The cost-effectiveness of behaviour change interventions designed to reduce Coronary Heart Disease: A thorough review of existing literature

Final Phase 1 Report for the project "Health Economic Analysis of prevention and intervention approaches to reducing incidence of Coronary Heart Disease"

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Foreword by Lesley Owen, Catherine Swann and Jane Huntley, NICE

The National Institute for Health and Clinical Excellence ('NICE' or 'the Institute') has been asked by the Department of Health to develop public health programme guidance on supporting knowledge, attitude and behaviour change. Specifically to produce guidance *on "The most appropriate means of generic and specific interventions to support attitude and behaviour change at population and community levels."*

This public health programme guidance will consist of recommendations on broad-ranging (those that may apply across a range of topics or behaviours) and specific interventions (those that relate to a particular activity like smoking) that aim to promote or support attitude, knowledge and behaviour change, in order to help reduce the risk of developing preventable diseases or conditions or help to promote healthier lifestyles. This guidance will provide recommendations for good practice, based on the best available evidence of effectiveness, including cost effectiveness.

Five reviews have been commissioned to inform the development of this guidance and these are as follows:

1. A review of the use of the Health Belief Model (HBM), the Theory of Reasoned Action (TRA), the Theory of Planned Behaviour (TPB) and the Trans-Theoretical Model (TTM) to study and predict health related behaviour change.
2. A review of the social and cultural context on the effectiveness of health behaviour change interventions in relation to diet, exercise and smoking cessation.
3. A review of the effectiveness of general interventions delivered outside public health (eg. marketing) at changing knowledge, attitudes and behaviour.
4. A review of the effectiveness of public health interventions including policy and legislative measures in changing knowledge, attitudes and behaviour,
5. A review of the effectiveness of interventions to support and maintain health producing knowledge, attitudes and behaviour.

Economic Evaluation

Rather than undertake separate health economic reviews for each of the areas identified above NICE has initiated a process that seeks ultimately to compare and contrast the cost-effectiveness of prevention, intervention and treatment strategies aimed at changing behaviour.

As a first step in this process NICE has narrowed the scope of the health economic analysis and focussed on prevention and intervention strategies aimed at reducing Coronary Heart Disease. The aim of the analysis is to synthesize and analyse information on a range of approaches within each of the following four broad strategies:

1. Prevention in childhood
2. General prevention in adulthood
3. Intervention in adulthood to change the behaviour of people with specific risk factors for CHD (eg. smoking, poor diet, lack of physical activity)
4. Treatment (primary, secondary and tertiary care) in adulthood for people with CHD (eg. statins, coronary heart by-pass, heart transplant).

Using QALYs as the key health outcome measure the analyses in the first step will help to inform the development of guidance on the most effective and cost-effective means of achieving behaviour change aimed at reducing Coronary Heart Disease [whilst recognising that prevention is concerned with maintaining healthy behaviours].

In the longer term it is anticipated that the full programme of work, which will include the present analysis, will help to inform other aspects of NICE's work including future guidance documents and methodological developments in health economic analyses. The study may also provide a useful input to discussions and debates about resource allocation.

Executive Summary

Aim and Objectives

The aim of this report is to summarise the available evidence on the cost-effectiveness of interventions and programmes designed to change knowledge, attitude and behaviour in the whole population and specific communities (including families and individuals) in order to help to promote healthier lifestyles and reduce the risk of developing CHD.

Methods

A systematic search of six databases was undertaken in June 2006 using a fully specified set of search terms as well as inclusion and exclusion criteria. Following a review of 4122 abstracts and 225 papers, 26 papers were retained for full review using a standard set of piloted questions. Data extraction included background data, population characteristics, interventions and alternatives, main features and findings of the study and 3 sets of quality review criteria.

Results

A set of evidence statements is provided, by paper, for

- Exercise (page 37)
- Smoking (page 39)
- Combined interventions (pages 41 to 42)
- Diet (pages 45 to 57)

Main Conclusions

1. Prevention in childhood

   None of the papers reviewed provided evidence on child-focussed health promotion programmes. Children were stated as being included in population level statistics in only two papers (Murray et al 2003, Services DoH, 2003) but data were not evaluated by subgroup[1].

2. General prevention in adulthood

   Three out of the four papers that focussed on combined packages of interventions aimed at multiple risk factors fell into the 'likely to be very cost-effective' category[2]. These included a mix of population and individual focussed interventions for adults over the age of 30. Whilst short term effects in two papers were based on RCTs, none of the studies were conducted in the UK and none investigated alternative packages of interventions. Two papers

[1] It is possible that children were also included in a number of other interventions aimed at populations, but age ranges were not always specified.
[2] The remaining paper(s) did not provide QALYs or number of life years saved.

compared the combination programme with no programme at all and one against a screening based alternative.

3. Intervention in adulthood to change the behaviour of people with specific risk factors for CHD (eg. smoking, poor diet, lack of physical activity)

Exercise: Both papers on the cost-effectiveness of interventions designed to increase exercise fall into the category 'likely to be very cost-effective' when compared with no intervention and a largely sedentary population aged over 35. However, the quality of short term effectiveness data was not strong.

Smoking: Two out of three papers[3] on smoking fall into the category 'likely to be very cost-effective'. One paper was the advice to individuals in Spain and the other was Heartbeat Wales. Unfortunately the quality of short term effectiveness data from Spain was not strong and the data from Wales very poor quality.

Diet: Of the 17 papers on diet, the cost-effectiveness of professional advisors in changing diet was consistently in the 'very cost-effective' category whereas there is no consistent pattern for any other types of diet interventions (population or screening based or diet alone) which fell in all categories between very likely and very unlikely to be cost-effective, including the 'standard' Step 1 diet which could be considered a more 'standardised' intervention.

Two non-advisory interventions also remained in the likely to be very cost-effective group; food labelling with trans fatty acid content (Services DoH, 2003) and a population-based health promotion programme on healthy food (Kristianson 1991). However, one of the reasons why the food labelling may rest only in one category is because neither sensitivity nor sub-group analysis was conducted, which is surprising given that only level 2 data was (and could be) available. Kristianson's (1991) model used a range of levels of data and undertook a basic sensitivity analysis.

When specified (n=12/17), most papers on diet focused on populations over the age of 35 with the exception of Murray et al (2003) who modelled the entire population. The quality of evidence varied by category of cost-effectiveness, with most RCT data for specifications of interventions in the >£50,000 category, followed by £0-20,000 and then £30-50,000. No RCT data supported interventions in the cost saving or £30-50,000 level of cost-effectiveness.

4. Treatment (primary, secondary and tertiary care) in adulthood for people with CHD (e.g. statins, coronary heart by-pass, heart transplant).

The majority of treatments provided and evaluated are not behaviour change interventions or are provided in conjunction with behaviour change interventions. This project was also defined with NICE to exclude secondary

[3] The remaining paper(s) did not provide QALYs or number of life years saved.

and tertiary care. This reviews found no evidence on the effectiveness of behaviour change interventions alone. Several papers were excluded because the effects of behaviour change interventions could not be isolated, particularly from pharmacological intervention.

5. Other findings

- A blanket statement on cost-effectiveness of targeted or population strategies cannot be made as the evidence is mixed; in some cases targeted strategies are more effective and in other cases mass treatment is.

- There is evidence suggesting that the cost-effectiveness of behavioural change interventions varies by age, gender and risk level but in an inconsistent way across intervention type.

- There is considerable uncertainty for a number of interventions around the threshold value of £30,000/QALY, indicating that future modelling may provide useful decisional information for a UK setting.

- Data from studies citing ICERs of between 0-£50,000/QALY was heavily reliant on uncontrolled primary studies

- Few economic evaluations rely on primary data and few modelling studies provide sufficient description to ascertain the methods used.

Evidence gaps

Content of evidence

- With the exception of evaluations that cover the whole population, no evidence is provided on the cost-effectiveness of behaviour change interventions for specified sub-groups e.g. age group 19-30yrs, low income groups, pregnant women, particular ethnic groups or specified disadvantaged groups.

- There is no economic evaluation of a solely child-focussed disease prevention programme targeted at reducing CHD.

- No cost-effectiveness analysis of interventions to reduce smoking or increasing exercise to reduce CHD has included children.

- Very few economic evaluations of behaviour change interventions to reduce CHD have been conducted from a UK perspective

- There is a lack of research looking at patient preferences. Little attention was paid to patient preferences for the type of interventions that would be preferred or how they would be delivered. In turn preference is likely to affect

compliance, which needs to be addressed (Murray et al, 2003) as it is key to the success of any behaviour intervention.

- Future research needs to include QALY weights for life years to facilitate comparison across a range of interventions

Quality of evidence

- Few economic evaluations of behaviour change interventions to reduce CHD are conducted alongside level 1 effectiveness evidence

- A lack of reliable data from which to extrapolate the long term health outcomes of behaviour change interventions from short term effects of behaviour change interventions (Kristiansen et al., 1991). For example, Kinlay et al. (1994) cited a lack of adequate information upon the impact of cholesterol and cholesterol reduction upon the risk of CHD among women.

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1.0 Background

Coronary heart disease (CHD) is a leading public health problem and the leading single cause of death in the UK. Around one in five men and one in six women die from the disease (British Heart Foundation, 2005) and, of the 110,000 people a year who die from CHD in England, 41,000 are under the age of 75 (Wanless 2002).

Recently, CHD mortality has fallen faster in the over 55 years category in the UK, compared with younger people (British Heart Foundation, 2005). However, the burden of CHD in the whole population is higher and has fallen less in the UK compared with many other countries (Wanless 2002). There are also large disparities across ethnic groups with death rates from CHD not falling as fast in South Asians, for example, compared with the rest of the population (British Heart Foundation, 2005).

In addition to the impact on people, CHD also places a heavy financial burden on the UK health care system - £1.73 billion in 1999 (Liu et al 2002). CHD accounted for 4.1% of the total health expenditure in the UK in 2003 and is among the highest healthcare costs in the EU (Leal et al, forthcoming). The National Service Framework (NSF) (DoH 2000) sets standards for every stage of CHD, from primary prevention through to treatment and cardiac rehabilitation. Wanless (2002) estimated that to implement the NSF would cost an additional £2.4 billion a year by 2010-11. This would roughly double existing NHS expenditure on CHD (Wanless, 2002).

As CHD is largely preventable (Wanless, 2002), the Government aims to reduce the death rate from CHD, stroke and related diseases in people under 75 by at least two fifths by 2010 (DH 1999). The 'fully engaged' scenario (Wanless 2004) set out a framework for action to tackle key health problems such as smoking and obesity that contribute to CHD. However, this scenario requires improved monitoring of the health of the UK population and improvements in the cost-effectiveness of the NHS. There is also concern that "even effective programmes for lifestyle changes in diet, exercise and behaviour can be intensive and expensive" (Avenell et al, 2004).

The paucity of knowledge about the cost-effectiveness of prevention methods, coupled with the need to ensure that effective interventions are used efficiently (Wanless 2002 & 2004) explains why NICE has been asked, by the Department of Health, to develop guidance on "the most appropriate means of generic and specific interventions to support attitude and behaviour change at population and community levels." The development of this guidance needs to draw on, and fit within, existing NICE frameworks for evaluating health technologies although the process of developing guidance could also provide an opportunity to consider the relevance of the 'reference case' (evaluation guidelines NICE 2004 & 2006) to evaluating public health interventions.

To date three reviews of the effectiveness of behaviour change interventions (a review of the effectiveness of general interventions delivered outside public health (eg. marketing) at changing knowledge, attitudes and behaviour; a review of the effectiveness of public health interventions including policy and legislative measures in changing knowledge, attitudes and behaviour and a review of the effectiveness of interventions to support and maintain health producing knowledge, attitudes and behaviour) plus two other reviews (a review of the use of the Health Belief Model (HBM), the Theory of Reasoned Action (TRA), the Theory of Planned Behaviour (TPB) and the Trans-Theoretical Model (TTM) to study and predict health related behaviour change; a review of the social and cultural context on the effectiveness of health behaviour change interventions in relation to diet, exercise and smoking cessation) have been commissioned by NICE. These reviews, together with the evidence in this report will help guide the choice of a forthcoming economic model examining the most cost-effective interventions to encourage behaviour change that will prevent the development of coronary heart disease. With an economic model of the selected interventions, this will constitute the evidence base considered by the programme development group in the development of NICE guidance on behaviour change interventions.

A life course approach has been adopted for this work; NICE has selected strategies that will facilitate comparison across four broad areas:

- Prevention in childhood;
- General prevention in adulthood;

- Intervention in adulthood to change the behaviour of people with specific risk factors for CHD (e.g. smoking, poor diet, lack of physical activity); and,
- Treatment (primary, secondary and tertiary care) in adulthood for people with CHD (e.g. statins, coronary heart by-pass, heart transplant).

For the purposes of developing the guidance in question, however, there is a need to focus most immediately on the first three areas, although we expect that the majority of evidence exists for the fourth area much of which has been previously reviewed.

With respect to this review and the forthcoming economic model, NICE has narrowed the scope to focus on the impact of prevention, intervention and treatment strategies aimed at changing behaviour and the reduction of CHD. Given the time and resources available, NICE suggested that the focus on behaviour change be directed to the areas of diet, exercise (including weight), smoking and alcohol.

This report first sets out the aims followed by the methods of searching, selecting and reviewing evidence. The results section begins with a presentation of the type and quality of papers found prior to summarising key findings and evidence statements by each selected area. The discussion draws together findings to consider the potential strength of evidence in this field as a whole and points to a series of gaps in knowledge.

2.0 Aim of health economics component

The aim of the health economics component has been split into two phases, the overall aim of which is to:

Phase 1

1. Summarise the available evidence on the cost-effectiveness of interventions and programmes designed to change knowledge, attitude and behaviour in the whole population and specific communities (including families and individuals) in order to help to promote healthier lifestyles and reduce the risk of developing CHD;

Phase 2

2. Provide the best possible model of cost-effectiveness of one or more behaviour change interventions to decrease CHD, given the resources and time available;

3. Provide the above information in an accessible way to help the PDG and NICE develop guidance on appropriate interventions & programmes for behaviour change.

This report presents phase 1, a thorough search for literature on the economic evaluation of interventions and programmes designed to change knowledge, attitude and behaviour in the whole population and specific communities (including families and individuals) in order to help to promote healthier lifestyles and reduce the risk of developing coronary heart disease with a view to constructing evidence statements on cost-effectiveness.

3.0 Methods

3.1 Databases selected

A structured search of electronic databases was conducted between the 9th and 13th of June 2006. To ensure that the maximum number of appropriate papers were identified, the Cochrane Library recommended procedure of using a combination of MeSh (medical subject heading) and free text search terms was used. The databases and type of search are presented in Table 1 below.

Table 1. Databases and type of search

Databases searched	Type of search
Medline	MeSh and Free Text
Embase	MeSh and Free Text
NHS EED	MeSh and Free Text
OHE HEED	Free Text
NCCHTA	Subject classification including 'coronary heart disease', 'men's health' and women's health'
CEA Registry (Harvard University)	Subject classification of cardiovascular diseases.

3.2 Development of search terms

The terms were designed with the intention of identifying literature on; the four coronary heart risk factors of poor diet/nutrition, lack of exercise, smoking and excessive alcohol consumption[4]; literature on behaviour modification and health promotion, these terms could then be combined with economic evaluations and coronary heart disease terms.

The list of MeSh and free text terms were generated by GG & JFR in conjunction with ongoing and completed effectiveness reviews funded by NICE, and consultation with the Public Health Programme Analysts, Lesley Owen and Catherine Swann, and the Associate Director Jane Huntley. The initial list of terms was piloted on the Ovid Medline search engine and refined based upon discussion of the results with Public Health Program officials and a NICE Information Specialist, Marta Calonge-Contreras.

It was necessary to refine the search strategy for subsequent search engines to comply with their download limits and to create an efficient and manageable review. Refinement of the coronary heart disease terms was done in consultation with Dr. Helen Chung of Nice and the Public Health team. In addition to the CHD terms, general terms such as 'cost*' which identified partial economic evaluations as well as full economic evaluations were excluded in favour of specific terms such as 'cost-utility'.

The final search strategy was reviewed and approved by NICE and subsequently implemented. The full list of MeSh and free text terms used in each database are presented in Appendix 1[5]

3.3 Inclusion and exclusion criteria

The criteria for including literature in this review were as follows:

[4] Weight was not included as a separate category as diet/nutrition and exercise were considered to capture this risk factor.
[5] NICE retains a copy of the development process of all terms

- Is the reduction of risk/behaviour change in relation to CHD the primary objective?
- Any of the following type of interventions:
  - Individual-level health promotion and disease prevention interventions (targeted and general).
  - Community-level health promotion and disease prevention interventions (including family interventions).
  - Community-level and area-based development and regeneration interventions and programmes.
  - School- and workplace-based interventions and programmes.
  - Mass media and communications interventions.
  - Work in public relations, marketing and advertising.
  - Interventions and approaches within social care, applied psychology, prison and probationary services.
  - Macro level and legislative interventions and policies, and the structures and systems that support their implementation.
- Primary studies published ≥1990.
- Reviews published ≥1995 (to identify additional relevant primary studies)
- Is data extractable for a stand alone behaviour change or health promotion programme that has a comparator?

The criteria for excluding literature in this review were as follows:

- Partial economic evaluations.
- Studies where reduction of risk/behaviour change in relation to CHD is not the primary objective.
- Interventions focusing on one or more of the following: screening techniques[6]; diagnostic approaches; drug interventions (including nicotine gum); psychiatric interventions delivered as part of the therapeutic process for people with mental ill health.

[6] Papers where individuals were screened to ascertain their risk or eligibility for a behaviour change intervention and the behaviour change intervention was the primary focus were included.

- Interventions aimed at secondary prevention of CHD.
- Interventions that can only delivered in secondary or tertiary care settings.
- Studies where behaviour change is assumed to occur but no intervention is stated.
- Non-English language papers

3.4 Search Results

In total 4,122 references were identified after the removal of exact duplicates from the Endnote reference management system (see Table 2). Examination of the abstracts and application of the inclusion and exclusion criteria to the identified abstracts by one author resulted in a list of 250 papers for retrieval and full examination (approximately 5% of abstracts were checked by another author at outset to ensure accuracy and consistency). Further review of the text and references of all review and empirical identified created an additional list of 78 empirical studies. Therefore a total of 328 papers were selected for retrieval.

Table 2. Papers identified and abstracts reviewed

Search Engine/Source	Papers identified	Output format	Selected for full review
Medline	2012	Endnote file	180
Embase	1475	Endnote file	37
NHS EED	304	Endnote file	17
OHE HEED	99	Endnote file	6
Total (exact duplicates removed)	3536		
NCCHTA			
Coronary Heart Disease	39	Electronic/Hard copy	2
Men's health	17	Electronic/Hard copy	0
Women's health	63	Electronic/Hard copy	0
CEA Registry (Harvard University)	462	Electronic/Hard copy	3
Nep: New Economic Papers Health Economics (via NICE)	5		5
Empirical papers identified from references	*78*		*78*
Total	*4200 (n=4122 from databases alone)*		*328*

Of the 328 papers identified for retrieval, 14 were not in English, a further 12 requested by inter-library loan did not arrive by the agreed deadline (12.00 on 18th

August 2006) and 77 were used solely for the purposes of identifying relevant primary studies. Therefore a total of 225 papers were retrieved and assessed in relation to the inclusion and exclusion criteria by one author. 199/225 papers were excluded. The number of papers failing each of the sequential exclusion criteria is set out in Table 3. This table shows that 125 papers passed the first 3 criteria (225 - (33+67)) but that 41 then failed the fourth criteria. Following the exclusion criteria 26 papers were retained for full review (see list in Table 4). All excluded papers are referenced in Appendix 2.

Table 3: Numbers of papers failing the sequentially applied exclusion criteria

Reasons for excluding papers from full review	N
1. Was not a full economic evaluation (costs & effects for at least two alternatives)	33
2. Reduction of risk/behaviour change in relation to CHD was not the primary objective	67
3. Focus on one or more of the following: screening techniques; diagnostic approaches; drug interventions (including nicotine gum); psychiatric interventions delivered as part of the therapeutic process for people with mental ill health.	41
4. Data was not extractable for a stand alone behaviour change or health promotion programme	3
5. The intervention needed to be delivered in a secondary or tertiary care setting.	2
6. A secondary prevention intervention (patients that have had a coronary event).	33
7. A study where behaviour change was assumed to occur but no intervention was stated.	7
8. Retrieved and found to be foreign language	12
9. Paper reporting details of a study that was reported elsewhere in more detail	1
Total excluded	199

The four main reasons papers were excluded were that the papers were: not focused primarily on CHD prevention; focused on diagnostic approaches; a secondary prevention, or; not a full economic evaluation. Several studies that failed on item 2 in Table 3 (reduction of risk/behaviour change in relation to CHD was not the primary objective) targeted risk factors common to several diseases, but they did not specifically report any impact on CHD, either in terms of avoided myocardial infarctions or quality adjusted life years saved due to reducing CHD. Examples of such interventions would be smoking cessation which affects many health conditions such as cancers and cardiovascular disease, not just CHD. Diet and nutrition frequently failed on the same grounds, as reduced weight or reduced blood pressure are all common risk factors to many long term health conditions such as stroke and diabetes.

Reason 3 in Table 3 was prominent as many studies had participants that were on medication or a proportion of study participants on medication and it was not possible to disaggregate the results for participants receiving a behaviour intervention alone from those receiving the same intervention and receiving drugs, so the study had to be excluded. Results presented in this way mask the true effects of the behaviour interventions being implemented.

Table 4. Included studies.

Assmann, G., & Schulte, H. (1990). Primary prevention of coronary heart disease in the Federal Republic of Germany. Analysis of cost-effectiveness. *DRUGS,* 40, 33-37.

Bendich, A., Mallick, R., & Leader, S. (1997). Potential health economic benefits of vitamin suplementation. *Western Journal of Medicine*, 166, 307-312.

Blake, G. J., Ridker, P. M., & Kuntz, K. M. (2003). Potential cost-effectiveness of C-reactive protein screening followed by targeted statin therapy for the primary prevention of cardiovascular disease among patients without overt hyperlipidemia. *American Journal of Medicine*, 114, 485-494.

Dalziel, K., Segal, L., & Mortimer, D. (2005). *Risk Factor Study - How to reduce the burden of harm from poor nutrition, tobacco smoking, physical inactivity and alcohol misuse: cost-utility analysis of 9 multi-risk factor interventions*. Victoria: Monash University.

Finkelstein, E. A., Troped, P. J., Will, J. C., & Palombo, R. (2002). Cost-effectiveness of a cardiovascular disease risk reduction program aimed at financially vulnerable women: the Massachusetts WISEWOMAN project. *Journal of Womens Health & Gender Based Medicine*, 11, 519-526.

Johannesson, M., & Fagerberg, B. (1992). A health-economic comparison of diet and drug treatment in obese men with mild hypertension. *Journal of Hypertension*, 10, 1063-1070.

Jones, T. F., & Eaton, C. B. (1994). Cost-benefit analysis of walking to prevent coronary heart disease. *Archives of Family Medicine*, 3, 703-710.

Kinlay, S., O'Connell, D., Evans, D., & Halliday, J. (1994). The cost-effectiveness of different blood-cholesterol-lowering strategies in the prevention of coronary heart disease. *Australian Journal of Public Health*, 18, 105-110.

Kristiansen, I. S., Eggen, A. E., & Thelle, D. S. (1991). Cost effectiveness of incremental programmes for lowering serum cholesterol concentration: is individual intervention worth while? *BMJ*, 302, 1119-1122.

Lindgren, P., Fahlstadius, P., Hellenius, M.-L., Jonsson, B., & De Faire, U. (2003). Cost-effectiveness of primary prevention of coronary heart disease through risk factor intervention in 60-year-old men from the county of Stockholm - A stochastic model of exercise and dietary advice. *Preventive Medicine*, 36, 403-409.

Lindholm, L., Rosen, M., Weinehall, L. & Asplund, K.,(1996). Cost effectiveness and equity of a community based cardiovascular disease prevention programme in Norsjo, Sweden. *Journal of Epidemiology and Community Health*, 50, 190-195.

Munro, J., Brazier, J., Davey, R., & Nicholl, J. (1997). Physical activity for the over-65s: could it be a cost-effective exercise for the NHS? *Journal of Public Health Medicine*, 19, 397-402.

Murray, C. J., Lauer, J. A., Hutubessy, R. C., Niessen, L., Tomijima, N., Rodgers, A., Lawes, C. M., & Evans, D. B. (2003). Effectiveness and costs of interventions to lower systolic blood pressure and cholesterol: a global and regional analysis on reduction of cardiovascular-disease risk.[erratum appears in Lancet. 2005 Jul 16-22;366(9481):204]. *Lancet,* 361, 717-725.

Nallamothu, B. K., Fendrick, A. M., Rubenfire, M., Saint, S., Bandekar, R. R., & Omenn, G. S. (2000). Potential clinical and economic effects of homocyst(e)ine lowering. *Archives of Internal Medicine*, 160, 3406-3412.

Olsen, J., Willaing, I., Ladelund, S., Jorgensen, T., Gundgaard, J., & Sorensen, J. (2005). Cost-effectiveness of nutritional counseling for obese patients and patients at risk of ischemic heart disease. *International Journal of Technology Assessment in Health Care,* 21, 194-202.

Ong, M. K., & Glantz, S. A. (2004). Cardiovascular health and economic effects of smoke-free workplaces.[erratum appears in Am J Med. 2005 Aug;118(8):933]. *American Journal of*

Medicine, 117, 32-38.
Phillips, C. J., & Prowle, M. J. (1993). Economics of a reduction in smoking: case study from Heartbeat Wales. *Journal of Epidemiology & Community Health*, 47, 215-223.
Phillips, C., Belsey, J., & Shindler, J. (2000). Flora pro.activ: A clinical and financial impact analysis. *Journal of Medical Economics*, 3, 61-76.
Plans-Rubio, P. (1997). Cost-effectiveness of dietary treatment of hypercholesterolemia in Spain. *Public Health*, 111, 33-40.
Plans-Rubio, P. (1998). Cost-effectiveness analysis of treatments to reduce cholesterol levels, blood pressure and smoking for the prevention of coronary heart disease: Evaluative study carried out in Spain. *PharmacoEconomics,* 13, 623-643.
Plans-Rubio, P. (2004). Allocation of resources between smoking cessation methods and lovastatin treatment of hypercholesterolaemia: based on cost effectiveness and the social welfare function. *Pharmacoeconomics*, 22, 55-69.
Prosser, L. A., Stinnett, A. A., Goldman, P. A., Williams, L. W., Hunink, M. G., Goldman, L., & Weinstein, M. C. (2000). Cost-effectiveness of cholesterol-lowering therapies according to selected patient characteristics.[see comment]. *Annals of Internal Medicine*, 132, 769-779.
Services, D. o. H. a. H. (2003). *Food labelling: trans fatty acids in nuitrition labelling; Consumer research to consider nutrient content and health claims and possible footnote or disclosure statements; final rule and proposed rule*. Rockville: Us Food and Drug Administration.
Stinnett, A. A., Mittleman, M., & Weinstein, M. C. (1996). Cost-effectiveness of dietary and pharmacological therapy for cholesterol reduction in adults. In M. R. Gold (Ed.), *Cost-effectiveness in Health and Medicine* (pp. 349-391). New York: Oxford University Press.
Tice, J. A., Ross, E., Coxson, P. G., Rosenberg, I., Weinstein, M. C., Hunink, M. G., Goldman, P. A., Williams, L., & Goldman, L. (2001). Cost-effectiveness of vitamin therapy to lower plasma homocysteine levels for the prevention of coronary heart disease: effect of grain fortification and beyond.[see comment]. *Journal of the American Medical Association*, 286, 936-943.
Tosteson, A. N., Weinstein, M. C., Hunink, M. G., Mittleman, M. A., Williams, L. W., Goldman, P. A., & Goldman, L. (1997). Cost-effectiveness of populationwide educational approaches to reduce serum cholesterol levels*. Circulation*, 95, 24-30.

3.5 Method of reviewing papers

A data extraction form was developed and piloted by two authors. The revised form was used to extract a range of data in a standardised and comparable way across papers. The type of data extracted (see Appendix 3 for full data extraction form and Appendix 4 for the accompanying manual) included the following:

1. *Background data* including; bibliographic data, funders of study, country;

2. *Population characteristics* including; target population, setting of the study, sample size, age, reported incidence of CHD, gender, ethnicity, risk-level of CHD;

3. *Intervention & alternatives* including*:* their content, duration, and mode of delivery;

4. *Features of the study* including:
    a. study design, analytic method, perspective, time horizon, discount rate
    b. effectiveness measures used and sources of data, type of sensitivity analysis undertaken
    c. type or and sources of data use for resource use and costs, reporting figures for costs;

5. *Main results* including specified types of ICERs (e.g. health service or societal perspective with and without health care savings), main conclusions;

6. Whether the reported data specifically addressed the key elements influencing the interventions' effective implementation[7].

In accordance with NICE guidance on research methods (NICE, 2006) the robustness of evidence included in the review was assessed. In addition to applying the Drummond 35 item checklist as is recommended by NICE, the applicability of the papers to economic modelling (phase 2 of this project), and the findings from reported sensitivity analysis were assessed. The generalisability of the findings of the papers were assessed in relation to Pang's 8 generalisability questions (Pang 2006). 40% of papers were double-reviewed (as funding did not allow for all papers to be double reviewed), with any discrepancies resolved in a subsequent meeting of reviewers. Data extraction forms from the remaining papers were checked over by at least one other person and all tabulated data was checked by another person.

[7] How does the content of the intervention influence effectiveness?
How does the way that the intervention is carried out influence effectiveness?
Does the effectiveness depend on the job title/position of the deliverer (leader)? What are the significant features of an effective delivery leader?
Does the site/setting of delivery of the intervention influence effectiveness?
Does the intensity (how much? how long? How often?) of the intervention influence effectiveness/duration of effect?
Does the effectiveness of the intervention vary with different characteristics within the target population such as age, sex class and ethnicity?
Does the intervention have differential impact on inequalities in health?
What are the barriers to implementing this intervention successfully?

3.6 Methods of analysis

Text from the data extraction exercise are tabulated in three main summary tables covering: objectives and main results (see Tables 14 to 17); context of the intervention and its alternatives (see Tables 5.1 to 5.4 in Appendix 5); and main methodological aspects of studies (see Tables 6.1 to 6.4 in Appendix 6). Categorical data extracted from the reviewed papers are presented as frequency or contingency tables and figures below.

Currency conversion

In order to allow direct comparison of results such as cost per life year saved, annual cost of programs, cost per avoided event etc., which were estimated in different currencies and at up to 15 years apart, results have been adjusted and converted from local currencies to UK £, 2006 prices. Conversion comprised of two steps; inflating to local 2006 prices and then converting to UK£. Costs were first inflated to 2006 prices using the local country's GDP deflator from the year of costing (or date of publication if not given). For countries that joined the European Monetary Union in 2001, results presented in the original currency (e.g. DM) and were adjusted in two steps; first inflating from the year of costing to the year that the country integrated the union and then translating to Euros at the point of joining the Euro. This conversion rate was then inflated to 2006 prices using the local GDP deflator. The second step converted all local 2006 prices to UK£ using PPP conversion rates and the quarterly average Official Exchange Rates (31st March- 30 June) (EconStats, Bank of England, 2006).

In cases where the results were reported in a currency different from that in the country of origin, the findings were deflated according with the country's GDP deflator but the currency conversion was based on the PPP value or OER of the currency of which they were stated. For, example the Spanish based study by Plans-Rubio (1998) presented results in $. Therefore figures were transformed to pesetas at the given or predicted (from Index values) exchange rate, inflated to 2006 prices, via a Euro conversion, and transferred to UK£ PPP.

3.7 Development of evidence statements

The development of evidence statements from each paper reviewed were constructed with respect to: the quality of effectiveness data; quality of economic evaluations; generalisability of evidence; and a judgement of likely cost-effectiveness. The criteria used are explained below.

Quality of effectiveness data

The quality of effectiveness data was categorised into short-term (up to one year and intended to capture whether a programme 'worked' in the short term, for example in changing specified behaviour or impacting on risk factors such as cholesterol levels) and long term (as an indicator of impact on CHD). We used a 4-point scale rating based on the NICE recognised criteria (NICE, 2006). However, as reporting details of effectiveness data was limited to referencing other papers, it was not possible to use the more detailed 8-point scale for the papers reviewed. The ratings, made by one of this review's authors, were based on Table 5.

Table 5: Grading of effectiveness evidence in economic evaluations

Grade of evidence	Type of evidence
1	Meta analyses, systematic reviews of RCTs, randomised controlled trials (including cluster trials),
2	Before & after, cohort or case-control studies
3	Non-analytical studies including case series and case reports
4	Expert opinion, formal consensus, author assumptions

Quality of economic evaluations

The quality of economic evaluations was judged in two ways. The main approach used was to quantify the % of Drummond's criteria adhered to (in cases where a 'not applicable' answer was logged, the question was excluded from the denominator). Yes was coded as a 1 and No or Not clear as 0. Only 31 items of the Drummond were used, as items 2, 4, 15 and 24 were considered inappropriate to this exercise[8]. We refrained from dividing the %-scores into arbitrary categorisations of excellent, good and poor quality studies for two reasons. First it adds a largely indefensible

[8] The 35 item Drummond checklist (Drummond and Jefferson, 1996) was developed as an aid to journal reviewers and not as a measure of quality.

layer of uncertainty because it is arbitrary. Secondly, a 100% adherence does not guarantee a perfect study as the questions are largely about whether particular data has been recorded and it was possible for a badly designed evaluation to report well. We are also aware that this % scoring of adherence is not a usual or accepted usage of the Drummond criteria. However, NICE were keen for some scaled judgement of quality.

We also designed a question that tapped into our own judgement of the usefulness of each paper to the second phase of research, developing an economic model. The question captures our views on how useful the paper would be in developing a future model structure, or providing data for transition probabilities, resource use, costs, outcomes or utilities. As such it could be viewed as an alternative judgement on the quality of papers. We use the % of positive responses to judge the field as a whole and to comment on how differently quality may be viewed (positive answers were coded as 1 and No as 0).

Generalisability of evidence

We characterise generalisability in two ways. First we note the country of study Second, we use Pang's transferability questions (Pang 2006) for reviewing economic evaluations. However, rather than produce a definitive statement on whether results are generalisable they give an indication of the extent to which data is reported in a sufficiently disaggregated way to allow cost-effectiveness ratios to be reconstructed in another setting. The questions address whether :

- the target decision-maker can be inferred
- the year of effectiveness data are recorded
- details of life expectancy are given
- details of compliance are given
- resources year was recorded
- details of technology availability are given
- details are given about how to transfer data to another setting are provided
- conclusions about generalisability are addressed

To reflect responses we simply provide a % adherence to these issues (in cases where a 'not applicable' answer was logged, the question was excluded from the denominator. Yes was coded as a 1 and No or Not clear as 0.

Judgement of likely cost-effectiveness

The degree of cost-effectiveness was judged to fall in one of the five levels (A. Fischer, personal communication September 26, 2006):

- Likely to be cost saving
- Likely to be very cost-effective (<£20,001/QALY)
- Likely to be reasonably cost-effective (£20,001-£30,000/QALY)
- Unlikely to be cost-effective (£30,001-£50,000/QALY)
- Very Unlikely to be cost-effective (>£50,000 QALY)
- Unclear whether or not cost-effective as QALYs or LY not used

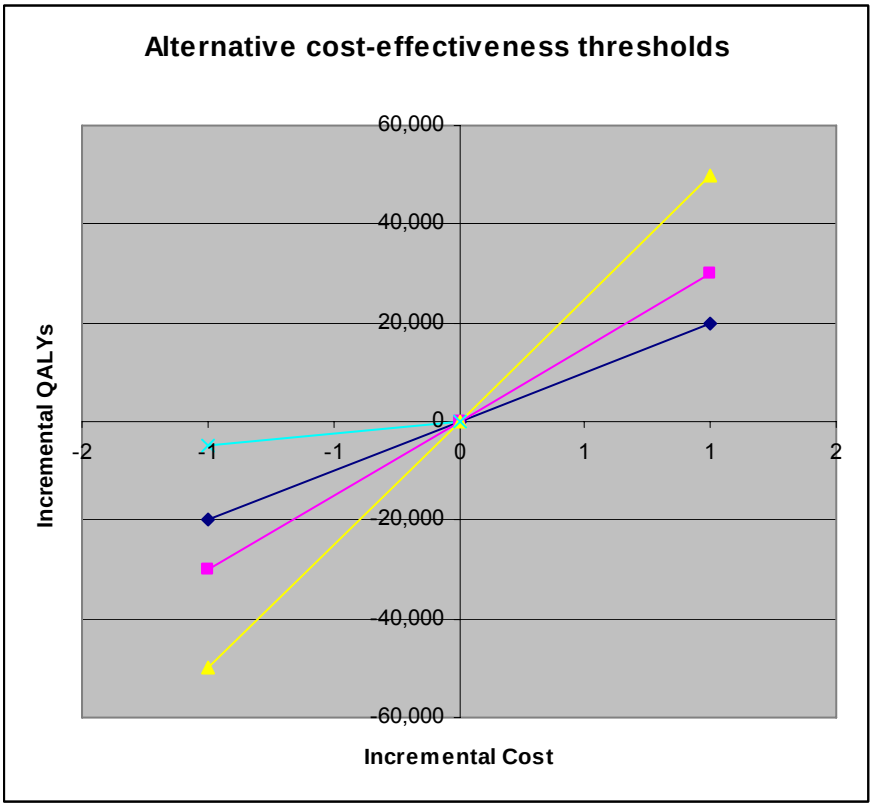
In many cases papers have just reported a cost per life year gained. In order to allow comparison between these studies and those that have estimated quality adjusted life years (QALYs), as is recommended by NICE (2004; 2006), life years have been converted to QALYs. This was done by applying a utility (QALY weight) to each life year (Carande-Kulis et al., 2000). In this case we assumed that each additional life year would be worth a minimum of 0.99 based on the utility value of a hypertensive patient (CEA Registry), which essentially makes little difference to results. This allows a conversion to QALYs and a judgement using the criterion above.

Some papers compared behavioural change therapies (as a control) with other, usually pharmacological, interventions. We therefore interpreted ICERs as a reduction in services offered to the point of a behavioural change therapy. In this case ICERs need to be interpreted slightly differently, as set out below:

- Very unlikely to be willing to cut back services (<£20,001)
- Unlikely to be willing to cut back services (£20,001 - £30,000)
- Likely to be willing to cut back services (£30,001 - £50,000)
- Very likely to be willing to cut back services (£>50,000)

Figure 1 shows the alternative cost-effectiveness thresholds. If an intervention's ICER fell to the right of the £20,000 threshold line in the north-east quadrant, an intervention would be considered likely to be very cost-effective. If an intervention's ICER fell to the right of the £20,000 threshold line in the south-east quadrant, an intervention would be considered cost-saving. If an intervention's ICER fell to the right of the £20,000 threshold line in the south-west quadrant, it is very likely that an intervention would be considered for service cut back. An intervention with a reduction of £5,000 per QALY lost, as indicated by the highest line in the south-west quadrant, would be considered very unlikely to be a good candidate for reduction of services.

Figure 1: Alternative cost-effectiveness thresholds



4.0 Results

4.1 Overview of papers reviewed

4.1.1 *Background data*

Figure 2 shows the spread of studies included by year. Six studies fall in the first third, and ten each in the latter two thirds. Most studies (43%) have a US-focus and only 3 (11%) papers provide a UK-based analysis. The remaining studies focus on mainland Europe, with the exception of 1 Australian study and one mixed European study which was used to develop costs for a cost-effectiveness analysis in Australia (see Figure 3).

Figure2: Year of publication of the 26 included papers

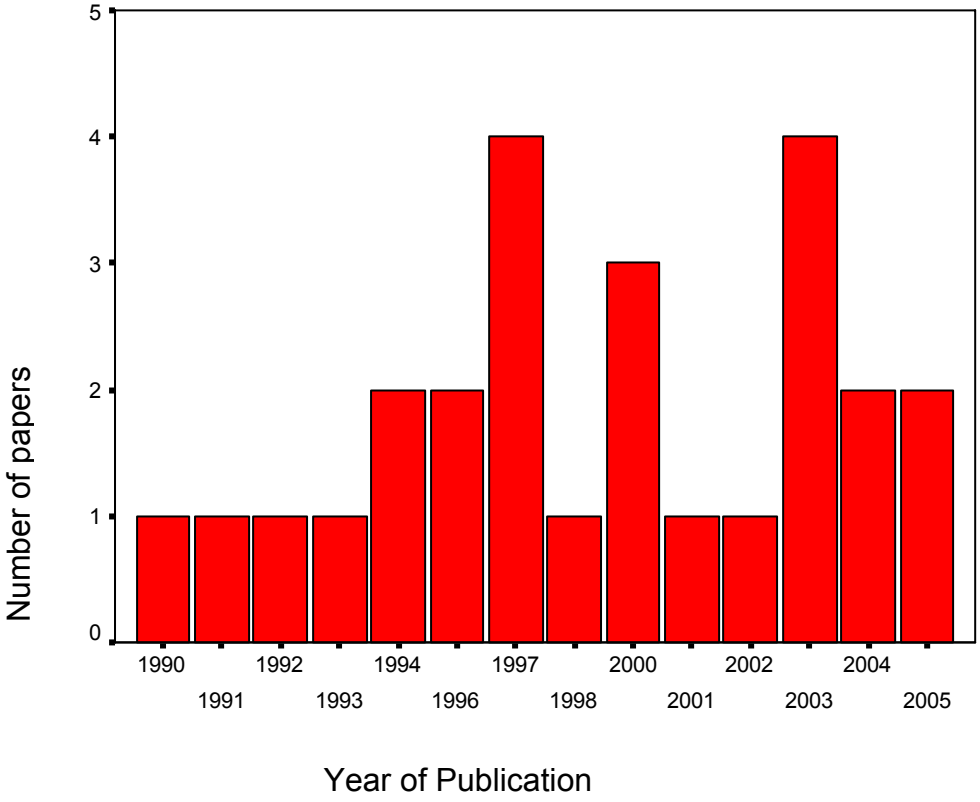
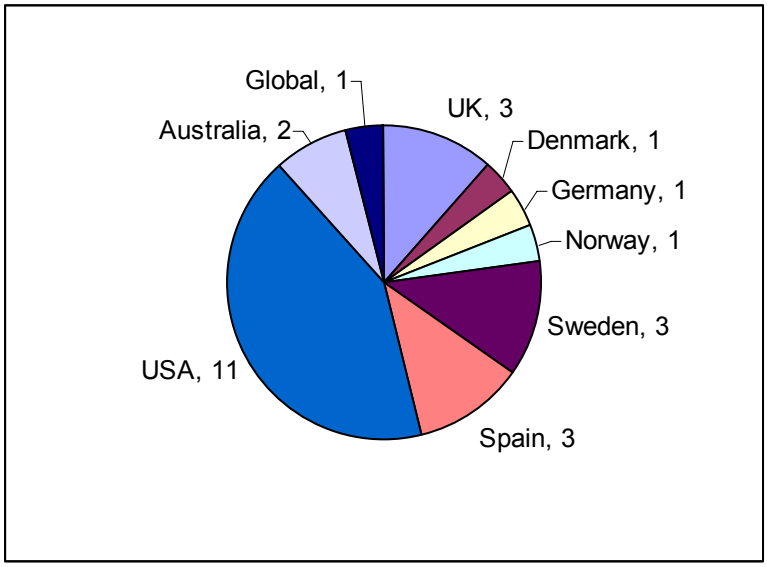


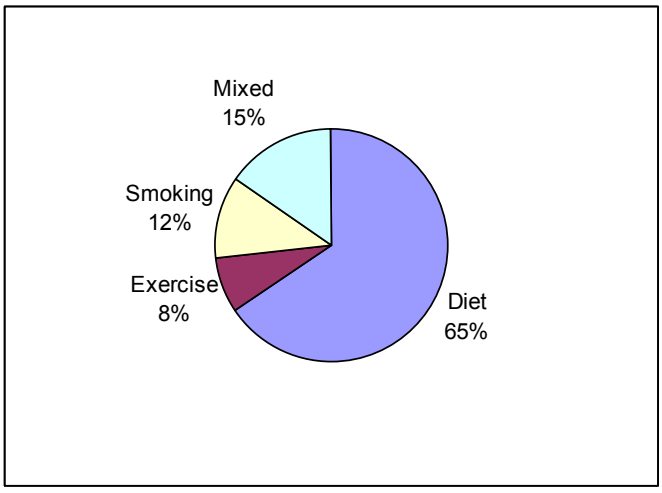
Figure 3: Study countries



Seven studies named the funding source for the evaluation and all received funding from publicly financed national or international bodies. Of the three studies that named the funders of the intervention studies, all were publicly funded. They included a county council, heart foundation, national delivery programme, department & school of public health and research institute.

Figure 4 shows that most papers focussed on diet related interventions (65%) followed by interventions aimed at multiple risk factors (15%), smoking cessation programmes and, lastly, programmes designed to change exercise behaviour.

Figure 4: Risk factor focus of papers studies



4.1.2 Population characteristics

The majority of studies (88%) considered adult and older adult populations and only diet-related interventions consider children (see Table 6). 77% of papers included both males and females and 20% of papers only males. Ethnicity was only reported in two studies and was confined to the categories 'white' and 'black'.

Table 6: Type of intervention by age grouping of population studied.

Age/Life stage	**Behaviour change intervention**				***Total***
	Diet	**Exercise**	**Smoking**	**Mixed**	
Older adults	0	1	0	0	*1*
Adults & older adults	15	1	3	4	*23*
All (children, teenagers, adults & older adults)	2	0	0	0	*2*
Total	*17*	*2*	*3*	*4*	*26*

Table 7 shows that most papers focussed on populations at increased risk and targeted both populations and individuals in equal proportions. The most common setting was primary care although it was not possible to determine the setting for 5/26 papers and 7 were 'not applicable' because they were diet and exercise interventions that did not require attendance at a fixed setting (4 of which were population level interventions). These patterns don't appear to vary much by type of intervention although the combination interventions tend to be more evenly distributed across all categories. Further cross-tabulations (see Table 8) showed that the primary care setting was the focus of interventions aimed both at higher risk individuals and population groups.

Table 7: Intervention group by Target population by disease risk, target population and setting

		Diet	Exercise	Smoking	Combination	Total
Disease risk	Increased risk	9	2	2	1	14
	Population risk	5	0	0	1	6
	Population & increased risk	3	0	1	2	6
	Total	17	2	3	4	26
Target population	Individual	8	0	1	1	10
	Population	7	1	2	1	11
	Individual & population	2	0	0	1	3
	Community	0	1	0	1	2
	Total	17	2	3	4	26
Setting of intervention	Primary Care	5	0	1	0	6
	Community / community centre	1	0	0	1	2
	Work	0	0	1	1	2
	Mixed	1	0	0	1	2
	Hospital	1	0	0	0	1
	Home	0	0	0	1	1
	Does not apply	5	2	0	0	7
	Cannot determine	4	0	1	0	5
	Total	17	2	3	4	26

See Appendix 4 (data extraction manual) for definition of terms

Table 8: Disease risk by setting of intervention

	Setting								*Total*
Disease Risk	**Hospital**	**Primary Care**	**Community & Community Centre**	**Work**	**Home**	**Mixed**	**Does not apply**	**Cannot determine**	
Population risk	0	1	0	0	1	0	2	2	*6*
Increased risk	1	5	1	0	0	1	4	2	*14*
Population & increased risk	0	0	1	2	0	1	1	1	*6*
Total	*1*	*6*	*2*	*2*	*1*	*2*	*7*	*5*	*26*

4.1.3 Interventions and their comparators

The majority of papers (70%) only compared interventions with no intervention. However, 2 studies (8%) compared behaviour change interventions with each type of the following; alternative ways of delivering a similar behaviour change intervention; drug therapies; screening plus treatment; and doing nothing as well as drug therapy.

Full details of the types of interventions are set out in Section 4.2 and Appendices 5 (Tables 5.1-5.4) and 6 (Tables 6.1-6.4).

4.1.4 Methodology of studies

Table 9 shows that cost-effectiveness analysis was the most common type of evaluation, followed by cost-utility analysis and that modelling dominated the study design of these evaluations. Only four studies conducted economic evaluations alongside primary studies of effectiveness and, of these, three were randomised controlled trials. Table 10 shows that the 'sample size' of studies was largely unreported and that this is attributable mostly to the modelling studies. Of the papers using modelling, 54% predominantly derived results from epidemiological / regression models and 35% from Markov models. We noticed frequently that there was insufficient detail given about the exact type of model used or about the key parameters such as the number of individuals in a cohort, base age or for state transition models the number of cycles run[9].

Table 9: Type of economic evaluation by type of study design

Study design	**Analytic method**					***Total***
	Cost-effectiveness	**Cost-utility analysis**	**Cost-benefit analysis**	**Cost-consequences analysis**	**Cost-effectiveness & Cost-benefit**	
Quasi experimental	1	0	1	0	0	*2*
Modelling	10	4	1	3	0	*18*
Modelling with RCT	3	2	0	0	1	*6*
Total	*14*	*6*	*2*	*3*	*1*	*26*

[9] The total number of cycles equals the total amount of time a model is run for. As a result life years gained and QALYs will be influenced by the length of a cycle and the numbers of cycles run.

Table 10: Sample size of different types of study designs

	Study design			*Total*
Sample size	**Quasi experimental**	**Modelling**	**Modelling with RCT**	
< 500	0	0	1	*1*
500 - 9999	1	0	3	*4*
10,000 – 200,000	0	2	1	*3*
No information	1	16	1	*18*
Total	*2*	*18*	*6*	*26*

The perspective of analysis adopted by papers tended to be societal (36%) followed by government (20%), health care provider (20%), societal & health care provider (8%), other government department (4%). Each of the 3 studies (12%) from the UK presented an NHS perspective, with one also providing a societal perspective. 1 study did not specify the perspective.

Table 11 depicts the types of outcome measures used in the evaluations. It shows that the main outcome measures used in these economic evaluations focussed on avoiding CHD related events or additional life years gained. Only 30% of studies provided information on QALYs or DALYs. It indicates a potential problem with this literature in being able to compare results with other NICE recommended procedures that do provide incremental cost effectiveness ratios (ICERs) using QALYs. The sources of data used to predict effectiveness varied widely in type and quantity across studies. Apart from extensive referencing of specific papers and studies, such as the North Karelia project and Stanford 3-city project, the most extensively referenced data was:

- The Framingham study (n=11),
- Population census, surveys and life tables (n=11),
- Other risk factor studies (n=9),
- Trial data (n=7),
- Meta analysis and other quantitative reviews (n=5),
- US National Health and Nutrition Examination Survey (versions 11 and 111) (n=5),

- Beaver Dam and other health outcomes studies (n=5),
- Hospital admission, discharge and death statistics (n=4),
- Patient/client questionnaires (n=3),
- Coronary Heart Disease Policy Model (amongst many other sources).

Table 11: Type of outcome measures used by focus of study

	Diet	Exercise	Smoking	Combination	Total
Cholesterol: LDL / HDL /Total	2	0	0	1	3
Smoking: stop / reduce / rate / currently	1	0	1	2	4
Avoided: CHD / MI / events / Hospital / Incidence	7	2	2	3	14
Death/avoided death from CHD/MI	3	0	2	2	7
Life years / survival	9	1	2	1	13
QALYs / DALYs	7	0	0	1	8
Hypertension blood pressure	1	0	0	3	4
Other benefit / health outcomes	6	1	1	2	10

Table 12 shows that, in nine studies (see darkened cells), the time frame of the intervention and time horizon of analysis was the same and that, of these, four lasted for up to 10 years. In seven studies neither the length of time the intervention ran nor was the analytic horizon clear. In four studies the intervention was assumed by the authors to be permanent whilst analysis covered 7, 20 and 45 years (with 1 unclear). Three papers presented an analytic horizon longer than the time horizon of the intervention, by 9 years, 22 years and infinity.

Table 12: Time horizon of intervention by analysis

Time horizon of intervention (years)	Time horizon of analysis (years)														Total
	1	5	6	7	10	20	25	30	45	49	50	58	Perm-anent	Un-clear	
1	1				1								1		3
3							1								1
5		2													2
10					1										1
20						1									1
25							1								1
30								1							1
50											1				1
58												1			1
100														1	1
Permanent				1		1			1					1	4
Unclear			1							1				7	9
Total	*1*	*2*	*1*	*1*	*2*	*2*	*2*	*1*	*1*	*1*	*1*	*1*	*1*	*9*	*26*

All papers reporting a discount rate (n=19) also reported QALYs, DALYs or life years saved and all used the same rate for costs and outcomes. Most studies (53%) selected a 3% discount rate, followed by 5% (in 32% of studies), with one study each using 4%, 6%, and 7%.

Of those undertaking sensitivity analysis (n=19), ten provided a one-way analysis, 6 undertook a two-way and 3 undertook a three/multi-way analysis. Eleven conducted deterministic sensitivity analysis and eight undertook a probabilistic analysis. The variables most frequently subjected to sensitivity analysis were; treatment cost (n=10), compliance or rate of decline in effectiveness (n=8), the relationship between short and long term impact (n=7), size of effect in the short and long term (n= 6 & 5), followed by utility scores, discount rates and life expectancy, each of which was examined in 5 papers. Noticeably, the cost of the intervention itself was only examined in 4 cases, as was the lag between implementation of an intervention and its effect.

The principal resource use costed was the change in annual or life-time treatment costs from CHD related events (n=16), with only one study specifically mentioning costing treatment of additional non-CHD events. Following this the direct costs of

staff time (n=10), drugs (n=6) and other consumables (n=11) connected with the intervention were assessed as well as costs of screening (n=4) and impacts on patient costs (n=6). The sources of resource use and cost data tended to be poorly reported. However, when stated, the most frequent sources used included published studies (n=14), local wage lists or fee schedules (n=9) followed by primary data (n=4) and routine data sources, including claims databases (n=4). 2 of the UK studies used national reference costs. Fuller details can be found in Appendix 6.

4.1.5 Availability of information on factors influencing the interventions' effective implementation

Only 30 of a possible 208 responses (8 questions applied to 26 papers) to the eight pieces of evidence were generated. No evidence was provided on how the way that the intervention is carried out affects the intervention and only one piece of evidence existed for three other questions. Most evidence was concentrated on how effectiveness and cost-effectiveness was influenced by characteristics (n=12) such as age (n=11), gender (n=12) risk factors (Murray et al, 2003; Plans-Rubio, 1998; Prosser, et al, 2000; Stinnet 1996; Tosteson et al, 1997), and one paper showed the impact of race (Bendich et al 1997).

Less evidence was presented on the impact on effectiveness and cost-effectiveness of the content of the intervention (n=5), barriers (n=6), and intensity of an intervention (n=3). Descriptions of 'content' are captured in section 4.2. With reference to the influence of the intensity of an intervention, Finklestein et al (2002) found that an enhanced intervention was more effective. Kristianson (1991) showed that whilst diet therapy was more effective than population wide promotion of healthier eating it was not as cost-effective, and Blake et al (2003) argued that targeted statin treatment was more cost-effective. The main barriers we noted mainly concerned the agencies required to implement an intervention. For example, firms need to take-up work based interventions, politicians and the public to accept central intervention in regulatory and legislative change such as food labelling or fortifying basic foods. Alternatively the strength of the tobacco industry may affect take-up of smoke-free work-place legislation. Finally, Johanesson (1992) pointed to the political will

required to take funding decisions for very expensive technologies in the face of other competing resources.

4.1.6 Robustness of evidence:

Table 13 shows the mean % scores and distribution for each of the areas of behaviour change. Overall it shows that the papers reported a reasonable level of data required by the Drummond criteria (See Appendix 7 for full list of items and results per paper). The better reported evidence to date appears to be focussed on exercise and smoking. Considering the distribution of % scores on the Drummond scale revealed 3 studies that were particularly badly reported (see Figure 5). Studying the count data for each individual question revealed that all studies reported their research question and stated the primary outcomes clearly. Other questions reported well included:

- Perspective
- Form of economic evaluation
- Sources of effectiveness data used
- Currency
- Presenting disaggregated outcome data relevant to the study question
- Reporting conclusions with appropriate caveats.

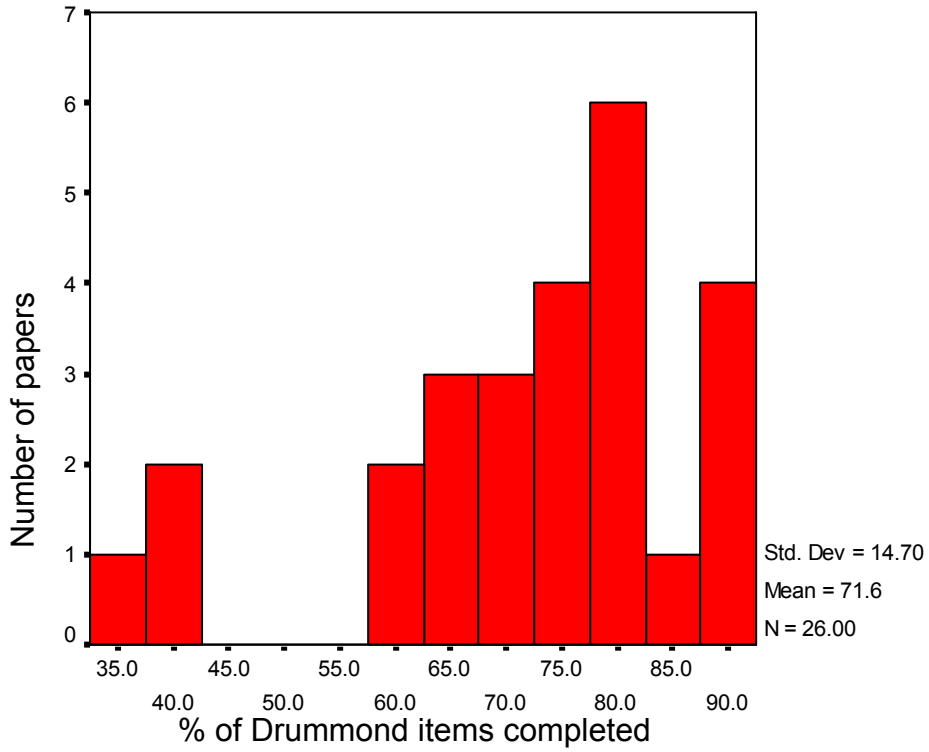
The aspects of studies that tended to be reported poorly (with at least 1/3rd not reporting information) were:

- Reporting the quantities of resource use and costs separately and their methods of construction,
- Adjustments to currencies and prices,
- Choice of model used and key parameters on which it is based, and
- Not justifying the lack of discounting
- Not justifying the choice of variables for sensitivity analysis

Taking the three questions on sensitivity analysis together raises concerns about how well the robustness of conclusions has been tested as over 25% of studies did not conduct any sensitivity analysis and, of those that did (n=19), over 63% did not

state the approach used and 30% did not give the ranges over which variables were tested.

Figure 5: Histogram of the Drummond % scores for all papers



The % of papers useful for our future modelling is disappointingly low (see Table 13). This data will be particularly unhelpful for specifying resource use, cost data and utility values although a few papers could help with structuring a future model as well as providing some relevant data on transition probabilities and outcomes.

Table 13: Mean scores for all three measures

		N	Mean	Std. Deviation	Minimum	Maximum
Relevance to modelling	Diet	17	21.0	19.0	0.0	57.1
	Exercise	2	35.7	10.1	28.6	42.9
	Smoking	3	14.3	14.3	0.0	28.6
	Mixed	4	10.7	7.1	0.0	14.3
	Total	***26***	***19.8***	***17.2***	***0.0***	***57.1***
Drummond 35 item	Diet	17	70.1	16.7	34.8	88.9
	Exercise	2	81.0	9.8	74.1	88.0
	Smoking	3	76.5	12.1	65.2	89.3
	Mixed	4	69.3	8.9	62.5	82.1
	Total	***26***	***71.6***	***14.7***	***34.8***	***89.3***
Transferability score	Diet	17	57.2	25.3	14.3	100.0
	Exercise	2	71.4	20.2	57.1	85.7
	Smoking	3	76.2	8.2	71.4	85.7
	Mixed	4	53.6	13.7	42.9	71.4
	Total	***26***	***60.0***	***22.5***	***14.3***	***100.0***

Table 13 also shows the reporting of Pang's transferability criteria. To date, evidence from the papers on smoking are most consistent and most easily transferable. Studying the individual count data by question showed that the target decision maker was easily inferred but that up to 40-60% of papers did not report: the year of effectiveness data; how generalisable results would be to another setting or provide any analysis to help such transfer; the life expectancy used; or anything about levels of compliance, either measured or assumed.

4.2 Evidence statements

This section summarises the quality of evidence and what is know on a paper by paper basis, with supplementary data including adherence to the Drummond guidelines on reporting economic evaluations and Pang's transferability criteria provided in a series of Tables (14-18). Interventions are also classified by how likely they are to be cost-effective additions (cost saving; £0-£20,000/QALY very cost-effective (CE); (£20,001-£30,000/QALY reasonably CE; £30,001-£50,000/QALY unlikely to be CE; ≥£50,000 QALY very Unlikely to be CE or cost-effective withdrawal

of service). Further information is presented in Appendices 5 and 6 upon the context of interventions and the methods used in the papers, by risk factor and the focus of interventions.

Information on study context in Appendix 5 includes who provides the behaviour change intervention, the target population of the intervention, where the intervention is set, the disease/state of the study participants e.g. at increased risk of developing CHD, details of the intervention, details of the study comparator e.g. no intervention of any kind, the time horizon of intervention and who funded the study. Appendix 6 contains details of the methods used in each paper/study; analytic model, perspective adopted, study design, health outcomes considered (measures and sources), costs (list of resources costed, sources of resource use data, sources of unit costs, year of costing, discount rates applied (benefits and costs), sensitivity analysis (type and variables used) and the time horizon of the analysis.

4.2.1 Exercise

The UK-based study by Munro et al (1997) suggested that regular aerobic exercise instruction in the over 65s led by a qualified instructor compared with no intervention is very cost-effective (varying between £111-£1661 per life year saved as a result of including savings or decreasing incidence rates). However, the authors felt that further testing of effectiveness was needed. Short and long term effectiveness data: both grade 2.

The US-based study by Jones et al (1994) suggested that if people aged 35-74 years walked 1 hour a day for 5 days a week compared with having a sedentary lifestyle it would be cost saving. Results were most sensitive to the monetary value placed on exercise time but not high rates of recidivism. Short and long term effectiveness data: 4 and 2 respectively.

Table 14: Summary, by paper of main finding on the cost-effectiveness of exercise interventions in reducing CHD

Ref.	Objective	Characteristics of sample		Main findings and conclusions	Findings of Sensitivity Analysis	Drummond %	Relevance to modelling score	Transferability score %	Short (long) term Effectiveness scores
		Size, age, gender	Country						
Munro et al. (1997)	To estimate the likely costs, health benefits and consequences for the National Health Service which might result from a publicly funded program of regular exercise made available to a population of 10000 people over the age of 65	10,000 males &females, aged over 65	UK	Annual cost of exercise programme is £946,141.9 per 10,000 participants with annual reduction of 52 CHD & hypertension deaths, 124 inpatient episodes averted plus a saving of £192,062.3. The promotion of physical activity in the elderly has considerable potential to contribute to the achievement of *the* targets of reduced coronary heart disease, stroke and mental health. Locally provided exercise facilities funded by NHS would be innovative and controversial. An RCT is needed to determine effectiveness. The cost per life year saved (coronary heart and hypertension) = £1,442.7 and the cost per avoided event is = £6,061.7.	Sensitive to inclusion of unmeasured savings (30% of the measured) and the decrease of incidence rates (by 50%) which increased cost/life year by £1602.9 for all health conditions. Cost per LYS varies £110.7-£1660.5	89	29	86	short grade 2 (long grade 2)
Jones et al. (1994)	To quantify the cost-benefit relationship of walking to prevent Coronary Heart Disease	Males & females aged 35-74	USA	Walking 1 hour per day for 5 days per week as an intervention to prevent CHD can have a significant impact from an economic and public health perspective. If 10% of sedentary adults with a relative risk of CHD of 1.9 took up this intervention it is estimated that $5.0 billion would be saved annually.	The cost-benefit of the walking programme was sensitive to the monetary value placed upon exercise time. Results were relatively insensitive to changing estimates of the costs and rates of injury and subsequent recidivism, even very high levels had relatively little impact on the overall cost-benefit.	79	43	57	Short grade 4 (long grade 2)

See Appendix 5 and 6 for context and methods

4.2.2 Smoking

A US-based study by Ong and Glantz (2004) suggested that implementing a nation-wide smoke-free workplace policy delivered by government and employers compared with no intervention could save 6250 myocardial infarctions and 1960 deaths in 7 years and therefore save £169.5 million in treatment costs. However as the cost of implementing programme was not included, neither an ICER nor internal rate of return is known. Short and long term effectiveness data: both grade 2.

The Spanish-based study by Plans-Rubio (2004) suggested that physician-led medical counselling targeting smoking cessation at people aged 40-69 compared with no intervention is very cost-effective (£3,764 per man, £8,821 per woman, and £206.8 per life year saved). Short and long term effectiveness data: both grade 2.

The Welsh-based study by Phillips et al (1993) suggested that the Heartbeat Wales Programme (targeted at 18-64yrs) compared with no intervention is very cost-effective (£116 per life year saved assuming a 10% impact of the programme). Short and long term effectiveness data: both grade 4.

Table 15: Summary, by paper of main finding on the cost-effectiveness of smoking interventions in reducing CHD

Ref.	Objective	Characteristics of sample		Main findings and conclusions	Findings of Sensitivity Analysis	Drummond %	Relevance to modelling %	Transferability score %	Short (long) term Effectiveness scores
		Size, age, gender	Country						
Ong and Glantz (2004)	To project the cardiovascular health and economic effects if all remaining US workplaces were made smoke-free	Males & females aged 35-64	USA	Making all US workplaces smoke free would result in health and economic benefits within one year. 1st year savings from prevented myocardial infarction (MI) and averted strokes were £38.6 & £8.9 million. Cumulative savings over 7yrs =£169.5 million from averted MI and £41.6 million from averted strokes. Assuming a steady state over 7 yrs would also prevent 6250 MIs and 1960 MI deaths. Reduction in passive smoking accounted for most (60%) benefits. Implementation of a nationwide smoke-free workplace policy would produce 1.3 million new non-smokers, cause a reduction in over 95 million packs smoked each year (from quitters and smokers), reducing cigarette consumption by 12.2%. The pre-tax value of forgone consumption = £1.7 billion.	None	65	14	71	Short grade 2 long (grade 2)
Pedro Plans-Rubio (2004)	To use the social welfare function to decide on allocation of resources between smoking cessation methods and lovastatin treatment of hypercholesterolemia for the primary prevention of CHD	2 samples used n=140 & n= 72,323. Males & females 40-69	Spain	Total annual treatment cost for smoking cessation using medical advice was £14,958,164.7 for men and £461,851.8 for women, the cost per person was £206.8 for either gender. Total health gain in life years for men was 3973.6 years or 0.055 per man. Women gained 665.3 life years in total and 0.028 per woman. The ICERs were £3,764.4 per life year for men and £8,821 per life year for women.	None	75	0	71	Short grade 2 long (grade 2)
Phillips, et al. (1992)	To apply economic principles and techniques in evaluating a health promotion programme	Males & females aged 18-64	UK, Wales	Large scale benefits to the NHS and the economy as a whole can be derived from reductions in smoking. The cost-benefit analysis, on both evaluation cases, showed that the HBW programme (public education campaigns along with supportive policy and infrastructure change) generates positive net present values even at impact rates as low as 10%. Combining the costs and savings of the programme with the number of working life years saved (assuming a 10% impact rate) produces the net cost per working life year saved of £116.4.	For all impact rates and for all variations the net present value of the economic appraisal is insensitive and always remains positive	89	29	86	Short grade 4 long (grade 4)

See Appendix 5 and 6 for context and method

4.2.3 Combination Interventions

The Swedish-based study by Lindgren et al (2003) suggested that advice on diet and exercise for people aged 60 or over from a physician or dietician compared with no intervention is very cost-effective (ICER is £7,574 per life year saved from a health service perspective assuming a declining effect over time and £893 under the most favourable assumption of a constant effect over time and from a societal perspective). Short and long term effectiveness data: 1 and 2 respectively.

The Swedish-based study by Lindholm et al (1996) suggested that health education, health promotion and advice on lifestyle factors through media, food labelling, sports clubs, screening and advice on risk factors by health care personnel and targeted at 30-60 year olds compared with annual screening[10] for cardiovascular risk factors by trained nurses ranges from cost saving to being likely to be very cost-effective (varying between net savings to £1,660 per life year saved from a societal perspective and between £123-£451 from a health sector perspective). The most optimistic scenario (societal perspective & regression compensation[11]) became cost saving even at 5% discount rates. Short and long term effectiveness data: both grade 2.

Finkelstein et al's (2002) US-based study suggested that providing women aged between 50 and 65 with CVD screening, computerised risk appraisal and individual life style counselling sessions (lasting between 3-8 hours) plus the opportunity to join group intervention activities to improve physical activity and nutrition compared with no intervention is very cost-effective (£3,635 per life year gained). However, no sensitivity analysis was conducted and the authors noted the difference in effects was not statistically significantly different after 1 year. Short and long term effectiveness data: 1 and 2 respectively.

The Australian-based study (using data from the UK, Italy and Belgium) by Dalziel et al (2005) suggested that screening men aged 40-59 and providing high risk men with 4x15 minute screening visits in 1 year (and contacting non-high risk men after 2

[10] No comparison of less frequent check ups was made
[11] Covarying out (removing) the impact of variables to leave the direct relationship between the variables of interest e.g. removing the impact of age.

years) by a workplace-based doctor or nurse that focussed on general health education on diet, smoking, exercise and treatment of hypertension compared with no intervention costs £43,389 to reduce one CHD event in the all risk population and £22,716 in the high risk population. However, as no information was given on expected change in life expectancy it is difficult to predict how cost-effective this would be relative to other interventions. Short and long term effectiveness data: both grade 2.

Table 16: Summary, by paper, of main finding on the cost-effectiveness of combination interventions in reducing CHD

Ref.	Objective	Characteristics of sample		Main findings and conclusions	Findings of Sensitivity Analysis	Drummond %	Relevance to modelling %	Transferability %	Quantity of short (long) term
		Size, age, sex	Country						
Lindgren et al. (2003)	Develop a general model to simulate costs and effects of various preventive measures. (Cost-effectiveness of exercise vs. diet vs. diet vs. both in preventing CHD)	813 males & females aged 60-109	Sweden	Model predicts lower costs and higher effectiveness for dietary advice compared to other strategies. Total life years saved (YLS) = 0.0228 compared to no intervention, but if there is no decline in the intervention effect LYS=0.0997. From a societal perspective incremental cost = £ 221.9(or £1,082.2 with no decline). Dietary advice is the most cost-effective strategy among 60-year-old men in Stockholm. The validity of that conclusion is independent of study's perspective (societal or health-care payers). ICER from health sector & other perspective = £7,573.9 (declining effect)/893.1 (remaining effect). ICER from societal (savings included) = £9,748.1 (declining effect), £10,859.7 (remaining effect) [savings included].	1. Remaining effects (extending survival) raises other health care costs making diet less cost-effectives from a societal perspective, 2. From the payer's perspective remaining effects (survival) improves ICER, 3. Diet gave most QALYs; Payer perspective + Remaining effects =£1,040.4 /QALY	82	14	43	Short grade 1 long (grade 2)
Lindholm et al (1996)	To evaluate the cost-effectiveness and equity of a CHD prevention programme.	3081 males & females aged 30-60	Sweden	Strategy resulted in a profound change in dietary habits and an appreciable lowering of cholesterol concentrations (mean serum cholesterol level in intervention group declined by nearly 20% in the first 6 years of the intervention) but with regard to smoking and blood pressure no change took place in the intervention area. Results differed by age and gender but not by social class. Interventions were most effective for the upper middle-aged group (55-64 years of age). Total cost per year = £5,687.3. Total societal cost for 10 years discounted at 5% = £40,440.6m. The intervention was cost-effective even under conservative assumptions. With a societal perspective, cost per life year saved ranged from net savings to £1,660. (£122.5- £451.2 with health system perspective).	1. Cholesterol is likely to significantly effect cost-effective 2. Most optimistic scenario (cost savings =societal & regression compensation) resulted in cost savings at 0% and 5% discount rates 3. Increasing costs by 50% and reducing savings by 50% increased the ICER to £17,970.4 per life year saved	64	14	43	Short grade 2 long (grade 2)

See Appendix 5 and 6 for context and

Finkelstein et al. (2002)	The cost-effectiveness of providing CVD screening and enhanced lifestyle interventions (EI) compared to CVD screening and minimum interventions (MI) to older uninsured and underinsured women.	1586 females aged 50-65	USA	The incremental cost of EI was $191. CHD risk was reduced but EI was not significantly better than MI. During the 1st year study period, the 10-year probability of CHD decreased from 9.4% to 9.2% in the MI group and from 10.3% to 9.8% in the EI group. Nearly £3,635.4 would be necessary for 1 extra life-year gained above and beyond any gains that result from participation in the MI. Health Sector Perspective (no cost savings) = £3,635.4 per life year gained Future research is needed to assess the impact of lifestyle interventions targeting financially disadvantaged women.	None	63	14	71	Short grade 1 long (grade 2)
Dalziel et al. (2005)	Cost-effectiveness of workplace-based multi-factorial prevention of coronary heart disease.	21,917 in the first year & 3,076 in the 4th year male subjects, aged 40-59 (sample mean 49)	UK, Italy & Belgium	Reduced CHD risk by 1% from baseline at a cost £874 per participant in the UK (Belgium = £1,765.5 and Italy = £1,826.6). In the UK the cost per 1,000 participants at 4 years was £143,662. Baseline predicted CHD was 3.4 for all and 7.0 for the high risk. The % change at 4 years was -12.8% for all and -19.1% for the high risk. Predicted CHD events at follow-up were 3.0 for all and 5.7 for high risk. Cost per reduction in 1 CHD event were £43,388.5 and £22,715.6 respectively for all and high risk (Health Sector Perspective, no cost savings)	None	68	0	57	Short grade 2 long (grade 2)

See Appendix 5 and 6 for context and method

4.2.4 Diet

The US-based study by Stinnett et al (1996) suggested that providing dietary advice based on the Step-1 diet with follow-up counselling in an out-patient setting to people aged 35-84 compared with treatment by Niacin reduced both costs and QALYs (at a rate of; £1150 for high risk women aged 55-84, £785 for moderate risk males, £2330 for moderate risk females, £2880 for low risk males and £5173 for low risk females). Therefore reducing Niacin to step-1 diet would be very unlikely to be considered a cost-effective cut back of services. Short and long term effectiveness data: 2 and 1-2 respectively.

Phillips et al's (2000) UK-based study suggested that using Flora pro.activ in conjunction with a healthy diet compared with no intervention would achieve a 14% reduction in total cholesterol, which has the potential to reduce 5-year cardiac mortality 38% and save £100.4m spending on treatment of myocardial infarction per year. However, as no information was given on expected change in life expectancy it is difficult to predict how cost-effective this would be relative to other interventions. Short and long term effectiveness data: 1+2 and 2 respectively.

The Australian-based study by Kinlay et al (1994) suggested that providing males aged 35-64 with *either* a population education programme via the mass media (based on the Stanford Three Cities Study) aimed at encouraging people to choose different food to reduce cholesterol *or* a moderate risk strategy that providing GP-based counselling plus the drug cholestramine for those with cholesterol >5.5mmol/L dominated the option of prescribing cholestramine for those with cholesterol >6.5mmol/L. The study also showed that the population option had a lower ICER (£316) per disease case averted compared with the moderate risk strategy (£9,054), although more benefits were potentially achievable with the latter and therefore would be preferred with a threshold value of £20,000/QALY. However, as no information was given on expected change in life expectancy it is difficult to predict how cost-effective this would be relative to other interventions. Short and long term effectiveness data: 1 and 2 respectively.

Table 17: Summary, by paper of main finding on the cost-effectiveness of diet-related interventions in reducing CHD

Ref.	Objective	Characteristics of sample		Main findings and conclusions	Findings of Sensitivity Analysis	Drummond %	Relevance to modelling %	Transferability score %	Quantity of short (long) term effectiveness data
		Size, age, sex	Country						
Stinnett, et al. (1996)	To evaluate the cost-effectiveness of alternative diet-and drug- based clinical strategies for cholesterol reduction in US adults according to patients' CHD risk factor characteristics.	Males & females aged 35-84	USA	Compared with Niacin, diet as a primary prevention strategy provided 18,591 less QALYs at a saving of £21,382,130 for high risk (LDL ≥ 190 mg/dL, HDL < 35 mg/dL, cigarette smoker, DBP ≥ 105 mmHg) females 55 to 84 years of age. For moderate risk (LDL ≥ 190 mg/dL, HDL < 35-49 mg/dL, non-smoker, DBP 94-104 mmHg) males' diet provided 150,432 fewer QALYs at a saving of £118,155,251 compared to Niacin and for females the reduced QALYs and savings were respectively 161,873 and £377,251,508.. For low risk (LDL 160-189 mg/dL, HDL ≥ 50 mg/dL, non-smoker, DBP <95 mmHg) males diet provided 303,806 less QALYs at a saving of £875m compared with Niacin and for females the reduced QALYs and savings were respectively 832,028 and £4,304m.. Transferring suitable adults from Niacin to diet as a prevention strategy would reduce QALYs in exchange for cost savings that could be invested in other health services.	Assuming that reduced serum TC caused an increase in non-CHD mortality, resulting in reduced quality adjusted survival compared to the base case. Results were relatively insensitive to changes in utilities. Substituting survival in favour of QALYs did not affect conclusions. Varying the discount rate had virtually no effect on results.	89	0	57	Short grade 2 long (grade 1+2)
Phillips et al. (2000)	To appraise the extent to which Flora pro. activ can be expected to reduce the risk of CHD and the cost implications of this approach to risk factor management	Males & females aged 40+	UK	It seems likely that when Flora pro. activ, in combination with a healthy diet, achieves a reduction in total cholesterol of 14%, this has the potential to reduce 5-year cardiac morbidity by approximately 38%. On this basis, if used by the adult population as a whole, NHS expenditure on MI could fall by £100.4 million per year (range £30.4-£212.6 million). A 25% reduction in the risk of CHD would equate to 250,000 coronary events prevented over a period of 5 years if the whole population aged 40+ were to use Flora pro. activ in conjunction with diet. Flora pro. activ not only is cost-effective, but can also be adopted into an existing risk factor management programme, at no additional cost to the NHS, and offers the potential to generate considerable future savings.	1. If we assume that only a 5% reduction in total cholesterol is achieved in practice, then the likely estimate for 5-year savings will be reduced to £273.3 million (£54.9 million per year) 2. If there is only a 15% reduction in risk for every 10% reduction in total cholesterol, then the saving could be reduced to as little as £151.8 million (£30.4 million per year).	42	14	43	Short grade 1+2 long (grade 2)

See Appendix 5 and 6 for context and method

Kinlay et al.(1994)	To compare the cost-effectiveness of two screening strategies and a population strategy for lowering blood-cholesterol to prevent coronary heart disease	Males aged 35-64	Australia	The population strategy reduced cholesterol by 3%, prevented 116 (5.46%) coronary heart disease events. The cost of implementing the strategy was £4,256,477.0. Cost per avoided event was £36,693.6 and the medical resource costs saved was £413,639.5. The moderate/high risk strategy reduced cholesterol by 4.9% with diet 8.5% by cholestyramine, prevented 144 (6.77%) coronary heart disease events. The cost of implementing the moderate/high risk strategy £41,713,313.2. Cost per avoided event was £290,216.3 and the medical resource costs saved was £513,483.6. The high risk strategy reduced cholesterol by 4.9% with diet 8.5% by cholestyramine, prevented 104 (4.9%) coronary heart disease events. The cost of implementing the high risk strategy was £39,410,721.5. Cost per avoided event was £379,165.7 and the medical resource costs saved was £370,849. After calculating the ICERs, the reviewers found that the high risk strategy was a dominated option and that the ICER (without cost savings) and that the population strategy had an ICER of £316.1 and mod/high risk strategy was £9,054.1 per disease event prevented. With medical resources saved both were cost saving.	1. For the "worst-case" assumptions the population strategy would cost less than one-tenth of the other strategies per CHD event saved (£110,045.3per discounted event saved), 2.For the "best-case" assumptions the population strategy would be less than one-tenth the costs of other strategies (£18,788.3 per discounted event saved), 3.Small changes in blood cholesterol across the whole community will lead to very large changes in the number of CHD events prevented.	81	14	57	Short grade 1 long (grade 2)
Johannesson & Fagerberg (1992)	To compare dietary and antihypertensive drug treatment in obese men with mild hypertension in economic terms	31 males aged 40-69	Sweden	The cost-effectiveness ratios in the cost-effectiveness scenarios were very high for diet treatment compared with no treatment and this is supported by the cost-benefit analysis, where treatment results in a loss. This trial had high treatment costs (total treatment cost was £744.8 for the diet group and £705.9 for the drug group), mainly due to the large number of consultations made. Total cost per patient ranged between £653.7 and £717.7, effects ranged between 0.002 and 0.31 life years gained and cost per life year gained ranged between £20,252.2 and £358,829.4. In 2/5 scenarios, diet was more effective & more costly (ICERS varied £4,104.0 – £18,289.4). In 3/5 scenarios diet was dominated (£79.6 -£98.9 more costly and providing 0.005 - 0.015 less life years than treatment with atenolol).	Not stated	79	0	86	Short grade 1+4 long (grade 2)
Services, D. o. H. a. H. (2003).	To estimate the costs and effects of stating the trans fatty acid content of food on labels.	Males & females	USA	Food labelling should be implemented. The median cost of the intervention including savings over 20 years discounted at 3% was £8,567,990.3. Assuming that only LDL-C changed due to trans fatty acid and this resulted in a reduction of CHGD risk of 0.052%. 2,600 life years were estimated to be saved over 20 years. The cost per life year saved was £3,213 from the perspective of the health service and other sector.	None	71	43	43	Short grade 2 long (grade 2)

See Appendix 5 and 6 for context and method

Bendich et al. (1997)	Translate risk reduction estimates based on vitamin intake into estimates of potential savings from avoidable US hospitalizations	Males & females	USA	Compared with other preventive interventions, vitamin supplementation appears to yield benefits relatively quickly. This is so for vitamin E-based cardiovascular disease prevention. Daily vitamin E supplementation at 100 IU/day or more could cut £3.3-£3.9billion in annual hospital charges for men and £2.7-£3.3billion for women. Potentially, as much as £4.0-£4.8billion of annual US hospital charges for all of these coronary outcomes could have been avoided if the 65.5 million Americans over the age 50 in 1992 had consumed at least 100 IU of supplement vitamin E daily.	Not stated	42	0	57	Short grade 1+2 long (grade 2+4)
Assmann & Schulte (1990)	Brief review of primary prevention strategy for CHD in West Germany and cost-benefit analysis of treatment strategy	Males & females	Germany	The number of CHD events will be reduced and the events will be transferred into higher age-bands, thus increasing quality of life. Cholesterol lowering interventions are unlikely to result in important direct savings to the health care system. Rather the benefit of treatment is reflected in terms of reduced mortality and improved quality of life. Approximate figures (taken from graph) indicated nutritional advice to the population saved 57 life years per 1000 individuals at a cost per life year saved of £6,319.8. The stringent diet (high risk strategy) saved 121 life years per 1000 individuals at a cost per life year saved of £8,005.2.	None	35	0	14	Short grade 2 long (grade 2)
Tosteson et al (1997)	"To estimate the cost-effectiveness of population-wide approaches to reduce serum cholesterol levels in the US adult population" See Appendix 5 and 6 for context and method	Males & females aged 35-84	USA	Educational interventions to lower serum cholesterol are likely to be reasonably cost-effective and possibly cost-saving over a broad range of assumptions, especially if total serum cholesterol is reduced by more then 2%. A population-wide programme with the costs (£4.2 per person per year) and cholesterol lowering effects (an average of 2% reduction in serum cholesterol levels of the Stanford 5 city) would prolong life at an estimated ICER of £2,740.3 per year of life gained (LYG). A programme with the costs £14.2 Per person in the first year and £7.2 each following year (as in the North Karelia study) would result in a reduction in serum cholesterol ≥ 2% and would prolong life at an ICER of £32,968.7/LYG. The ICER always falls below £30,000/LYG when programme cost per person is £4.2 except when non CHD mortality increases and serum cholesterol falls only by 1%. At an average programme cost of £14.2 educational interventions are never cost effective when non-CHD mortality rises or when serum cholesterol falls by less than 3%. Applying utilities to survival resulted in ICERS of £2,483.4 per QALY and £29,800.2 per QALY for the £4.20 and £14.2 interventions respectively.	1.The annual cost per person is very sensitive 2.Changes in serum cholesterol would have a greater impact on non-CHD death among individuals with low serum cholesterol than among individuals with high serum cholesterol	74	0	29	Short grade 2 long (grade 2)

Tice et al. (2001)	To examine the potential effect of grain fortification with folic acid on CHD events and to estimate the cost-effectiveness of additional vitamin supplementation (folic acid and cyanocobalamin) for CHD prevention	Both males & females aged 35-84	USA	Grain fortification with folic acid was predicted to decrease CHD events by 8% in women and 13% in men, with comparable reductions in mortality. Compared with grain fortification alone, treating all patients with known CHD with folic acid and cyanocobalamin over a 10-year period would result in 310000 fewer deaths and lower costs Providing vitamin supplementation beyond grain fortification to all men ≥45 years = £7,138.9 per QALY compared with screen and treat. Extending to men 35 to 44 had an ICER of £79,320.9/QALY and was not recommended. For women ≥75 yrs, the ICER for Vitamin supplementation compared with fortification was £951.9/QALY whereas the ICER for screening & treating women aged 65-74 was £4,362.6/QALY compared to treating all women ≥75 years. The ICER for treating all women ≥65 compared with screening & treatment £6,980.2 /QALY, rising to £30,935.1/QALY for ages 55-64. Folic acid and cyanocobalamin supplementation may be cost-effective among many population subgroups and could have a major epidemiologic benefit for primary and secondary prevention of CHD if ongoing clinical trials confirm that homocysteine-lowering therapy decreases CHD event rates	If the RRR of vitamin supplementation is 9% rather than 29%, primary prevention strategies treating everyone without measuring homocysteine levels would remain attractive at <£31,728.3/QALY gained for men aged 65+ and women aged 75+. If compliance with vitamin supplementation is only 50%, the treat-all strategy's incremental CE ratios remains <£39,660.4/QALY gained for men aged 45+ and women aged 65+.	89	29	71	Short grade 1 long (grade 2)
Plans- Rubio (1997)	To answer the questions: What are the estimated costs and benefits from a programme of individual dietary treatment in Spain? What is the CE ratio associated with the programme according to age, sex and cholesterol concentration? To which population groups should priority for detection and treatment be given?	Males & females aged 35-84	Spain	Programmes of individual dietary treatment of hypercholesterolemia could be considered an efficient use of health resources especially in men aged 35-64 years with very high cholesterol concentrations. Cost per life year gained ranged from £8,821 to £86,435.7 in men and £39,486.2 to £241,217.7 in women, according to age and initial cholesterol concentration. The lowest cost-effectiveness ratio was obtained in individuals with a cholesterol concentration of 9.7mmol/l (380mg/dl) aged 45-49 years in men and 50-54 years in women, and the highest one was obtained in those men and women with a cholesterol concentration of 5.7 mmol/l (220 mg/dl) aged 60-65 years. Cost per life year gained was lower than £35,171.3 in men aged 35 to 64 years with a cholesterol concentration higher than 6.2mmol/l (240mg/dl) and it was lower than £49,239.9 in women aged 35 to 64 years with a cholesterol concentration higher than 9.3mmol/l (360mg/dl)	1. Cost-effective results were sensitive to variations in cholesterol reduction, discount rates and programme costs 2.In contrast, cost-effective results were less sensitive to variations in non-compliance rate, lag period and CHD treatment costs 3.The highest effect (a reduction of 65%) was observed when a 0% discount rate was used for the health effects.	81	29	100	Short grade 2 long (grade 2)

See Appendix 5 and 6 for context and method

Prosser et al. (2000)	Evaluate how the cost-effectiveness ratios of cholesterol-lowering therapies vary according to different risk factors	Males & females aged 35-84	USA	Cost-effectiveness of treatment strategies varies significantly when adjusted for age, sex and the presence or absence of additional risk factors. However, it depends on the specific risk factor combination, not just the total number of risk factors. When risk factors were considered cost-effectiveness ranged from £1,507.1 per QALY for men 75-84 years old with four risk factors to £396,604.3 per QALY for women 35-44 years old with no risk factors Primary prevention with a step I diet seems to be CE for most risk subgroups but may not be CE for healthy young women. Health sector plus other ICER= £65,043.1 men 35-44 £30,141.9 women 75-84, £187,197.2 women 35-44	1. Lag time of less than two years resulted in better CE ratios for older patients and less favourable for younger patients. No lag resulted in 10% decline in CE for 50 year-old men 2. Varying the effectiveness of step I diet resulted in CE doubling for men 35-44 years old. CE decreased by 40% for women 75-84 years old. CE increased by 50% for women younger than 55 years old. 3. CE results were sensitive to assumptions about preference weights for quality of life. If QALYs were not calculated CE ratios would be reduced by 20%	78	14	71	Short grade 2 long (grade 2)
Olsen et al. (2005)	To compare costs and effects of providing nutritional counselling by a general practitioner with counselling by a dietician.	503 males & females	Denmark	The effects in terms of life years gained and life years gained without IHD were greatest and more distinct in the GP group, and the costs were greatest in the dietician group given the applied cost method. As a consequence, the GP group was the most cost-effective nutritional counselling strategy but it should be noted that both counselling strategies were relatively CE. The effect of nutritional counselling comparing GPs and dieticians is greatest when counselling is performed by a GP 0.919 years versus 0.0274 years. Even though the effects are significant, the gains were moderate (number of life years gained in the interval of 0.0384-0.1210 year with an average of 0.0528 year). The GP group was most cost-effective. The probability of acceptance of GP counselling would have been much greater than acceptance of dietician counselling: If the maximum willingness-to-pay for a life year gained was £2,303.4, counselling by a GP would have been accepted with certainty, whereas counselling by a dietician would not have been accepted at all. Health Sector Perspective (no cost savings_ ICER for intervention 1 = GP group was most cost-effective (£756.7 per LYS) compared with the dietician group (ICER =£5,526.9)	1. Identical time estimates for dieticians and GPs, resulted in lower intervention costs for the dietician group compared with the GP group. However, counselling by a GP was still the most cost-effective. 2. The inclusion of patient's use of time in the estimates, increased costs, and decreased cost-effectiveness but still showed that the GP group was most cost-effective.	81	14	86	Short grade 1 long (grade 2)

See Appendix 5 and 6 for context and method

Nallamothu et al. (2000)	To address the question "What are the potential clinical benefits and economic costs associated with a strategy of universal folic acid supplementation in at-risk groups within the general population?"	40-85 year-old men, 50-85 year-old-women	USA	Homocyst(e)ine lowering with folic acid and vitamin B12 supplementation could result in substantial clinical benefits at reasonable costs. Although the treat-all strategy was slightly more effective overall, If homocyst(e)ine lowering is considered, a screen and treat strategy is likely to be more cost-effective than universal supplementation. The screen and treat strategy remained cost-effective under rather unfavourable scenarios such as when a low level of CHD risk reduction was assumed. Health sector plus other ICER = (for treat-all strategy) = £486,395.9 per LYS in men & £996,327.1 per LYS in women. Screen & treat strategy = £10,669.3 per LYS in men and £21,574per LYS in women compared with no intervention	1. Cost per LYS in the screen and treat strategy remained below £39,225.5 when the relative risk of CHD-related death was reduced by at least 11% in men and 23`% in women 2 .In the treat-all strategy more than 25% in men and 60% in women were required for cost-effectiveness ratios to remain lower than £39,225.5 per life year saved. 3.After varying the threshold for treatment from 11 to 15µmol/L, it was found that a tHcy level of 11µmol/Lwas the most cost-effective for initiating supplementation in the screen and treat strategy 4.Cost-effectiveness ratios remained less than £251,043 per life-year saved even at extreme values, suggesting that uncertainty in cost-parameters had only a modest effect on outcomes.	85	43	100	Short grade 2,3+4 long (grade 4)

See Appendix 5 and 6 for context and method

Murray et al. (2003)	To assess the health effects, costs and cost-effectiveness of personal and population-based interventions designed to reduce the risks associated with high cholesterol concentrations and blood pressure in areas of the world in 14 different epidemiological sub-regions. It addresses the relative roles of both types of interventions and considers whether management of blood pressure and cholesterol concentrations should be based on thresholds for each risk factor in isolation or based on the absolute risk of CVD for a given individual accounting for their risks.	Male and female children, teenagers, adults and older adults (60+)	Global and world regions (including European Region)	In all regions of the world, the 4 non-personal interventions had the lowest ICERs but also the least potential to reduce burden of disease when resources are extremely scarce, these interventions will be funded first. In all regions the most efficient strategy is a combination of the population-wide and individual based intervention based on the absolute risk approach. In the European region the most cost-effective non-personal intervention was Health education through mass-media and with more funding arable, the next choice of programme would be to add population wide salt intake reduction through legislation. All 17 interventions were cost-effective (using 3x GNP per capita as decision threshold value). Health Sector Perspective (no cost savings) ICER for intervention 1 (health education versus doing nothing) = £12.1/DALY averted. ICER for intervention 2 (health education via mass-media plus salt reduction by legislation versus doing nothing)= £15.9	1. Despite uncertainty, the 4 non-personal interventions are always chosen as the first strategy to reduce CVD. However, the choice between non-personal strategies becomes more uncertain as to which it is best to fund first. 2. Halving the effectiveness of non-personal interventions did not change conclusions.	61	43	38	Short grade 1+2 long (grade 2)
Kristiansen et al. (1991)	To evaluate the relative cost-effectiveness of three main strategies to reduce cholesterol concentrations.	200,000 males aged 40-49	Norway	Population approach gave 3100 life years and 3000 QALYs over no action. The net incremental effects of dietary treatment were 400 QALYs. Over 20 years of a population based strategy was projected to be £1.4 per life year gained. For an individual strategy based on dietary treatment the cost was about £1,427.4 per life year gained. Individual intervention should be implemented cautiously and within more selected groups than currently recommended. From perspective of health sector plus other, ICER for intervention 1 compared with no action =£1.2 per QALY. ICER for intervention 2 compared with intervention 1 = £11,574.5 per QALY	Varying unit cost up and down influenced total cost in the same direction.	61	57	29	Short grade 2+4 long (grade 1,2+4)

See Appendix 5 and 6 for context and method

Blake et al. (2003)	To compare the potential cost-effectiveness of c-reactive protein screening followed by targeted statin treatment for elevated c-reactive protein compared with dietary therapy alone to prevent cardiovascular disease.	Males & females aged 35-85 (sample mean 58)	USA	C-reactive protein therapy would be cost-effective and in some cases cost-saving compared with dietary counselling alone. For 58-year old men with no C-reactive protein (under usual care-dietary, counselling, screening) lifetime costs, life expectancy and health benefits were calculated to be £7,190, 14.471 and 12.217QALYs respectively. While for a 58-year old woman they are £5,676, 16.766 and 13.910 QALYs respectively. The incremental cost per QALY for screening and targeted treatment compared with dietary counselling was therefore £36,403 for men and £71,445 for women. [*NB. Results should be interpreted as for the south west quadrant*)	Sensitive to relative risk of MI, lost of statins and efficacy of statin therapy. C-reactive protein becomes cost saving if the annual cost of statin therapy is reduced to £378.4 or an efficacy of ≤45%. Results were moderately sensitive to utility of MI states, discount rate, cost of cardiovascular events and efficacy of stroke prevention.	75	43	50	Short grade 1+4 long (grade 2)
Plans-Rubio (1998) et al.	To assess the efficiency of diet interventions (amongst others) in preventing CHD	Both males & females. Sample size and age not stated	Spain	Average cost-effectiveness ratios for dietary treatment according to age, gender and blood cholesterol level. It ranged from £18,741 to £56,796 per life year gained in men and from £67,629 to £217,548 per life year gained in women. The annual total cost per individual was £182 for dietary treatment. Cost-effectiveness ratios were lower for men than for women. For blood cholesterol levels of 7.7mmolL (mg/dl), CERs were £23,850 per LYG in men aged 40-49 and £29,782 in men aged 50-59. In women aged 40-49 CERs were £91,829 and £84,473 in ages 50-59. The higher the cholesterol level, the more cost-effective it is to intervene at earlier ages for men. In women it is most cost-effective to intervene at ages 45-49.	Cost-effectiveness ratios were sensitive to variations in programme costs, health effects and discount rates. In contrast, cost-effectiveness results were less sensitive to variations in treatment costs for coronary Heart Disease and treatment compliance.	69	14	43	Short grade 2 long (grade 2)

See Appendix 5 and 6 for context and method

The Swedish-based study by Johannesson & Fagerberg (1992) suggested that providing obese males aged 40-69 with 13 nurse and 4 GP visits over a 6 week period aimed at reducing body weight, salt intake and alcohol consumption compared with no intervention varies from being not cost-effective to possibly being very cost-effective: In 2/5 scenarios, diet was more effective & more costly than Atenolol (ICERS varied £4,104.0 – £18,289.4) but in 3/5 scenarios diet was dominated (£79.6 to £98.9 more costly and providing 0.005 - 0.015 less life years than treatment with Atenolol). This was supported by cost-benefit analysis that suggested costs exceeded benefits. Nevertheless there appears to be considerable uncertainty surrounding the results. Short and long term effectiveness data: 1+4 and 2 respectively.

The Department of Health and Health Services' (2003) US-based study suggested that labelling food with the trans fatty acid content compared with no intervention is very cost-effective (ICER: £3,213 per life year saved). Short and long term effectiveness data: both grade 2.

The US-based study by Bendich et al (1997) suggested that providing at least 100IU/day vitamin E supplementation for 2+ years to men and women compared with no intervention could cut annual hospital charges by £4.0-£4.8bn annually in the USA. However, as no information was given on expected change in quality or quantity of life therefore the relative cost-effectiveness is unknown. Short and long term effectiveness data: 1+2 and 2+4 respectively.

The German-based study by Assman & Schulte (1990) suggested that stringent dietary advice with compliance controls for selected patients (those with LDL cholesterol <4.14 mmol/l, HDL cholesterol $\geq$ 0.9 and triglyceride <2.3) compared with no intervention is very cost-effective (£8,005 per life year saved). Short and long term effectiveness data: both grade 2.

The US-based study by Tosteson et al (1997) suggested that a cholesterol intervention programme such as that delivered in North Karelia, Stanford 3 community study or Stanford-5 city project (which involved health education media campaigns, community activities and face to face instruction) compared with no

programme is likely to be very cost-effective (£2,740 per life year saved) if serum cholesterol falls by at 1% and there is no change in non-CHD mortality. However, if the programme cost £14.2 per person and serum cholesterol falls by less than 3%, then education is unlikely to be cost-effective (£32,969/QALY) and if non-CHD mortality rose it is very unlikely to be considered cost-effective (>£65,000/QALY). Short and long term effectiveness data: both grade 2.

Tice et al's (2001) US-based study suggested that a diet that includes grain-enriched products (e.g. fortified flour) to increase folic acid by 100ug/d compared with no intervention would reduce myocardial infarctions by 13% in men and 8% in women although no costs for the fortification were provided and therefore no ICER was provided. Comparing the fortification with fortification plus treatment for all CHD patients with 1mg folic acid & 0.5mg of Cyanocobalamin would be very to just above reasonably cost-effective (ICER ranges between £952 - £30,935/QALY depending on gender, age and whether screening tests are used). Short and long term effectiveness data: 1 and 2 respectively.

The Spanish-based study by Plans-Rubio (1997) suggested that an 8-year diet low in fat and cholesterol compared with no intervention ranges from being very cost-effective to being unlikely to be considered cost-effective (£8,821 - £86,436 in men and £39,486-£241,218 in women). At a willingness to pay of £30,000 per QALY dietary therapy is never cost-effective for women of any age or cholesterol level or for men over the age of 65. However, at a willingness to pay of £30,000/QALY dietary therapy is cost-effective for men aged 35-59 if cholesterol levels are around or above 6.7 mmol/l and cost-effective for men aged 60-64 when cholesterol levels are around or above 7.8 mmol/l. Results were sensitive to discount rates (when assuming 0% for health effects cause cost-effectiveness ratios to fall by 65%) and programme costs although less sensitive to variations in non-compliance rate, lag period and CHD treatment costs. Short and long term effectiveness data: both grade 2.

The US-based study by Prosser et al (2000) suggested that the Step 1 diet (low intake of saturated fat, rich in fruit, vegetables, whole grains, fat free and low fat dairy, meat fish and poultry) delivered by physicians over a 30 year period compared with no intervention is reasonably cost-effective (£30,142/QALY) for women aged 75-

84 and very cost-effective (£1,507/QALY) in men aged 75-84 with four risk factors. However, it is unlikely to be cost-effective in women or men aged 35-44 (£187,197 and £65,043 per QALY respectively). In men of any age and in women over the age of 55 with 3 or 4 risk factors, diet therapy is always very cost-effective whereas diet therapy is unlikely to ever be cost-effective when there are no risk factors. With 2 risk factors, diet therapy becomes cost-effective (at a WTP for £30,000/QALY) in men around the age of 55 and in women around the age of 65. Results were sensitive to assumptions of the lag time between programme and benefits (<2 yrs resulted in better CE ratios for older patients and no lag resulted in 10% decline in CE for 50 year-old men) as well as of the effectiveness of the Step 1 diet (results increased or decreases up to 50%) and utility weights (excluding them reduced ICERs by 20%). Short and long term effectiveness data: both grade 2.

The Danish-based study by Olsen et al (2005) suggested that 5 nutritional counselling sessions by a GP (1x30 mins, 4x12 mins) that focussed on general advice plus written materials in diet compared with 5 sessions by a dietician (1 x 60 mins, 4x 30 mins) focussing on good nutrition, shopping, meal preparation and exercise is very cost-effective (£757 per life year saved for the GP option and £5,527 for the dietician-led option). The GP option was consistently favourable under different assumptions about cost (e.g. equalising time estimates of GPs and dieticians, including patient costs). Short and long term effectiveness data: 1 and 2 respectively.

The US-based study by Nallamothu et al (2000) suggested that mass treatment with daily intake of folic acid and vitamin B12 for all at-risk people compared with “screen and treat” those with tHcy levels ≥11 umol/L with the same daily supplement was unlikely to be cost-effective for mass treatment (£486,396 per life year saved) but very to reasonably cost-effective for the targeted strategy (£10,669 and £21,574 per life year saved in men and women). After varying the threshold for treatment from 11 to 15μmol/L, it was found that a tHcy level of 11μmol/Lwas the most cost-effective for initiating supplementation in the screen and treat strategy. Short and long term effectiveness data: 2,3+4 and 4 respectively.

The global study by Murray et al (2003) suggested that, in the European region health education through the mass-media alone or with salt reduction through voluntary agreements with industry compared with doing nothing were both very cost-effective (£12 and £16 per disability adjusted life year averted respectively). Compared with personal interventions these non-personal interventions always had lower ICERs. Short and long term effectiveness data: 1+2 and 2 respectively.

The Norwegian-based study by Kristianson et al (1991) suggested that population level promotion of health eating using information from many sources via the mass media, levying taxes on fatty foods and subsidising low-fat foods compared with no intervention is very cost-effective (£1.2/QALY a 20 year period) and that screening for hypercholesterolemia plus dietary advice to individuals for high risk patients compared with doing nothing was also likely to be cost-effective (£11,575/QALY). Short and long term effectiveness data: 2+4 and 1,2+4 respectively.

The US-based study by Blake et al (2003) indicated that moving to Step 1 dietary counselling from C-reactive protein screening and targeted statin therapy reduces both QALYs and costs for 58-year old men and women at a rate of £36,403 and £71,445 respectively. However, in some cases (a male who smokes and is hypertensive) QALYs may not fall (so diet therapy is dominated). Results were sensitive to relative risk of myocardial infarction, cost and efficacy of statin therapy and moderately sensitive to utility of myocardial infarction states, discount rate, cost of cardiovascular events and efficacy of stroke prevention. Short and long term effectiveness data: 1+4 and 2 respectively.

The Spanish-based study by Plans-Rubio (1998) suggested that 4 medical visits and 4 lipid analyses plus dietary treatment of hypercholesterolemia for the first year with visits halved in the follow-up year compared with no intervention is reasonably cost-effective in men (£23,850 per LYG for ages 40-49 and £29,782 in ages 50-59) but unlikely to be cost-effective in women (£91,829 in ages 40-49 and £84,473 in ages 50-59). Cost-effectiveness ratios were sensitive to variations in programme costs, health effects and discount rates but less sensitive to variations in treatment costs for coronary Heart Disease and treatment compliance. Short and long term effectiveness data: both grade 2.

5.0 Overview of evidence and discussion

5.1 Cost per QALY

This review has shown that the majority of evidence on behaviour change interventions to reduce CHD has focussed on changing diet and on adults. Table 18 summarises the quality of evidence by category of ICER across the whole field to date. One intervention was cost saving, 19 interventions (17 diet, 1 exercise, 2 smoking, 3 combination) were very cost effective, five diet interventions were reasonably cost effective, three diet interventions were unlikely to be cost effective and nine were very unlikely to be cost effective. However, it is interesting to note that the quality of evidence for the cost saving intervention and one of the two interventions (Blake et al 2003) that were potentially cost saving were significantly dependent on assumptions and relatively poorly reported data and that 5/9 interventions suggesting that QALYs might be bought at a rate >£50,000 both included RCT evidence and well reported data.

Data from studies citing ICERs of between 0-£50,000/QALY were heavily reliant on uncontrolled primary studies and this appears to be a significant evidence gap. Indeed only 10 studies indicated use of RCT level evidence for short term effectiveness of programmes. Of these, 8 showed ICERs to be very cost-effective and 2 were 'reasonably' cost-effective. No intervention for smoking or exercise used data from RCTs but 1 combination intervention did. Thus the majority of better quality evidence was on diet, although 3 of the 6 papers on diet supplemented this with data from additional sources within the models used. There was little variation in the type of data used for long term effects, with most focussed on long term cohort data. Again, the better quality data was in the diet area where 2 studies used a mix of trial and longitudinal data.

Table 18 shows that interventions to reduce smoking, increase exercise or combination interventions all fall below £20,000/QALY whereas the more numerous diet-related interventions spread across all positive categories from very cost-effective to very unlikely to be cost-effective.

There appears to be little consistent patterning of results by intervention for diet. For example, different types of screening and treatment programmes fall into several categories, as does diet. The Step 1 diet is interesting because it is possibly the most consistent in content of interventions studied by more than one set of authors. However the estimates of cost-effectiveness differ markedly across studies and this may be due to the varying context and methods of implementing the diet across studies. Perhaps the strongest piece of evidence overall is that interventions providing dietary advice all fall in the 'very cost-effective' category.

We examined which studies fell ±£6,000 above the threshold value of £30,000/QALY and found six estimates of ICERs in the 'reasonably' and 'unlikely to be' cost-effective categories were close to the threshold value. The varying estimates came from five studies (Tosteson et al, 1997; Tice et al., 2001; Plans-Rubio, 1997; Blake et al, 2003; Plans-Rubio, 1998). This highlights our concerns with, and the danger of, over-interpreting Table 18 to direct current policy. However, one of the differences (Plans-Rubio, 1998) was attributed to differently aged males and females. If the same NICE behavioural change advice were to be applied without differentiation by gender, then dietary treatment of hypercholesterolemia is less likely to be considered cost-effective. Nevertheless, the variation in other papers suggests that the interventions from these papers may benefit from further investigation through modelling, with the proviso that any sub-group analysis is based on politically decisional information rather than only descriptive social, demographic or epidemiological information. These interventions include:

- Educational programmes similar to North Karelia to reduce serum cholesterol for population aged 35-84
- Low fat low cholesterol diet in males 35-64
- Screening and treatment
- C-reactive protein screening and targeted statin treatment compared with diet only
- Dietary treatment for hypercholesterolemia

It would not be worth developing a model in phase 2 if a paper fulfilled the following conditions; an intervention set in a UK context with RCT level evidence in the short and longer term that showed evidence of effectiveness and an ICER <£30,000/QALY and whose conclusions were supported with similar evidence outside the UK. Unfortunately this situation does not arise for any type of intervention. Indeed one of the 2 UK based studies suffers from very poor quality effectiveness data. Therefore modelling may be useful.

In examining papers that fall in the category of 'very cost-effective', it is important to note that two papers need to be viewed in the light of whether they offer potentially efficient reductions in services. Blake et al, (2003) suggested that moving from a screening and targeted statin treatment programme to health education is likely to be a cost-effective reduction in services whereas Tice et al. (2001) provided mixed evidence of cost-effectiveness that depend on gender and age.

Table 18: Summary of ICERs by intervention area and quality of evidence

Likely cost-effectiveness	Type Intervention	Study No.	Sub-group intervention	Gender, age & risk group (where stated)	Short term effect	Long term effect	Drummond Score	Relevance to modelling	Transferability	Perspective
Cost saving	Exercise	E2	Walking 1 hour per day	M&F. 35-74 yrs.	4	2	79%	43%	57%	Societal
£0-20,000 "Very cost-effective"	Diet		**Diet:**							
		D4	Dietary programme that aimed to reduce body weight, restrict sodium, and to reduce alcohol consumption. Duration:6 weeks/13 visits to the nurse and 4 to the physician.	M 40-69 (BMI ≥ 26, blood pressure 90-104mmHg, DBP= expected, HDL= expected, Cholesterol = HDL + 1% - CHD risk – 1.5%	1+4	2	79%	0%	86%	Societal
		D11	Step I Diet - low intake of saturated and fat, rich in fruit, vegetables, whole grains, fat free and low fat dairy, meat, fish and poultry. Diet delivered by physicians	M 75-84 (4 risk factors)	2	2	78%	14%	71%	Societal
		D15	Intervention (II) dietary treatment	M 40-49 (serum cholesterol concentration >= 6.0 mmol/L)	2+4	1,2+4	61%	57%	29%	Health Care Provider
			Population based:							
		D5	Labelling food with trans fatty acid content	M & F	2	2	71%	43%	43%	Government
		D9#	Vitamin supplementation & grain fortification	M 35-44	1	2	89%	29%	71%	Health Care Provider
			Advisory:							
		D7	Nutritional advice to the population	M & F	2	2	35%	0%		
		D8	Educational interventions to lower serum cholesterol; similar to the Stanford 5-city project	M & F 35-84	2	2	74%	0%	29%	Not Clear
		D12	Nutrition counselling by a GP or dietician	M & F (Obese)	1	2	81%	14%	86%	Health Care Provider & Societal
		D15	Intervention (I) promotion of healthy eating habits. Information to agricultural sector, food industry etc.	M 40-49	2+4	1,2+4	61%	57%	29%	Health Care Provider
		D14	Intervention 1 (health education versus doing nothing)	M & F children to older adults	1+2	2	61%	43%	38%	Government
		D14	Intervention 2 (health education via mass-media plus salt reduction by legislation versus doing nothing)	M & F children to older adults	1+2	2	61%	43%	38%	Government

		D16#	Cut back C-reactive protein screening & targeted statin therapy to dietary counselling alone	F 58	1+4	2	75%	43%	50%	Societal
			Screen & treatment:							
		D13	Screen and treat (Folic acid and vitamin B12)	M 40-85 tHcy levels of 11µmol/L or more	2,3+4	4	85%	43%	100%	Government
	Exercise	E1	Aerobic style exercise with a qualified instructors for 1.5 hours, twice a week	M & F 65+	2	2	89%	29%	86%	NHS
	Smoking	S2	Medical counselling targeting at smoking cessation and delivered by physicians	M & F 40-69	2	2	75%	0%	71%	Societal
		S3	The Heartbeat Wales Program, public education campaigns along with supportive policy and infrastructure change, aimed to reduce smoking prevalence	M & F 18-64	4	4	89%	29%	86%	Societal NHS
	Combination	C1	Check-up and advice on diet and/or exercise from a physician or dietician	M & F 60-109	1	2	82%	14%	43%	Societal
		C2*	Health education/promotion and advice on lifestyle factors delivered through media, food labelling, sports clubs, screening and advice on risk factors by health care personnel	M & F 30-60	2	2	64%	14%	43%	Societal & Health Care Provider
		C3	Enhanced intervention (EI) - screening tests and further counselling sessions and group intervention activities on improving physical activity levels & nutrition compared with screening tests and brief individual lifestyle counselling session	F 50-65	1	2	63%	14%	71%	Health Care Provider
£20,001-30,000 "Reasonably cost-effective"	Diet	D8	Educational interventions to lower serum cholesterol; similar to the North Karelia study	M & F 35-84	2	2	74%	0%	29%	Not Clear
		D13	Screen and treat (Folic acid and vitamin B12)	F 50-85 tHcy levels of 11µmol/L or more	2,3+4	4	85	43	100	Government
		D9#	(Vitamin supplementation & grain fortification) treat all compared to screen and treatment	F 55-64	1	2	89%	29%	71%	Health Care Provider
		D16#	Cut back C-reactive protein screening & targeted statin therapy in favour of dietary counselling alone	M 58	1+4	2	75%	43%	50%	Societal
		D17	Dietary treatment of Hypercholesterolaemia	F 40-49 (cholesterol levels of 7.7mmolL (mg/dl)	2	2	69%	14%	43%	Government
£30,001-50,000 "Unlikely to be cost-effective"	Diet		**Diet:**							
		D10	Diet low in fat and cholesterol	M 35-64 (cholesterol concentration higher than 6.2mmol/l (240mg/dl)) F 35-64 (cholesterol concentration higher than 9.3mmol/l (360mg/dl))	2	2	81%	29%	100%	Societal
		D11	Step I Diet - low intake of saturated and fat, rich in fruit, vegetables, whole grains, fat free and low fat dairy, meat, fish and poultry. Diet delivered by physicians	F 75-84 (No risk factors)	2	2	78%	14%	71%	Societal

		D17	Dietary treatment of Hypercholesterolaemia	M 50-59 (cholesterol levels of 7.7mmolL (mg/dl)	2	2	69%	14%	43%	Government
£+50,001 "Very unlikely to be cost-effective"	Diet		**Diet:**							
		D1#	Step 1	M or F. 55-84 yrs. Low & mod. & F high risk.	2	1&2	89%	0%	57%	Societal
		D11	Step I Diet - low intake of saturated and fat, rich in fruit, vegetables, whole grains, fat free and low fat dairy, meat, fish and poultry. Diet delivered by physicians	M & F 35-44 (No risk factors)	2	2	78%	14%	71%	Societal
		D4	Dietary programme that aimed to reduce body weight, restrict sodium, and to reduce alcohol consumption. Duration:6 weeks/13 visits to the nurse and 4 to the physician.	M 40-69 (BMI ≥ 26, blood pressure 90-104mmHg, DBP= 0.5 expected or no effect, HDL= No effect or 0.5 expected, Cholesterol= HDL +1% - CHD risk 0.75% or no effect	1+4	2	79%	0%	86%	Societal
		D17	Dietary treatment of Hypercholesterolaemia	F 40-59 (cholesterol levels of 7.7mmolL (mg/dl)	2	2	69%	14%	43%	Government
			Population based:							
		D9#	Vitamin supplementation & grain fortification	M ≥ 45	1	2	89%	29%	71%	Health Care Provider
		D9#	Vitamin supplementation compared with fortification	F ≥ 75	1	2	89%	29%	71%	Health Care Provider
		D13	Treat all (Folic acid and vitamin B12)	M 40-85 & F 50-85	2,3+4	4	85	43	100	Government
			Screen & treatment:							
		D9#	(Vitamin supplementation & grain fortification) screen & treatment compared to treating all women ≥ 75	F 65-74	1	2	89%	29%	71%	Health Care Provider
		D9#	(Diet without folic acid fortification) treat all compared to screen & treatment	F ≥ 65	1	2	89%	29%	71%	Health Care Provider

*Potentially cost saving when a societal perspective and regression compensation applied
Interpret as a reduction in services towards the behavioural change intervention
E1: Munro et al. (1997) E2: Jones et al. (1994)
S2: Plans-Rubio (2004) S3: Phillips, et al. (1993)
C1: Lindgren et al. (2003) C2: Lindholm et al (1996) C3: Finkelstein et al. (2002)
D1: Stinnett, et al. (1996) D4: Johannesson & Fagerberg (1992) D5: Services, D. o. H. a. H. (2003). D7: Assmann & Schulte (1990) D8: Tosteson et al (1997) D9: Tice et al. (2001) D10: Plans-Rubio (1997) D11: Prosser et al. (2000) D12: Olsen et al. (2005) D13: Nallamothu et al. (2000) D14: Murray et al. (2003) D15: Kristiansen et al. (1991) D16: Blake et al. (2003) D17: Plans-Rubio (1998)
Note: the following papers are not reported as they did not record QALYs or survival: S1: Ong and Glantz (2004), C4: Dalziel et al. (2005)
, D2: Phillips et al. (2000) D3: Kinlay et al.(1994), D6: Bendich et al. (1997)

5.2 Factors influencing cost-effectiveness

One of the most influential factors on cost-effectiveness ratios is the nature of the intervention itself. In many other interventions evaluated by NICE the nature of the intervention is specified in great detail, for example a specified dose of a specific drug for a specific disease which may be delineated by severity and for a specific age group. The literature we have reviewed is noticeably different, although some studies have been careful to document the relationship between cost-effectiveness and age or specified what information is given by who and how many times. However, the majority of papers fail to provide sufficient detail about the exact nature of the intervention. This means that advice on what interventions are cost-effective can only be given very cautiously. For example, stating that 'drugs are cost-effective in treating X' could be construed as being similar to stating that 'advice on diet is cost-effective in reducing CHD'. Neither provides sufficient guidance for practitioners and both can be interpreted inappropriately, leading to inefficiency or even potential harm.

In looking at the cost-effectiveness of combination treatments, ideally they would indicate which risk behaviours are influenced by the intervention. Whilst this was not possible to separate out in the selected papers it is theoretically possible for combination interventions to have less than unitary additionality or for one risk factor to 'lose out' when combined with other interventions (Wonderling et al., 1996; Langham et al., 1996).

Part of the reason for the lack of precision about interventions evaluated may be related to their complexity and because interventions are implemented differently in different sites. Published papers may not offer the space for a full enough description. However, there are two possibilities for improving the description of interventions. Firstly it would be useful to consider and adopt a standard way of describing interventions. Drummond's recommendation to describe who does what to whom, where and how often is a good starting point, and should be applied routinely to both the intervention and its comparator. However, other conventions exist and an agreed approach might usefully be added to the CONSORT guidance. If public health interventions and programmes are very complex, a second approach would for journals or authors to provide additional descriptions online such as copies of the protocols for the interventions.

Of the 17 diet interventions, 7 specifically compared population wide interventions with targeted interventions, where candidates for behaviour change interventions are identified by one or more risk factor. No such comparisons were made in the smoking, exercise or mixed studies identified in this review. Of the 7 studies, one (Nallamothu et al., 2000) found that providing folic acid and vitamin B12 to all was more effective than a targeted approach but was less cost effective. Screening and treating with folic acid and vitamin B12 was reasonably cost-effective for men 40-85 and very cost-effective for women 50-85, whilst treating all was unlikely to be cost effective for men or women. In their comparison of diet with stations, Blake et al. (2003) found that targeted drug use was more cost-effective than administering stations to the population. Whilst screening and treating 58 year old men and women was more cost-effective than a population strategy it was still 'unlikely to very unlikely' to be cost-effective. All remaining studies (Kinlay et al. (1994), Asssman and Schulte (1990), Tice et al. (2001), Murray et al. (2003) and Kristiansen et al. (1991)) found that population strategies were more cost-effective although Kristiansen et al. (1991) concluded that individual interventions should be implemented cautiously and with select groups; Prosser et al. (2000) also found convergent evidence in their study when cost effectiveness was compared by type and number of risk factors.

Age and gender emerged as prominent mediating factors for effectiveness and cost-effectiveness, with eleven studies (Assmann and Schulte, 1990; Blake et al., 2003; Lindgren et al., 2003; Lindholm et al., 1996; Nallamothu et al., 2000; Plans-Rubio, 1997; 1998; 2004; Prosser et al. (2000); Stinnett et al., 1996; Tice et al., 2001) presenting results in relation to these factors (1 smoking, 2 mixed, 8 diet). With the exception of four studies (Phillips et al., 2000; Kinlay et al., 1994; Kristiansen et al., 1991; Tosteson et al., 1997), cholesterol levels were combined with age and/or gender and were found to influence cost-effectiveness.

Smoking cessation using medical advice (Plans-Rubio,2004), homocyst(e)ine lowering with folic acid and vitamin B12 (Nallamothu et al., 2000) and other dietary interventions (Lindgren et al., 2003; Plans-Rubio, 1997; 1998) were all found to be more cost-effective for men, although this does not necessarily mean they were not cost-effective for women, controlling for age.

All the studies looking at cost-effectiveness by age and gender found interventions to be more cost-effective for men. With the exception of Assmann and Schulte (1990) who found nutrition advice to be more cost-effective for individuals less than 60 years of age than those 60 to 64 years, all found in general that cost-effectiveness increased with the age of intervention participants. Interventions were least cost-effective for young women (Blake et al., 2003; Stinnett et al., 1996). More evidence of cost-effectiveness at a younger age was found for men than for women. For example Tice et al. (2001) found grain fortification and folic acid supplements to be cost-effective for men from the age of 45 years and for women around the age of 55.

5.3 Methodological issues

In this study currency and ICERs were converted to World Bank purchasing power parity (PPP) exchange rates, the number of units of a country's currency required to buy the same amounts of goods and services in the domestic market as a UK £ would buy in the UK, rather than using official exchange rates. Comparison of the impact of this method with official exchange rates revealed very little difference most studies reviewed, with the impact on cost varying between -0.14% and 5.55%.

However, for Scandinavian studies, there was a marked impact both in total costs and in movement of interventions from being reasonably cost-effective to being unlikely to be cost-effective. For the latter studies, using standard exchange rates would have resulted in substantial underestimation of costs.

Application of Drummond's checklist for a sound economic evaluation and Pang's transferability score revealed substantial deficiencies in key information that should be recorded in peer reviewed studies. In particular costs were not presented in a disaggregated form (quantities and unit costs not reported separately), adjustment to currencies and prices were inadequately described, the choice of model used and the key parameters upon which it was based were poorly reported, as were the choice of variables for sensitivity analysis and any justification for failing to discount costs. Pang's questionnaire highlighted authors failing to address how generalisable their results would be to another setting. Finally, there is clearly a difficulty in transferring results from one country to another if the comparator of an intervention differs from current practice in the UK. For example, Lindholm et al (1996) compared a health promotion programme to annual screening for cardiovascular risk but there is no annual screening programme in the UK.

We are aware that creating a score from the Drummond questions is not usual practice and that there has been debate about whether and how this might be done (Shaya 2003; Hoffman et al, 2002; Gonzalez-Perez, 2002; Gerard et al, 2000,). The approach we have used is probably better at identifying the lower quality studies rather than distinguishing between better quality studies as no additional indicators were used to weight for effectiveness (Gonzalez-Perez, 2002). However, specifying a 1-4 score for short and long-term effectiveness data goes someway to improving this situation. We investigated the relationship between each of the scoring mechanisms (for short term & long term effectiveness, the Drummond 31 score, relevance to modelling and transferability) through a Pearson correlation matrix. 3/10 correlations were statistically significant using 2 tailed tests; short term effectiveness scores were positively related to long-term effectiveness scores ($r = 0.49$ $p<0.05$) and relevance to modelling ($r = 0.41$ $p<0.05$) and the Drummond score was positively related to Pang's transferability score ($r = 0.61$ $p=0.001$). This suggests that better quality short term studies are more likely to be useful for economic evaluations

because they are also more likely to have better quality long term data. It also suggests that the Drummond scores could be roughly reasonable predictors of the ability to transfer data across settings.

One of the challenges of the summary in Table 18 is that the studies are presented using a variety of different perspectives. 11 include a societal perspective and 13 include a health provider or government perspective. This raises questions of what 'ought' to be considered. NICE currently recommends an NHS perspective for the reference case and it is known that the perspective will have an important impact on the type of costs considered. For example, a programme focussed on changing the dietary habits of a population will not account for any change in costs borne by families if an NHS or personal and social services perspective is used. This might be considered correct for two reasons; firstly, families are unlikely to consider cost-effectiveness (at least in terms of limiting 'effectiveness' to QALYs gained) in deciding on their food choices; secondly, considering whether a behaviour change programme is a 'good use' of public funds will only matter if it is demonstrated that people do change their diet. The challenge to this narrow view comes from considering the opportunity cost that families face in adopting a new diet. If, for example, expenditure has to increase and the opportunity cost is not being able to support a child to follow tertiary education, the new diet might lead to a welfare loss. It is difficult to judge what impact a different perspective would have on ICERs or decision but is worth further investigation, particularly in terms of whether there is a systematic differential impact in evaluations of behavioural change versus pharmacological interventions.

Another challenge to interpreting Table 18 for the context of current decision-making by NICE is that no study has used the recommended discount rates (3.5%), although most did use the same rates for costs and effects. 47% of studies used 5% or higher and only 5 papers investigated the impact of discount rates in a sensitivity analysis.

Table 18 treats information on cost per life year gained and cost per QALY as virtually synonymous, given the assumption of a quality weighting of 0.99 for additional life years. This allows more papers to be compared and allows consideration about orders of magnitude with respect to cost-effectiveness.

However, it is also pertinent to consider the five papers that have been excluded from this table; 3 diet-related interventions (Phillips et al 2000; Bendich et al. 1997; Kinlay et al, 1994), 1 on smoking cessation (Ong & Glantz, 2004) and 1 combination intervention (Dalziel et al, 2005). Of these, three involved at least some evidence on short term effectiveness from RCTs although two had very low scores for the Drummond questions. On the whole these five papers scored lower than average on both the Drummond, modelling and transferability scores. Nevertheless, given the paucity of data, it would be very useful to find a system to convert findings from these studies into LYG and QALYs. Unfortunately this went beyond the resources of this project.

5.4 Evidence gaps

Evidence or research gaps areas are listed below:

Content of evidence

- With the exception of evaluations that cover the whole population, no evidence is provided on the cost-effectiveness of behaviour change interventions for specified sub-groups e.g. age group 19-30yrs, low income groups, pregnant women, particular ethnic groups or specified disadvantaged groups.

- There is no economic evaluation of a solely child-focussed disease prevention programme targeted at reducing CHD.

- No cost-effectiveness analysis of interventions to reduce smoking or increase exercise to reduce CHD has included children.

- Very few economic evaluations of behaviour change interventions to reduce CHDhave been conducted from a UK perspective

- There is a lack of research looking at patient preferences in this area. Little attention was paid to patient preferences for the type of interventions that

would be preferred or how they would be delivered. In turn preference is likely to affect compliance, which needs to be addressed (Murray et al, 2003) as it is key to the success of any behaviour intervention.

- Future research needs to include QALY weights for life years to facilitate comparison across a range of interventions

Quality of evidence

- There is a lack of reliable data from which to extrapolate the long term health outcomes of behaviour change interventions from short term effects of behaviour change interventions (Kristiansen et al., 1991). For example, Kinlay et al. (1994) cited a lack of adequate information upon the impact of cholesterol and cholesterol reduction upon the risk of CHD among women.

- Few economic evaluations of behaviour change interventions to reduce CHD are conducted alongside level 1 effectiveness evidence

5.5 Implications for modelling

As was stated in the introduction, phase two will be guided by three reviews of the effectiveness of behaviour change interventions and two reviews (on the relationship between knowledge, attitudes, behaviour and outcomes and on optimal conditions for bringing about change) in addition to this review. The following findings will have to be subsequently considered in conjunction with those of the other reviews.

Given that 80% of the literature identified in this review related to single (65%) or mixed (15%) interventions with respect to diet, the findings of this review dictate that a dietary intervention must be considered for inclusion in phase two of this project. Section 5.1 highlighted a number of specific interventions that could be considered.

We would also suggest that a range of type of intervention were also considered, such as a population wide intervention and personally focussed intervention. As age, gender and other CHD risk factors affect cost effectiveness, sub-group analysis may be relevant – although only useful if of decisional value.

Despite the prominence of modelling studies amongst the literature identified in this review, data that could be used to replicate or create new models was sparse. Only one paper reported data relating to utility values and two on resource use and costs. These problems will be addressed in phase 2 when model specific parameter estimates will be sought.

6.0 Summary and Conclusions

1. Prevention in childhood

    None of the papers reviewed provided evidence on child-focussed health promotion programmes. Children were stated as being included in population level statistics in only two papers (Murray et al 2003, Services DoH, 2003) but data were not evaluated by subgroup[12].

[12] It is possible that children were also included in a number of other interventions aimed at populations, but age ranges were not always specified.

2. General prevention in adulthood

Three out of the four papers that focussed on combined packages of interventions aimed at multiple risk factors fell into the 'likely to be very cost-effective' category[13]. These included a mix of population and individual focussed interventions for adults over the age of 30. Whilst short term effects in two papers were based on RCTs, none of the studies were conducted in the UK and none investigated alternative packages of interventions. Two papers compared the combination programme with no programme at all and one against a screening based alternative.

3. Intervention in adulthood to change the behaviour of people with specific risk factors for CHD (eg. smoking, poor diet, lack of physical activity)

Exercise: Both papers on the cost-effectiveness of interventions designed to increase exercise fall into the category 'likely to be very cost-effective' when compared with no intervention and a largely sedentary population aged over 35. However, the quality of short term effectiveness data was not strong.

Smoking: Two out of three papers[14] on smoking fall into the category 'likely to be very cost-effective'.. One paper was the advice to individuals in Spain and the other was Heartbeat Wales. Unfortunately the quality of short term effectiveness data from Spain was not strong and the data from Wales very poor quality.

Diet: Of the 17 papers on diet, the cost-effectiveness of professional advisors in changing diet was consistently in the 'very cost-effective' category whereas there is no consistent pattern for any other types of diet interventions (population or screening based or diet alone) which fell in all categories between very likely and very unlikely to be cost-effective, including the 'standard' Step 1 diet which could be considered a more 'standardised' intervention.

[13] The remaining paper(s) did not provide QALYs or number of life years saved.
[14] The remaining paper(s) did not provide QALYs or number of life years saved.

Two non-advisory interventions also remained in the likely to be very cost-effective group; food labelling with trans fatty acid content (Services DoH, 2003) and a population-based health promotion programme on healthy food (Kristianson 1991). However, one of the reasons why the food labelling may rest only in one category is because neither sensitivity nor sub-group analysis was conducted, which is surprising given that only level 2 data was (and could be) available. Kristianson's (1991) model used a range of levels of data and undertook a basic sensitivity analysis.

When specified (n=12/17), most papers on diet focused on populations over the age of 35 with the exception of Murray et al (2003) who modelled the entire population. The quality of evidence varied by category of cost-effectiveness, with most RCT data for specifications of interventions in the >£50,000 category, followed by £0--20,000 and then £30-50,000. No RCT data supported interventions in the cost saving or £30-50,000 level of cost-effectiveness.

4. Treatment (primary, secondary and tertiary care) in adulthood for people with CHD (e.g. statins, coronary heart by-pass, heart transplant).

The majority of treatments provided and evaluated are not behaviour change interventions or are provided in conjunction with behaviour change interventions. This project was also defined with NICE, to exclude secondary and tertiary care. This reviews found no evidence on the effectiveness of behaviour change interventions alone. Several papers were excluded because the effects of behaviour change interventions could not be isolated, particularly from pharmacological intervention.

5. Other findings

- A blanket statement on cost-effectiveness of targeted or population strategies cannot be made as the evidence is mixed; in some cases targeted strategies are more effective and in other cases mass treatment is.

- There is evidence suggesting that the cost-effectiveness of behavioural change interventions varies by age, gender and risk level but in an inconsistent way across intervention type.

- There is considerable uncertainty for a number of interventions around the threshold value of £30,000/QALY, indicating that future modelling may provide useful decisional information for a UK setting.

- Data from studies citing ICERs of between 0-£50,000/QALY was heavily reliant on uncontrolled primary studies

- Few economic evaluations rely on primary data and few modelling studies provide sufficient description to ascertain the methods used.

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