at population level

[Question 1; cost-effectiveness]

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West Midlands Health Technology Assessment Collaboration

The West Midlands Health Technology Assessment Collaboration (WMHTAC) is an organisation involving several universities and academic groups who collaboratively undertake research synthesis to produce health technology assessments. Most of our members are based in the Department of Public Health & Epidemiology, University of Birmingham, however other members are drawn from a wide field of expertise including economists and mathematical modellers from the Health Economics Facility, University of Birmingham.

WMHTAC produce systematic reviews, health technology assessments and economic evaluations for NHS R&D HTA programme (NCCHTA), the National Institute for Health and Clinical Excellence (NICE), and for the health service in the West Midlands. WMHTAC also undertakes methodological research on research synthesis, and provides training in systematic reviews and health technology assessment.

Name of other institution(s) involved

WMHTAC work in close collaboration with the Peninsula Technology Appraisal Group (PenTAG) with respect to providing support to the CPHE. They were not however involved in this report.

Contents

Executive Summary

Objectives:

This report is a cost-effectiveness review which complements three previous reports forming an effectiveness review. The four reports together address:

Which multiple risk-factor interventions are effective and cost effective in the primary prevention of CVD within a given population? Where the data allows, how does the effectiveness and cost effectiveness of interventions vary between different population groups?

Groups to be covered were populations defined on a geographical basis.

The interventions included were multiple risk-factor approaches to preventing CVD among a given population. These included addressing two or more risk factors through one or more of the following types of intervention:

- educational/behavioural (including the use of mass media)
- fiscal
- environmental
- legislative

The expected outcomes of interest were population changes in: rates or levels of CVD mortality or morbidity; the biochemical or physiological precursors of CVD; behaviour associated with the risk of developing CVD.

Methods:

Working to a pre-determined protocol a systematic review was conducted. The main component of the search addressing the review question was 8 major bibliographic databases. These were searched from 1970 to August 2008 for evaluative studies addressing the review question and published in the English language.

The results of the data extraction and quality assessment for each programme identified in the included studies were presented in a narrative summary and combined in a summary evidence table. Evidence statements were then generated. Meta-analysis was not employed.

There was particular focus on whether sufficient economic evaluations already exist to address issues of cost-effectiveness and in existing models how the evidence of impact on CVD risk factors is translated into estimates of impact on CVD morbidity and mortality.

Synthesis was narrative and meta-analysis was not employed. Evidence statements are given below.

Cost effectiveness evidence statements

Three studies gave results in cost per life-year gained for population based programmes compared to no intervention. The results ranged from cost-saving to £240,000 per life-year gained.

Two studies gave results in cost per QALY or DALY for population based programmes compared to no intervention. Results ranged from £10/QALY to £96/DALY.

Two studies gave results in cost per case prevented for population based programmes compared to no intervention. Results ranged from cost saving to £22,000 per case prevented.

Five studies reported results in cost per life year gained for some form of screening strategy compared to no intervention. Results ranged from cost saving to £140,000 per life year gained.

Two studies gave results in cost per case prevented for screening compared to no intervention. Results ranged from £10,000 to £730,000 per case prevented.

Two studies gave results per 1% reduction in coronary risk for screening compared to no intervention. Results ranged from £2.25 to £5.30 per 1% reduction for one person.

One study gave a result of £0.80 per pound weight lost for a screening programme compared to no intervention.

One study gave results ranging from £12,000 to £120,000 per life year gained and £100,000 to £230,000 per QALY for screening compared to a population based approach.

One study gave results from cost saving to £39,000 per life year gained for some form of exercise training.

Conclusions:

This review suggests that some primary preventative population programmes involving education, mass media and screening in members of general populations can be cost-effective in improving some CVD risk factors and behaviours. There is, however, considerable uncertainty about the effect on health outcomes summarised across all programmes. Whether the observed findings of the programmes that were conducted many years ago remain generally applicable in the UK at the current time is not clear.

1 Introduction

The National Institute for Health and Clinical Excellence ('NICE' or 'the Institute') has been asked by the Department of Health (DH) to develop guidance on a public health programme aimed at preventing cardiovascular disease (CVD) in different populations.

NICE public health programme guidance supports implementation of the preventive aspects of national service frameworks (NSFs) where a framework has been published. The statements in each NSF reflect the evidence that was used at the time the framework was prepared. The public health guidance published by the Institute after an NSF has been issued will have the effect of updating the framework. Specifically, in this case, the guidance will support NSFs on the following: cancer, coronary heart disease (including obesity), diabetes, and older adults (including stroke services) (DH 2000a; DH 2000b; DH 2001a; DH 2001b).

This guidance will support a number of related policy documents including:

- 'Delivering choosing health: making healthier choices easier' (DH 2005a)
- 'Health challenge England – next steps for choosing health' (DH 2006a)

- 'National stroke strategy' (DH 2007)
- 'Our health, our care, our say' (DH 2006b)
- 'Tackling health inequalities: what works' (DH 2005b)
- 'The NHS in England: the operating framework for 2006/7' (DH 2006c)
- 'Wanless report: securing good health for the whole population' (Wanless 2004).
- 'Tackling Health Inequalities – A Programme for Action' (DH 2003)
- 'Tackling Health Inequalities: 2007 Status Report on the Programme for Action' (DH 2008)
- Commissioning framework for health and well-being (DH 2007)
- 'The NHS in England: The operating framework for 2008/9' (DH 2007)
- 'Healthy Weight, Healthy Lives: A Cross Government Strategy for England' (DH 2008)
- 'Putting prevention first – vascular checks: risk assessment and management' (DH 2008a)

This guidance will provide recommendations for good practice, based on the best available evidence of effectiveness, including cost effectiveness. It is aimed at professionals, commissioners and managers with public health as part of their remit working within the NHS, local authorities and the wider public, private, voluntary and community sectors. It may also be of interest to members of the public.

The guidance will complement and support NICE guidance on alcohol, CVD risk assessment, obesity, physical activity and smoking cessation.

This report is the economic review to be delivered to the Programme Development Group (PDG). It complements three effectiveness reports addressing question 1 defined in the final scope as:
Which multiple risk-factor interventions are effective and cost effective in the primary prevention of CVD within a given population? Where the data allows, how does the effectiveness and cost effectiveness of interventions vary between different population groups?

Subsequent reports will address the second question, defined in the final scope as:

What barriers and facilitators influence the effectiveness of multiple risk-factor programmes aimed at reducing CVD (or the risk factors associated with CVD) among a given population (including sub-groups experiencing health inequalities where the data allows)?

1.1 Background

A large number of preventable illnesses and deaths are associated with CVD (CVD includes coronary heart disease [CHD], heart failure, stroke and peripheral arterial disease). In 2005, there were 171,021 deaths from circulatory diseases in England, including 45,620 from CHD and 18,013 from stroke (Health Survey for England 2005, cited in Allender et al. 2007). In that year, over 40% of deaths in the UK were caused by CVD. More than 4 million UK patients are currently affected and it costs the UK approximately £30 billion annually. A large proportion of the risk of a first heart attack (over 90%) comes from nine easily or potentially modifiable risk factors (Yusuf et al. 2004).

Despite recent improvements, UK death rates from CVD are relatively high compared with other developed countries (only Ireland and Finland have higher rates). There is also considerable variation within the UK itself – geographically, ethnically and socially. For instance, premature CVD death rates are three times higher among lower socioeconomic groups than among more affluent groups – and death rates from CVD are approximately 50% higher than average among South Asian groups (Allender et al. 2007). Circulatory disease makes a substantial contribution to the gap in life expectancy between the Spearhead areas (the areas with the worst health and deprivation indicators) and England generally. For males, 35% of the gap is due to differences in circulatory diseases (70% of this being due to CHD), and for females the figure is 30% of the gap (63% of this being due to CHD) (DH 2008b).

CVD is influenced by a variety of 'upstream' factors (such as access to a safe environment for physical activity and a person's educational level) and 'downstream' behavioural issues (such as diet and smoking). The British Heart Foundation identifies nine key risk factors that can be modified: smoking/tobacco use, poor diet, insufficient physical activity, high blood pressure, obesity/overweight, diabetes, psychosocial stress (linked to people's ability to influence the potentially stressful environments in which they live), high alcohol consumption and high blood cholesterol. Other factors, such as maternal nutrition and air pollution may also be linked to the disease (Allender et al. 2007). Changes in risk factors, such as a reduction in cholesterol or blood pressure, or quitting using tobacco, can rapidly reduce the risk of developing CVD.

Evaluating complex changes between populations is problematic for a number of reasons, for example: it is difficult to design studies which evaluate entire cities, regions or countries; control sites can become 'contaminated' (that is, if the intervention affects people living in the control area); unreasonable expectations about the speed of effect; and failure to address 'upstream' influences such as policy or manufacturing practices. Some population programmes have been accompanied by a substantial reduction in the rate of CVD deaths. However, the degree to which these are attributable to the programme is debatable.

1.2 Research Objectives

This report, together with three others, addresses the question:
Which multiple risk-factor interventions are effective and cost effective in the primary prevention of CVD within a given population? Where the data allows, how does the effectiveness and cost effectiveness of interventions vary between different population groups?

The expected outcomes are population changes in: rates or levels of CVD mortality or morbidity; the biochemical or physiological precursors of CVD; behaviour associated with the risk of developing CVD.

The precise nature of the populations and interventions to be covered, and those which are not included are defined in the final scope as follows:

POPULATION	
COVERED BY GUIDANCE	**NOT COVERED BY GUIDANCE**
Groups to be covered are populations defined on a geographical basis. The	The guidance will not focus on individuals who are clinically

area will usually be at least a region of a country (such as Merseyside) or an urban or rural area (such as Paisley and Nottingham or New Forest). In the UK, the geographical area would not be less than what is currently covered by a Primary Care Trust. A population could also be made up of people living in a designated geographical area that fulfils the criteria above who also share a specific characteristic, such as all South Asian men over 50 who live in Sheffield. Populations will include both adults and children.	diagnosed as being at high risk of developing – or who have already been diagnosed with – CVD. However, as populations include people at different stages of disease, it will have some relevance for them. (Individuals at high risk of developing CVD are covered by other NICE guidance, see section 6.)
ACTIVITIES /INTERVENTIONS	
COVERED BY GUIDANCE	**NOT COVERED BY GUIDANCE**
Multiple risk-factor approaches to preventing CVD among a given population. These include addressing two or more risk factors through one or more of the following types of intervention: • educational/behavioural (including the use of mass media)	Secondary prevention activities and those aimed only at people who are at high risk of developing CVD. (If an intervention covers both primary and secondary prevention, it will only be included if the primary component is sufficiently disaggregated and can be reported separately.)

• fiscal • environmental • legislative	
OR Programmes that include a pharmacological element alongside a broader, non-pharmacological multiple risk-factor approach (as indicated in 4.2.1a) will be included when they involve a primary prevention element and where data can be disaggregated to allow consideration of the impact of the non-pharmacological elements.	OR Interventions which focus on screening for CVD risk factors (for example, cholesterol-level screening) and do not attempt to modify them
OR Natural experiments, such as changes in the diet of Eastern Europeans brought about by social change, where relevant evidence is available	

A number of secondary questions were posed should sufficient data be available:

- The target audience, actions taken and by whom, context, frequency and duration.
- Whether it is based on an underlying theory or conceptual model.
- Whether it is effective and cost effective.

- Critical elements. For example, whether effectiveness and cost effectiveness varies according to:
    - the diversity of the population (for example, in terms of the user's age, gender or ethnicity)
    - the status of the person (or organization) delivering it and the way it is delivered
    - its frequency, length and duration, where it takes place and whether it is transferable to other settings
    - its intensity.
- Any trade offs between equity and efficiency.
- Any factors that prevent – or support – effective implementation.
- Any adverse or unintended effects.
- Current practice.
- Availability and accessibility for different population groups.

The study designs of particular interest were for:

Effectiveness: RCT; Controlled before and after; Cohort; Case control; Before and after; Interrupted time series; and for
Cost effectiveness: Cost benefit analyses; Cost effectiveness analyses; Cost utility analyses

1.3 Structure of report

The structure of this report is as follows:

- Chapter 2 discusses how the literature search was conducted, the retrieval of papers, the selection of studies for inclusion, data extraction and quality assessment.
- Chapter 3 provides the cost-effectiveness findings.
- Chapter 4 discusses the review findings, highlighting their applicability, limitations and any gaps.

Appendices present supporting documents, namely protocol, example search strategies, inclusion/exclusion checklists, list of excluded studies, and quality assessment tools.

2 Methodology

The protocol governing the conduct of the literature review for all phases of the review, including costs and cost-effectiveness, addressing question 1 is appended in Appendix 1. The following sections emphasise the features which particularly apply to the review of evidence on cost-effectiveness and costs. There were no major departures from the originally stated protocol. In a minor departure from the protocol the list of included study designs was extended to include cost-consequences analyses at the suggestion of the CPHE technical team

2.1 Identifying potentially relevant studies

The focus was identifying studies on cost-effectiveness and cost of population level, multi-component CVD prevention programmes. The search strategy was developed by the information specialists at WMHTAC in consultation with CPHE who signed off the final version before implementation.

2.1.1 Bibliographic databases searches

The following databases were searched from 1970 to August 2008:

- NHS EED database (Cochrane Library Wiley)
- ECONLIT (ovid)
- MEDLINE (ovid)
- EMBASE. (ovid)

The key components of the search question - 'cardiovascular diseases' (population), 'health promotion' (intervention) and thirdly the concept of 'Programmes tackling at least two CVD risk factors' (focus of the intervention) - were combined, ready to be used with the appropriate study design terms. The strategy for health economic evaluations was based on one developed by the NHS Centre for Reviews and Dissemination. The search was limited to articles published from 1970 onwards and in the English language. The precise search strategies employed are listed in Appendix 2.

In addition to the general bibliographic database searches, specific searches targeting each of the included programmes were conducted to ensure that all published evaluations, particularly economic evaluations, of any included programmes were identified. These were run using the strategies again detailed in Appendix 2.

Archives of all the studies identified in the searches were stored on Reference Manager databases.

2.1.2 Studies tagged in the effectiveness review and other components of search

A number of possible reviews of economic evaluations and primary studies were identified in the course of the review of effectiveness described in reports 1-3. These were formally considered for inclusion into the review of cost effectiveness.

Suggestions from the PDG and items highlighted in the key UK public health web-sites (see list in protocol appendix 1) were similarly considered.

2.2 Selection of studies for inclusion

2.2.1 Title and abstract appraisal

Cost-effectiveness studies possibly relevant to this review were identified by screening retrieved titles/abstracts from the bibliographic database searches. 12, 689 citations/abstracts were examined for inclusion and 121 potentially relevant studies had their full text ordered. One study was not available from the British Library. The process was undertaken by one reviewer (CH) who focused particularly on the nature of the intervention and the type of evaluation. There was no double-checking of decisions. Reasons for not ordering a hard copy of any particular citation were not formally recorded.

2.2.2 Full text appraisal

To the 120 hard copies obtained from scanning the bibliographic databases were added 55 identified from additional searching activities, particularly tagging of studies in the effectiveness reviews. Four of these 55 could not be obtained in the time available. 171 full text articles were thus assessed using the inclusion/exclusion tool included in Appendix 3. This form was developed from the inclusion criteria used in the effectiveness review and checked by the CPHE. It focused on the nature of the study (economic evaluations) and whether the activity aimed to address CVD, targeted multiple risk factors, targeted a population and was mainly aimed at primary prevention. Studies reporting weight and physical activity interventions were included if the interventions were deemed to affect two or more risk factors.

The process was undertaken by one reviewer (CH). There was no double-checking of decisions. The reasons for exclusion of studies/programmes were recorded according to the first inclusion criterion failed on the in/exclusion list. Some excluded studies were tagged as providing potentially important information for the economic modelling exercise, but these are not reported here.

2.2.3 Summary of effectiveness studies identified for inclusion

The following 16 articles were included:

Table 2.1 included articles

Assmann et al. (1990) Primary prevention of coronary heart disease in the Federal Republic of Germany. Analysis of cost-effectiveness.

Baxter et al. (1997) A cost effective, community based heart health promotion project in England: prospective comparative study.

Field et al. (1995) Strategies for reducing coronary risk factors in primary care: which is most cost-effective?

Hall et al. (1998) A cost-effectiveness analysis of alternative strategies for the prevention of heart disease.

Kinlay et al. (1994) The cost-effectiveness of different blood-cholesterol-lowering strategies in the prevention of coronary heart disease.

Kristiansen et al. (1991) Cost effectiveness of incremental programmes for lowering serum cholesterol concentrations: Is individual intervention worth while?

Langham et al. (1996) Costs and cost effectiveness of health checks conducted by nurses in primary care: the Oxcheck study

Lasater et al. (1991) Community-based approach to weight loss: the Pawtucket "weigh-in".

Lindholm et al. (1996) Cost effectiveness and equity of a community based cardiovascular disease prevention programme in Norsjo, Sweden.

Lowensteyn et al. (2000) The cost-effectiveness of exercise training for the primary and secondary prevention of cardiovascular disease.

Murray et al. (2003) Effectiveness and costs of interventions to lower systolic blood pressure and cholesterol: a global and regional analysis on reduction of cardiovascular-disease risk.

Norinder et al. (2002) Costs for screening, intervention and hospital treatment generated by the Malmo Preventive Project: A large-scale community screening programme.

Rasmussen et al. (2007) Preventive health screenings and health consultations in primary care increase life expectancy without increasing costs.

Tosteson et al. (1997) Cost-effectiveness of populationwide educational approaches to reduce serum cholesterol levels.

Wonderling et al. (1996) Costs and cost effectiveness of cardiovascular screening and intervention: the British family heart study.

Wonderling et al. (1996) What can be concluded from the Oxcheck and British Family Heart studies: commentary on cost effectiveness analysis.

2.2.4 Excluded studies

155 studies were excluded on the basis of assessment of full text. A summary of the reasons for exclusion of studies is given in Table 2.2 below, with further explanation of the categories in Table 2.3. The full list of excluded studies appears in Appendix 4.

Table 2.2 Reasons for exclusion of studies obtained in full text

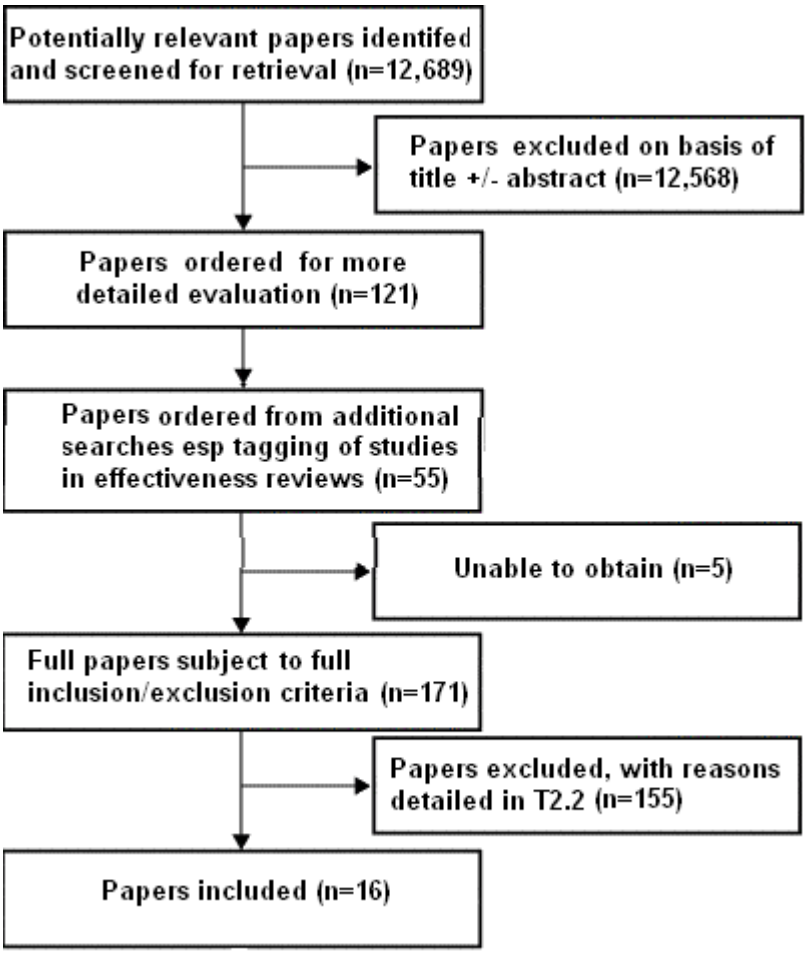
Reason for exclusion	**Number**
Full text ordered	176
Full text obtained	171
Published before 1970	0
Does not address general purpose	72
Inappropriate setting and population	48
Does not contain an appropriate intervention	22
Inappropriate design	13
Number of articles "included"	16

Table 2.3 Definitions of reasons for exclusion of studies obtained in full text

Reason for exclusion	**Definition**
Does not address general purpose	Assessed as answering "No" to one or both of: • Does the paper broadly consider some sort of change which might affect CVD or CVD risk? • Does the paper consider the cost or cost-effectiveness of this change in some way?
Inappropriate setting and population	Assessed as meeting general purpose, but answering "No" to one or more of: • Is the study set in a developed/OECD country?

	• Does the approximate target population exceed 100,000 (or similar to a PCT) or does the study involve a population living within a certain geographical area (which should not be smaller than primary care trust)? • In one of the alternative approaches evaluated are the vast majority of participants likely to have low or minimal risk of CVD?
Does not contain an appropriate intervention	Assessed as meeting general purpose and appropriate setting and population but answering "No" to one or more of: • Is the primary aim of the alternatives considered to address CVD? • Does one of the alternatives considered tackle 2 or more of the risk factors below? (9 listed: smoking; poor diet; insufficient physical activity; high blood pressure; high cholesterol; obesity/overweight; diabetes; psychosocial stress; high alcohol consumption) • Could one of the alternatives considered be described as one/more of the following? (4 listed; educational/behavioural including use of mass media; fiscal; environmental; legislative).
Inappropriate design	Assessed as meeting general purpose and appropriate setting and population and appropriate intervention but answering "No" to : • Does the study assess cost-effectiveness, cost-benefit or cost-utility?

Figure 2.1 QUOROM diagram for review of evaluations of cost-effectiveness



2.3 Data extraction and quality appraisal

The study type of each included cost-effectiveness paper was identified using standard nomenclature.

An evidence form based on the *Methods for development of NICE public health guidance* was adapted to reflect the parameters of this review and supplemented with questions from the Drummond checklist (Guidelines for authors and peer reviewers

of economic submissions to the BMJ, M F Drummond, 1996, on behalf of the BMJ Economic Evaluation Working Party). One reviewer (LA or PB) extracted data for each full paper using this form. Any doubtful points were resolved by discussion with the other reviewer. An example of a completed quality assessment form is included in Appendix 5.

Studies were also assessed for applicability in a current UK context. A study was only deemed to be directly applicable if:

- the population was equivalent to the current UK population;
- it was carried out using rules equivalent to those currently applied by NICE, in particular with reference to costing perspective and discount rates.

2.4 Synthesis and formulation of evidence statements

The results of the data extraction and quality assessment for each programme identified in the included studies were presented in a narrative summary and combined in a summary evidence table. An evidence statement was then generated. Meta-analysis was not employed.

There was particular focus on whether sufficient economic evaluations already exist to address issues of cost-effectiveness and in existing models how the evidence of impact on CVD risk factors is translated into estimates of impact on CVD morbidity and mortality.

3 Cost Effectiveness Findings

The bibliographic database searches described in Chapter 2 yielded 12,689 hits, yielding 121 potentially relevant articles requiring scrutiny of the full text, yielding in turn 16 included articles, as listed in Table 3.1. These articles can be grouped into effectiveness study based articles, and model-based articles. For convenience, the two papers by Wonderling and colleagues are considered in the same section. For the effectiveness study based articles, the table shows the name of the programme and which of the three effectiveness reviews considered that programme. We have reported results from the cost-effectiveness articles reviewed: in some cases, this means information which goes beyond, or differs in some other way from, the information quoted in the effectiveness review. Monetary results are reported as given, and, if no value in sterling was quoted by the authors, we have converted the results into sterling using exchange rates at the time of publication.

Table 3.1 Included articles

Articles	Study type	Programme name	Effectiveness review
Assmann et al. (1990)	Model based		
Baxter et al. (1997)	Effectiveness study based	Action Health	2
Field et al. (1995)	Model based		
Hall et al. (1998)	Model based		
Kinlay et al. (1994)	Model based		
Kristiansen et al. (1991)	Model based		
Langham et al. (1996)	Effectiveness study based	Oxcheck	1
Lasater et al. (1991)	Effectiveness study based	Pawtucket	1
Lindholm et al. (1996)	Effectiveness study based	Norsjo	1
Lowensteyn et al. (2000)	Model based		
Murray et al. (2003)	Model based		
Norinder et al. (2002)	Effectiveness study based	Malmo	3
Rasmussen et al. (2007)	Effectiveness study based	Ebeltoft	3
Tosteson et al. (1997)	Model based		
Wonderling et al. (1996a)	Effectiveness study based	BFHS	1
Wonderling et al. (1996b)	Effectiveness study based		

3.1 Effectiveness study based articles

Eight of the included economic evaluations were based on a single effectiveness study. Of these, four articles reported interventions conducted in the United Kingdom (Baxter *et al.* 1997; Langham et al. 1996; Wonderling et al., 1996a (Cost and cost effectiveness) ; Wonderling et al., 1996b (What can be concluded)) while three of the other articles related to studies conducted in Europe (Lindholm *et al.,* 1996; Norinder et al., 2002; Rasmussen et al., 2007) and one in the USA (Lasater et al., 1991). The UK based studies are described first, followed by the non-UK based studies.

3.1.1 Baxter et al. (1997)[2] A cost effective, community based heart health promotion project in England: prospective comparative study

Overview

The article by Baxter and colleagues aimed to assess the cost effectiveness of the Action Heart community-based health promotion programme, as well as evaluate whether such a programme is associated with changes in the prevalence of lifestyle risk factors known to affect the development of coronary heart disease. The study was conducted in Rotherham, an area with a high incidence of coronary heart disease, and involved a combination of health promotion approaches such as stop smoking support groups, weight control clinics, healthier eating activities, information leaflets, nicotine patch scheme etc. The effectiveness of the intervention was assessed on the basis of participants' answers to pre and post-intervention questionnaires. The authors reported costs discounted at 6% rate and undiscounted health benefits.

Effectiveness

The study estimated changes in prevalence of lifestyle risk factors between the control and intervention groups from 1991 to 1995 from participants' answers to relevant questionnaires using univariate analysis and multiple logistic regression techniques. The results of the study show significant reductions in smoking in the intervention group as well as significant increases in consumption of lower fat milk. Using a computer model based on an American Cancer Society's study, the authors predicted a health gain of 3581 life years for the 14500 people in the intervention group.

Cost

The estimated cost of the project was £110,000. The authors acknowledged that there is uncertainty around the estimated NHS costs and assessed doubling these costs in sensitivity analyses.

Cost effectiveness

The results of the study suggest a cost between £31 and £42 for an additional life year gained (£117 and £160 discounted at 6% rate).

Limitations

1) Additional health benefits gained (such as quality of life improvement from non-fatal CVD avoided) and health care services use avoided from quitting smoking were not considered.
2) The study measured only the programme-related costs. Costs that might arise in relation to other health resource use were not considered.
3) Costs and benefits may have been ignored due to short follow up period.
4) Estimates of total life years gained appear to be calculated from median gain in model not mean.

Comments

The article was rated +. The results are deemed not directly applicable, because of the age of the study and the discount rates used.

3.1.2 Langham et al.[7] Costs and cost effectiveness of health checks conducted by nurses in primary care: the Oxcheck study

Overview

The study by Langham and colleagues measured the costs and cost effectiveness of the Oxcheck cardiovascular risk factor screening and intervention programme conducted in five general practices in Luton and Dunstable, England. Registered patients who returned a lifestyle questionnaire were randomly allocated to receive a health check in one of the four study years. Health checks were performed by nurses who recorded the participants' medical history and lifestyle characteristics and measured their blood pressure, height and weight. Participants with a risk factor level above a predetermined cut-off were invited to attend for follow up visits. The intervention group comprised patients who attended their first health check in year one of the study while the control group comprised those who attended their first health check in the fourth year. The authors reported costs discounted at 6% rate and undiscounted health benefits, which were expressed as an overall reduction in coronary risk: this was calculated using the Dundee risk score for the purpose of the cost-effectiveness analysis and thus does not appear in the effectiveness review.

Effectiveness

The findings show a 13% overall reduction in coronary risk for patients in the intervention group (20% reduction for those in the intervention group who attended the final examination). The effect was greater for women (17%, 24%) than for men (7%, 18%).

Cost

Total costs (excluding re-examination costs) were estimated at £237,400. Approximately 64% of this amount was attributed to nurses' time input. Uncertainty around the time spent on health checks and follow up appointments was explored in sensitivity analysis.

Cost effectiveness

According to the findings of the study, per patient cost amounted to £2.25 per 1% reduction in coronary risk for patients in the intervention group.

Limitations

1) Assumptions were made with relation to discriminating between programme costs and research costs, hence some research costs might have been included in the programme costs, while some programme costs may have been omitted along with the research costs.
2) Estimated costs do not include the costs that might have arisen in relation to other subsequent health care use.
3) Reduction in coronary risk was not converted into a broader unit of effectiveness.
4) The study's follow up period is unlikely to capture all the relevant costs and benefits.

Comments

The article was rated +. The results are partially applicable, because of the short time frame of the analysis, the measure of outcomes and the discount rates used.

3.1.3 Wonderling et al. (1996)[15] Costs and cost effectiveness of cardiovascular screening and intervention: the British Family Heart study

Overview

The study by Wonderling et al. aimed to determine the cost and cost effectiveness of the British Family Heart Study (BFHS) programme. This was a nurse led programme that combined cardiovascular screening to determine an overall risk score for each participant and follow-up appointments, the frequency of which vary according to each participant's score at the initial screen. The authors reported results in terms of total cost and cost per 1% reduction in coronary risk at one year. Costs were discounted at a 6% annual rate.

Effectiveness

The authors derived the coronary risk reduction from the observed reduction in Dundee risk score. The intervention was associated with a 7% and 13% reduction in coronary risk for men and women, respectively.

Costs

Total programme cost included the costs of screening and follow-up appointments, as well as additional health service costs such as drug cost and cost attributed health service visits. The total cost of implementing the programme for one year was estimated at £63 per person.

Cost effectiveness

The cost per 1% reduction in coronary risk was estimated at £5.30 per person when only direct programme costs are considered and £4.30 when costs include additional health service costs.

Limitations

1) The analysis is focused only on the short term costs and benefits of the British Family Heart study intervention.

2) The size of the study limits the reliability of the overall cost effectiveness results of the intervention.

3) Reduction in coronary risk was not converted into a common unit of effectiveness

4) The article considers only programme-related costs and costs due to resource use at general practice level.

Comments

The article was rated ++. The results are considered partially applicable. The applicability of this study is limited by the short time frame of the analysis, the employed measure of outcomes and the discount rates used.

3.1.4 Wonderling et al. (1996)[16] What can be concluded from the Oxcheck and British Family Heart studies: commentary on cost effectiveness analysis

Overview

The article by Wonderling et al. aimed to provide a direct comparison of the relative effectiveness and cost effectiveness of the Oxcheck (Langham et al. 1996) and British Family Heart studies (Wonderling et al. 1996). As already mentioned, both studies assessed the cost effectiveness of nurse led, population based programmes that involved health checks and follow-up appointments. The main difference between these two studies is that while in the Oxcheck intervention follow up was negotiated between the nurse and participant on an individual basis, the British Family Heart

study involved an intensive follow-up approach where participants at high risk were invited for follow up according to a strict protocol. Both costs and benefits for this article were discounted at a 6% annual rate.

Effectiveness

Effectiveness results, expressed in terms of reduction in coronary risk in both the Oxcheck and British Family Heart studies, were converted to life years gained.

Assuming that the effect of the intervention persists for a year, men and women in the British Family Heart study gained on average 0.0062 and 0.0011 life years, respectively. Under the same assumption men and women in the Oxcheck study gained 0.0034 and 0.0018 life years, respectively.

Costs

The cost of the intervention per participant in the Oxcheck study was estimated at £29. In the British Family Heart study the cost was estimated at £66 and £58 for men and women, respectively.

Cost-effectiveness

The cost per life year gained associated with the British Family Heart study ranged between £1100 (assuming a 20 year effect) and £24,400 (assuming a one year effect) for men and between £3,300 (20 year effect) and £144,500 (one year effect) for women. The cost per life year gained associated with the Oxcheck study ranged between £900 (assuming a 20 year effect) and £20,900 (assuming a one year effect) for men and between £1,000 and £41,800 for women.

Limitations

1) There is substantial uncertainty on the duration of the observed risk reductions, which affects the cost-effectiveness of the interventions.

2) Long term effects and costs might have been ignored due the studies' short time horizon.

Comments

The article was rated ++. The results are considered partially applicable, mainly because of the short time frame of the analysis and the discount rates used.

3.1.5 Lasater et al.(8) Community-based approach to weight loss: the Pawtucket "weigh-in"

Overview

The article by Lasater et al. aimed to assess the effectiveness and the costs associated with the Pawtucket Heart Health weight loss programme (PHHP), conducted in Pawtucket, United States. The programme involved adult Pawtucket residents getting weighed and setting a 10-week weight loss goal. At the end of 10 weeks, participants returned to assess whether they achieved the predetermined goal. To assist participants in achieving the weight loss goals, the programme provided a weight loss kit (calorie guide, weight loss reading list, tip sheets on weight loss etc) as well as group talks delivered by nutritionists. Costs and benefits were not discounted.

Effectiveness

The study compared participants' weight at baseline and 10-week follow up and found significant weight loss of 8.2 lb and a 29mg/dL reduction in blood cholesterol levels.

Costs

The total cost of the programme was estimated at $2,840 (£1,900). Cost per participant was $6.80 (£4.50).

Cost effectiveness

The authors estimated the cost per pound of weight lost at $1.30 (£0.86)

Limitations

1) The study did not involve a control group.

2) Non-randomly selected sample consisted of volunteers.

3) Weight loss was not converted into a CVD-related measure of effectiveness

Comments

The article was rated -. The results are not considered applicable in a UK context, due to the age and design of the study and the employed measure of outcomes.

3.1.6 Lindholm et al. (1996)[9] Cost effectiveness and equity of a community based cardiovascular disease prevention programme in Norsjo, Sweden

Overview

The article by Lindholm et al. evaluated the cost effectiveness of a community-based cardiovascular disease prevention programme in Norsjo, Sweden. The programme aimed at changing dietary habits and reducing cholesterol concentration in both the general population level and individuals thought to be at high risk of cardiovascular disease, and involved a number of health promotion activities undertaken in the community by adult education associations, sports clubs, media, food retailers (food labelling), companies, and local authorities. The programme also involved risk factor screening followed by a counselling programme. The authors reported undiscounted and discounted at 5% rate costs and undiscounted health benefits.

Effectiveness

The results of the study showed a 1.0 mmol/l and 1.4 mmol/l reduction in mean serum cholesterol for men and women in the intervention group, respectively. No change in blood pressure or proportion of smokers among the population was found.

Cost

The total annual cost of the programme amounted to £51,500. The total discounted cost over 10 years was estimated at £363,000.

Cost-effectiveness

The authors estimated the intervention to result in £14,900 per life year saved under the most pessimistic scenario (assuming that cholesterol levels revert after the end of the intervention plus the intervention is associated with 50% higher costs and 50%

lower savings) and £1,200 per life year saved under the optimistic scenario where cholesterol remains at low levels in the future.

Limitations

1) The intervention combined individual and population-based strategies, hence it is not possible to determine with certainty which of these approaches was most effective in bringing about the observed benefits

2) The utilised logistic regression model to convert the observed cholesterol reduction into morbidity does not take into account possible interactions between risk factors and they may underestimate the effects of reduction in the population risk factor levels.

Comments

The article was rated ++. The results are considered partially applicable in a UK context, mainly because of the used discount rate and differences in baseline rate of CVD between the population in the study and the UK population.

3.1.7 Norinder et al. (2002)[12] Costs for screening, intervention and hospital treatment generated by the Malmo Preventive Project: A large-scale community screening programme

Overview

The article by Norinder et al. aimed to assess the costs and savings associated with the Malmö Preventive Project in Sweden. This community-based programme lasted from 1974 to 1992 and aimed at reducing morbidity and mortality attributed to cardiovascular disease by identifying people in high risk of developing

cardiovascular disease and offering follow-up counselling. Costs were discounted at a 3% rate.

Effectiveness

The article did not report effectiveness results.

Costs

The net health care costs of the programme were estimated at SEK 110.5m (£9.13m). Including the opportunity cost of devoting this amount to fund the programme, the total health care costs approached SEK 202.7m (£16.75m).

Cost effectiveness

The cost effectiveness of the programme was not assessed

Limitations

1) The article is a cost analysis, so it does not assess the cost-effectiveness of the intervention.
2) The reported cost estimates are based on authors' calculations and assumptions.
3) Costs in terms of patients' use of health care resources may have been underestimated as the study assessed only in-patient resource use.

Comments

The article was rated -. The results did not consider the effectiveness of the programme and are deemed not applicable in a UK context.

3.1.8 Rasmussen et al. (2007)[13] Preventive health screenings and health consultations in primary care increase life expectancy without increasing costs

Overview

Based on the results of the Ebeltoft Health Promotion Project (EHPP) conducted in Aarhus, Denmark in 1991, the article by Rasmussen et al. aimed to investigate the cost effectiveness of preventive health checks with or without a follow-up health consultation in 30-49 year old adults. The authors assessed two intervention groups against a control group. The intervention group A involved participants receiving a health test followed by a planned consultation with their family physician, while the intervention group B received the same health test without follow-up consultation. The authors estimated mean direct and total cost per participant and life years gained. Costs and benefits were discounted at 3% annual rate.

Effectiveness

The results of the study show that both the intervention groups have significantly better life expectancy compared to the control group. Patients who received health check and follow-up consultation gained on average 0.14 more life years than those in the control group, while patients who received health check without pre-arranged consultation gained 0.8 life years more than patients in the control group.

Costs

Both interventions were associated with lower cost compared to control. The total cost for the health check with consultation and health check only interventions amounted to €10,410 (£7,000) and €9,400 (£6,400) respectively, while the cost of no intervention was €10,670 (£7,200).

Cost-effectiveness

The interventions were cost saving as well as improving health. Accordingly, the authors did not report incremental cost effectiveness ratios.

Limitations

1) Absolute estimated life years gained may be overestimated since the model assumes that the intervention effect lasts lifelong, which may not be the case.
2) The authors acknowledge limitations in the calculation of indirect and productivity costs, as in some occasions resource use data and unit costs were not available.
3) Analysis of uncertainty is limited to identifying significant differences at $p<0.05$, $p<0.01$ and $p<0.001$ levels. No exact P values or confidence intervals were reported.

Comments

The article was rated +. The results are considered partially applicable in a UK context, mainly because of the discount rates used and differences in population characteristics.

3.2 Model-based articles

Eight model based papers were included in this review. One of these (Murray *et al*, 2003)[11] was a global analysis stratified by regions of the world, each continent being divided into groups of countries according to general levels of adult and child mortality. The other seven papers applied modelling methods to populations within a single country: two of these were based in Australia, with one each for Canada, Germany, Norway, the United Kingdom, and the United States. The global analysis is listed first, followed by the UK based article. The remaining articles follow in

alphabetical order of first author, which has the effect of keeping the two Australian articles together.

3.2.1 Murray et al (2003)[11] Effectiveness and costs of interventions to lower systolic blood pressure and cholesterol: a global and regional analysis on reduction of cardiovascular-disease risk

Overview

Murray and colleagues (2003) considered a range of interventions that could be applied in any country: their analysis was stratified by groups of similar countries. The United Kingdom was included in the "EurA" region of 26 countries, essentially covering the whole of Western Europe. The region was defined (in world terms) by very low adult and child mortality. The interventions most relevant to this report are (N3) health education through mass media and (N4) N3 combined with legislation aimed at population-wide reduction in salt intake. Comparators included "no intervention". Costs were measured in "international dollars": that is, converted to US dollars according to purchasing power parity rather than official exchange rates. Costs and effects were discounted at 3%.

Modelling method used

Effects were measured in disability adjusted life years (DALYs) averted, and estimated using a multi-state modelling tool, PopMod, which is a cohort simulation model.

Effectiveness

The study estimated that each year of intervention N3 would save 1.2 million DALYs across the whole region and intervention N4 would save 2.4 million DALYs.

Cost

Estimated annual costs of interventions N3 and N4 are $202 million (£120 million) and $499 million (£300 million) respectively.

Cost effectiveness

The ICER for N3 compared to do nothing is $160 (£96)/DALY: for N4 compared to N3 $250 (£150)/DALY.

Limitations

1) An important limitation of this work is the aggregation at multinational level.
2) Cost savings related to the prevention of CVD events are not included.

Comments

The article was rated +. While the accounting rules used are similar to those required for economic evaluations by NICE, the use of DALYs as a measure of outcome means that the results are not directly applicable.

3.2.2 Field et al (1995)[3] Strategies for reducing coronary risk factors in primary care: which is the most effective?

Overview

The only UK based modelling article was that by Field and colleagues (1995). They considered a range of interventions from minimal screening (blood pressure and personal history only) to intensive screening of the whole population, measuring blood pressure, height and weight, and blood cholesterol, and asking about personal and family history, smoking, and diet. For all but the most intensive strategy, those identified as "at risk" at the screening would then be screened for the remaining risk

factors. Those found to be at risk would be given lifestyle advice and drug therapy if no reduction in cholesterol followed. Results presented (for men and women separately aged 35-64) included undiscounted life years gained, discounted total costs, undiscounted ICERs for each strategy compared to no intervention and to the previous strategy and discounted ICERs for each strategy compared to no intervention only. The undiscounted ICERs compared to no intervention were presented by age groups 35-49, 50-59, and 60-69. Sensitivity analysis considered the effect of intervention and were given as best and worst case ICERs, undiscounted and compared to no intervention only. A secondary analysis considered a range of different protocols for treatment for raised cholesterol level for the basic strategy. These were reported as ICERs compared to basic strategy and to previous protocol.

Modelling method used

Life years gained and cost of the programme were estimated using the Framingham parametric model, both undiscounted and discounted at 6%. Only health service costs were included.

Effectiveness

Results were reported for 7,840 men and women aged 35-64. The undiscounted life years gained for men ranged from 132 for the least intensive strategy up to 227 for the most intensive. For women, the range was 78 to 133.

Costs

Only discounted total costs were reported. For men, these ranged from £97,000 to £287,000 according to strategy; for women, from £206,000 to £503,000.

Cost effectiveness

ICERs compared to no intervention increased with the intensity of the strategy. Undiscounted figures ranged from £730 to £1,270 per life year gained for men and from £2,650 to £3,780 per life year gained for women. The corresponding figures based on discounted results were £1,240 to £2,180 for men and £4,730 to £6,850 for women. ICERs compared to previous strategy were only given undiscounted. These ranged from £180 to £2,720 per life year gained for men, and from £3,470 to £12,470 for women.

Limitations

1) The authors did not include cost of blood pressure screening and treatment. They stated that this was the same for all strategies, but it could increase the ICERs for the strategies compared to no treatment.
2) They also did not include the cost of treating existing coronary heart disease.
3) They did not consider savings generated by lower morbidity, hence lower demand for medical care, nor did they consider costs of care for additional survivors.

Comments

The article was rated +. Because of the costing perspective, the discount rates used, and the age of the study, the results are not directly applicable.

3.2.3 Assmann and Schulte (1990)[1] Primary Prevention of Coronary Heart Disease in the Federal Republic of Germany: Analysis of Cost-Effectiveness

Overview

Assmann and Schulte considered the adult population of Germany: the programme described stratifying the population into five groups. The lowest risk group was deemed to require no treatment, the next two groups required dietary advice, and the two highest risk groups required dietary advice together with medication. The intervention for each group was aimed at reducing LDL cholesterol to 4.15 mmol/l. Costing perspective was restricted to those costs which would be reimbursed from sickness funds. A discount rate of 4% for both costs and benefits was used.

Modelling method used

A model based on Framingham risk equations was used to assess the number of CHD events and their impact on life expectancy with and without intervention and hence the cost-effectiveness of the overall programme.

Cost-effectiveness

Numerical results were only given as cost-effectiveness ratios. ICERs were reported of DM 30,000 (£10,000) per life year gained (LYG) for men under 60, DM 40,000 (£14,000) per LYG for men aged 60 to 64, with corresponding figures for women under 60 of DM 86,000 (£29,000) per LYG and DM 110,000 (£37,000) per LYG for women aged 60 to 64.

Limitations

1) No account is taken of improved quality of life from delayed onset of coronary heart disease.

2) An important limitation of the article is the lack of any sensitivity analysis.

Comments

The article was rated +. The results are not directly applicable in a UK context because of the age of the study, no account is taken of quality of life gains, and the medication used would not reflect current UK practice.

3.2.4 Hall et al (1988)[4] A cost-effectiveness analysis of alternative strategies for the prevention of heart disease

Overview

Hall and colleagues considered a range of interventions applied to men in Australia. Those of relevance to this report are a whole population approach consisting of media campaigns, a screening programme to identify high risk individuals, and an approach which combines the previous two. A five-year time horizon was used, with costs discounted at 6%.

Modelling method used

Literature-based estimates of the reduction in incidence of ischaemic heart disease that could be expected.

Effectiveness

Results were expressed as number of myocardial infarctions prevented within five years in a population of 60,000 men. The whole population approach would prevent

264 cases, while the screening programme would prevent 169 cases. The combined approach would prevent 348 cases.

Costs

The whole population approach would cost Aus$331,000 (£120,000) to run over 5 years, but saving in treatment costs as a result of myocardial infarctions prevented would mean an overall net saving of $919,000 (£340,000). The screening programme would cost $5,455,000 (£2,000,000) to run, with a net cost after savings of $4,655,000 (£1,700,000). For the combined approach, the total cost would be $6,092,000 (£2,300,000), with a net cost of $4,445,000 (£1,700,000).

Cost-effectiveness

The whole population approach is cost-saving while producing an improvement in health outcomes. The screening programme has a net cost of $27,544 (£10,000) per case prevented, while the combined approach costs $12,773 (£4,800) per case prevented compared to no intervention.

Limitations

1) The effectiveness of each strategy might be overestimated if myocardial infarctions are postponed rather than prevented.
2) Costs are underestimated as they do not include strategy design and initiation costs.
3) Indirect costs due to increased productivity are not included.
4) The follow-up period was limited to 5 years.

Comments

The article was rated -. The results are not directly applicable because of the age of the study and the short time frame.

3.2.5 Kinlay et al (1994)[5] The cost-effectiveness of different blood-cholesterol-lowering strategies in the prevention of coronary heart disease

Overview

Kinlay and colleagues consider a screening strategy for men in Australia between 35 and 64 years old. This strategy aims to identify individuals with high cholesterol for diet and drug treatment. This is compared to the screening strategy recommended by the National Heart Foundation of Australia, and also to a strategy that does not rely on screening, but involves diet change at population level. For the purpose of this report, the population based strategy is considered as the main intervention, with the two screening strategies as comparators. Cost-effectiveness ratios were estimated with no discounting in the main analysis (5% in sensitivity analysis).

Modelling method used

A logistic regression equation was used to translate risk factor profiles provided by Hunter Risk Factor Prevalence Study, reduction in CHD events. This reduction was modelled to estimate the number of primary and secondary CHD events saved in the Lower Hunter region (67,651 men aged 35 to 64 years).

Effectiveness

The outcome measure was heart disease events prevented. The population based strategy is estimated to save 104 (sensitivity analysis range 39 to 226) CHD events, compared with 144 (53 to 184) CHD events saved by the screening strategy with treatment for moderate and high risk patients, and 116 (42 to 137) CHD events saved by the screening strategy with treatment for high risk patients only.

Costs

The population based strategy is estimated to cost Aus$5,413,400 (£2,600,000) to provide the intervention for five years. The screening strategies cost $53,051,115 (£25,000,000: moderate and high risk) and $50,122,672 (£24,000,000: high risk). Sensitivity analysis results did not report the total costs.

Cost-effectiveness

Compared to no intervention, the population strategy costs $46,667 (£22,000: sensitivity analysis range $23,953 to $138,805, £11,000 to £66,000) per CHD event saved, while the cost per CHD event for the screening strategies is $369,098 ($263,691 to $1,293,597: £170,000, £120,000 to £610,000: moderate and high risk) or $482,224 ($335,825 to $1,537,697: £230,000, £160,000 to £730,000: high risk). Discounting costs and effects at 5% changes these figures to $46,652 ($23,895 to $139,956: £22,000, £11,000 to £66,000) for the population strategy, $368,424 ($264,981 to $1,253,266: £170,000, £130,000 to £590,000: moderate and high risk) and $472,424 ($331,693 to $1,503,684: £220,000, £160,000 to £710,000: high risk) for the screening strategies.

Limitations

1) The analysis is restricted to men only due to lack of data.
2) Costs due to adverse effects of medication provided in the moderate/high risk and high risk "identify and treat" strategies were not included.
3) Cost and effectiveness estimates were obtained from a study conducted 20 years earlier than this article.

Comments

The article was rated +. The results are not directly applicable because of the age of the study. It is also unclear whether the populations are comparable.

3.2.6 Kristiansen et al (1991)[6] Cost effectiveness of incremental programmes for lowering serum cholesterol concentration: is individual intervention worth while?

Kristiansen and colleagues consider a cholesterol lowering programme for the Norwegian male population aged 40 to 49. The interventions considered are: (1) a population based approach consisting of targeted use of the mass media; (2) mass screening with dietary treatment for those with high cholesterol level; (3) mass screening with dietary and drug treatment for high-risk patients. Costs and effects were discounted at 7% as recommended by the Norwegian Treasury. A feature of this analysis is an assumption of a 0.2% reduction in quality of life in individuals identified as being at risk and given dietary treatment, with a reduction of 0.5% if drug treatment was used.

Modelling method used

A range of literature-based assumptions were used to convert from cholesterol lowering through reduced incidence of coronary heart disease to life years gained and QALYs.

Effectiveness

In a population of 200,000, the population based approach gains 3,100 life years (3,800 QALYs) compared to no intervention. The QALY figure reflects both life years gained, and improved quality of life for non-fatal myocardial infarctions avoided. Mass screening with dietary treatment gains a further 3,100 life years (400 QALYs): here the QALY gain is severely reduced because of the assumption of reduced

quality of life in those identified as "at risk". Adding drug treatment gains a further 900 life years (800 QALYs).

Costs

Measured in 1990 UK£, the population based approach costs £36,700 compared to no intervention. Mass screening with dietary treatment costs an additional £38.2 million, while adding drug treatment costs a further £99.2 million.

Cost-effectiveness

Compared to no intervention, the base-case ICER for the population based approach is £12 per life year gained (£10 per QALY). Screening with dietary treatment costs £12,440 per life year gained (£100,546 per QALY) compared to the population based approach. Adding drug treatment to this costs a further £111,549 per life year gained (£125,860 per QALY). The differences in the figures according to outcome measure reflect the differences noted above under effectiveness.

In univariate sensitivity analysis, the population based approach was cost-saving in some cases, but the ICER was as high as £1,600 per life year gained in the worst case considered. The ICER for screening with dietary treatment (compared to the population based approach) ranged from £8,000 to £20,000 per life year gained, while the ICER for adding drug treatment to the screening approach ranged from £57,000 to £166,000 per life year gained. Sensitivity analysis results were not reported in cost per QALY.

Limitations

The main limitation of this analysis is the range of assumptions used. Although these were tested in a range of univariate sensitivity analyses, and the conclusions were largely robust to these assumptions, the results were expressed as cost per life

year gained only. There was no report on the effect on the cost per QALY estimates of changing the assumption about quality of life loss for those identified as high risk.

Comments

The article was rated +. The results are not directly applicable because of the age of the study and the likelihood of differences in population characteristics between Norway and the UK.

3.2.7 Lowensteyn et al (2000)[10] The Cost-Effectiveness of Exercise Training for the Primary and Secondary Prevention of Cardiovascular Disease

Overview

Lowensteyn and colleagues considered the general Canadian population between the ages of 35 and 74. The intervention involved supervised and unsupervised exercise training, defined as aerobic exercise performed at least 3 times per week for 30 minutes per session within 65% to 85% of an individual's maximum heart rate. This was compared to no intervention. Costs and effects were discounted at 3%.

Modelling method used

The Cardiovascular Disease Life Expectancy Model was used to estimate costs and life expectancy of a cohort of 1000 patients.

Effectiveness

Unsupervised exercise training gains 0.7 life years for a man without CVD aged 35 to 54 assuming 100% lifetime adherence. Gains are less for older men and for all women.

Costs

Again assuming 100% lifetime adherence, and taking savings in medical costs into account, unsupervised exercise training is cost-saving compared to no intervention in most groups.

Cost-effectiveness

Assuming 100% adherence, unsupervised exercise training dominates no intervention for men without CVD aged 35 to 74, and women without CVD aged 55 to 74. For women without CVD aged 35 to 54, unsupervised exercise training costs $4,915 (£2,200) per life year gained. The ICER for supervised exercise training is between $15,000 and $23,000 (£6,700 to £10,000) per life year gained for men, and between $42,000 and $61,000 (£19,000 to £27,000) per life year gained for women.

Assuming adherence of 50% for the first year and 30% for subsequent years, the ICER for unsupervised exercise compared to no intervention is still under $4,000 (£1,800) per life year gained for men without CVD and between $6,000 and $12,000 (£2,700 to £5,400) per life year gained for women without CVD. For supervised exercise, the ICER is between $20,000 and $31,000 (£8,900 to £14,000) per life year gained for men, and between $51,000 and $88,000 (£23,000 to £39,000) for women.

Limitations

1) The authors did not incorporate in the analysis potential benefits of exercise on aspects other than lipid and blood pressure lowering.

2) The authors did not take into account the benefits of exercise on quality of life.

3) Neither indirect costs of exercise training nor potential cost savings associated with non-CVD events as a result of exercise training were considered.

4) No adjustments for differences in US versus Canadian healthcare costs were made.

5) No separate cost estimates were given for the supervised exercise.

Comments

The article was rated +. The results are not directly applicable because of the limitations identified above.

3.2.8 Tosteson et al (1997)[14] Cost-effectiveness of population wide educational approaches to reduce serum cholesterol levels

Overview

Tosteson and colleagues (1997) considered populationwide approaches to reduce serum cholesterol levels in the US adult population. Programmes considered were the North Karelia, Stanford Three-Community, and Stanford Five-City programmes. Costs and outcomes were discounted at 5% in the base case analysis (3% in sensitivity analysis).

Modelling method used

The analysis was based on an existing model called the Coronary Heart Disease Policy Model. For each programme considered, the cost and effects on cholesterol reduction were entered as parameters into the CHD Policy Model, and results were obtained in the form of costs per life-year saved.

Cost-effectiveness

A programme with the costs and benefits of the Stanford Five-City project ($4.95, £3 per person per year; 2% reduction in serum cholesterol) would cost $3,200 (£1,900) per year of life saved.

A programme with the costs and benefits of the North Karelia project ($16.55, £10 in year 1 and $8.28, £5 each year thereafter; 3% reduction in serum cholesterol) would cost $6,100 (£3,700) per year of life saved.

Under the assumptions that cost is $16.55 (£10) and reduction in cholesterol is equal to or less than 2%, the intervention would cost $38,500 (£23,000) per year of life saved.

Varying the model inputs over a wide range gave cost-effectiveness results ranging from cases where the programme is cost-saving but still gains years of life to a cost of over $400,000 (£240,000) per life year gained in the worst case considered.

Limitations

1) The baseline analysis did not include adverse events because such events had not been found in two recent large RCTs.

2) Costs associated with following a diet or costs due to potential increase in non-CHD medical costs incurred by individuals as a result of prolonged life owing to lower cholesterol levels were not included. Similarly, potential benefits of cholesterol reduction for other diseases (e.g. peripheral vascular disease) were not included.

Comments

The study was rated +. The results are not directly applicable because of differences in the underlying population characteristics between the US and the UK.

3.3 Summary of the evidence

In this section, the evidence reported in Sections 3.1 and 3.2 is summarised. The effectiveness study based articles have been considered in two groups. The evidence for the UK-based studies is summarised in Section 3.3.1, and for the non-UK based studies in Section 3.3.2. Model-based articles are summarised in Section 3.3.3, and an overall summary with evidence statements for the cost-effectiveness review follows in Section 3.3.4.

3.3.1 Summary of the evidence for effectiveness study based articles carried out in the UK

Interventions

All the three studies were population based.

Two of the three studies (Oxcheck and BFHS) involved screening for risk factors and follow-up appointments. In these studies, screening focused on several risk factors, including blood pressure, cholesterol concentration, smoking, weight and alcohol consumption. The main difference between Oxcheck and BFHS is that while in Oxcheck follow up appointments were negotiated between nurse and participant, in BFHS follow up appointments were arranged according to a strict protocol.
In contrast, the study by Baxter and colleagues evaluated the Action Heart intervention, which involved a combination of health promotion approaches such as stop smoking support groups, weight control clinics, healthier eating activities, information leaflets, nicotine patch scheme etc.

Effectiveness

The effectiveness of the Oxcheck and BFHS programmes was assessed in terms of reduction in coronary risk. However, in the article by Wonderling and colleagues comparing the Oxcheck and BFHS studies, the effectiveness is measured in life years gained. The Baxter study assessed the observed difference in smoking and consumption of low fat milk between the intervention and control area and converted these estimates to life years gained. Life years gained were reported undiscounted in the Baxter study, but they were discounted at 6% in the Wonderling study (Oxcheck and BFHS).

Costs

All of the three UK-based studies measured the programme related costs. In addition, Langham et al, measured the cost of prescribed medication, while Wonderling et al, also included the costs of health services used at the general practice level. In all the articles, costs were discounted at 6% annual rate.

Cost-effectiveness

The articles by Wonderling et al and Langham et al reported cost-effectiveness in terms of cost per 1% reduction in coronary risk compared to "do-nothing". However, in the article by Wonderling and colleagues that compared Oxcheck and BFHS the results were presented in terms of cost per life year gained.

The Baxter study also reported cost per life year gained.

Limitations

All three studies suffered from limited follow up period that is likely to ignore important costs and benefits accruing in the future.

Another limitation relates to the measurement of costs. While Langham and colleagues measured programme costs, medication cost and health services cost at GP level, Wonderling costing was limited to programme costs and medication costs and Baxter estimated only the programme related costs. It is likely there are other costs (for example, those arising in secondary care) that are ignored.

In addition, there is substantial uncertainty around the duration of the effect of the intervention, and this has a major effect on the cost-effectiveness of the intervention.

3.3.2 Summary of the evidence for non-UK effectiveness study based articles

Intervention

All the non-UK based studies assessed programmes that combined screening for identification of patients in high risk and CVD-related education (Lasater et al., 1991; Lindholm et al., 1996; Norinder *et al.*, 2002 and Rasmussen *et al.*, 2007).

Effectiveness

Most of the studies (Lasater *et al.*, 1991; Lindholm et al., 1996 and Rasmussen *et al.*, 2007) measured and reported the effectiveness of the assessed interventions. On the contrary, Norinder and colleagues did not provide effectiveness results as their study evaluated only the costs of the assessed intervention.

All the articles reporting effectiveness found positive evidence. The assessed intervention in the studies by Lindholm et al, and Lasater et al, were associated with reduction in serum cholesterol levels, and, similarly, Rasmussen et al, found patients in the intervention group to be associated with more life-years gained than those in the control group.

Costs

All the studies measured costs associated with implementing the programme. In addition, Lindholm and Rasmussen measured costs incurred by patients (productivity loss) and the health care system (CVD related health services use). The article by Norinder and colleagues took into account only health care system costs that arise from in-patient health services use.

Cost-effectiveness

Only Lindholm and colleagues calculated incremental cost effectiveness ratios (£1,200 to £14,000 per life year gained). Lasater et al stated that the intervention cost $1.30 (£0.86) per pound of weight loss; Rasmussen et al found the assessed interventions being more effective and cost saving. The article by Norinder et al is a cost-analysis, therefore cost effectiveness ratios could not be calculated.

Limitations

The main limitations with regards to the Lasater et al article are associated with the design of the study, not involving a control group and non-randomly selected participants. The articles by Rasmussen et al and Norinder et al presented limitations related to measuring the cost of the programme. On the other hand, Lindholm et al acknowledged limitations associated with the logistic regression model used to translate risk reduction into cardiovascular morbidity.

3.3.3 Model based articles

Interventions

Interventions covered are mass media campaigns (5 articles), some form of screening with treatment for high-risk individuals (5 articles) and a population based exercise training campaign (one study).

Modelling method used

Two articles used a series of literature-based assumptions to convert changes in risk factors to changes in outcomes. Three articles used risk equations (two Framingham, one Australian). Three articles used cohort simulation models.

Effectiveness

The two Australian articles measured outcomes in terms of events prevented, while five others made an attempt to estimate life years gained, one of which also estimated QALYs. One article used DALYs averted as the only outcome measure.

Costs

All articles included the costs of any population campaign and screening programme, together with any treatment included as part of that programme. One article (Murray et al) explicitly excluded cost savings as a result of treatment no longer required for cases of CVD averted while one article (Hall et al) explicitly included such cost savings. Most of the articles did not comment explicitly on this issue.

Cost-effectiveness

Results were reported in terms of an incremental cost-effectiveness ratio, with the denominator as described above under effectiveness. Of the two studies which covered UK populations, one used a 3% discount rate, while the other used 0 and 6% discount rates. No article used the currently recommended rate of 3.5%.

3.3.4 Overall summary and evidence statements

Of the seven effectiveness study based articles, six assess interventions that combine screening and provision of CVD-related education. The remaining intervention involves provision of CVD-related education only.

Cost-effectiveness results have been reported in terms of cost per life year gained (Baxter et al. 1997; Wonderling et al. 1996b; Lindholm et al. 1996 and Rasmussen et al. 2007); cost per 1% reduction in coronary risk (Wonderling et al. 1996a; Langham et al. 1996) and cost per pound of weight lost (Lasater et al., 1991). One article evaluated only costs, thus it did not provide cost-effectiveness results (Norinder et al., 2002).

One article (Rasmussen et al. 2007; rated +) found the assessed intervention to be more effective and less costly. In the rest of the studies that conducted incremental analysis, the results ranged from £31 per life year gained (Baxter et al 1997; rated +) to £144,500 (British Family Heart intervention, reported by Wonderling et al 1996a; rated ++). In the majority of the studies, the reported ICERs did not exceed £20,000 per life year gained. Similarly, in articles that did not report results in terms of life years gained, the assessed interventions were associated with improved effectiveness in terms of reduction in risk factors for a small additional cost (Langham et al., 1996, rated +; Wonderling et al (1996a), rated ++; Lasater et al 1991, rated -).

Three modelling articles (Murray et al, 2003, Kristiansen et al, 1991, Tosteson et al, 1997, all rated +) have assessed mass media campaigns and given results in life years gained (2), QALYs (1) and DALYs (1). According to the range of assumptions used, results vary from cases where the campaign is overall cost saving while still effective to cases with a cost of over US$400,000 (£240,000) per life year gained. The majority of cases reported were within a range equivalent to £20,000 per QALY.

Two modelling articles gave results for mass media campaigns in terms of cases prevented. One (Hall et al, 1998, rated -) suggested that the whole population approach would be cost saving while also reducing the number of cases, while the

other (Kinlay et al, 1994, rated +) gave a cost per case prevented of Aus$47,000 (£22,000: sensitivity analysis range $24,000 to $140,000, £11,000 to £66,000).

One article (Field et al, 1995, rated +) reported a range of screening options in which all ICERs compared to no intervention or a less intensive screening programme were below £13,000/LYG. Another article (Assmann et al, 1990, rated +) gave results for screening compared to no intervention and gave results between DM 30,000 (£10,000)/LYG (for men under 60) and DM 110,000 (£37,000)/LYG (for women aged 60 to 64).

One article (Kristiansen et al, 1991, rated +) compared screening with a population based approach and reported an ICER of £12,000 per life year gained (£100,000 per QALY). Adding drug treatment for some high risk cases had an ICER of £110,000 per life year gained (£130,000 per QALY).

Two articles reported results for screening strategies in terms of cases prevented. One (Hall et al, 1998, rated -) reported an ICER of Aus$28,000 (£10,000) per case prevented while the other (Kinlay et al, 1994, rated +) reported ICERs ranging from Aus$260,000 to Aus$1,500,000 (£120,000 to £730,000) per case prevented.

One article (Lowensteyn et al, 2000, rated +) reported the effects of exercise training. Assuming 100% adherence, unsupervised exercise could be cost saving while improving health outcomes in some age groups, but could cost as much as Can$5,000 (£2,200) per life year gained in women aged 35 to 54. With a more realistic assumption about adherence, ICERs remained below Can$12,000 (£5,400) per life year gained in all groups. Supervised exercise could cost up to Can$88,000 (£39,000) per life year gained.

Table 3.2 summarises the cost-effectiveness results for all studies considered in this review. Evidence statements have been generated following the structure of this table.

Table 3.2 Cost-effectiveness Results Summary

Population based programmes	
Results per LYG	
Baxter	£31 to £42
Kristiansen	Cost saving to £1,600
Tosteson	Cost saving to £240,000
Per QALY or DALY	
Murray	£96
Kristiansen	£10
Per case prevented	
Hall	Cost saving
Kinlay	£22,000
Screening compared to no intervention	
Per LYG	
Wonderling (BFHS)	£1,100 to £140,000
Wonderling (Oxcheck)	£900 to £42,000
Lindholm	£1,200 to £15,000
Rasmussen	Cost saving
Field	£1,200 to £6,900
Assmann	£10,000 to £37,000
Results per case prevented	
Hall	£10,000
Kinlay	£170,000 to £230,000
Per 1% reduction in coronary risk	
Wonderling (BFHS)	£4.30 to £5.30
Langham	£2.25
Per pound weight lost	
Lasater	£0.80
Screening compared to population approach	
Per LYG	
Kristiansen	£12,000 to £120,000
Per QALY	
Kristiansen	£100,000 to £230,000
Exercise training	
Per LYG	
Lowensteyn	Cost saving to £39,000

Interventions described as "Cost saving" in the above table are associated with reduced costs and improved outcomes.

Cost effectiveness evidence statements

Three studies gave results in cost per life-year gained for population based programmes compared to no intervention. The results ranged from cost-saving to £240,000 per life-year gained.

Two studies gave results in cost per QALY or DALY for population based programmes compared to no intervention. Results ranged from £10/QALY to £96/DALY.

Two studies gave results in cost per case prevented for population based programmes compared to no intervention. Results ranged from cost saving to £22,000 per case prevented.

Five studies reported results in cost per life year gained for some form of screening strategy compared to no intervention. Results ranged from cost saving to £140,000 per life year gained.

Two studies gave results in cost per case prevented for screening compared to no intervention. Results ranged from £10,000 to £730,000 per case prevented.

Two studies gave results per 1% reduction in coronary risk for screening compared to no intervention. Results ranged from £2.25 to £5.30 per 1% reduction for one person.

One study gave a result of £0.80 per pound weight lost for a screening programme compared to no intervention.

One study gave results ranging from £12,000 to £120,000 per life year gained and £100,000 to £230,000 per QALY for screening compared to a population based approach.

One study gave results from cost saving to £39,000 per life year gained for some form of exercise training.

3.4 Evidence tables

Assmann and Schulte (1990)[1]

Study details	Population and setting	Intervention/comparator	Outcomes and methods of analysis	Results	Notes
Authors: Assmann and Schulte **Year:** 1990 **Aim of study:** To assess the cost-effectiveness of a primary prevention strategy for coronary heart disease in West Germany **Type of Economic Analysis:** Cost-effectiveness	**Source population/s:** Adult population of Federal Republic of Germany **Setting:** Population **Data Sources:** Published sources	**Intervention/s description:** Population stratified into five groups. No therapy for group I, nutritional advice for group II, stringent diet for group III, diet plus fibrate/nicotinic acid (niacin) for group IV, diet plus ion exchange resin/HMG CoA reductase inhibitor for group V **Comparator/Control/s description:** No intervention **Sample sizes:** Model based analysis – no new primary data	**Primary Outcomes** Lifeyears gained **Secondary outcomes** None **Time Horizon:** Lifetime **Discount Rates:** ▪ Benefits 4% ▪ Costs 4% **Modelling Method:** Framingham risk equations	**Primary analysis:** ▪ ICERs men under 60: 30,000 DM per life year gained men 60 to 64: 40,000 DM per life year gained women under 60: 86,000 DM per life year gained women 60 to 64: 110,000 DM per life year gained **Secondary analysis:** None	**Limitations identified by author:** No account taken of improv quality of life from delayed onset of coronary heart dise **Limitations identified by review team**: No sensitivity analysis. Not clear whether Framingham equations are transferrable to German population Medication used would not reflect current UK practice **Evidence gaps and/or recommendations for futur research:** None stated

[1]Assman and Schulte. Modelling the Helsinki Heart Study by means of risk equations obtained from the PROCAM study and the Framingham Heart Study. *Drugs* 1990; 40:13-18

Study details	Population and setting	Intervention/comparator	Outcomes and methods of analysis	Results	Notes
Economic Perspective: Only costs reimbursed by sickness funds **Study Quality: +** **Applicability:** Not applicable					**Source of funding:** Not stated.

Baxter *et al.* (1997)[2]

Study details	Population and setting	Intervention/comparator	Outcomes and methods of analysis	Results	Notes
Authors: Baxter et al **Year:** 1997 **Aim of study:** To assess effectiveness and cost effectiveness of a community based coronary heart disease health promotion project **Type of Economic Analysis:** Cost effectiveness analysis **Economic Perspective:**	**Source population/s:** United Kingdom (public health care system) Intervention and control populations of adults aged 18-64 in Rotherham (urban areas with high incidence of coronary heart disease) **Setting:** Community **Data Sources:** primary research, published sources	**Intervention/s description:** Combination of health promotion approaches, including stop smoking support groups, weight control clinics, healthier eating activities, information leaflets, library resources, Action Heart Club, blood pressure screening, Action Heart body check ups, nicotine patch scheme **Comparator/Control/s description:** No intervention **Sample sizes:** **Total n=** not stated **Intervention n=** not stated **Control n=** not stated	**Primary Outcomes** Life years gained **Secondary outcomes** None **Time Horizon:** Lifetime **Discount Rates:** ▪ Benefits not discounted ▪ Costs 6% **Modelling Method:** Computer model based on American Cancer Society study	**Primary analysis:** ▪ Benefits 3581 life years gained in intervention group of 14,500 people ▪ Costs Total project cost £110,000 ▪ ICERs £31 per life year gained **Secondary analysis:** None	**Limitations identified by author:** ▪ Outcome measure based o life years gained at end of ex-smoker's life, with no attempt to measure other health benefits to be gaine from quitting smoking (su as quality of life improvement from non-fa CVD avoided). ▪ Health care costs avoided due to the likely reduction in smoking-related diseas has not been estimated ▪ Costs and benefits may ha been ignored due to short follow up period **Limitations identified by review team**: ▪ Estimate of total life years gained appears to be calculated from median g in model not mean ▪ Incomplete description of the intervention **Evidence gaps and/or**

[2] Baxter *et al*. A cost effective, community based heart health promotion project in England: a prospective comparative study. *BMJ* 1997; 315:582-585

Study details	Population and setting	Intervention/comparator	Outcomes and methods of analysis	Results	Notes
Health Authority (Rotherham) **Study Quality: +** **Applicability:** Not applicable					**recommendations for futur research:** Longer follow up is required to assess fully the long term effectiveness and overall cos effectiveness of the project. **Source of funding:** Rotherham Health Authorit

Field (1995)[3]

Study details	Population and setting	Intervention/comparator	Outcomes and methods of analysis	Results	Notes
Authors: Field et al **Year:** 1995 **Aim of study:** To examine the relative cost effectiveness of a range of screening and intervention strategies for preventing coronary heart disease in primary care **Type of Economic Analysis:** Cost effectiveness analysis **Economic**	**Source population/s:** United Kingdom. Men and women aged 35-64 years. **Setting:** Primary care **Data Sources:** published sources including risk factors measured during OXCHECK trial	**Intervention/s description:** Initial screening followed by additional screening for those at risk. Patients found to have high risk factors offered lifestyle counselling plus drug treatment as appropriate. Risk factors as follows: A. systolic blood pressure >140mmHg, history of ischaemic heart disease, stroke or transient ischaemic attack B. smoking C. body mass index >28 D. fat intake >110 g/day E. first degree relative with ischaemic heart disease, stroke, or transient ischaemic attack before 60 years F. total cholesterol >7.5 mmol/l Strategy 1 applied screening for risk factor A to whole population, then factors BCDEF to those at risk. Strategy 2 applied screening for risk factors AB to whole population, then factors CDEF to those at risk. Strategy 3 applied screening	**Primary Outcomes** Life years gained **Secondary outcomes** None **Time Horizon:** Lifetime **Discount Rates:** ▪ Benefits: 0, 6% ▪ Costs: 0, 6% **Modelling Method:** Framingham risk equation applied to estimate expected avoided deaths from intervention	**Primary analysis:** For 7840 men and women aged 35-64 ▪ Benefits Life years gained undiscounted by strategy: 1. men 132, women 78 2. men 182, women 103 3. men 211, women 121 4. men 216, women 124 5. men 218, women 125 6. men 227, women 133 ▪ Costs Discounted (£000) by strategy 1. men, 97, women 206 2. men 173, women 295 3. men 250, women 421 4. men 263, women 444 5. men 263, women 465 6. men 287, women 503 ▪ ICERs (£/life year gained) Undiscounted compared to no screening by strategy 1. men 730 women 2650 2. men 950 women 2850 3. men 1190 women 3470 4. men 1220 women 3590 5. men 1210 women 3700 6. men 1270 women 3780	**Limitations identified by author:** Did not include cost of bloo pressure screening and treatment, which was the sa for all strategies, or cost of treating existing coronary heart disease. Did not consi savings generated by lower morbidity, hence lower demand for medical care. D not consider costs of care fo additional survivors. **Limitations identified by review team**: Only health service costs **Evidence gaps and/or recommendations for futur research:** Further research, preferably by randomised trials, on the effectiveness of health promotion interventions. Need for information on the long term changes that can b expected from health

[3] Field *et al*. Strategies for reducing coronary risk factors in primary care: which is most cost-effective? *BMJ* 1995; 310: 1109-1112

Study details	Population and setting	Intervention/comparator	Outcomes and methods of analysis	Results	Notes
Perspective: Health service **Study Quality: +** **Applicability:** Not applicable		for risk factors ABC to whole population, then factors DEF to those at risk. Strategy 4 applied screening for risk factors ABCD to whole population, then factors EF to those at risk. Strategy 5 applied screening for risk factors ABCDE to whole population, then factor F to those at risk. Strategy 6 applied screening for risk factors ABCDEF to whole population. **Comparator/Control/s description:** No screening **Sample sizes:** Not relevant as model based analysis		Undiscounted compared to previous strategy 2. men 1530 women 3470 3. men 2650 women 6970 4. men 2490 women 9570 5. men 180 women 12470 6. men 2720 women 5040 Discounted compared to no screening 1. men 1240 women 4730 2. men 1640 women 5150 3. men 2040 women 6270 4. men 2090 women 6480 5. men 2080 women 6700 6. men 2180 women 6850 Discounted compared to previous strategy not reported **Secondary analysis:**	promotion interventions and the effects that these change have on the future risk of disease. **Source of funding:** Health Education Authority North West Thames Region Health Authority, Imperial Cancer Research Fund.

Hall *et al.*(1988)[4]

Study details	Population and setting	Intervention/comparator	Outcomes and methods of analysis	Results	Notes
Authors: Hall *et al.* **Year:** 1988 **Aim of study:** To measure the costs and cost-effectiveness associated with a number of strategies for the prevention of heart disease **Type of Economic Analysis:** Cost effectiveness analysis **Economic**	**Source population/s:** Austalia (developed, public health care system) **Setting:** Community **Data Sources:** Published studies	**Intervention/s description:** The following were assessed: ▪ Whole population approach: Involves medial campaigns to promote behavioural changes in the population ▪ Identification of high-risk individuals approach: Involves screening and provision of long term counselling to those who are in the top 15% of the distribution for overweight, smoking, lack of exercise, blood pressure and blood cholesterol levels ▪ Combined approach: Involves advice on risk-factor modification in the total population and screening to identify a high-risk group in need for more intensive counselling **Comparator/Control/s**	**Primary Outcomes** ▪ Mean cost ▪ Net cost per prevented case **Secondary outcomes** NA **Time Horizon:** Unclear **Discount Rates:** ▪ Benefits: NA ▪ Costs: 6% **Modelling Method:** No formal modelling techniques were utilised	**Primary analysis:** **Benefits** Expressed as number of myocardial infarctions prevented within five years in a population of 60,000 men ▪ Whole population approach: 264 cases prevented ▪ Identification of high-risk individuals approach: 169 cases prevented ▪ Combined approach: 348 cases prevented **Costs** Expressed as total cost and net cost (cost less potential savings as a result of the intervention) of implementing the intervention for 5 years ▪ Whole population approach: Total cost: $331,000 Net cost: -$919,000 (this approach results in savings)	**Limitations identified by author:** ▪ The effectiveness of each strategy might be overestimated if myocard infarctions are postponed rather than prevented ▪ Costs are underestimated they do not include strate design and initiation costs ▪ Indirect costs due to increased productivity are not included **Limitations identified by review team**: Follow-up period was limite to 5 years **Evidence gaps and/or recommendations for futur research:** ▪ Studies with longer follow up period would be neede to capture costs and benef occurring in the long term

[4] Hall *et al.* A cost-effectiveness analysis of alternative strategies for the prevention of heart disease. *Med J Aust* 1988; 148: 273-277

Study details	Population and setting	Intervention/comparator	Outcomes and methods of analysis	Results	Notes
Perspective: Health care system (Australia) **Study Quality: -** **Applicability:** Not applicable		**description:** The comparator involved no intervention **Sample sizes:** not relevant-model based analysis		▪ Identification of high-risk individuals approach: Total cost: $5,455,000 Net cost: $4,655,000 ▪ Combined approach: Total cost: $6,092,000 Net cost: $4,445,000 **ICERs** Expressed as net cost per prevented case ▪ Whole population approach: $919,000 saved and 264 cases prevented ▪ Identification of high-risk individuals approach: $27,544 per case prevented ▪ Combined approach: $12,773 per case prevented **Secondary analysis:** NA	**Source of funding:** Not reported

Translation of CVD-risk factor related reductions to broader benefits: p. 274 left " It has been estimated that an 8%... strategies 1, 2 and 3 ".

Kinlay *et al.*[5](1994) *Prevention of CVD*

Study details	Population and setting	Intervention/comparator	Outcomes and methods of analysis	Results	Notes
Authors: Kinlay *et al.* **Year:** 1994 **Aim of study:** to measure the cost effectiveness of two identification and treatment strategies and a population-based educational strategy for lowering blood cholesterol as a means	**Source population/s:** Australia (developed, public health care system) Men between 35 and 64 years old **Setting:** Population in Lower Hunter region, New South Wales, Australia **Data Sources:** Primary research (the Stanford Three Cities Study)	**Intervention/s description:** Effectiveness data were obtained from the Stanford Three Cities Study. This study involved a community-based intervention that provided information about common risk factors of cardiovascular disease (high blood pressure, high cholesterol levels, smoking) via mass media, face-to-face instructions or combination of the two.[6] **Comparator/Control/s description:** The comparator involved two identification and treatment strategies for patients in high (blood cholesterol >6.5mmol/L) and moderate/high (>5.5 mmol/L) blood cholesterol. Both the strategies offered screening and treatment with	**Primary Outcomes** Cost per coronary heart disease (CHD)event averted **Secondary outcomes** NA **Time Horizon:** 5 years **Discount Rates:** ▪ Benefits: No discounting (5% in sensitivity analysis) ▪ Costs: No discounting (5% in sensitivity analysis) **Modelling Method:** A logistic regression equation was used to translate risk factor profiles provided by Hunter Risk Factor Prevalence Study,	**Primary analysis:** For population of Lower Hunter region (67,651 men aged 35 to 64 years) **Benefits** Number of CHD events averted ▪ Intervention: 104 CHD events averted ▪ Control: Moderate/high risk: 144 CHD events ▪ High risk: 116 CHD events **Costs** ▪ Intervention: $5,413,400 (cost to provide the intervention for 5 years) ▪ Control:	**Limitations identified by author:** ▪ The analysis is restricted t men only due to lack of d ▪ Costs due to adverse effec of medication provided in the moderate/high risk an high risk "identify and treat" strategies were not included ▪ Cost and effectiveness estimates were obtained from a study conducted 2 years before this study **Limitations identified by review team**: None **Evidence gaps and/or recommendations for futur research:** None **Source of funding:**

[5] Kinlay *et al.* The cost-effectiveness of different blood-cholesterol-lowering strategies in the prevention of coronary heart disease. *Australian journal of public health* 1994, 18(1): 105-110

[6] Farquhar *et al.* Community intervention for cardiovascular disease. *Lancet* 1977; i: 1192-5

Study details	Population and setting	Intervention/comparator	Outcomes and methods of analysis	Results	Notes
of preventing coronary heart disease **Type of Economic Analysis:** Cost effectiveness analysis **Economic Perspective:** Societal (government and patients) **Study Quality:+** **Applicability:** Not applicable		medication and diet counselling **Sample sizes:** **Total n=** NA **Intervention n=** NA **Control n=** NA (model based analysis- no new samples)	reduction in CHD events. This reduction was modelled to estimate the number of primary and secondary CHD events saved.	Moderate/high risk: $53,051 115 (undiscounted population cost for providing the intervention for 5 years) High risk: $50,122,672 (undiscounted population cost for providing the intervention for 5 years) **ICERs** ▪ Intervention $44,667 per CHD event averted ▪ Control Moderate High Risk: $369,098 per CHD event averted High Risk: $482,224 per CHD event averted **Secondary analysis:** NA	Not reported

Kristiansen et al(1991)[7]

Study details	Population and setting	Intervention/comparator	Outcomes and methods of analysis	Results	Notes
Authors: Kristiansen et al **Year:** 1991 **Aim of study:** To evaluate the relative cost effectivness of various cholesterol lowering programmes **Type of Economic Analysis:** Cost effectiveness analysis **Economic Perspective:** Health care costs only	**Source population/s:** Norway (developed, public health care system) Men aged 40-49 **Setting:** Population **Data Sources:** published sources, assumptions	**Intervention/s description:** 1. Population approach , consisting of targeted use of the mass media as well as tax incentives to improved diet 2. Screening for hypercholesterolaemia and following up subjects whose serum values exceed defined limits. Specifically, over 5.0 mmol/l a confirmatory cholesterol test. Over 6.0 mmol/l dietary treatment with visits to the doctor at 1.5 per year (2 per year at 8.0 mmol/l). 3. Use of lipid lowering drugs in combination with dietary treatment for half of patients over 8.0 mmol/l **Comparator/Control/s description:** No action	**Primary Outcomes** Life years gained, QALYs. **Secondary outcomes** None **Time Horizon:** 20 years **Discount Rates:** ▪ Benefits: 7% ▪ Costs: 7% ▪ (varied from 0 to 10% in sensitivity analysis) **Modelling Method:** Simple cohort calculations	**Primary analysis:** (For population of 200,000) ▪ Benefits Life years 1 over do nothing: 3,100 2 over 1: 3,100 3 over 2: 900 QALYs 1 over do nothing: 3,800 2 over 1: 400 3 over 2: 800 ▪ Costs (1990 UK£) 1 over do nothing: £36,700 2 over 1: £38.2 million 3 over 2: £99.2 million ▪ ICERs (£/life year gained) 1 over do nothing: 12 2 over 1: 12,440 3 over 2: 111,549 (£/QALY) 1 over do nothing: 10 2 over 1: 100,546 3 over 2: 125,860 **Secondary analysis:** None	**Limitations identified by author:** Analysis based on numerou assumptions **Limitations identified by review team**: As noted by authors **Evidence gaps and/or recommendations for futur research:** Further studies on the long term effects of individual intervention on both biologi processes and quality of life are needed **Source of funding:** Not reported

[7] Kristiansen *et al* Cost effectiveness of incremental programmes for lowering serum cholesterol concentration: is individual intervention worth while? *BMJ* 1991; 302:1119-22

Study details	Population and setting	Intervention/comparator	Outcomes and methods of analysis	Results	Notes
Study Quality: + **Applicability:** Not applicable		**Sample sizes:** **Total n=** NA **Intervention n=** NA **Control n=** NA (model based analysis; no new samples)			

Langham *et al.* (1996)[8] *Prevention of CVD*

Study details	Population and setting	Intervention/comparator	Outcomes and methods of analysis	Results	Notes
Authors: Langham *et al* **Year:** 1996 **Aim of study:** To measure the costs and cost effectiveness of the Oxcheck cardiovascular risk factor screening and intervention programme **Type of Economic Analysis:** Cost effectiveness analysis **Economic Perspective:** General	**Source population/s:** UK (developed, public health care system) Primary care patients (men and women) between 35 and 64 years **Setting:** Community (5 general practices in Luton and Dunstable, UK) **Data Sources:** Primary research (multicentre randomised controlled trial)	**Intervention/s description:** The intervention involved health checks, carried out by nurses, that aimed to record each participants' medical history, lifestyle characteristics and level of blood cholesterol. Patients with high risk factor levels were invited to attend 10-20 minutes follow up appointment with a nurse. As part of the intervention, participants who received health check in the first year (1989-90) were invited to attend a 30 minutes re-examination in the fourth year (1992-93). **Comparator/Control/s description:** The control group comprised patients who attended a health check in the fourth (last) year of the study **Sample sizes:** **Intervention n=** 2,205	**Primary Outcomes** ▪ Mean cost ▪ Mean cost per 1% reduction in coronary risk **Secondary outcomes** NA **Time Horizon:** 4 years **Discount Rates:** ▪ Benefits: Not discounted ▪ Costs: 6% **Modelling Method:** No modelling techniques were utilised	**Primary analysis:** **Benefits** Overall reduction in coronary risk: ▪ 20% for patients who attended the year 4 examination only ▪ 13% including non-attenders of the year 4 examinations The authors also stated that the effect of the intervention in terms of reduced risk was greater for women at 24% compared to men at 18%. **Costs** ▪ Average cost for the health check cardiovascular risk factor screening and intervention programme was estimated to be £29.27 ▪ Programme costs was estimated to be	**Limitations identified by author:** ▪ Some research costs migh have been included in the programme costs, while some programme costs m have been omitted along with the research costs ▪ Estimated costs do not include costs that might have arisen in relation to other subsequent health care. **Limitations identified by review team**: ▪ Reduction in coronary ris was not converted into a broader unit of effectiven ▪ The study's follow up period is unlikely to captu all the relevant costs and benefits **Evidence gaps and/or recommendations for futur research:** Translation of coronary risk

[8] Langham *et al.* Costs and cost effectiveness of health checks conducted by nurses in primary care: the Oxcheck study. *BMJ* 312: 1265-1268

Study details	Population and setting	Intervention/comparator	Outcomes and methods of analysis	Results	Notes
practice (England) **Study Quality:** + **Applicability:** Partially applicable		participants attending a health check in the first year (1989 – 1990) **Control n=** 1,916 participants attending for their first check in the fourth year (1992-93)		approximately £47,000 for a 7,500 general practice **ICERs** Cost per 1% risk reduction for men who ▪ attended the year 4 examination only: £1.22 ▪ did not attend the year 4 examination: £1.72 Cost per 1% risk reduction for women who ▪ attended the year 4 examination only: £1.63 ▪ did not attend the year 4 examination: £4.18 Cost per 1% risk reduction per person who ▪ attended the year 4 examination only: £1.46 ▪ did not attend the year 4 examination: £2.25 **Secondary analysis:** NA	reduction into a common un of effectiveness **Source of funding:** Imperial Cancer Research Fund

Lasater et al. (1991)[9]

Study details	Population and setting	Intervention/comparator	Outcomes and methods of analysis	Results	Notes
Authors: Lasater et al **Year:** 1991 **Aim of study:** To assess a community based programme aimed at reducing obesity **Type of Economic Analysis:** Cost-effectiveness analysis **Economic Perspective:** Non-personnel costs only **Study**	**Source population/s:** US (developed, private health care system). Adult residents of Pawtucket, Rhode Island. **Setting:** Community. **Data Sources:** primary research.	**Intervention/s description:** The intervention involved provision of weigh loss kits (including guidelines for setting weight loss and calorie goals and record keeping, calorie guide, explanation of the energy balance principles, tip sheets on weight loss and cholesterol reduction etc.) to assist participants to achieve a self-determined 10-week weigh loss goal **Comparator/Control/s description:** No control group **Sample sizes:** **Total n=** 213 **Intervention n=** 213 **Control n=** 0	**Primary Outcomes** Weight loss achieved. **Secondary outcomes** Proportion who returned for second weighing Reduction in cholesterol level. **Time Horizon:** 10 weeks **Discount Rates:** ▪ Benefits: not discounted ▪ Costs: not discounted **Modelling Method:** No modelling techniques were utilised	**Primary analysis:** ▪ Benefits Mean weight loss 8.2 lb in those who returned (61%) Mean reduction in cholesterol level 29 mg/dL ▪ Costs Total cost of the programme $2,840 ($6.80 per participant) ▪ ICERs $1.30 per measured pound loss **Secondary analysis:** Not reported	**Limitations identified by author:** No control group was involved Non-randomly selected sample consisted of volunteers. **Limitations identified by review team**: No attempt to translate the observed effectiveness resul to CVD-related benefits (e.g events prevented, life years gained) **Evidence gaps and/or recommendations for futur research:** Future research would be useful to compare similar interventions in controlled studies. **Source of funding:**

[9] Lasater *et al.* Community-based approach to weight loss: the Pawtucket "weigh-in". *Addictive Behaviors* 1991; 16: 175-181

Study details	Population and setting	Intervention/comparator	Outcomes and methods of analysis	Results	Notes
Quality: - **Applicability:** Not applicable					Not stated

Lindholm (1996)[10]

Study details	Population and setting	Intervention/comparator	Outcomes and methods of analysis	Results	Notes
Authors: Lindholm et al **Year:** 1996 **Aim of study:** To evaluate the cost effectiveness and equity of a community based cardiovascular disease prevention programme **Type of Economic Analysis:** Cost effectiveness analysis **Economic Perspective:**	**Source population/s:** Sweden (developed, public health care system) Rural population aged 30-60 **Setting:** Rural community **Data Sources:** Primary research	**Intervention/s description:** Health promotion activities undertaken in the community by adult education associations, sports clubs, media, food retailers (food labelling), companies, and local authorities, combined with screening and followed by appropriate advice focussed on the main risk factors for cardiovascular disease **Comparator/Control/s description:** No intervention (control group comprised population of another part of northern Sweden) **Sample sizes:** **Total n=** 7500 **Intervention n=** 5500 **Control n=** 2000	**Primary Outcomes** Mean serum cholesterol, mean diastolic blood pressure, proportion of daily smokers **Secondary outcomes** None **Time Horizon:** 15 years of follow up **Discount Rates:** ▪ Benefits 0, 5% ▪ Costs 5% **Modelling Method:** Estimated mortality from Framingham equation	**Primary analysis:** ▪ Benefits Mean serum cholesterol fell in intervention population by 1.0 mmol/l in men, 1.4 mmol/l in women; control group no change in men, fell by 0.2 mmol/l in women No change in blood pressure or proportion of smokers ▪ Costs Annual cost of the programme £51,500 (discounted total over 10 years £363,000) Savings estimated at £326,000 ▪ ICERs Base case result £1,200 per life year saved Worst case £14,000 per life year saved **Secondary analysis:** None	**Limitations identified by author:** ▪ Cardiovascular outcomes estimated using Framingham equation ma underestimate or overestimate the effects of the intervention (due to n allowing for interactions between risk factors) ▪ The intervention combine individual and population based strategies, hence it i not possible to determine with certainty which of these approaches was mo effective in bringing abou the observed benefits **Limitations identified by review team**: As noted by author **Evidence gaps and/or recommendations for futur research:** Knowledge of indirect effec

[10] Lindholm *et al*. Cost effectiveness and equity of a community based cardiovascular disease prevention programme in Norsjö, Sweden *Journal of Epidemiology and Community Health* 1996; 50:190-195

Study details	Population and setting	Intervention/comparator	Outcomes and methods of analysis	Results	Notes
Study Quality: ++ **Applicability:** Partially applicable					of screening (such as the possibility that effects diffus from a screened member of household to others) is incomplete. **Source of funding:** Not reported

Lowensteyn *et al.* (2000)[11] *Prevention of CVD*

Study details	Population and setting	Intervention/comparator	Outcomes and methods of analysis	Results	Notes
Authors: Lowensteyn *et al* **Year:** 2000 **Aim of study:** To measure benefits and cost effectiveness of long-term aerobic exercise training among patients with and without symptomatic cardiovascular disease (CVD) **Type of Economic Analysis:** Cost effectiveness	**Source population/s:** Canada (developed, publicly-funded health care system) Men and women 35-74 years old with and without symptomatic CVD **Setting:** Community and primary care in Canada **Data Sources:** Risk factor data were obtained from the Canadian Heart Health Survey. Effectiveness data (decrease in cholesterol levels and blood pressure) were obtained from randomised controlled trials published between 1980 and 1999 and a review of published studies (Arroll and Beaglehole, 1992)	**Intervention/s description:** The intervention involved supervised and unsupervised exercise training, defined as aerobic exercise performed at least 3 times per week for 30 minutes per session within 65% to 85% of an individual's maximum heart rate. **Comparator/Control/s description:** The comparator involved no exercise training **Sample sizes:** **Total n=** Not reported **Intervention n=** Not reported **Control n=** Not reported	**Primary Outcomes** Life years saved **Secondary outcomes** NA **Time Horizon:** Maximum time horizon of 67 years **Discount Rates:** ▪ Benefits: 3% ▪ Costs: 3% **Modelling Method:** The Cardiovascular Disease Life Expectancy Model was used to estimate costs and life expectancy of a cohort of 1000 patients	**Primary analysis:** **Benefits** The authors reported that adherence to the exercise training resulted in 0.7 life-years saved 35-54 years old men without CVD; less life years gained for older men and all women without CVD . The estimated number of life-years gained was greater for those with CVD compared with their age and sex-matched counterparts without CVD. **Costs** An unsupervised exercise programme with 100% adherence would cost approximately $180 less that no exercise when the costs of exercise, fatal and non-fatal CVD events, medical procedures medicall follow up are considered). This estimate	**Limitations identified by author:** ▪ The authors did not incorporate in the analysi potential benefits of exerc on aspects other than lipi and blood pressure lowering. Also, the autho did not take into account benefits of exercise on quality of life. ▪ Neither indirect costs of exercise training nor potential cost savings associated with non-CVD events as a result of exerc training were considered ▪ No adjustments for differences in US versus Canadian healthcare cost were made **Limitations identified by review team**: No separate cost estimates were given for the supervis exercise.

[11] Lowensteyn *et al.* The cost-effectiveness of exercise training for the primary and secondary prevention of cardiovascular disease. *Journal of Cardiac Rehabilitation* 2000 20(3): 147-155

Study details	Population and setting	Intervention/comparator	Outcomes and methods of analysis	Results	Notes
analysis **Economic Perspective:** Not reported **Study Quality:** + **Applicability:** Not applicable				vary according to age-group, gender, disease status and type of exercise programme. **ICERs** Assuming 100% adherence, an unsupervised exercise programme would result in a cost per life-year gained ratio between: ▪ $645 (men, 35-54 years old) and $4,915 (women, 35-54 years old) for patients without CVD ▪ $356 (men, 35-54 years old) and $3,154 (women, 34-54 years old) for patiens with CVD Assuming 100% adherence, a supervised exercise programme would result in a cost per life-year gained ratio between: ▪ $15,015 (men, 55-64 y.o.) and $60,283 (women, 65-74 y.o.) for patients without CVD	**Evidence gaps and/or recommendations for futur research:** Future research that incorporate the broader clinical benefits of exercise i terms of reduced CVD relat mortality/morbidity would beneficial **Source of funding:** Not reported

Study details	Population and setting	Intervention/comparator	Outcomes and methods of analysis	Results	Notes
				▪ $5,871 (men, 55-64 y.o.) and $34,667(women, 35-54 y.o.) for patients with CVD Adherence rates of 50% for the first year and 30% for each year thereafter result in similar ratios, with ▪ Unsupervised exercise showing ratios lower than $11,200/ life year gained for all patients with or without CVD ▪ Supervised exercise showing ratios between $8,562 (men, 55-64 y.o. with CVD) and $87,166 (women, 65-74 without CVD) **Secondary analysis:** NA	

Murray *et al* (2003)[12]

Study details	Population and setting	Intervention/comparator	Outcomes and methods of analysis	Results	Notes
Authors: Murray et al **Year:** 2003 **Aim of study:** To provide estimates of the population health effects and costs of selected interventions to reduce the risks associated with high cholesterol concentrations and bllod pressure **Type of Economic Analysis:** Cost-	**Source population/s:** Whole population of various regions. Results here shown for region including UK **Setting:** Population level. **Data Sources:** systematic reviews of RCTs where possible, meta-analyses	**Intervention/s description:** Relevant interventions are N3: health education through broadcast and print media focusing on body mass index and cholesterol concentrations N4: N3 combined with legislation to decrease salt content in processed foods and appropriate labelling **Comparator/Control/s description:** No intervention **Sample sizes:** Not applicable	**Primary Outcomes** Annual costs (in international dollars with price year 2000), DALYs averted. **Secondary outcomes** None **Time Horizon:** Lifetime **Discount Rates:** ▪ Benefits 3% ▪ Costs 3% **Modelling Method:** Standard multi-state modelling tool (PopMod) – a cohort simulation model	**Primary analysis:** ▪ Benefits N3: 1.2 million DALY N4: 2.4 million DALY ▪ Costs N3: $202 million N4: $499 million ▪ ICERs Do nothing to N3: $160/DALY N3 to N4: $250/DALY (N.B. correction to printed ICERs published in 2005) **Secondary analysis:** None	**Limitations identified by author:** Aggregation at multinationa level Cost savings related to the prevention of CVD events n included **Limitations identified by review team**: **Evidence gaps and/or recommendations for futur research:** **Source of funding:** Not reported

[12] Murray *et al.* Effectiveness and costs of interventions to lower systolic blood pressure and cholesterol: a global and regional analysis on reduction of cardiovascular-disease risk. *Lancet*2003; 361:717-725

Study details	Population and setting	Intervention/comparator	Outcomes and methods of analysis	Results	Notes
effectiveness analysis **Economic Perspective:** Societal **Study Quality: +** **Applicability:** Partly applicable					

Norinder et al (2002)[13]

Study details	Population and setting	Intervention/comparator	Outcomes and methods of analysis	Results	Notes
Authors: Norinder et al **Year:** 2002 **Aim of study:** To estimate retrospectively the costs of health care resources used in the Malmö Preventive Project (Sweden) and estimate the costs of in-patient care avoided because of early intervention **Type of Economic Analysis:** Cost-analysis	**Source population/s:** Sweden (developed, public health care system) **Setting:** Community **Data Sources: primary study** (Malmö Preventive project)	**Intervention/s description:** The intervention involved identifying people in high-risk of developing cardiovascular disease and providing them with drug therapy and lifestyle modification approaches **Comparator/Control/s description:** The comparator involved no intervention **Sample sizes:** **Total n=** NR **Intervention n=** 33,346 males and females **Control n=** NR	**Primary Outcomes** Total net health care cost of the programme (excludes opportunity cost) Cost of recruitment (includes cost of buildings, materials and health care staff for delivering the intervention) Cost of in-patient care (difference in in-patient use of services between patients who received the intervention and those who did not) **Secondary outcomes** NA **Time Horizon:** 24 years **Discount Rates:**	**Primary analysis:** ▪ Benefits NR ▪ Costs: Total net health cost: £9.13m (SEK 110.5m) Opportunity cost for resources capitalised: £7.61m (SEK 92.2m) Recruitment cost: £14.05m (SEK 170m) In-patient care costs: -£11.78m (SEK -146.6m) (cost savings) ▪ ICERs NR **Secondary analysis:** NA	**Limitations identified by author:** Cost calculations are based estimates, as the exact cost could not be determined. **Limitations identified by review team**: ▪ The cost difference betwe patients who received the intervention and those wh were in the control group was assessed only in term of in-patient resource use. There might be difference in costs between groups d to consumption of other health care resources. ▪ No summary measure of cost per patient receiving the intervention **Evidence gaps and/or recommendations for futur research:** None

[13] Norinder *et al.* Costs for screening, intervention and hospital treatment generated by the Malmö Preventive Project: a large scale community screening programme. *Journal of Internal Medicine* 2002; 251: 44-52

Study details	Population and setting	Intervention/comparator	Outcomes and methods of analysis	Results	Notes
Economic Perspective: **Study Quality:** **Applicability:** Not applicable			▪ Benefits: NA ▪ Costs: 3% **Modelling Method:** No modelling techniques were utilised		**Source of funding:** Swedish Medical Associatio Malmö City Council)

Rasmussen *et al.* (2007)[14]

Study details	Population and setting	Intervention/comparator	Outcomes and methods of analysis	Results	Notes
Authors: Rasmussen *et al.* **Year:** 2007 **Aim of study:** To investigate whether preventive health checks and health discussions are cost effective **Type of Economic Analysis:** Cost consequence analysis **Economic Perspective:** Direct and total	**Source population/s:** Patients at GPs in Ebeltoft, Aarhus county, Denmark **Setting:** Primary care **Data Sources:** Primary research, published sources	**Intervention/s description:** Initially, all GPs took part in meetings to increase their knowledge and to learn how to give appropriate dietary advice and engage in patient discussions. Intervention consisted of health screenings with (B) or without (A) additional GP health counselling. Baseline health screenings included assessment of total cholesterol, blood pressure, BMI and tobacco use. A cardiovascular disease risk score was calculated based on these measures and on gender and family history of CVD. A few weeks later, participants received written feedback from their GPs with results and, where appropriate, lifestyle change recommendations. All participants with high cardiovascular risk scores	**Primary Outcomes** Life years gained **Secondary outcomes** NR **Time Horizon:** Lifetime **Discount Rates:** ▪ Benefits 3% ▪ Costs 3% **Modelling Method:** Life expectancy calculated based on Framingham risk equations applied to individual results together with	**Primary analysis:** ▪ Benefits Men: LYG in Control group 0.09, Intervention A 0.27, Intervention B 0.31 Women: LYG in Control group 0.22, Intervention A 0.21, Intervention B 0.30 ▪ Costs Men: Control group €4,953, Intervention A €6,893 Intervention B €5,818 Women: Control group €16,006, Intervention A €11,770 Intervention B €14,822 ▪ ICERs Not reported	**Limitations identified by author:** Absolute estimated LYG ma be overestimated since the model assumes that the intervention effect lasts lifelong, which may not be t case. **Limitations identified by review team**: Analysis of uncertainty limited to identifying significant differences at p<0.05, p<0.01 and p<0.001 levels. No exact P values or confidence intervals **Evidence gaps and/or recommendations for futur research:** None reported **Source of funding:** Danish Centre for Evaluatio

[14] Rasmussen *et al.* Preventive health screenings and health consultations in primary care increase life expectancy without increasing costs. *Scandinavian Journal of Public Health* 2007; 35:365-372

Study details	Population and setting	Intervention/comparator	Outcomes and methods of analysis	Results	Notes
productivity costs **Study Quality: +** **Applicability:** Partly applicable		encouraged to visit their GPs, all received a pamphlet on how to lead a healthy lifestyle. A 45 minute GP consultation was offered to those randomised to receive additional health counselling (half the intervention group). After the consultation, health-related lifestyle goals set through GP/patient discussion (maximum of 3) for the following year. A year later participants received another questionnaire and invited to health screening. Those in the additional health counselling group were offered GP consultations every year until the final evaluation (5 years from baseline) **Comparator/Control/s description:** No intervention **Sample sizes:** **Total n=** 1507 **Intervention A n=** 502 **Intervention B n=** 504 **Control n** = 501		**Secondary analysis:** Not reported	and Health Technology Assessment

Tosteson *et al.* (1997)[15]

Study details	Population and setting	Intervention/comparator	Outcomes and methods of analysis	Results	Notes
Authors: Tosteson *et al.* **Year:** 1997 **Aim of study:** To measure the costs and cost effectiveness of populationwide educational approaches to reduce cholesterol levels in the US adult population **Type of Economic Analysis:** Cost effectiveness analysis; Cost Utility analysis **Economic Perspective:**	**Source population/s:** USA (developed, privatehealth care system) General population between 35 and 84 years old **Setting:** Population **Data Sources:** Primary research (multicentre randomised controlled trial)	**Intervention/s description:** The interventions under consideration were the Stanford Three-Community Study, Stanford Five-City Project and the North Karelia project. **Comparator/Control/s description:** The comparator is no educational programme **Sample sizes:** **Total n=** NR **Intervention n=** NR **Control n=** NR (model based analysis)	**Primary Outcomes** Cost-effectiveness ratio, (change in projected costs divided by the change in projected life-years for patients which received the intervention compared to those without intervention) **Secondary outcomes** NA **Time Horizon:** 25 years (1995-2020) **Discount Rates:** ▪ Benefits: 5% ▪ Costs: 5% **Modelling Method:** The Coronary Heart Disease Policy Model was used to analyse each intervention's costs and effectiveness. This consists of the following submodels:	**Primary analysis:** **Benefits** Data on each intervention's effectiveness were obtained from primary effectiveness studies: ▪ Stanford Three-Community Study: 3% serum cholesterol reduction ▪ Stanford Five-City Project: 2% serum cholesterol reduction; 4% diastolic blood pressure reduction and 13% smoking rate reduction ▪ The North Karelia Study Serum cholesterol reduction of 3% and 1% in men and women respectively; diastolic blood pressure reduction of 1% and 2% in men and women respectively, and smoking rate reduction of 28% and	**Limitations identified by author:** ▪ The baseline analysis did not include adverse even because such events had not been found in two recent large RCTs. ▪ Costs associated with following a diet or costs d to potential increase in no CHD medical costs incur by individuals as a result prolonged life owing to lower cholesterol levels were not included. ▪ Similarly, potential benef of cholesterol reduction f other diseases (e.g. peripheral vascular disea were not included **Limitations identified by review team**: None **Evidence gaps and/or recommendations for futu**

[15] Tosteson *et al.* Cost-effectiveness of populationwide educational approaches to reduce serum cholesterol levels. *Circulation.* 1997; 95: 24-30

Study details	Population and setting	Intervention/comparator	Outcomes and methods of analysis	Results	Notes
Unclear (US federal government) **Study Quality:** + **Applicability:** Partially applicable			▪ Demographic-Epidemiologic Submodel (assessed each individual's risk of developing CHD and death on the basis of risk factors) ▪ Bridge Submodel (assessed the coronary events during the first 30 days after the patient develops CHD) ▪ Disease History Submodel (used to track subsequent development of recurrent CHD events, case-fatality rates and resource costs).	14% in men and women respectively. **Costs** Cost estimates were available for the Stanford Five-City Project and North Karelia study ▪ Stanford Five-City Project: $4.95 per person per year ▪ North Karelia Project: $8.66 per person per year **ICERs** A programme with the costs and benefits of the Stanford Five-City project ($4.95 per person per year; 2% reduction in serum cholesterol) results in $3200 per year of life saved. A programme with the costs and benefits of the North Karelia project ($16.55 in year 1 and $8.28 each year thereafter; 3% reduction in serum cholesterol) would result in $6100 per year of life	**research:** None **Source of funding:** Agency for Health Care Pol and Research and National Heart, Lung and Blood Institute, US.

Study details	Population and setting	Intervention/comparator	Outcomes and methods of analysis	Results	Notes
				saved. Under the assumptions that cost is $16.55 and reduction in cholesterol is at least 2%, the intervention would cost at most $38500 per year of life saved. Varying the model inputs over a wide range gave cost-effectiveness results ranging from cases where the programme is cost-saving but still gains years of life to a cost of over $400,000 per life year gained in the worst case considered.	

Wonderling *et al.*(1996)[16] *Prevention of CVD*

Study details	Population and setting	Intervention/comparator	Outcomes and methods of analysis	Results	Notes
Authors: Wonderling *et al.* **Year:** 1996 **Aim of study:** To measure costs and cost effectiveness of the British family heart study cardiovascular screening and intervention programme **Type of Economic Analysis:** Cost effectiveness analysis **Economic**	**Source population/s:** UK (developed, public health care system) Men aged 40-59 and their partners **Setting:** 13 general practices across Britain **Data Sources:** Primary research (multicentre randomised controlled trial)	**Intervention/s description:** The intervention involved selecting a matched pair of practices from each of 13 towns across Britain. Of each matched pair, one practice was randomly allocated to the intervention while the other served as "external comparison" arm. Within the practices allocated to intervention, men were randomised to either intervention or "internal comparison" arm. Men allocated to receive the intervention together with their partners were offered screening and lifestyle advice, and were followed-up according to the results of their screening test. **Comparator/Control/s description:** The comparator involved no screening and no intervention.	**Primary Outcomes** ▪ Mean cost ▪ Mean cost per 1% reduction in coronary risk **Secondary outcomes** NA **Time Horizon:** Unclear **Discount Rates:** ▪ Benefits: NA ▪ Costs: 6% **Modelling Method:** No modelling techniques were utilised	**Primary analysis:** **Benefits** Overall reduction: ▪ Dundee risk score: 16.5% ▪ Coronary risk: 12% Reduction in men's score: ▪ Dundee risk score: 17.6% ▪ Coronary risk: 13% Reduction in women's score: ▪ Dundee risk score: 13.2% ▪ Coronary risk: 10% **Costs** ▪ Estimated 1 year running costs per person: £63. ▪ Overall short term cost to the health service per man: £77 ▪ Overall short term cost ot the health service per woman: £13 ▪ Programme cost was approximately 58,000 per	**Limitations identified by author:** ▪ The analysis is focused on on the short term costs an benefits of the British fam heart study intervention. ▪ The size of the study limi the reliability of the overa cost effectiveness results the intervention **Limitations identified by review team**: As stated by the authors **Evidence gaps and/or recommendations for futu research:** ▪ Much larger studies are needed to determine the cost effectiveness of such interventions ▪ Reduction in coronary ris needs to be translated int common unit of effectiveness

[16] Wonderling *et al.* Costs and cost effectiveness of cardiovascular screening and intervention: the British family heart study. *BMJ* 1996; 312:1269-73

Study details	Population and setting	Intervention/comparator	Outcomes and methods of analysis	Results	Notes
Perspective: Health Service (NHS) **Study Quality:** ++ **Applicability:** Partially applicable		**Sample sizes:** **Total n=** 4185 men and their 2827 partners **Intervention n=** 2011 men and their 1425 partners **Control n=** 2174 men and their 1402 partners		year for a 4-partner 7500 patient practice. ▪ Mean incremental cost (intervention-control): £51.63 (95% CI: £12 -£91) **ICERs** Cost per 1% risk reduction for men if ▪ Only direct programme cost are included: £5.08 ▪ Direct programme and broader NHS costs are included: £5.92 Cost per 1% risk reduction for women if: ▪ Only direct programme cost are included: £5.78 ▪ Direct programme and broader NHS costs are included: £1.28 Cost per 1% risk reduction per person if: ▪ Only direct programme cost are included: £5.26 ▪ Direct programme and broader NHS costs are included: £4.30	**Source of funding:** Heart Family Association, central and local health authorities and educational grant from private company

Study details	Population and setting	Intervention/comparator	Outcomes and methods of analysis	Results	Notes
				Secondary analysis: NA	

Wonderling *et al.*(1996)[17] *Prevention of CVD*

Study details	Population and setting	Intervention/comparator	Outcomes and methods of analysis	Results	Notes
Authors: Wonderling *et al.* **Year:** 1996 **Aim of study:** To compare the effectiveness and cost effectiveness of the Oxcheck and British family heart studies (BFHS) **Type of Economic Analysis:** Cost-effectiveness	**Source population/s:** UK (developed, public health care system) **Setting:** Community **Data Sources:** Primary research (Oxcheck study, BFHS)	**Intervention/s description:** ▪ BFHS: allocated to receive the intervention together with their partners were offered screening and lifestyle advice, and were followed-up according to the results of their screening test. ▪ Oxcheck study: Health checks, carried out by nurses to determine level of risk factor. Patients with high risk factor levels were invited for follow up with 10-20 minutes. **Comparator/Control/s description:** No intervention **Sample sizes:** **Total n=** **Intervention n=** **Control n=**	**Primary Outcomes** **Secondary outcomes** **Time Horizon:** **Discount Rates:** ▪ Benefits: 6% ▪ Costs: 6% **Modelling Method:** No modelling techniques were utilised	**Primary analysis:** **Benefits** BFHS ▪ Reduction in coronary risk: 13% (men) and 10% women ▪ Mean life years gained per man: 0.0062 (assuming a one year effect); 0.2035 (assuming a 20 year effect). Mean life years gained per woman: 0.0011 (assuming a one year effect); 0.0626 (assuming a 20 year effect). Oxcheck ▪ Reduction in coronary risk: 7% (men) and 17% (women) ▪ Mean life years gained per man: 0.0034 (assuming a one year effect); 0.1093 (assuming a 20 year effect). Mean life years gained per woman: 0.0018 (assuming a one year effect); 0.1065 (assuming a 20 year effect).	**Limitations identified by author:** ▪ The authors acknowledge comparability problems a imprecision of estimates, a there are differences in th design and methods of analysis for the 2 studies. ▪ The results are critically dependent on the assume length of effect **Limitations identified by review team**: None **Evidence gaps and/or recommendations for futur research:** Research to provide information on the duration health effects in similar community-based interventions **Source of funding:** NR

[17] Wonderling *et al.* What can be concluded form the Oxcheck and British family heart studies: commentary on cost effectiveness analyses. *BMJ* 1996, 312:1274-1278

Study details	Population and setting	Intervention/comparator	Outcomes and methods of analysis	Results	Notes
analyses **Economic Perspective:** Health care system **Study Quality: ++** **Applicability:** Partially applicable				**Costs** **BFHS:** £66 for men, £58 for women **Oxcheck:** £29 (for men and women) **ICERs** BFHS: For men: £1100 per life year gained (20 years effect) to £24,400 (1 year effect) For women: £3300 per life year gained (20 years effect) to £144,500 (1 year effect) Oxcheck: For men: £900 per life year gained (20 years effect) to £20,900 (1 year effect) For women: £1000 per life year gained (20 years effect) to £41,800 (1 year effect) BFHS against Oxcheck £1300 (20 year effect) to £45,900 (1 year effect) **Secondary analysis:** NR	

4 Discussion

As noted at the beginning of this report, the National Institute for Health and Clinical Excellence has been asked by the Department of Health to develop guidance on a public health programme aimed at preventing cardiovascular disease in different populations.

If such a programme is to be supported and funded through a budget limited health service, then it must be cost-effective compared to other possible programmes, bearing in mind the competing demands on health service funding. The main question addressed by this review is the cost-effectiveness of programmes aimed at prevention of CVD through modification of multiple risk factors.

The articles reviewed have been divided into two groups. The first group consists of effectiveness study based articles, where a specific programme has been tested in a community and the effectiveness results have been directly measured. The second group consists of articles which have used a modelling approach, combining evidence from a range of sources to estimate the costs and effects of one or more possible programmes without actually testing them in practice.

Considering first the effectiveness study based articles, the majority of these considered some form of screening to determine the participants' risk level, with action by health

professionals to reduce the risks depending on the measured risk level. Only one study evaluated a programme that involves provision of CVD-related education only.

Such interventions seem to provide an effective way of reducing CVD-related risk and, as a result, reducing CVD-related morbidity and mortality. Most of the assessed interventions were associated with reductions in risk levels, which could be converted into positive health outcomes.

On the other hand, it is more difficult to draw general conclusions on the cost of such interventions. Studies varied in terms of which cost components were measured and included in the analysis. As a result, none of the studies gives a result that is directly applicable to the main question addressed in this review.

Similarly, none of the modelling studies is directly applicable, because of differences in costing perspective and discount rates. However, they cover a range of issues which will be important in modelling in a UK context.

The results for mass media intervention suggest that this is a potentially cost-effective approach, and may even be cost saving when account is taken of the cost of treatment no longer needed.

The results on screening programmes vary considerably. This reflects a wide range of different programmes. The results of the one UK based study (Field *et al*, 1995) reported favourable cost-effectiveness ratios for screening programmes of six different intensities, not only for each screening programme individually, but also when each is compared to the previous programme. The difference in ICERs between 0 and 6% discount rates was not substantial, and suggests that similar results would be obtained using a discount rate

of 3.5%. However, there are concerns about the treatment strategies used in all of the studies, and some explicit modelling of treatments likely to be used in the UK today is desirable.

An important note of caution is raised by Kristiansen and colleagues (1991). When they compared a strategy of screening with dietary treatment against a population based approach, they reported an ICER of around £12,000 per life year gained, but just over £100,000 per QALY. Although their results are not directly applicable because of the age of the study and the likelihood of differences in population characteristics between Norway and the UK, the difference is startling and reflects an issue that is applicable in a UK context. Their model includes a 0.2% reduction in quality of life for those identified as being at risk. Given that a substantial proportion of the population would be identified as high risk individuals, this is a potentially important consideration to include in any analysis that takes quality of life into account.

While many of the studies identified in this review suggest that some of the interventions considered are highly cost-effective, there are grounds for caution in the interpretation of these results. Many of the studies were conducted some time ago, and it is possible that population characteristics may have changed. In particular, if background population habits with relation to cardiovascular risk factors have changed substantially over time then the effects of either an information campaign or screening programme will change accordingly.

Further, the methods used in producing the articles are not necessarily up to the standards that are now expected for cost-effectiveness analysis. This applies in particular in relation to the issue of handling uncertainty, where methods such as probabilistic sensitivity analysis have now become generally accepted as routine requirements. It is

likely that the articles reviewed have considerably underestimated the uncertainty in the results reported.

4.1 Limitations of the Review

This review is limited by the concentration on existing analyses of cost-effectiveness. Whereas all published evidence as to the effectiveness of an intervention can be expected to be found through an effectiveness review, evidence on cost-effectiveness cannot necessarily be found by reviewing existing cost-effectiveness studies. Rather, the evidence that a particular intervention is cost-effective in a given setting is likely to be found by applying local costings to the results of an effectiveness review.

It is, of course, necessary to apply caution in transferring effectiveness results from one setting to another, particularly when considering interventions which are aimed at altering behaviour. The effectiveness of such interventions will depend to a greater or lesser extent on existing behaviour patterns. With cost-effectiveness, transferring results from one setting to another is even more problematic. Variation in unit costs means that an intervention may be cost-saving in one setting, but not even cost-effective in a different setting. To some extent, there is also the problem that different jurisdictions apply different rules for cost-effectiveness analysis. Thus there may be variations in such factors as costing persepective and discount rates, which limit the direct applicability of a cost-effectiveness analysis.

A further limitation of the review is determined by its scope, which means that it is limited to multiple risk factor interventions. This has required some interpretation. Interventions which act through a single mechanism such as weight reduction may have been included if that mechanism is deemed to affect multiple risk factors. However, interventions which only affect a single risk factor are excluded from this review.

4.2 The Way Forward

To address the issues raised so far in this discussion, some new modelling will be required. Issues pertinent to such modelling relate to costs and effects.

On the issue of costing, there is an important difference in the way in which costs are reported in the primary studies. In screening programmes, high risk cases are identified and treated and the cost of the treatment will naturally be included in the analysis. In the case of mass media programmes, a likely consequence of the programme will be an increase in the rate at which high risk cases present to primary care. In such cases, a link to the programme may well not be made. Even if the individual presenting tells the clinician that he or she has been prompted to attend because of the campaign, it is by no means certain that such information will have been passed back to the programme researchers, and so the cost of treating such cases may well not be included in the analysis. Explicit modelling offers the opportunity to make plausible assumptions about the extent to which costs are incurred through such means.

On the effectiveness side, outcome measures such as population means can be expected to have included any effects of high risk individuals seeking treatment, thus giving an unbiased estimate of the effectiveness of any intervention tried in practice. However, such summary measures as reduction in population mean risk factors can be misleading, as has been discussed in the effectiveness reviews to which the present review is a complement. The relationship between the measured value of a risk factor and the probability of developing some form of CVD is almost invariably nonlinear (even ignoring interaction effects). In such cases, the number of cases prevented by a given reduction in the population mean risk factor will depend on the distribution of the risk reductions within the population. In particular, a constant reduction will produce a

different number of expected cases prevented from a reduction that is correlated to the initial value of the risk factor. In the case of screening programmes, where the intervention to reduce risk factors depends on the size of the measured risk factor, it is particularly important to consider the effects on each intervention group separately.

To obtain cost-effectiveness results in a form that are useful for comparison with other demands on health service funding, it is necessary to measure the effects of any programme in appropriate units such as quality adjusted life years. The modelling studies considered in this review have used three different methods to do this.

The first method is an approach that may be called "chaining". In this method, changes in risk factors are converted to changes in event rate, which in turn are converted into QALYs gained. Data requirements for such an approach are the expected changes in risk factors from the programme, and conversion rates, which can be estimated from other studies.

The second method involves considering the distribution of risk factors within the population, and then explicitly modelling the effects of the programme. This can be done either by stratifying the population into a suitable number of sufficiently homogeneous subgroups, or by sampling a sufficient number of individuals (from an actual or hypothetical population). The choice here is largely driven by the degree of population heterogeneity to be modelled. In either case, the model works by applying risk factor equations to patient characteristics to estimate the number of cases prevented. The QALY gain from each case prevented can be estimated at subgroup level: for example it can be made to depend on age group, thus accounting for variability in life expectancy in the absence of CVD.

The third approach is to simulate full patient histories including both pre-disease states and the full course of disease history. Again this can be done through either stratifying the population into subgroups or sampling individuals, depending on the degree of heterogeneity. This approach differs from the second approach in that conversion from cases prevented to QALYs gained is explicitly modelled. This is the only approach that would allow variation in treatment to be considered directly.

The principle of parsimony suggests that the simplest adequate model should be selected. For the purpose of modelling disease prevention programmes, it seems unnecessary to model explicitly the course of treatment, and therefore the second approach appears to be indicated.

Appendix 1: Protocol to Address Question 1

Primary research questions

What multiple risk-factor interventions are effective and cost-effective in the primary prevention of CVD within a given population? Where the data allows, how does the effectiveness and cost-effectiveness of interventions vary between different population groups?

Secondary research questions

Any study identified addressing the primary research questions will also be interrogated for information addressing the following potential considerations of the Programme Development Group identified in the final scope (Appendix B):

- The target audience, actions taken and by whom, context, frequency and duration.
- Whether it is based on an underlying theory or conceptual model.
- Whether it is effective and cost effective.
- Critical elements. For example, whether effectiveness and cost effectiveness varies according to:
    - the diversity of the population (for example, in terms of the user's age, gender or ethnicity)
    - the status of the person (or organization) delivering it and the way it is delivered

    - its frequency, length and duration, where it takes place and whether it is transferable to other settings
    - its intensity.
- Any trade offs between equity and efficiency.
- Any factors that prevent – or support – effective implementation.
- Any adverse or unintended effects.
- Current practice.
- Availability and accessibility for different population groups.

Some of these are implicit in the primary question e.g. bullet 3; others are more relevant to review question 2 e.g. bullet 6 any factors that prevent – or support – effective implementation, covered in a separate protocol.

General plan

The research questions will be addressed in a single evidence review. In order to provide the information to the PDG in a timely fashion in manageable quanta the evidence review will be delivered in two phases:

- Phase 1 – initial findings from the included studies in the first components of the search to be presented at September 2008 PDG meeting
- Phase 2 – completed evidence review to be presented at October 2008 PDG meeting

Although there is a single evidence review, there will be different lead reviewers for the effectiveness and cost-effectiveness components. Integration will be achieved by common senior reviewers and second reviewers working on both effectiveness and cost-effectiveness. There will also be co-ordination with the evidence review being undertaken as part of question 2, for which there is a separate protocol. The health

economic modellers will be part of the review team addressing question 1, particularly the cost-effectiveness components, which will achieve integration of this part of the programme with the subsequent health economic modelling, which is again not covered directly in this protocol. There will be regular joint meetings of all researchers working on all components of the programme.

Search Strategy and Search Protocol

Proposed resources:

Phase 1:

- Primary studies identified in existing systematic reviews relevant to the research question, the systematic reviews being identified from searches of bibliographic databases (see below)

Phase 2:

- Additional primary studies identified from searches of bibliographic databases (see below)
- Additional potentially missing studies identified by PDG
- Searches of key UK public health web-sites (see appendix 1.1)
- Checking of bibliographies of included studies

Bibliographic databases:
Given the volume of material in the topic area and the time constraints we feel that concentrating principally on a limited number of electronic databases will be the most appropriate strategy.

Studies for review 2 will therefore be derived from the following bibliographic databases:

Cochrane (CDSR, DARE, HTA, EED, CENTRAL)
MEDLINE
MEDLINE In Process
EMBASE
CINAHL

PsycINFO
HMIC
ASSIA

Searches for cost effectiveness studies will be conducted on NHS EED database (Cochrane Library), ECONLIT, MEDLINE and EMBASE.

Bibliographic database search strategies:
The general approach will be to perform a search which captures all components relevant to the general topic (subject specific search terms) which will be combined with a series of "design filters" focusing on specific sub-types of literature. A review filter will be used to identify reviews for phase 1; a sensitive RCT filter combined with a selected number of other appropriate study design terms will be used to target primary studies providing evidence on effectiveness; an economic studies filter will be used to target studies providing evidence on cost-effectiveness.

Studies will be limited to those in the English language published since 1970.

Bibliographic database search strategies (content terms):
Scoping searches have been conducted to estimate the nature and volume of the literature. Our initial scoping searches targeted systematic reviews, evidence briefings and guidelines as well as a brief search for primary studies. The key concepts of the search question are 'cardiovascular diseases' (population), 'health promotion' (intervention) and 'nature of the intervention' (focusing on the multiple-risk factor aspect of the intervention).

We submit our search strategy below which combines all three key concepts. The sensitive strategy has been preferred to ensure a comprehensive search and illustrates results for both reviews (line 45) and primary studies (line 55).

Database: Ovid MEDLINE(R) <1950 to June Week 3 2008>
Search Strategy:
---
1 cardiovascular disease$.mp. or exp Cardiovascular Diseases/ (1484533)

2 CVD.mp. (6382)
3 coronary disease$.mp. (122405)
4 heart disease$.mp. (140976)
5 atherosclerosis.mp. (56204)
6 arteriosclerosis.mp. (65345)
7 hypertension.mp. (275687)
8 blood pressure.mp. (286797)
9 exp Hyperlipidemias/ or hyperlipidaemia$.mp. (47567)
10 hyperlipidemia$.mp. (26227)
11 exp Cholesterol/ or cholesterol.mp. (166774)
12 exp Stroke/ or stroke$.mp. (125458)
13 peripheral vascular disease$.mp. (12988)
14 peripheral arterial disease$.mp. (3132)
15 hypercholesterol$.mp. (29117)
16 hyperlipid$.mp. (28816)
17 or/1-16 (1837113)
18 health education.mp. or exp Health Education/ (112537)
19 health promotion.mp. or exp Health Promotion/ (38318)
20 primary prevention.mp. or exp Primary Prevention/ (96681)
21 campaign$.mp. (15632)
22 media.mp. or exp Mass Media/ (279445)
23 exp Counseling/ or advice$.mp. (43805)
24 counsel$.mp. (60062)
25 program$.mp. (426510)
26 (policy or policies).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (134656)
27 or/18-26 (1057511)
28 exp Smoking/ or smoking.mp. (135469)
29 exp Tobacco/ or tobacco.mp. (56047)
30 exp Diet/ or diet.mp. (248737)
31 exercise.mp. or exp Exercise/ (159441)
32 obesity.mp. or exp Obesity/ (109574)
33 diabetes.mp. or exp Diabetes Mellitus/ (287258)
34 stress.mp. or exp Stress/ (341439)
35 exp Cholesterol/ or cholesterol.mp. (166774)
36 exp Hypertension/ or hypertension.mp. (275687)
37 blood pressure.mp. or exp Blood Pressure/ (294128)
38 alcohol$.mp. (220914)
39 drinking.mp. or exp Alcohol Drinking/ (86568)
40 (cardiovascular adj3 risk$).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (34276)
41 multiple risk$.mp. (2128)
42 or/28-41 (1836612)
43 17 and 27 and 42 (43707)

44 limit 43 to (english language and humans and yr="1970 - 2008") (33237)
45 limit 44 to "reviews (specificity)" (577)
46 limit 44 to "therapy (sensitivity)" (13483)
47 epidemiologic studies/ (4126)
48 longitudinal studies/ (52280)
49 (control$ before and after).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (1064)
50 cohort.mp. (150206)
51 case control.mp. (113097)
52 interrupted time series.mp. (362)
53 or/47-52 (299591)
54 44 and 53 (3403)
55 46 or 54 (15574)

Bibliographic database search strategies (study design filters):

Searches for systematic reviews will be based on Evidence Based resources and specific sources of Health Technology Assessments as recommended in the ARIF search protocol (see appendix 1.2), including bibliographic databases.

All study designs will be included, however, searches for primary studies will focus in the first instance on RCTs by using specialist search filters. A broad filter (the Haynes "Therapy – sensitive" in-built filter on Ovid) should capture a wider range of study designs beyond RCTs with the addition of selected terms to capture other appropriate study designs.

A study design filter based on the CRD model will be used when searching for studies relevant to cost-effectiveness (illustrated below)

Database: Ovid MEDLINE(R) <1950 to June Week 3 2008>
Search Strategy:
---
1 cardiovascular disease$.mp. or exp Cardiovascular Diseases/ (1484533)
2 CVD.mp. (6382)
3 coronary disease$.mp. (122405)
4 heart disease$.mp. (140976)
5 atherosclerosis.mp. (56204)

6 arteriosclerosis.mp. (65345)
7 hypertension.mp. (275687)
8 blood pressure.mp. (286797)
9 exp Hyperlipidemias/ or hyperlipidaemia$.mp. (47567)
10 hyperlipidemia$.mp. (26227)
11 exp Cholesterol/ or cholesterol.mp. (166774)
12 exp Stroke/ or stroke$.mp. (125458)
13 peripheral vascular disease$.mp. (12988)
14 peripheral arterial disease$.mp. (3132)
15 hypercholesterol$.mp. (29117)
16 hyperlipid$.mp. (28816)
17 or/1-16 (1837113)
18 health education.mp. or exp Health Education/ (112537)
19 health promotion.mp. or exp Health Promotion/ (38318)
20 primary prevention.mp. or exp Primary Prevention/ (96681)
21 campaign$.mp. (15632)
22 media.mp. or exp Mass Media/ (279445)
23 exp Counseling/ or advice$.mp. (43805)
24 counsel$.mp. (60062)
25 program$.mp. (426510)
26 (policy or policies).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (134656)
27 or/18-26 (1057511)
28 exp Smoking/ or smoking.mp. (135469)
29 exp Tobacco/ or tobacco.mp. (56047)
30 exp Diet/ or diet.mp. (248737)
31 exercise.mp. or exp Exercise/ (159441)
32 obesity.mp. or exp Obesity/ (109574)
33 diabetes.mp. or exp Diabetes Mellitus/ (287258)
34 stress.mp. or exp Stress/ (341439)
35 exp Cholesterol/ or cholesterol.mp. (166774)
36 exp Hypertension/ or hypertension.mp. (275687)
37 blood pressure.mp. or exp Blood Pressure/ (294128)
38 alcohol$.mp. (220914)
39 drinking.mp. or exp Alcohol Drinking/ (86568)
40 (cardiovascular adj3 risk$).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (34276)
41 multiple risk$.mp. (2128)
42 or/28-41 (1836612)
43 17 and 27 and 42 (43707)
44 limit 43 to (english language and humans and yr="1970 - 2008") (33237)
45 economics/ (25685)
46 exp "costs and cost analysis"/ (138513)
47 cost of illness/ (10679)

48 exp health care costs/ (31269)
49 economic value of life/ (5041)
50 exp economics medical/ (11755)
51 exp economics hospital/ (15540)
52 economics pharmaceutical/ (1933)
53 exp "fees and charges"/ (23893)
54 (econom$ or cost or costs or costly or costing or price or pricing or pharmacoeconomic$).tw. (271202)
55 (expenditure$ not energy).tw. (11542)
56 (value adj1 money).tw. (11)
57 budget$.tw. (11609)
58 quality of life/ (69271)
59 life style/ (29162)
60 health status/ (38738)
61 health status indicators/ (12882)
62 quality-adjusted life years/ (3488)
63 "Value of Life"/ (5041)
64 SF$.mp. (37692)
65 EQ-5D.mp. (776)
66 TTO.mp. (291)
67 Time trade off.mp. (406)
68 HUI$.mp. (3820)
69 health utilit$.tw. (501)
70 cost utilit$.tw. (1207)
71 or/45-70 (545016)
72 44 and 71 (5779)

Documentation:
The search process will be clearly documented (databases searched, date searched, time span searched, results of individual searches) to ensure it is transparent and repeatable.

Search results will be saved as textfiles and also stored in a Reference Manager database which will be managed by the reviewers.

Inclusion / Exclusion criteria
Inclusion criteria will be developed mirroring the research question elements detailed in the final scope. In general inclusion/exclusion decisions will be made in two stages; step 1 decisions on studies sufficiently likely to included on the basis of title +/- abstract for the full copy of the paper to be ordered; step 2 final decisions based on the full text of the potentially included study. Only a sub-set of the complete inclusion criteria will be used

to make the step 1 decisions. Inclusion decisions at each step will be operationalised as checklists which will be piloted and discussed with CPHE prior to final use. Slightly different criteria may be required for the inclusion/exclusion of systematic reviews from which primary studies will be identified in phase 1 from the criteria which will be used to identify primary studies in phase 2. In both cases the final criteria will be agreed with CPHE.

Population:

Populations including children and adults from developed / OECD countries or a WHO region. Populations may be defined geographically (local, regional or national) with a minimum size no less than that covered by a Primary Care Trust in the UK, or according to other characteristics such as workplace, age, sex, social class, ethnicity. Studies confined to populations clinically diagnosed as being at high risk of CVD or diagnosed with CVD will not be included.

Intervention:

Multiple risk factor intervention programmes that include primary prevention strategies to tackle at least two of the following CVD risk factors: Smoking, poor diet, insufficient physical activity, high blood pressure, high blood cholesterol, obesity/overweight, diabetes, psychosocial stress (linked to an individual's ability to influence the potentially stressful environments in which they live) and high alcohol consumption. Intervention programmes should specifically aim to address CVD with the goal of reducing morbidity/mortality from CVD or reducing CVD risk factors. Interventions may include one or more of: educational/behavioural approaches; fiscal changes; environmental changes, legislative changes. Interventions that include a pharmacological component and/ or a secondary prevention component will only be included where data can be disaggregated to allow consideration of the impact of primary prevention and non-pharmacological elements. Interventions including screening for CVD risk factors will only be included if accompanied by interventions to modify these risk factors.

Outcomes:

- Primary outcomes:

CVD mortality

CVD morbidity

Biochemical precursors of CVD including lipid levels, HDL/LDL ratio, triglyceride levels.

Physiological precursors of CVD including blood pressure, metabolic syndrome.

Behaviours associated with the risk of CVD including use of tobacco, diet, physical activity, alcohol consumption.

- Secondary outcomes:

Knowledge, attitudes and intentions with regard to behaviours related to CVD.

Adverse events

Study designs:

Effectiveness: RCT; Controlled before and after; Cohort; Case control; Before and after; Interrupted time series;

Cost effectiveness: Cost benefit analysis; Cost effectiveness analyses; Cost utility analyses

Systematic reviews will be considered as a source of primary studies only.

The following will be excluded: books; book chapters; thesis; dissertations; studies which describe the relationship between health and ill/health and CVD risk factors (i.e. correlates studies or non-evaluative studies). Any studies undertaken in non-developed or non-OECD countries will also be excluded.

Inclusion decisions will be made by one reviewer from the review team, with reference to a co-reviewer in the case of uncertainty in step 2 decisions in particular. Uncertainty about a decision concerning inclusion of a study relevant to cost-effectiveness will always be referred to one of the review team members with experience in reviewing and appraising economic evaluations. A final list of

included studies after phase 2 will be sent to the PDG to offer an opportunity for them to suggest possible omissions to the included studies before completion of the evidence review for question 1. Lists of studies excluded at the retrieval of hard copy stage will also be compiled with reasons for exclusion and made available to the PDG.

As part of the inclusion/exclusion process we will also tag studies of potential relevance to other parts of the programme particularly:

- Studies relevant to the evidence review for question 2 on enhancers or barriers to CVD risk reduction population programmes. There will be liaison with researchers working on question 2 advising on the precise nature of the studies of potential relevance.
- Studies which contain costs and consequences data but are neither comparative economic evaluations as defined above in the included economic primary studies or effectiveness studies as defined in above included effectiveness primary studies which may be potentially relevant for supporting modelling work

Data extraction and quality assessment

Data extraction of included studies will be performed directly into evidence tables, based on the proforma outlined in appendix D of the Methods for development of NICE public health guidance 2006. The final format will be agreed with CPHE prior to implementation. Key data, particularly study results will be checked for accuracy by a second reviewer any differences being resolved by consensus and any irresolvable items being arbitrated by a third reviewer.

Quality assessment of included studies will be undertaken based on relevant checklists provided in appendix A of the Methods for development of NICE public health guidance 2006 and where an appropriate checklist is not provided in the NICE guidance form other sources such as the Cochrane collaboration and NHS CRD. Checklists will be

modified for the topic area where necessary and approved by CPHE team prior to use. Study quality information will be abstracted by two reviewers independently, differences being resolved by consensus and any irresolvable items being arbitrated by a third reviewer.

External validity (i.e. applicability) of each included intervention will be assessed according to the 'Methods for development of NICE public health guidance'.

During data abstraction particular attention will be paid to aspects raised by the secondary research questions:

- Nature of the target audience, particularly diversity in terms of age, gender and ethnicity
- Whether intervention is based on an underlying theory or conceptual model.
- Precise nature of the intervention including :
  - status of the person (or organization) delivering it and the way it is delivered
  - its frequency, length and duration, where it takes place and whether it is transferable to other settings
  - its intensity
  - factors with a bearing on the availability or accessibility for different population groups.

Concerning studies pertinent to cost-effectiveness, particular attention will be focused on results suggesting trade offs between equity and efficiency.

Data synthesis

A narrative synthesis based on tabulated study characteristics and results will be undertaken and if appropriate data synthesis will proceed to meta-analysis. Data synthesis will culminate in evidence statements constructed as outlined in the Methods for development of NICE public health guidance 2006.

Further development of protocol

The protocol may be further finessed in the light of feedback from NICE. Experience during phase 1 and feed back from the PDG may also suggest modifications to the conduct of phase 2. Any modifications will be agreed with NICE and a record of changes kept and reported in the methods of the full review presented in the October 2008 PDG meeting.

Appendix 1.1
Public Health websites

Centre for the Evaluation of Public Health Interventions London School of Hygiene & Tropical Medicine http://www.lshtm.ac.uk/cephi/

Cochrane Public Health Group http://www.ph.cochrane.org/en/index.html

The Campbell Collaboration http://www.campbellcollaboration.org/

The Evidence for Policy and Practice Information and Co-ordinating Centre (EPPI-Centre Social Science Research Unit Institute of Education, University of London http://eppi.ioe.ac.uk/cms/

The Trials Register of Promoting Health Interventions (TRoPHI) http://eppi.ioe.ac.uk/webdatabases/Intro.aspx?ID=5

List on heart disease http://eppi.ioe.ac.uk/webdatabases/SearchHistory.aspx

Public Health Specialist Library http://www.library.nhs.uk/publichealth/

Faculty of Public Health http://www.fphm.org.uk/

NICE public health guidance
http://www.nice.org.uk/guidance/index.jsp?action=byType&type=5

Health evidence.ca http://health-evidence.ca/

DoH Public Health http://www.dh.gov.uk/en/Publichealth/index.htm

UK Public Health Association http://www.ukpha.org.uk/

Association of Public Health Observatories http://www.apho.org.uk/

Appendix 1.2

SEARCH PROTOCOL FOR ARIF ENQUIRIES
(October 2007)

In the first instance the focus of ARIF's response to requests is to identify systematic reviews of research. The following will generally be searched, with the addition of any specialist sources as appropriate to the request.

1. Cochrane Library

- Cochrane Reviews
- Database of Abstracts of Reviews of Effects (DARE)
- Cochrane Central Register of Controlled Trials (CENTRAL)
- Health Technology Assessment (HTA) database

2. ARIF Database

An in-house database of reviews compiled by scanning current journals and appropriate WWW sites. Many reviews produced by the organisations listed below are included.

3. NHS CRD

- DARE
- Health Technology Assessment Database
- Completed and ongoing CRD reviews

4. Health Technology Assessments

- NICE guidance (all programmes)
- West Midlands Health Technology Assessment Collaboration
- Evidence Based Commissioning Collaboration (Trent R & D Support Unit). Links to Trent Purchasing Consortia reports and Wessex DEC reports (both no longer published)
- SBU – Swedish Council on Technology Assessment in Health Care
- NHS Coordinating Centre for Health Technology Assessments

- Canadian Agency for Drugs and Technologies in Health
- New Zealand Health Technology Assessment
- Agency for Healthcare Research and Quality (AHRQ)
- Alberta Heritage Foundation
- McGill Medicine Technology Assessment Unit of MUHC (McGill University Health Centre)
- Monash reports – Centre for Clinical Effectiveness, Monash University
- US Department of Veterans Affairs
- NHS QIS (Quality Improvement Scotland)
- SIGN (Scottish Intercollegiate Guidelines Network)

5. Clinical Evidence

6. Bandolier

7. National Horizon Scanning Centre

8. TRIP Database

9. Bibliographic Databases

- Medline – systematic reviews
- Embase – systematic reviews
- Other specialist databases

10. Contacts

- Cochrane Collaboration (via Cochrane Library)
- Regional experts, especially Pharmacy Prescribing Unit, Keele University (& MTRAC) and West Midlands Drug Information Service for any enquiry involving drug products.

Appendix 2: Search Strategies

Cost effectiveness searches

Database: MEDLINE(Ovid) 1950 to June Week 3 2008
Search Strategy:

1 cardiovascular disease$.mp. or exp Cardiovascular Diseases/
2 CVD.mp.
3 coronary disease$.mp.
4 heart disease$.mp.
5 atherosclerosis.mp.
6 arteriosclerosis.mp.
7 hypertension.mp.
8 blood pressure.mp.
9 exp Hyperlipidemias/ or hyperlipidaemia$.mp.
10 hyperlipidemia$.mp.
11 exp Cholesterol/ or cholesterol.mp.
12 exp Stroke/ or stroke$.mp.
13 peripheral vascular disease$.mp.
14 peripheral arterial disease$.mp.
15 hypercholesterol$.mp.
16 hyperlipid$.mp.
17 or/1-16
18 health education.mp. or exp Health Education/
19 health promotion.mp. or exp Health Promotion/
20 primary prevention.mp. or exp Primary Prevention/
21 campaign$.mp.
22 media.mp. or exp Mass Media/
23 exp Counseling/ or advice$.mp.
24 counsel$.mp.
25 program$.mp.
26 (policy or policies).mp.

27 or/18-26
28 exp Smoking/ or smoking.mp.
29 exp Tobacco/ or tobacco.mp.
30 exp Diet/ or diet.mp.
31 exercise.mp. or exp Exercise/
32 obesity.mp. or exp Obesity/
33 diabetes.mp. or exp Diabetes Mellitus/
34 stress.mp. or exp Stress/
35 exp Cholesterol/ or cholesterol.mp.
36 exp Hypertension/ or hypertension.mp.
37 blood pressure.mp. or exp Blood Pressure/
38 alcohol$.mp.
39 drinking.mp. or exp Alcohol Drinking/
40 (cardiovascular adj3 risk$).mp.
41 multiple risk$.mp.
42 or/28-41
43 17 and 27 and 42
44 limit 43 to (english language and humans and yr="1970 - 2008")
45 economics/
46 exp "costs and cost analysis"/
47 cost of illness/
48 exp health care costs/
49 economic value of life/
50 exp economics medical/
51 exp economics hospital/
52 economics pharmaceutical/
53 exp "fees and charges"/
54 (econom$ or cost or costs or costly or costing or price or pricing or pharmacoeconomic$).tw.
55 (expenditure$ not energy).tw.
56 (value adj1 money).tw.
57 budget$.tw.
58 quality of life/
59 life style/
60 health status/
61 health status indicators/
62 quality-adjusted life years/
63 "Value of Life"/
64 SF$.mp.
65 EQ-5D.mp.
66 TTO.mp.
67 Time trade off.mp.
68 HUI$.mp.
69 health utilit$.tw.

70 cost utilit$.tw.
71 or/45-70
72 44 and 71

Database: EMBASE (Ovid) 1980 to 2008 Week 26
Search Strategy:

1 cardiovascular disease$.mp. or exp Cardiovascular Disease/
2 cvd.mp.
3 coronary disease$.mp. or exp Coronary Artery Disease/
4 heart disease$.mp. or exp Heart Disease/
5 atherosclerosis.mp. or exp ATHEROSCLEROSIS/
6 arteriosclerosis.mp. or exp ARTERIOSCLEROSIS/
7 exp HYPERTENSION/ or hypertension.mp.
8 blood pressure.mp. or exp Blood Pressure/
9 hyperlipidaemia$.mp. or exp Hyperlipidemia/
10 hyperlipidaemia$.mp.
11 cholesterol.mp. or exp CHOLESTEROL/
12 exp STROKE/ or stroke.mp.
13 peripheral vascular disease$.mp. or exp Peripheral Vascular Disease/
14 peripheral arterial disease$.mp. or exp Artery Disease/
15 exp Hypercholesterolemia/ or hypercholesterol$.mp.
16 hyperlipid$.mp.
17 or/1-16
18 health education.mp. or exp Health Education/
19 health promotion.mp. or exp Health Promotion/
20 primary prevention.mp. or exp Primary Prevention/
21 campaign$.mp.
22 media.mp.
23 exp Mass Medium/
24 advice.mp.
25 counsel$.mp.
26 exp COUNSELING/
27 program$.mp.
28 (policy or policies).mp.
29 or/18-28
30 exp SMOKING/ or smoking.mp.
31 tobacco.mp. or exp TOBACCO/
32 exp DIET/ or diet.mp.
33 exercise.mp. or exp EXERCISE/
34 exp OBESITY/ or obesity.mp.
35 diabetes.mp. or exp Diabetes Mellitus/
36 exp STRESS/ or stress.mp.
37 cholesterol.mp. or exp CHOLESTEROL/

38 exp HYPERTENSION/ or hypertension.mp.
39 blood pressure.mp.
40 alcohol$.mp.
41 drinking.mp.
42 exp Drinking Behavior/
43 (cardiovascular adj3 risk$).mp.
44 multiple risk$.mp.
45 or/30-44
46 17 and 29 and 45
47 limit 46 to (human and english language and yr="1974 - 2008")
48 cost benefit analysis/
49 cost effectiveness analysis/
50 cost minimization analysis/
51 cost utility analysis/
52 economic evaluation/
53 (cost or costs or costed or costly or costing).tw.
54 (economic$ or pharmacoeconomic$ or price$ or pricing).tw.
55 (technology adj assessment$).tw.
56 quality adjusted life.ti,ab.
57 health status indicators/
58 health utili$.tw.
59 time trade off.tw.
60 tto.tw.
61 "Quality of Life"/
62 value of life.mp.
63 quality adjusted life year$.mp.
64 cost utilit$.tw.
65 qaly.mp. or exp Quality Adjusted Life Year/
66 or/48-65
67 47 and 66

Database: Cochrane Library (Wiley) 2008 Issue 2 *(NHS EED)*

Search strategy:

#1 cardiovascular next disease*
#2 cvd
#3 coronary next disease*
#4 MeSH descriptor Cardiovascular Diseases explode all trees
#5 heart next disease*
#6 atherosclerosis
#7 arteriosclerosis
#8 hypertension
#9 blood next pressure

#10 hyperlipidaemia*
#11 hyperlipidemia*
#12 MeSH descriptor Hyperlipidemias explode all trees
#13 cholesterol
#14 MeSH descriptor Cholesterol explode all trees
#15 stroke*
#16 MeSH descriptor Stroke explode all trees
#17 "peripheral vascular disease*"
#18 "peripheral arterial disease*"
#19 hypercholesterol*
#20 hyperlipid*
#21 (#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20)
#22 health next education
#23 MeSH descriptor Health Education explode all trees
#24 health next promotion
#25 MeSH descriptor Health Promotion explode all trees
#26 primary next prevention
#27 MeSH descriptor Primary Prevention explode all trees
#28 campaign*
#29 media
#30 MeSH descriptor Mass Media explode all trees
#31 advice
#32 counsel*
#33 MeSH descriptor Counseling explode all trees
#34 program*
#35 policy
#36 policies
#37 (#22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36)
#38 smoking
#39 MeSH descriptor Smoking explode all trees
#40 tobacco
#41 MeSH descriptor Tobacco explode all trees
#42 diet
#43 MeSH descriptor Diet explode all trees
#44 exercise
#45 MeSH descriptor Exercise explode all trees
#46 obesity
#47 MeSH descriptor Obesity explode all trees
#48 diabetes
#49 MeSH descriptor Diabetes Mellitus explode all trees
#50 stress
#51 MeSH descriptor Stress explode all trees

#52 cholesterol
#53 MeSH descriptor Cholesterol explode all trees
#54 hypertension
#55 MeSH descriptor Hypertension explode all trees
#56 blood next pressure
#57 MeSH descriptor Blood Pressure explode all trees
#58 alcohol*
#59 drinking
#60 MeSH descriptor Alcohol Drinking explode all trees
#61 cardiovascular near/3 risk*
#62 multiple next risk*
#63 (#38 OR #39 OR #40 OR #41 OR #42 OR #43 OR #44 OR #45 OR #46 OR #47 OR #48 OR #49 OR #50 OR #51 OR #52 OR #53 OR #54 OR #55 OR #56 OR #57 OR #58 OR #59 OR #60 OR #61 OR #62)
#64 (#21 AND #37 AND #63)
#65 <nothing>, from 1970 to 2008
#66 (#64 AND #65)

Database: Econlit (Ovid) 1969 to June 2008
Search Strategy:

1 cardiovascular disease$.tw.
2 cvd.tw.
3 coronary disease$.tw.
4 heart disease$.tw.
5 hypertension.tw.
6 blood pressure.tw.
7 stroke.mp. tw.
8 or/1-7
9 health education.mptw.
10 health promotion.mp. tw.
11 primary prevention.mp. tw.
12 campaign$.mp. tw.
13 media.mp. tw.
14 counsel$.mp. tw.
15 program$.mp. tw.
16 policy.mp. tw.
17 policies.mp. tw.
18 or/9-17
19 8 and 18
20 limit 19 to yr="1970 - 2008"

Reference tracking search strategies 21 August 2008

Database: MEDLINE(Ovid) 1950 to August Week 1 2008
Search Strategy:

1 norsjo.mp.

Database: MEDLINE(Ovid) 1950 to August Week 1 2008
Search Strategy:

1 minnesota heart health.mp.
2 minnesota heart.mp.
3 1 or 2

Database: MEDLINE(Ovid) 1950 to August Week 1 2008
Search Strategy:

1 oxcheck.mp.

Database: MEDLINE(Ovid) 1950 to August Week 1 2008
Search Strategy:

1 BFHS.mp.
2 British Family Heart.mp.
3 1 or 2

Database: MEDLINE(Ovid) 1950 to August Week 2 2008
Search Strategy:

1 bootheel.mp.

Database: MEDLINE(Ovid) 1950 to August Week 2 2008
Search Strategy:

1 danish municipality.mp.
2 slangerup.mp.
3 1 or 2

Database: MEDLINE(Ovid) 1950 to August Week 2 2008
Search Strategy:

1 german cardiovascular prevention study.mp.

Database: MEDLINE(Ovid) 1950 to August Week 2 2008

Search Strategy:

1 stanford five city.mp.

Database: MEDLINE(Ovid) 1950 to August Week 2 2008
Search Strategy:
1 pawtucket heart.mp.

Database: MEDLINE(Ovid) 1950 to August Week 2 2008
Search Strategy:

1 north karelia project.mp.
2 north Karelia.mp.

Database: MEDLINE(Ovid) 1950 to August Week 2 2008
Search Strategy:

1 heart to heart.mp.
2 south carolina cardiovascular disease prevention project.mp.
3 1 or 2

Database: MEDLINE(Ovid) 1950 to August Week 3 2008
Search Strategy:

1 (stanford adj2 community).mp.
2 stanford 3.mp.
3 stanford three.mp.)
4 or/1-3

Database: MEDLINE(Ovid) 1950 to August Week 3 2008
Search Strategy:

1 heartbeat wales.mp.

Database: MEDLINE(Ovid) 1950 to August Week 3 2008
Search Strategy:

1 action heart.mp.

Database: MEDLINE(Ovid) 1950 to August Week 3 2008
Search Strategy:

1 epernon town.mp.
2 epernon.mp.

3 or/1-2

Database: MEDLINE(Ovid) 1950 to August Week 3 2008
Search Strategy:

1 sezze.mp.

Database: MEDLINE(Ovid) 1950 to August Week 3 2008
Search Strategy:

1 national research program.mp.
2 nrp 1A.mp.
3 swiss.mp.
4 switzerland.mp.
5 or/3-4
6 1 and 5
7 2 or 6

Database: MEDLINE(Ovid) 1950 to August Week 3 2008
Search Strategy:

1 schleiz.mp.

Database: MEDLINE(Ovid) 1950 to August Week 3 2008
Search Strategy:

1 finnmark.mp.
2 cape.mp.
3 1 and 2
4 cardiovascular.mp.
5 1 and 4
6 5 and 2
7 batsfjord.mp.
8 7 and 5
9 3 or 5 or 6 or 8

Database: MEDLINE(Ovid) 1950 to August Week 3 2008
Search Strategy:

1 a su salud.mp.

Database: MEDLINE(Ovid) 1950 to August Week 3 2008
Search Strategy:

1 coeur en sante.mp.

Database: MEDLINE(Ovid) 1950 to August Week 3 2008
Search Strategy:

1 kilkenny.mp.
2 kilkenny health project.mp.

Database: MEDLINE(Ovid) 1950 to August Week 3 2008
Search Strategy:

1 otsego.mp.
2 (otsego adj schoharie).mp.

Database: MEDLINE(Ovid) 1950 to August Week 3 2008
Search Strategy:

1 dutch heart health.mp.

Appendix 3 In/exclusion Screening Checklists

Prevention of CVD at population level
Initial screening criteria for cost-effectiveness review

Starting point: Titles and abstracts from

- Database searches for "reviews" (looking for reviews of cost and cost-effectiveness studies)
- Included studies in any reviews of cost and cost-effectiveness
- Database searches for economic evaluations
- Reference tracking of included programmes in effectiveness reviews
- Suggestions from PDG

Item	Y	N
1. Is there reference to prevention of CVD OR risk reduction in CVD in the title or the abstract?		
2. Is there reference to economic evaluation, particularly cost-effectiveness, cost-utility or cost-benefit analyses OR collection of data on resource use or costs?		
If "Y" to both, order hard copy of paper		

Prevention of CVD at population level
Full paper inclusion/exclusion criteria for cost-effectiveness review

Starting point: Full text of studies obtained as a result of positive decision at screening stage

COST-EFFECTIVENESS REVIEW				
Title:				
Date: **Ref ID:**		Note: In case of ? use left or right arrow to indicate whether final decision is Y/N		
Study feature	Yes	? (Refer to 2nd reviewer)	No	Comments
DATE				
Was the paper published after 1970?				
• If Yes continue. • If No STOP and exclude study as "PUBLICATION PRIOR TO 1970"				
GENERAL				
Does the paper broadly consider some sort of change which might affect CVD or CVD risk?				
Does the paper consider the cost or cost-effectiveness of this change in some way?				
• If Yes to both continue. • If No to either STOP and exclude study as "DOES NOT ADDRESS GENERAL PURPOSE" • If excluding study do you want to TAG it as possibly of value in developing the economic model. If so state reason in space below:				
Reason for TAGGING:				
SETTING & POPULATION				
Is the study set in a developed/OECD country?				
Does the approximate target population exceed 100,000 (or similar to a PCT) or does the study involve a population living within a certain geographical area (which should not be smaller than primary care trust)?				
In one of the alternative approaches evaluated are the vast majority of participants likely to have low or minimal risk of CVD.				
• If Yes to all continue. • If No to any STOP and exclude study as "INAPPROPRIATE SETTING or POPULATION"				
COST-EFFECTIVENESS REVIEW				

Full paper inclusion/exclusion criteria for cost-effectiveness review – page 2

COST-EFFECTIVENESS REVIEW					
INTERVENTION or PROGRAMME					
Is the primary aim of the alternatives considered to address CVD?					
Does one of the alternatives considered tackle 2 or more of the risk factors below (tick those applicable ⇓)					
Smoking					
Poor diet					
Insufficient physical activity					
High blood pressure					
High cholesterol					
Obesity/overweight					
Diabetes					
Psychosocial stress					
High alcohol consumption					
Could one of the alternatives considered be described as one/more of the following (tick those applicable⇓)					
Educational/behavioural including use of mass media					
Fiscal					
Environmental					
Legislative					
• If Yes to all in INTERVENTION sub-section, continue. • If No to any exclude as "DOES NOT CONTAIN AN APPROPRIATE INTERVENTION"					
DESIGN					
Does the study assess cost-effectiveness, cost-benefit or cost-utility?					
• If Yes, INCLUDE • If No, exclude as "INAPPROPRIATE DESIGN", and answer last two questions					
Does the study assess resource use or cost in some way?					
• If Yes, TAG for possible use in economic model • If No, continue					
Is there any other reason why it may be helpful to TAG this paper for possible use in the economic model. If so state below.					

Reason for TAGGING:	
OVERALL DECISION	Tick
INCLUDE	
EXCLUDE, but TAG for MODEL	
EXCLUDE without TAGGING	
COST-EFFECTIVENESS REVIEW	

Appendix 4: Studies excluded on basis of full text

“Does not address general purpose”

Assessed as answering “No” to one or both of:

- Does the paper broadly consider some sort of change which might affect CVD or CVD risk?
- Does the paper consider the cost or cost-effectiveness of this change in some way?

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3 Aldana SG, Jacobson BH, Harris CJ, Kelley PL, Stone WJ. Influence of a Mobile worksite health promotion program on health care costs. *American Journal of Preventive Medicine* 1993; **9**(6):378-383.

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"Inappropriate setting or population"

Assessed as meeting general purpose, but answering "No" to one or more of:

- Is the study set in a developed/OECD country?
- Does the approximate target population exceed 100,000 (or similar to a PCT) or does the study involve a population living within a certain geographical area (which should not be smaller than primary care trust)?
- In one of the alternative approaches evaluated are the vast majority of participants likely to have low or minimal risk of CVD.

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”Does not contain an appropriate intervention”

Assessed as meeting general purpose and appropriate setting and population but answering “No” to one or more of:

- Is the primary aim of the alternatives considered to address CVD?
- Does one of the alternatives considered tackle 2 or more of the risk factors below (9 listed: smoking; poor diet; insufficient physical activity; high blood pressure; high cholesterol; obesity/overweight; diabetes; psychosocial stress; high alcohol consumption)
- Could one of the alternatives considered be described as one/more of the following (4 listed; educational/behavioural including use of mass media; fiscal; environmental; legislative).

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"Inappropriate Design"

Assessed as meeting general purpose and appropriate setting and population and appropriate intervention but answering "No" to :

- Does the study assess cost-effectiveness, cost-benefit or cost-utility?

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Appendix 5: Example Completed Quality Assessment Checklist

Methodology checklist for economic evaluations (Langham *et al.* 1996)

Study identification:		
Evaluation criterion		**Comments**
1	**Was a well-defined question posed in answerable form?**	
1.1	Did the study examine both costs and effects of the service(s) or programme(s)?	Yes
1.2	Did the study involve a comparison of alternatives?	Yes
1.3	Was a viewpoint for the analysis stated and was the study placed in any particular decision-making context?	Yes
2	**Was a comprehensive description of the competing alternatives given (that is, can you tell who? did what? to whom? where? and how often?)?**	
2.1	Were any important alternatives omitted?	No
2.2	Was (should) a do-nothing alternative (be) considered?	Yes
3	**Was the effectiveness of the programmes or services established?**	

3.1	Was this done through a randomised, controlled clinical trial? If so, did the trial protocol reflect what would happen in regular practice?	Yes/Yes
3.2	Was effectiveness established through an overview of clinical studies?	No
3.3	Were observational data or assumptions used to established effectiveness? If so, what are the potential biases in results?	Assumptions- risk reduction (Dundee risk scores) was obtained using the methodology employed in the British Family Heart Study (Wonderling *et al.* 1996). This method estimates cardiovascular risk as a number between -1 and -5. No further details were reported.

4	**Were all the important and relevant costs and consequences for each alternative identified?**	
4.1	Was the range wide enough for the research question at hand?	The measured costs included programme costs, cost of medications and general practice consultations. Additional health care services that may have resulted from the intervention were not considered.
4.2	Did it cover all relevant viewpoints? (Possible viewpoints include the community or social viewpoint, and those of patients and third-party payers.)	Health care system (NHS) only
4.3	Were capital costs, as well as operating costs, included?	Yes
5	**Were costs and consequences measured accurately in appropriate physical units (for example, hours of nursing time, number of physician visits, lost work-days, gained life-years)?**	
5.1	Were any of the identified items omitted from measurement? If so, does this mean that they carried no weight in the subsequent analysis?	Unclear
5.2	Were there any special circumstances (for example, joint use of resources) that made measurement difficult? Were these circumstances handled appropriately?	No
6	**Were costs and consequences valued credibly?**	

6.1	Were the sources of all values clearly identified? (Possible sources include market values, patient or client preferences and views, policy-makers' views and health professionals' judgements.)	Yes
6.2	Were market values employed for changes involving resources gained or depleted?	Yes
6.3	Where market values were absent (for example, volunteer labour), or did not reflect actual values (for example, clinic space donated at reduced rate), were adjustments made to approximate market values?	Unclear
6.4	Was the valuation of consequences appropriate for the question posed (that is, has the appropriate type or types of analysis – cost-effectiveness, cost-benefit, cost-utility – been selected)?	Yes
7	**Were costs and consequences adjusted for differential timing?**	
7.1	Were costs and consequences which occur in the future 'discounted' to their present values?	Only costs were discounted, as consequences were expressed in terms of coronary risk reduction
7.2	Was any justification given for the discount rate used?	No
8	**Was an incremental analysis of costs and consequences of alternatives performed?**	
8.1	Were the additional (incremental) costs generated by one alternative over another compared to the additional effects, benefits or utilities generated?	Yes- Incremental cost per 1% coronary risk reduction
9	**Was allowance made for uncertainty in the estimates of costs and consequences?**	
9.1	If data on costs or consequences were stochastic, were appropriate statistical analyses performed?	Yes
9.2	Were study results sensitive to changes in the values (within the assumed range for sensitivity analysis, or within the confidence interval around the ratio of costs to consequences)?	No

10	**Did the presentation and discussion of study results include all issues of concern to users?**	
10.1	Were the conclusions of the analysis based on some overall index or ratio of costs to consequences (for example, cost-effectiveness ratio)? If so, was the index interpreted intelligently or in a mechanistic fashion?	Yes
10.2	Were the results compared with those of others who have investigated the same question? If so, were allowances made for potential differences in study methodology?	Yes/Yes
10.3	Did the study discuss the generalisability of the results to other settings and patient/client groups?	No
10.4	Did the study allude to, or take account of, other important factors in the choice or decision under consideration (for example, distribution of costs and consequences, or relevant ethical issues)?	Yes
10.5	Did the study discuss issues of implementation, such as the feasibility of adopting the 'preferred' programme given existing financial or other constraints, and whether any freed resources could be redeployed to other worthwhile programmes?	No
OVERALL ASSESSMENT OF THE STUDY		
How well was the study conducted? *Code ++, + or –*		+
Are the results of this study directly applicable to the patient group targeted by this guideline?		Partially applicable

++	All or most of the criteria have been fulfilled. Where they have not been fulfilled the conclusions of the study or review are thought very unlikely to alter.
+	Some of the criteria have been fulfilled. Those criteria that have not been fulfilled or not adequately described are thought unlikely to alter the conclusions.
–	Few or no criteria fulfilled The conclusions of the study are thought likely or very likely to alter.

The code allocated here, coupled with the study type, will decide the level of evidence that this study provides. The aim of the other two questions in this section is to summarise your view of the quality of this study and its applicability to the patient group targeted by the guideline you are working on. Section 3 asks you to summarise key points about the study that will be added to an evidence table at the next stage of the process.

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