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Executive Report

RISK FACTOR STUDY

How to Reduce the Burden of Harm from Poor Nutrition, Tobacco Smoking, Physical Inactivity and Alcohol Misuse: Cost-Utility Analysis of 29 Interventions

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The content of the report remains the responsibility of the study team.

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RISK FACTOR STUDY: Cost-Utility Analysis Of Interventions To Reduce Harm From Lifestyle Behaviours: Executive Report

SUMMARY

Objectives

The risk factor project was commissioned by the Department of Health and Ageing, Population Health Division. The aim is to determine how best to reduce the burden of harm on the Australian community attributable to physical inactivity, poor nutrition, alcohol misuse and tobacco smoking, by determining which interventions are most effective and cost-effective, and thus able to make the greatest contribution to harm reduction for resources allocated.

This is a technical analysis. To the extent that health (reflected in mortality and quality of life), is the primary objective of health policy, in identifying the most efficient means for its achievement can inform resource allocation decisions. While there are other potential objectives and other issues that might be relevant to policy decisions, it was decided not to attempt to incorporate other objectives, which has the effect of introducing a level of subjectivity into the analysis. Similarly such matters as 'acceptability' or 'implementability' are not only highly subjective but also highly dependent on the specific policy and practice and organisation environment at a point of time and place, and thus excluded from this technical analysis.

Reporting

The project has been completed in several stages. It commenced with a literature review of evidence concerning interventions designed to modify these four lifestyle behaviours (Segal, Dalton, Robertson et al 2003). The primary purpose of this task was to identify a set of interventions for economic analysis that met nominated selection criteria related to quality of evidence etc. In practice, in order to achieve comprehensiveness, interventions were also included that did not meet the quality of evidence criteria. This is, in itself a comment on the literature. The interventions selected through this process for economic analysis are listed in Table 1. This list also includes a small number of newly published studies, subsequently added, which fit the inclusion criteria. The primary research task has involved the assessment of economic performance of the identified interventions, largely using cost-utility analysis, wherever possible. The aim was to assess the performance of 28 interventions. We identified 35 interventions for assessment and have been able to report 29 cost-utility (C-U) analyses – 22 based on models we developed, 3 based on published models, 2 'scenario analyses', whilst 2 interventions were dominated (C-U infinite). We were able to complete few C-U analyses for physical activity interventions, due to a combination of poor quality studies and dominated interventions. See Table 2.

The results of these analyses are reported in 6 volumes - this Executive Report, which includes a summary, plus 5 technical volumes covering each of the 4 risk factors, plus one for multiple risk factor interventions.

Table 1 Interventions selected for economic evaluation

MULTI-FACTORIAL	
Adult Interventions	**School-based Interventions**
▪ Fighting Fit, Fighting Fat Media Campaign ▪ Stanford 5 City media/community Project ▪ GutBusters Workplace Program ▪ Workplace prevention of heart disease * ▪ Oxcheck – Primary care nurse health checks	▪ Student TV viewing and obesity ▪ Interdisciplinary student intervention and obesity ▪ Cardiovascular disease risk factors in children ▪ Cardiovascular disease risk reduction in children
PHYSICAL ACTIVITY	
▪ Australian GP Active Script * ▪ New Zealand GP Active Script ▪ Community based exercise for over 65 year olds	▪ General practice exercise referral for cardiovascular disease risk factors ▪ Physical activity program and individualised advice for over 60 year olds
NUTRITION	
▪ Nutritional counselling in general practice * ▪ Mediterranean diet in those with previous myocardial infarction ▪ Reduced fat diet for those with impaired glucose intolerance	▪ Orlistat plus diet for obesity ▪ Lifestyle changes to prevent type 2 diabetes ▪ Talking computer for nutrition * ▪ Nurse nutritional counselling in general practice ▪ Multi-media '2 fruit 5 veg' campaign
SMOKING	
▪ US mass media smoking campaign – Massachusetts Tobacco Control Program ▪ Australian mass media campaign – Phase 1 National Tobacco Campaign ▪ Meta-analysis of 16 Bupropion SR trials	▪ Meta-analysis of 34 trials evaluating minimal to intensive advice in general practice ▪ Meta-analysis of 86 trials comparing brief intervs, NRT and behavioural interventions * ▪ Phone counselling as adjuvant therapy for NRT
ALCOHOL	
▪ US mass media alcohol campaign * ▪ Meta-analysis of 8 trials evaluating brief interventions in primary care for problem drinking ▪ Brief interventions for heavy drinkers	▪ MOCE and BSCT for moderately dependent drinkers ▪ MET and NDRL for mildly to moderately dependent drinkers ▪ Meta-analysis of 7 trials evaluating Naltrexone and psychosocial therapy

Notes * Cost-utility analysis not completed due to insufficient evidence, interventions too complex or resource and time constraints. NRT: Nicotene replacement therapy; MOCE: Moderation-Orientated Cue Exposure. BSCT: Behavioural Self-Control Training. MET: Motivational Enhancement Therapy. NDRL: Non-directive Reflective Listening.

Methods

The relationship between the intervention, behaviour and health outcomes are complex and not necessarily directly observable. We have thus adopted a 2-staged approach to measuring economic performance that distinguishes the impact on behaviour from the consequent impact on health. We have in most cases generated an 'intermediate' measure of performance, a *cost-effectiveness ratio,* in which interventions are analysed in terms of the cost to achieve an observed change in lifestyle, based on trial results. Interventions that target the same lifestyle behaviour can in this way be directly compared, without having to understand the relationship between behaviour and health.

This technique is applicable where behaviour is consistently and simply described, (for example with cigarette smoking). It is less useful where the life style attribute is complex, such as nutrition or physical activity. It also cannot be used to compare interventions which target several behaviours or that address different behaviours or that aren't focused on behaviour change. The preferred measure of performance is thus a *cost-utility analysis* in which interventions are assessed in terms of the cost to enhance quality of life and reduce mortality, expressed as cost/QALY gain. The capacity to complete cost-utility analyses depends on access to evidence on the cost of the intervention, on

behaviour change, and the effect of behaviour change on mortality and quality of life. The methods we have used to derive estimates of costs and QALYs are outlined below.

Costs

Costs are calculated in Australian dollars and expressed in 2003 dollars, (A$ 2003). A societal perspective is taken, which means all costs are to be included, regardless of on whom they fall. This differs from a government or agency perspective. In practice however, some costs have not been measured, such as private costs on consumers to access services, (such as waiting time, transport costs etc.) and costs to others, such as carers as well as productivity impacts. While these may be important, methodologies are insufficiently developed to provide reliable estimates. Furthermore, they are not typically included in program descriptions or in the economic evaluation of health programs.

Direct costs of the intervention have been calculated using one of two methods:

- Calculated costs: based on description of the intervention documented in the literature to establish resource inputs, to which Australian published unit costs are applied. These are derived from a range of sources including the Pharmaceutical Benefits Schedule (PBS) and the Medicare Benefits Schedule (MBS);
- As reported: using the published costs of an intervention, adjusted by the health price index and relevant exchange rate.

Downstream cost impacts: The base case for our analyses does not include possible downstream cost impacts, essentially because of the complexity and uncertainty that surrounds such estimates. Unless direct evidence is available of the impact on health service use and cost, which generally requires many years (or even decades) of follow-up, estimation of downstream cost impacts requires large data inputs. These include; a well documented relationship between change in current behaviour and change in future behaviour, between behaviour (current and future) and health; and between health (current and future) and health service use (current and future). The longer into the future before health benefits are likely to be realised, the less confidence in estimates of potential downstream cost savings. Given the generally poor standard of evidence relating to interventions to modify lifestyle behaviours and of the other relationships critical to this analysis, it was considered prudent to exclude downstream cost savings from the base-case.

Downstream cost savings were only included in the base-case, where data on health-care costs and/or health-care events are collected and reported as part of the clinical trial. This information was only reported for the Mediterranean diet intervention, which thus includes expected impact on health service costs as part of the base-case analysis. Potential downstream cost savings are included in the sensitivity analysis for 'disease-based models' where potential downstream cost savings can be estimated from published data on the cost of managing the specific condition. In other cases a threshold analysis is performed, in which we calculate the size of downstream cost savings that, if realised, would make the intervention becomes cost neutral, (additional cost of the intervention offset by downstream cost savings).

Impact on behaviours

Estimating the impact of an intervention on lifestyle behaviour requires two pivotal pieces of evidence:

- First of the magnitude and direction of lifestyle behaviour *change in the presence of the intervention*; and
- Second of the persistence (or otherwise) of any lifestyle behaviour *change after the intervention has been discontinued.*

Evidence of the treatment effect on lifestyle behaviour was drawn from a meta-analysis of well-conducted randomised control trials (RCT) where available. This class of evidence was available for pharmaco-therapies and some primary care interventions, given relatively little variation in interventions, patient profiles and costs allowing the results of several studies to be combined. However, in other cases, wide variation in intervention characteristics, preclude meta-analyses. For complex and unique interventions, the only approach is to derive costs based on the resources applied, related to the observed outcomes derived from single studies. Our strategy was thus to locate all well constructed studies that met basic criteria for suitability for generation of evidence; i) address one or more of the four subject life style behaviours; ii) use an RCT design (or met-analysis of several RCTs), iii) report objective measure of outcomes, iv) include a full description of the intervention from which costs can be calculated, v) include long term follow-up. Any studies that met all those criteria were included. Unfortunately few trials were located that met all these criteria, so in order to maintain breadth of scope of interventions studied, trials were also included which only partially met these criteria.

The major compromise related to the length of the trial and period of follow-up. Evidence of persistence of treatment effect cannot really be gained in any other way. Behaviours need to be described against normal lifetime patterns. (For instance alcohol misuse tends, even in the absence of specific interventions, to reduce with age). In estimating downstream changes in behaviour, the aim is to determine this relative to what it would have been without the intervention.

Impact on quality of life and mortality

The impact of the intervention on quality of life and mortality was estimated from direct observation, or in the absence of such observed data, indirectly.

The first-best approach is to directly observe any divergence in mortality and morbidity (quality of life) between intervention and control groups. However, for life style interventions, this approach is rarely available. It is unusual for trial participants to be followed up for the requisite time for an expected change in risk of death or quality of life to be able to be observed. An exception is the Mediterranean diet intervention for persons post heart attack (deLorgeril 1999). This RCT included 4 year follow-up in a high risk population which allowed for significant differences in cardiac event rate and all-cause mortality to be observed in the Mediterranean diet group. More commonly, direct observation of intervention and control groups is limited to short periods of 6 to 24 months, during which time effects on mortality and morbidity are unlikely to manifest.

The second-best approach relies on supporting evidence of the link between intermediate outcomes, such as smoking cessation, increased physical activity levels or clinical parameters that are directly observed in the trial and quality of life and mortality, or through published relationships between lifestyle behaviour and health. Where this was not available then we resorted to a third best approach that of relating behaviour change via clinical parameters to disease incidence and health.

Estimating the impact on health via clinical parameters is common in the economic evaluation literature[1] using published risk equations derived from large-scale cohort studies (eg, Anderson et al, 1991; D'Agostino et al, 2000; Knuiman et al 1998). These published multiple risk equations which describe the determinants of disease-specific mortality or morbidity can be applied to the findings of clinical trials, given a relevant set of independent variables. However, the potential application of these equations in the current context is limited, as the independent variables do not match well with the outcomes reported in the clinical trials. For instance they rarely include nutrition or physical activity variables, and moreover the behaviour or clinical parameter used in the published risk

[1]For example NICE in the UK are known to employ rigorous methods and have used published equations to establish relationships-such as Framingham (see reports such as, Sibutramine#31), and the Australian PBAC accept submissions relying on similar methods (details are commercial in confidence).

equation must match how they are reported in the clinical trial. Furthermore, the majority of published risk equations link intermediate outcomes to only one disease pathway, which is not very useful when considering exposure to risk factors such as diet, exercise, alcohol and tobacco that operate via multiple disease pathways.

We have primarily used the 'second-best' approach and have sought evidence relating lifestyle behaviour (smoking status, alcohol consumption, physical activity levels etc.,) to health-related quality of life (HRQoL) and all-cause mortality. The potential errors in this approach, (as with all indirect approaches) relate to confounding and not allowing for possible reverse causation when analysing observational data.

Effects that extend beyond the individual

Health benefits can extend beyond the individual to family members and the wider community. It is not common to capture these wider influences in economic evaluations. This is partly because of the sheer complexity of the relationships, but also because such influences may not be quantitatively important relative to the health impact on the individual. Simply measuring individual benefit will, for many health interventions, represent an acceptable simplification. It is the adopted base-case in all our models. However, in relation to interventions targeted at alcohol a major part of the disease burden of alcohol misuse is borne by families and others. Thus confining measurement to individual impact is demonstrably incomplete. But data relating to the impact on families and how this changes with the adoption of 'safe drinking behaviour' is limited. But, if these wider impacts are excluded altogether the potential benefits of these interventions will be understated and performance undervalued. We have therefore developed an alternative family model for alcohol, which includes an estimate of the possible effect on family members in a way that is exploratory.

Transferability and generalisability

Australian-based trials have been used wherever possible to maximise relevance to Australia. Given the small number of high quality Australian trials that address the four subject risk factors the international literature, notably European and North American trials have also been used. Transferability of cost-utility estimates depends on transferability of outcomes as well as costs, both in translating trial results to a normal clinical/population setting and relevance to Australia today. It has not been possible to explore this issue in any detail, although we do comment where there is a particular concern, for instance where the process of recruitment suggest likely selection bias, or where there is a mismatch between the comparator used in the trial and current Australian practice. How well performance derived in the clinical trial setting would transfer to the community or clinical practice setting is not known.

Key assumptions of the economic models

For each risk factor and specific intervention, the approach adopted for estimating the impact on quality of life and mortality follows the broad principles above. We have, where data allows, estimated QALYs from observed impact on health outcomes, otherwise using published relationships between lifestyle behaviours and health or clinical parameters and health. In short we draw on a combination of trial evidence and pertinent epidemiological and other data in a standard cost-utility analysis. Most use a markov model structure, with the primary input the probability of moving control and intervention cohorts between pertinent health states. Full details of each model and the assumptions adopted are described in the chapters of this Executive Report and the five Technical Reports, one for each risk factor and are summarised in Table 2. Where possible, consistent assumptions are used across all interventions. The impact of alternative assumed values

for uncertain parameters have been explored via univariate sensitivity analysis or probabilistic sensitivity analysis (where data quality allows).

Table 2 Key assumptions underlying the economic modelling

Description	Details
Base case	
Discount rate	5% for costs and benefits.
Cycle length	1 year for all Markov models except the diabetes Gutbusters model of 5 years and the alcohol model with cycles 3 or 6 months.
Time horizon	Chosen to match the disease process, age of participants and reflecting available evidence; ranging between 5 years & life expectancy.
Evidence of treatment effect	Ideally drawn from meta-analyses or if unavailable from key RCTs.
Length of intervention benefit	Generally in the base case the length of intervention benefit is not extended beyond the duration of the trial evidence.
Direct costs of intervention	Estimated in Australian dollars 2003, based on described resource use or published costs adjusted by health price index and exchange rate.
Indirect costs	Indirect costs such as transportation, waiting times, costs to careers and productivity losses have not been included.
Comparator	Usual care, current practice, placebo or no intervention. If the comparator was inappropriate, an own-control comparison was made of intervention group, comparing final outcomes and baseline values.
Downstream costs	Excluded in base case analysis.
Model structure- Examples	
Smoking interventions	Markov model, containing ex-smoker tunnel sequence. Cohort initially distributed across smoker states according to prevalence in Australian population. Mortality differential commences from age 25 years.
Alcohol interventions	Tunnel sequences used to delay the health effects of moving from one state to another, quality of life gain directly attributable to alcohol moderation varies depending on severity of alcohol problems.
Hypothetical scenario analysis	Was performed for selected multi-factorial school based interventions given gap in key effectiveness data.
Modification of published model	Where a sound published model was available Australian costs were applied, and in some cases model assumptions were modified.
Sensitivity analysis - examples	
Discount rate	0%,3% and 7%
Downstream costs	Included for interventions targeted at specific disease such as diabetes or heart disease. Otherwise a threshold analyses was performed to show the downstream cost offset associated with intervention dominance.
External effects	Health effects for family members are considered for alcohol interventions
Other variables frequently varied	Time horizon, length of intervention benefit, utilities, costs, treatment effect, characteristics of starting population, relapse rates.

Results

Despite the many challenges in a study of this breadth, there are also benefits of such a comprehensive research program in the potential for comparison of interventions that address different risk factors and target populations through various modalities. It extends knowledge of the relative performance of interventions and of the important gaps in research knowledge.

In this research program we have compared the performance of 29 interventions which address the four life style behaviours through 27 cost-utility analyses with 2 interventions identified as dominated. From the analysis we can suggest where resources should be focussed to reduce burden of harm from the nominated lifestyle behaviours. We can draw strong conclusions, where there is good quality evidence. The research program has focused on the technical task of deriving measures of performance, expressed in cost/QALY. We recognise that in making decisions about resource allocation, other criteria might be considered. However, rather than incorporate other issues, which tend to be subjective and value laden, we simply report the technical result. This research thus identifies resource allocation decisions that will maximise QALYs gained and the loss of potential QALYs if other choices are made.

The performance of interventions is specified in terms of cost/QALY, the lower the cost to achieve a QALY gain the better, see Table 5 and Figure 1. As the steps taken to model each intervention use data inputs of varying quality, the confidence which can be placed on the estimates of cost/QALY varies. This is important in interpreting the results. We have therefore classified interventions according to both cost/QALY and confidence in the estimates. (A more comprehensive schema is used in the full report).

In Table 3 we list those interventions that perform extremely well, with an estimated cost/QALY <$15,000 and where quality of evidence is good. In Table 4 we list interventions found to perform less well cost/QALY >$25,000, but also based on reasonable quality evidence. Other interventions may perform well or poorly but the evidence is of insufficient quality to be confident in the result.
The cost effectiveness of each intervention, together with costs, absolute health gain and quality of evidence is summarised in Table 5. These base case cost/QALY estimates have been derived using conservative assumptions, as is the tradition in health economic evaluation, and thus will tend to provide a high estimate of cost/QALY.

The most outstanding interventions that perform exceptionally well based on good quality evidence are:

- *Mediterranean diet for persons post AMI,* at $340/QALY. Or taking account the differential rate of health events such as subsequent heart attack and stroke as observed in the clinical trial, substantial net cost savings should be generated, estimated at $14,000 saving per person (present value). This intervention also yields the highest absolute level of benefit of over 1 QALY gain per person.
- *Brief interventions for alcohol* misuse also appear highly cost effective, based on good quality data, at less than $700/QALY.
- *Lifestyle modification for persons with IGT,* at $1,900/QAY based on good quality evidence. This intervention is likely to be cost saving, taking account of projected cost savings.
- Other potentially highly cost-effective interventions are as listed in Table 3.

Comments

Critical data gaps

The capacity to assess performance of interventions depends on access to evidence on; i) behaviour change (and other outcomes) contemporaneous with the intervention; ii) maintenance of behaviour/clinical change and iii) the link between behaviour change/clinical parameters and health and wellbeing. There are critical gaps in the evidence relating to lifestyle interventions across all these areas, but varies across risk factors and modalities. As a general rule, evidence related to nutrition interventions, especially those targeted at high risk groups is of high quality, as is evidence concerning tobacco interventions, especially for clinic-based interventions. In general, evidence from which to assess community-wide interventions is incomplete and what is available is of poor quality. There is strong evidence concerning alcohol programs, in terms of impact on current behaviours, but

with less known about maintenance of behaviours, although there is some information from one long-term (10 year trial). Less is known about the impact of change in alcohol consumption on health and wellbeing of family members. Least satisfactory is the evidence concerning physical activity and multiple risk factor interventions, particularly in relation to retention of behaviour change. As a generalisation, evidence concerning maintenance of behaviour change is poorest as it requires long term follow-up, from well designed studies. Unless interventions are followed up for an appropriate period beyond the end of the trial, it is not possible to presume that behaviour change is maintained. Rather the limited evidence related to physical activity suggest otherwise.

Comparative performance

Clinical interventions targeted at those at high risk were often found to be both highly effective and highly cost-effective, especially in the areas of nutrition and alcohol and smoking. The evidence relating to physical activity interventions is more equivocal, partly due to an almost entire absence of follow-up data[2].

We find that there is much that can be done to modify harmful lifestyle behaviours. There are many interventions that are both highly effective and highly cost-effective, performing extremely well relative to social norms. Drugs are typically listed in the PBS where $/QALY < $40,000 (George et al 2000). As can be seen from Table 5 many life style interventions fit well within this 'acceptable range'. And given that the cost/QALY estimates in this Table do not incorporate, what are almost certain, downstream cost savings, the net performance will be even better. Our research supports funding of clinical approaches to life style modification, where these are targeted at high risk groups, using proven interventions. If society invests in such interventions, the potential health gain is large.
There is less certainty around population-based approaches to life style change. The research suggests that, whilst population based interventions (including those directed at school children) have the potential to be highly cost-effective, the evidence is generally of too poor quality, to be confident that this is the case. We also note that the estimated benefit per person for many of the studied interventions is very small. If size of health gain is also important, then some interventions that are potentially cost-effective due to low costs may not be suitable for funding. Such issues are beyond the scope of the current study but should be considered in any associated policy debate.

Table 3 Interventions that are highly cost-effective (<$12,000/QALY) based on good quality evidence

Intervention	***Estimated performance $/QALY gain #***
Mediterranean diet post AMI (deLorgeril et al, 1999)	*300*
Brief Interventions in primary care for problem drinking or heavy drinkers (Wilk et al, 1997; Saunders et al, 1991)	*100 to 900*
Lifestyle change to prevent type 2 diabetes (Eriksson et al, 1999)	*1,900*
Minimal physician advise to quit smoking (Silagy et al, 2004)	*m = 5,300 f = 8,600*
Intensive physician advise to quit smoking (Silagy et al, 2004)	*m = 6,600 f = 10,700*
Reduced fat diet for IGT (Swinburn et al, 2001)	*10,000*
Nurse nutritional counselling in general practice (Steptoe et al, '03)	*10,600*
Naltrexone + psychotherapy for alcohol dependence (Streeton et al, 2001)	*5,200 to 13,000*
Buprorion SR + counselling to quit smoking (Hughes et al, '04)	*m = 10,500 f=14,000*

Note # Base case, excluding downstream cost savings, rounded to nearest $100; m male; f female

[2] This conclusion does not relate to physical activity interventions pertinent to diseases management, such as exercise and strength training for osteoarthritis, which were outside the study scope, but found in other studies to be highly cost-effective, (Segal et al 2004).

Table 4 Interventions that perform relatively poorly based on good quality evidence $/QALY gain >$40,000

Intervention	*Estimated performance $/QALY gain*
Cardiovascular disease risk factors in children (Harrell et al, 1996)	*Control dominates*
GP exercise referral for CHD risk factors (Taylor et al, 1998)	*Control dominates*
Individualised exercised advice for persons 60+ (Halbert et al, 1999)	*575,000*
Orlistat + diet for obesity (Padwal et al, 2003)	*83,700*
School-based interdisciplinary lifestyle (Gortmaker et al, 1999)	*50,000*

Note # Base case, excluding downstream cost savings

Performs poorly against many life style interventions (the focus of this study), but well compared with medications listed on the Pharmaceutical Benefits Schedule. (George et al 2000).

Table 5 Summary of cost-utility analyses of interventions for physical activity, nutrition, smoking and alcohol, including multi-factorial interventions

	Intervention (key study)	Incremental QALY gain per person (0% disc rate)	Incremental program cost $/person	Incremental $ cost/QALY [2]	Quality of evidence
MULTI-RISK FACTOR (Nutrition + Physical activity +/- alcohol +/- smoking)					
1	Fighting fat, fighting fit media campaign (Wardle et al, 2001)	0.0546	$308	$5,600	##
2	Stanford 5 City project (Farquhar et al, 1990)	NA	$103	$14,700	##
3	Student TV viewing and obesity (Robinson, 1999)	~ 0.0006 to 0.002	$167	Hypothetical $74,600 to $298,600	#
4	Interdisciplinary student intervention for obesity (Gortmaker et al, 1999)	~ 0.001	$69	$50,100	##
5	CVD risk factors in children (Harrell et al, 1996)	NA	$323	Control dominates	##
6	CVD risk reduction in children, (Killen et al, 1988)	~ 0.0006 to 0.002	$87	Hypothetical $37,100 - $148,000	#
7	GutBusters workplace program (Egger et al, 1996)	0.02	$356	$19,800	#
8	Workplace prevention of heart disease (WHO European Collaborative, 1986)	NA	UK: $90 Belgium: $224 Italy: $461	Not modelled	#
9	Oxcheck: Primary care nurse health checks (Imperial Cancer Research Fund '95)	0.0045	$57	$12,600 to $65,200	###
PHYSICAL ACTIVITY					
10	Australian Active Script (Nacerrella & Huang, 2001)	NA	NA	Not modelled	
11	New Zealand Green Prescription (Elley et al, 2003)	0.01439	$417	$29,000	##
12	GP Exercise referral for CHD risk factors (Taylor et al, 1998)	NA	$223	Control dominates	##
13	Community based exercise for over 65 year olds (Munro et al, '02)	0.009	$144	$15,650	#
14	Physical activity program for 60+ year olds (Halbert et al, 1999)	Approx 0.0002	$126	$575,300	###

	Intervention (key study)	Incremental QALY gain per person (0% disc rate)	Incremental program cost $/person	Incremental $ cost/QALY [2]	Quality of evidence
NUTRITION					
15	Nutritional counselling in GP (Pritchard et al, 1999)	NA	$88	Not modelled	#
16	Mediterranean diet in those with previous MI (deLorgeril et al, 1999)	1.44	$488	$340	####
17	Reduced fat diet for IGT (Swinburn et al, 2001)	0.024	$241	$10,000	###
18	Orlistat and diet for obesity (Padwal et al, 2003)	NA	$1,492	$83,700	##
19	Lifestyle changes to prevent type 2 diabetes (Eriksson et al, 1999)	0.41	$769	$1,900	####
20	Talking computer for nutrition (Delichatsios et al, 2001)	NA	NA	Not modelled	#
21	Nurse nutritional counselling in GP (Steptoe et al, 2003)	0.087	$917	$10,600 to $39,000	##
22	Multi media 2 fruit 5 veg (Dixon et al, 1998)	0.0048	$0.20	$50	#
SMOKING – modelled over more than 20 years in a wide range of contexts/settings					
23	US mass media smoking campaign: MTCP (Beiner et al, 2000; Rigotti et al, 2002)	0.0211	$44	$2,100	#
24	AUS mass media campaign: Phase 1 National Tobacco Campaign (Wakefield et al, 1999)	0.0006	$0.71	$1,100	#
25a	Minimal smoking advice in GP (Silagy et al, 2004)	M = 0.0027 F = 0.0017	$14.30	M = $5,300 F = $8,600	##
25b	Intensive smoking advice in GP (Silagy et al, 2004)	M = 0.0093 F = 0.0057	$61.06	M = $6,500 F = $10,700	##
26	Meta-analysis of, brief, NRT, behav. interventions (Baille et al, 1994)	NA	NA	Not modelled	###
27	Phone counselling as adjuvant therapy for NRT (Zhu et al, 2000)	M=0.0426 F=0.0251	$501	M=$11,800 F=$20,000	#
28	Meta-analysis of 16 Bupropion SR trials (Hughes et al, 2004)	M = 0.0544 F = 0.0407	$570	M = $10,500 F = $14,000	###
ALCOHOL – modelled over more than 20 years in a wide range of contexts/settings					
29	US mass media campaign (Holden and Treno, 1997)	NA	NA	Not modelled	#
30	Brief interventions in primary care for problem drinking (Wilk et al, 1997)	0.091 to 0.330	60.98	$185 to $670	###
31	Brief interventions to extended advice for heavy drinkers, (Saunders et al, 1991)	0.068 to 0.757	Simple: $15 Brief: $30 Extended: $90	$35 to $888	###
32	MOCE vs BSCT, (Heather et al, 2000)	0.116 to 0.244	$249	$1,000 to $2,100	###
33	MET vs control (Sellman et al, 2001)	0.1157 to 0.2865	$389	$1,360 to $3,370	##
34	Naltrexone + psychotherapy (Streeton et al, 2001)	0.0528 to 0.132	$685	$5,200 to $13,000	###

Note # Very poor quality evidence: Eg lack of control group, lack of ITT, minimum follow-up, limited evidence of relationship between behaviour and health

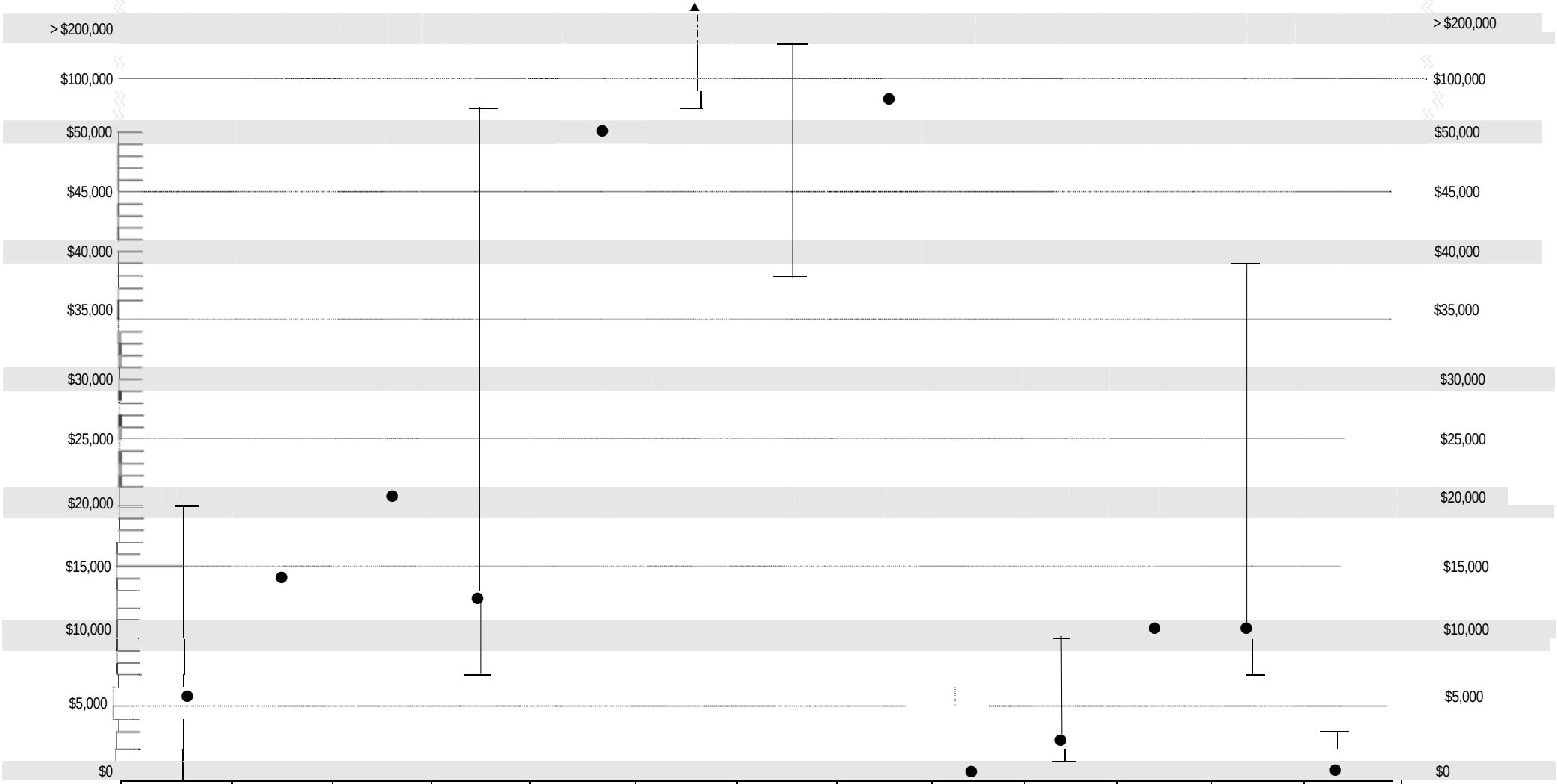
Poor quality evidence

Acceptable quality evidence

Good quality evidence. Eg; RCT, ITT analysis, appropriate outcomes (behavioural as well as health), appropriate follow-up period and minimal loss to follow up)

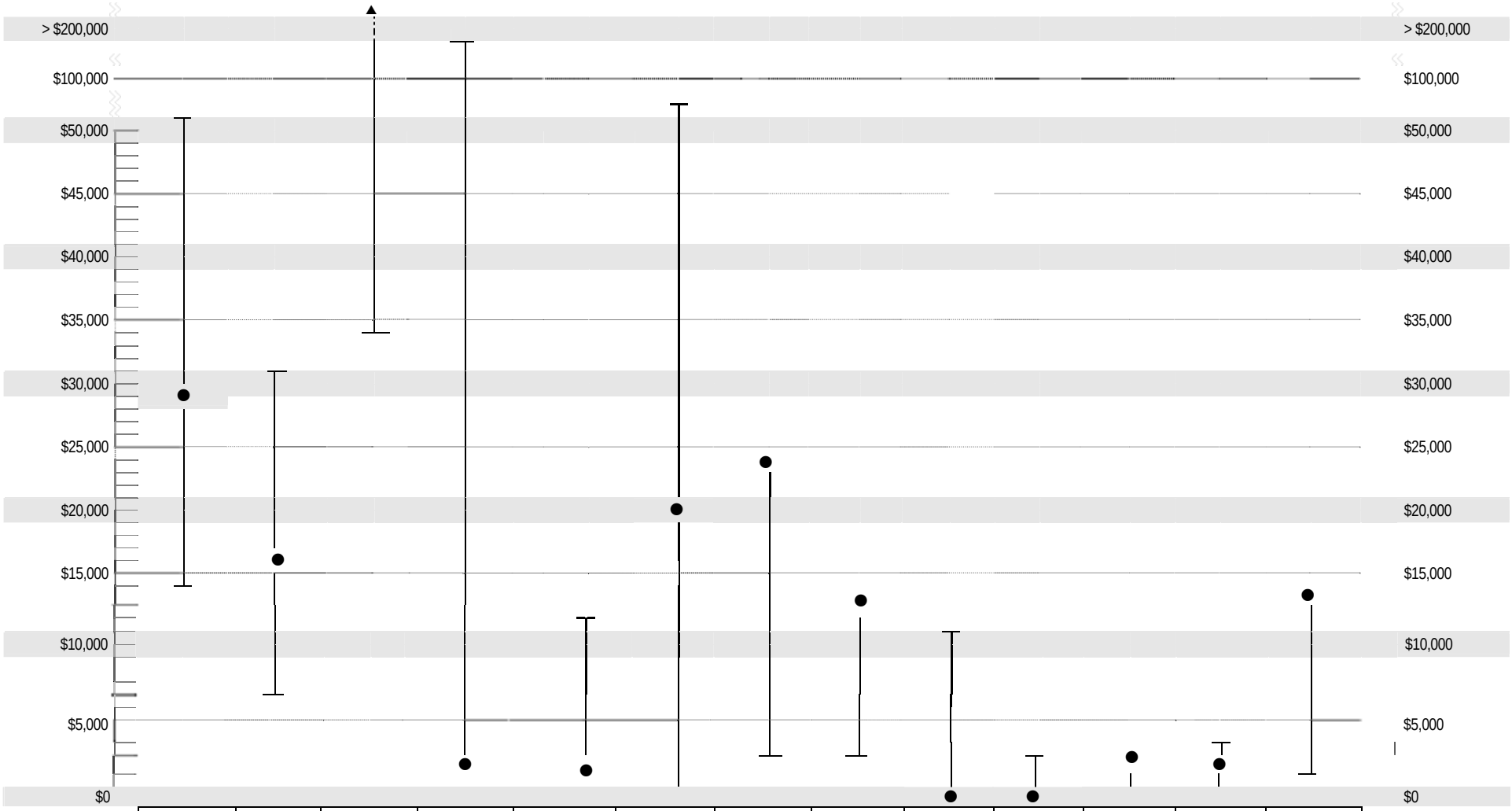
NA data not available

Figure 1 Sensitivity analysis and ranking of interventions (QALYs discounted at 5%)



	FFFF	Stanford 5	GutBusters	Oxcheck	Mass 10-school intervention	TV & obesity	CVD risk reduction	Orlistat	Mediterranean Diet	Lifestyle change for diabetes	Reduced fat diet	Nurse Counselling	2 fruit 5 veg media campaign	
Best Estimate	$5,600	$14,600	$ 19,800	$12,600	$50,000			$83,600	$300	$1,900	$10,000	$ 10,500	$ 50	Best Estimate
Upper Range	$20,200			$65,200		$299,000	$148,000	?	$700	$10,000		$39,000	$2,500	Upper Range
Lower Range	$ 10			$6,800		$74,500	$37,000	?	$200	$ 1,100		$6,500	$20	Lower Range
	Multi-factorial - Adults				*Multi-factorial – School based*				*Nutrition*					

Figure 1 (continued)



	Active Script	Ex Sessions	Ex Advice	MTCP	Aust Tobacco Campaign	GP advice for smoking	Phone counsel + NRT	Bupropion	BIs problem drinking	BIs heavy drinkers	MOCE vs BEST	MET	Naltrexone	
Best Estimate	$29,000	$15,600	$ 575,000	$2,000	$1,100	$20,000	$24,200	$12,500	$600	$300	$2,100	$1,360	$ 13,000	Best Estimate
Upper Range	$58,000	$31,300		$190,000	$21,500	$69,000			$10,500	$2,600		$ 3,400		Upper Range
Lower Range	$ 14,500	$7,200	$ 33,000	$900	$600	$200	$1,500	$2,100	$ 100	$ 15	$1100	$300	$1,500	Lower Range
	Physical Activity			*Smoking*					*Alcohol (base case excluding external family effects)*					

SECTION I INTRODUCTION AND METHODS

Chapter 1 Introduction

1.1 Background

The risk factor project was commissioned by the Department of Health and Ageing, Population Health Division, to establish the optimal (most cost-effective) means to reduce burden of harm from physical inactivity, poor nutrition, alcohol misuse and tobacco smoking.

The health of the community and its members is influenced by non-modifiable and modifiable factors. Of the latter, most important are use of health care services, lifestyle behaviours and social and economic variables. The incidence and progression of the common chronic diseases of modern societies of heart disease, type 2 diabetes, stroke, some types of cancers and arthritis are highly influenced by lifestyle behaviours. The most important of these lifestyle behaviours are tobacco use, physical inactivity and nutrition - the latter relevant separately but also for their influence on obesity. Alcohol misuse is important in part for its impact on disease, but also for the direct burden of harm of alcohol dependence on the individual and his/her family.

Governments have a potential role to encourage and support members of the community to adopt more healthy lifestyle behaviours. The role of government arises from several considerations:

- that citizens should have adequate information to make informed choices;
- that citizens should be protected from making 'unwise' choices; whereby society accepts an obligation to promote healthy lifestyle choices - regardless of expressed preferences, as consumer choices are compromised by the various distorting influences on the health care market and the wider market place;
- lifestyle behaviours can have consequences for persons other than the person indulging in the high risk behaviour. This applies most notably to alcohol abuse and tobacco smoking;
- high risk behaviours are not without cost consequences for society, for instance the downstream costs of treating associated illness and addressing harms, which are not necessarily considered adequately by the individual.

Based on the above arguments, the research program presumes that modifying high-risk behaviours, which are associated with an expected loss in quality of life and/or increased mortality and/or harm to others is a valid social objective.

1.2 Study objectives and scope

The possible means to influence lifestyle behaviours are wide ranging and include: i) programs to inform, educate and empower citizens and patients, ii) information and training for providers, iii) modification to financial incentives, for instance through taxation and subsidies or adjusting the level of co-payments, iv) direct service provision and v) regulatory arrangements and enforcement. Each set of policies or strategies for influencing lifestyle behaviours will have cost or resource use implications, for individuals, the community and governments, and a level of influence on lifestyle behaviours and subsequent health status of individuals directly affected and for the wider community.

The purpose of this study was to compare the performance of a range of options for modifying the four target lifestyle behaviours of physical inactivity, poor nutrition, alcohol misuse and tobacco smoking. Recognising that resources are limited, the aim was to determine how best to reduce the burden of harm on the Australian community from these risk factors, by determining which

interventions are most effective and cost-effective and able to make the greatest contribution to harm reduction.

This is a technical analysis. The results can provide an important input to resource allocation decisions. To the extent that health (reflected in mortality and quality of life), is the primary objective of health policy, the research in identifying the most efficient means for its achievement can inform resource allocation decisions efficiency. While there are other potential objectives and other issues that might be relevant to policy decisions, in the absence of agreed society standards it was decided not to attempt to incorporate other objectives. This would otherwise introduce a layer of subjectivity, that it was considered would undermine the independence of the analysis. Similarly such matters as 'acceptability' or 'implementability' are not only highly subjective but also highly dependent on the specific policy and practice and organisation environment and cannot be taken as givens.

1.3 Reporting

The project has been completed in several stages. It commenced with a literature review, to gain familiarity with the substantial literature relating to evidence concerning interventions designed to modify these four lifestyle behaviours (Segal, Dalton, Robertson et al 2003). The primary purpose of this task was to select a set of interventions for economic analysis that met documented criteria concerning quality of evidence, primarily trial design, nature of outcome data and period of follow-up. However there was also an over-riding requirement for comprehensiveness - across risk factors, setting, modalities etc., which necessitated substantial compromise in the application of these criteria, given the quality of the evidence. The interventions selected through this process for economic analysis are listed in Table 1.1. This list also includes a small number of newly published studies, subsequently added, which fit the inclusion criteria.

The primary project task has involved the assessment of economic performance of the identified interventions through cost-utility analysis, wherever possible. The results of these analyses are reported in 6 volumes; in this Executive Report, plus Five Technical Reports, one for each of the four risk factors, plus one for interventions targeting multiple risk factors.

Table 1.1 Interventions and level of analysis completed

		PROGRAM TYPE AND MODALITY	BRIEF DESCRIPTION : KEY REFERENCES
Multi-factorial: Nutrition + Physical activity +/- alcohol +/- smoking			
1	**Y**	Large scale media + community	A 7 week program on BBC radio, called FFFF 'Fighting Fit Fighting Fat'. (Waedle et al, 2001)
2	**P**	5 yr media/ community-wide education for CVD risk factors.	The "Stanford Five-City Project." (Farquhar et al, 1990)
3	**S**	School-based, focused on reduced TV viewing	USA school-based intervention aimed at increasing physical activity and improving diet by reducing TV, video and computer game viewing. Parents also targeted (Robinson et al 1999)
4	**P**	School-based- interdisciplinary program to reduce obesity	School-based program designed to reduce obesity amongst children in grades 6 to 8. The interdisciplinary intervention was administered over two school years. (Gortmaker et al, 1999)
5	**D**	School-based - class room lessons on exercise, nutrition and smoking	RCT field trial: Regular classroom and physical education teachers, 8 weeks of classes on nutrition and smoking + 8-week exercise program.(Harrell et al, 1996)
6	**S**	20-session school based- risk-reduction education	All 1447 tenth graders in four senior high schools from two school districts participated in a cardiovascular disease risk-reduction trial, 'matched control school'. (Killen et al, 1988)
7	**Y**	Workplace/ community group obesity program for overweight males.	GutBusters: Self-help group program conducted in the workplace, through self help tapes/booklet, group sessions moderated by allied health professional (Egger et al 1996, 1999)

		PROGRAM TYPE AND MODALITY	BRIEF DESCRIPTION : KEY REFERENCES
8	N	Workplace - multi-factorial prevention of CHD.	60, 881 men in 80 factories in Belgium, Italy, Poland, UK. Multifactorial prevention of CHD. (WHO European Collaborative Group, Lancet 1986 (1): 869-72)
9	Y	Primary care: health checks by practice nurse. The OXCHECK study	Health checks, performed by nurses in primary care, to improve life style behaviours and reduce risk factors for CVD and cancer. (Imperial Cancer Research Fund, BMJ 1994, 1995 Whiteman et al '99)
Physical activity			
10	N	GP active script – Australia (subsumed in 11)	GP script for increased activity levels by persons considered sedentary. Program on-going supported by VicFit. (Nacerrella and Huang, 2001)
11	Y	GP active script - New Zealand	RCT of 878 sedentary patients. Program consisted of written and oral tailored advice from GP's to exercise and telephone follow up from exercise specialists. (Elley et al, 2003)
12	D	GP + active script +/- access to supervised exercise, UK	Primary care -based exercise. Prescribed 20 exercise sessions at leisure centre (half price) over 10 weeks. Moderate/vigorous aerobic activity, semi supervised. (Taylor et al, 1998)
13	Y	Free community exercise programs for the elderly	A 2-year program in the UK for over 65's to attend free supervised exercise sessions in community. (Munro et al, 2002)
14	Y	Allied health in primary care setting	Counselling by exercise specialist – Australian study initial sessions, reinforced at 3, 6 months. 12 month follow-up. (Halbert et al, 1999)
Nutrition			
15	N	Primary care, Dietician +/- GP counselling re nutrition	Australian study. 6 counselling sessions on nutrition by GP + dietician, or dietician alone. Target at risk patients. (Pritchard et al, 1999)
16	Y	Nutrition counselling for persons post AMI by cardiologist and dietician	RCT: 1-hr dietary advice session from a cardiologist and dietician advising Mediterranean-type diet. (de Lorgeril et al, 1999)
17	Y	Group education for persons with IGT	5-year follow-up of a 1-year RCT of a reduced-fat diet versus usual diet. Intervention group participated in monthly small-group education sessions on reduced-fat eating for 1 year. (Swinburn et al, 2001)
18	P	Diet +/- pharmacotherapy (orlistat) for obesity	Review of 11 RCTS of orlistat in combination with diet for obesity compared to placebo plus diet. (Padwal et al, 2003 (Cochrane Review))
19	Y	Consultations with nutritionist. Targeted at persons with IGT. *'The Finnish Diabetes Prevention study'*	523 overweight subjects with IGT received information about lifestyle change to prevent diabetes. Annual follow-up visits. 7 sessions with nutritionist in yr 1, + 3 mnthly visit thereafter to ↓ weight, ↓ saturated fat, ↑ dietary fibre, + advice to increase physical activity. (Eriksson et al, 1999)
20	N	Clinician advice using information technology	RCT. Weekly communication for 6 months via automated, computer-based voice system. For intervention group IT monitoring of dietary habits and provided educational feedback, advice and behavioural counselling. Control group received physical activity counselling. (Delichatsios et al, 2001)
21	Y	Advice by practice nurse to increase fruit and veg	UK intervention designed to measure the effect of brief behavioural counselling by practice nurses on the consumption of fruit and vegetables. Target adults from low income populations. (Steptoe et al, 2003)
22	Y	State wide media campaign- fruit and veg	The 2 Fruit 'n' 5 Veg Every Day campaign was a state-wide nutrition promotion conducted in Victoria over four years in the early 1990s. (Department of Health 2002, Dixon et al 1998)
Smoking			
23	Y	Mass media aimed at entire population.	Massachusetts Tobacco Control anti-smoking campaign. (Beiner et al, 2000, Rigotti et al, 2002)

		PROGRAM TYPE AND MODALITY	BRIEF DESCRIPTION : KEY REFERENCES
24	Y	Mass media campaign aimed at smokers aged 18-40 yrs	Advertising campaign + quit line phone support to assist smokers to quit. (Wakefield et al, 1999) *Australian National Tobacco Campaign (NTC)*
25 a	Y	Minimal Advice from clinicians to support smoking cessation	Brief advice versus no advice or usual care from a GP; (Silagy et al, 2004 meta-analysis)
25 b	Y	More Intensive advice from clinicians to support smoking cessation	Intensive advice versus no advice, or brief advice from a GP (Silagy et al, 2004)
26	N	Behavioural and nicotine replacement therapy (NRT)	Older meta-analysis of clinician advice of varying intensities, with/without NRT. (Baille et al, 1994)
27	Y	Telephone counselling and NRT, to support people who had decided to quit	Telephone support with NRT compared to NRT only for 12 months aimed at maintaining cessation of smoking. (Zhu et al, 2000)
28	Y	Pharmacotherapy (+ psychotherapy), bupropion SR	Use of bupropion SR + psychotherapy or psychotherapy alone. (Hughes et al, 2004)
Alcohol			
29	N	Mass media, aimed at entire population	US Community project, media advocacy focussed upon community awareness and support for local policies. (Holder and Treno 1997)
30	Y	GP counselling, aimed at those with alcohol problems	Meta-analysis of 34 studies of GP counselling. Distinguished between treatment seeking and non-treatment seeking populations. (Wutzke et al 2002; Wilk et al, 1997)
31	Y	Brief interventions, aimed at heavy drinkers	Study of >1500 subjects (in 8 countries) considered at risk of alcohol-related problems but with no history of dependency. (WHO Brief Intervention Study Group 1996, Saunders et al, 1991)
32	Y	Cognitive and behavioural therapy (MOCE vs BSCT)	Moderation Oriented Cure Exposure, compared with Behavioural self-control training in heavy drinkers. (Heather et al, 2000)
33	Y	Cognitive behavioural therapy compared (MET)	Motivational enhancement therapy compared to no counselling and non-directive reflective listening for 122 patients with mild to moderate alcohol dependence. (Sellman et al, 2001)
34	Y	Pharmacotherapy, Naltrexone (NTX) and psychological therapy	Australian RCT, comparing 12 weeks NXT with placebo or other active drug in patients >18 years with diagnosis of alcohol dependence or abuse. (Streeton et al, 2001)

Notes:

Y Yes - Cost-utility analysis completed incorporating published evidence

S Scenarios - Cost-utility analysis completed based on assumed data

D Intervention dominated – cost-utility analysis not applicable

N Not modelled, see discussion section III, but generally due to no evidence of effectiveness

P Cost-utility result reported from existing published model that appears robust

Table 1.2 Reporting Status

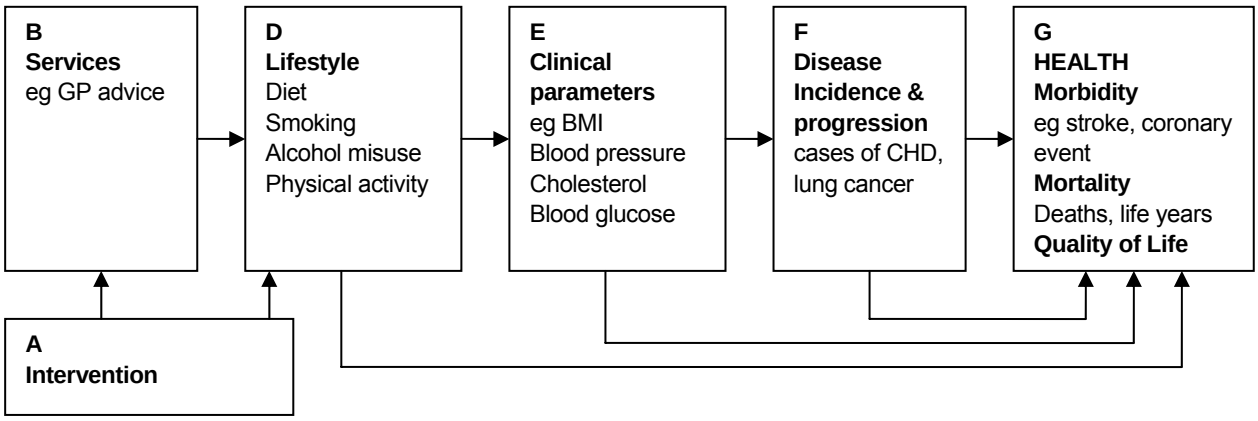
Status	Multi-risk factor	Physical activity	Nutrition	Smoking	Alcohol	Total
C-U analysis completed	3	3	5	6	5	22
Published C-U of acceptable quality	2	-	1	-	-	3
Scenario analysis	2	-	-	-	-	2
Intervention dominated	1	1	-	-	-	2
C-U not completed due to lack of trial data	-	1	2	1	1	5
C-U not completed due to complexity of model	1	-	-	-	-	1
Total	9	5	8	7	6	35

Chapter 2 Methods

2.1 Introduction

The primary methodological challenge in comparing the performance of a wide range of interventions designed to change behaviours is to translate reported outcomes into a universal measure of effectiveness. The challenge here is 2-fold; firstly relating the change in lifestyle to health and secondly establishing whether any observed change in behaviour is maintained. The nature of the relationship between Interventions A and Health G is illustrated in Figure 2.1. This Figure is a partial representation most relevant to the current study and does not include all possible influences on health and wellbeing, (such as age, gender and socio-economic status and broad economy-wide or societal factors).

Figure 2.1 Relationship between Intervention, Lifestyle, Mortality/Quality of Life: Modifiable Factors



Intervention A is designed to modify lifestyle D, either directly (as in a media campaign) or indirectly by changing clinician behaviour (as in the Active Script program). Any change in lifestyle may potentially influence health in several ways:

i. *Directly:* for instance when a person feels better when they stop smoking through improvement in their sense of taste or smell (such impacts will be contemporaneous with the intervention);
ii. *Indirectly and over time (ie with a lag) through disease pathways* (F) usually mediated through changes in observable clinical parameters (E). An example is improved nutrition resulting in lower incidence of type 2 diabetes avoiding associated loss in quality of life and life expectancy; or via secondary prevention (ie as part of disease management), such as a reduction in smoking in persons with heart disease reducing the rate of complications;
iii. *Inversely:* observed behaviour may be influenced by a change in health status which in turn results in deterioration of health. For instance an exogenous decline in health status (such as loss of mobility or sensory function) may lead to a change in lifestyle (such as reduced physical activity or poor appetite/compromised nutrition), resulting in a second-order decline in health status;
iv. *Via externalities:* Health impacts from the behaviour change of an individual may accrue to others. For example, alcohol misuse (or adoption of safe drinking) can have major consequences for family members and others in the community. Such impacts may be direct and contemporaneous (as in foetal alcohol syndrome), or mediated through disease (as in the effect of alcoholic dementia on family burden, or risk of smoking related disease via passive smoking).

Given the complexity of this relationship, we have where possible, in assessing performance, adopted a 2-stage approach, distinguishing the impact on behaviour from the consequent impact on health.

The first measure of performance is *comparative cost-effectiveness ratios* in which interventions are analysed in terms of the cost to achieve an observed change in lifestyle based on trial results ($A/∆D). This creates an intermediate measure of performance, whereby interventions that target the same lifestyle behaviour can be compared, without having to understand the relationship between behaviour and health. However, it is most useful where lifestyle is consistently and simply described, as is possible with smoking. It is far less useful for something like nutrition or physical activity given the range of ways that behaviour can be described and the lack of precisely definable at-risk behaviours. Furthermore, it does not allow comparison across all interventions, given the range of lifestyle behaviours being considered in this study. The approach cannot be used to describe the performance of interventions targeted at a number of behaviours and does not allow comparison between interventions targeted at life style and other health interventions.

The preferred measure of performance is thus *cost-utility analysis* in which interventions are assessed in terms of the cost to achieve an estimated gain in quality of life and mortality ($A/∆G). Our capacity to complete these calculations is dependent on the nature of evidence. It requires evidence on $A (cost of the intervention) and ∆G (impact of the intervention on mortality and quality of life). The latter can in theory be measured directly or via modelling for instance; the relationship between change in lifestyle and change in clinical parameters and or disease state and health. We now discuss in broad terms the methods used to estimate costs and impact on health. More information on the specific models and assumptions are provided in the summary chapters on each risk factor (see below), and in more detail in the Technical Report.

2.2 Costs/resource use

Determining costs requires an understanding and capacity to estimate the resource inputs for delivering the intervention in question. This is primarily made up of the direct costs of delivery – for clinician time, pertinent diagnostic tests, consumables etc., but also for program management, training of clinicians, and identification and recruitment of eligible participant group where that is central to the intervention. However, costs specifically related to the trial setting should be excluded.

Direct costs have been calculated using one of two methods:

i. *Calculated costs:* careful documentation of the intervention described in the literature to establish resource inputs and the application of Australian published unit costs to each input. Unit costs are derived from a range of sources including the Pharmaceutical Benefits Scheme (PBS) and the Commonwealth Medicare Benefits Schedule (MBS), published charge-out rates for specific health disciplines etc.;

ii. *As reported*: the use of published costs of an intervention, adjusted by the health price index and relevant exchange rate as necessary. While this latter method might be considered more robust in that it uses actual program costs, there can be some doubt about which costs have been included. There is the further concern with overseas programs that resource inputs and costs may not reflect the Australian setting.

Costs are calculated in Australian dollars and expressed in 2003 dollars, ($A 2003).

Downstream cost impacts: Interventions may also result in changes in downstream health service use resulting from a change in disease incidence and/or rate of disease progression and/or a change in resources needed to address harm or side-effects. The benefits of any downstream cost savings is in the freeing up of resources that can then be reallocated to yield benefits elsewhere. However, the base case for the models excludes downstream cost impacts, largely due to the uncertainty in these estimates. (See discussion below).

In addition, the calculations are complex, due to the wide range of health conditions that might plausibly be affected, reflecting the breadth of scope of the research program and the wide-ranging impacts of life style behaviours. We also note that excluding downstream cost savings provides for a conservative estimate of potential benefits.

This treatment is consistent with the PBAC Guidelines (1995), which highlight the need for caution in modelling from intermediate to final outcomes. High quality evidence is required of the relationship between reported outcomes (eg clinical parameters) and health. In relation to downstream cost savings from interventions designed to modify lifestyle behaviours, the steps and assumptions required in the modelling are many. Assumptions must be made to go from evidence of change in current behaviour, to impact on future behaviour, and further assumptions to impact on future clinical/health outcomes and finally to health resource impact. Especially in relation to primary prevention, where health benefits are not expected to accrue for many years into the future, when health care management and costs cannot possibly be predicted, any estimate of potential downstream cost savings must be highly speculative.

On the other hand, where impact on clinical outcomes is more immediate and resource impacts are collected as part of a clinical trial, then consequential effect on resource use can be estimated with some confidence. Thus downstream cost savings are included in the base-case where health care costs or health care events are collected and reported as part of the clinical trial and the results are significant. In relation to the interventions analysed, this applies only to the Mediterranean diet intervention, for which downstream cost impact is included in the base case. Elsewhere, potential downstream cost savings have been included in the sensitivity analysis. In the case of disease based models (such as interventions targeted at persons with diabetes) estimates of potential downstream cost savings are developed, using published data on the cost of managing diabetes. In other cases a threshold analysis is performed to calculate what downstream cost savings would need to be, for the intervention to become cost neutral. This is most appropriate for interventions that have very wide potential impacts across several disease groups and for which the calculations involved in estimating potential savings are extremely complex. Given the number of interventions analysed and the very large number of diseases potentially implicated and the quality of the available data, it simply was not possible to take the downstream cost analysis further. (It was expected the AIHW would complete an analysis of disease costs attributable to lifestyle behaviours that could have been used to estimate downstream cost savings. However, this study did not however proceed at that time.)

A societal perspective was taken, which means all costs are to be included, regardless on whom they fall. This is different from a government or agency perspective. In practice some costs have not be measured – specifically private costs to access services, such as waiting time, transport costs and costs to others (such as carers) and productivity impacts. While these may be important, methodologies are insufficiently developed to provide reliable estimates. Furthermore, they are not typically included in program descriptions or in the economic evaluation of health programs. Finally in the context of a large priority setting exercise in which over 30 interventions are to be modelled it simply was not possible to allocate the time and research resources to this complex issue.

2.3 Estimating the impact on lifestyle

Estimating the impact of an intervention on lifestyle requires two pivotal pieces of evidence:

i. evidence of the magnitude and direction of lifestyle behaviour change *in the presence of the intervention*; and
ii. evidence of the persistence (or otherwise) of any lifestyle behaviour change *after the intervention has been discontinued.*

The evidence of the treatment effect on lifestyle behaviours was drawn from a meta-analysis of well-conducted randomised control trials (RCT) where available. This was the case for pharmacotherapies, and some primary care interventions, where there is little variation in the interventions, patient profiles and costs so that the results of several studies can be combined. However, in evaluating other types of interventions where there is considerable variation in the components of the intervention, the patient profile/target group and resource inputs, these do not lend themselves to meta-analyses. Thus meta-analyses were generally not available as a source of evidence. Further, in undertaking cost-utility analyses of complex and unique interventions, the only way that costs can be derived, based on the resources applied and related to the observed outcomes, is to work with individual studies. Our main strategy was to locate all well constructed studies that met basic criteria for suitability for generation of evidence; i) addressed one or more of the four subject life style behaviours; ii) an RCT, iii) report objective measure of outcomes, iv) full description of the intervention that can be used to calculate costs, v) long term follow-up. Any studies that met all those criteria were included. Very few trials were identified that met all these criteria, therefore in order to maintain a breadth of scope for the comparison, trials were also included which did not; (for example for which there was no follow-up after completion of the intervention.) A full discussion of the process for selecting the interventions for evaluation is contained in a previous report to the Department.

Due to the relatively short duration of follow-up in the majority of trials, evidence of the persistence of a treatment effect was invariably drawn from observational rather than experimental studies. Where possible the influence of effect modifiers, such as the duration of changed behaviour, exposure to stressor/temptation events and patient characteristics (such as age and gender), has been allowed for[3]. This also means that in estimating the likely long term treatment effect, in the absence of clinical trial data, typical changes in patterns of behaviour need to be recognised and not attributed to an intervention. (For instance alcohol misuse tends to reduce with age, whilst obesity tends to increase with age and then decline). This has important implications for estimating downstream changes in behaviour, which must be relative to what it would have been without the intervention.

Transferability and generalisability: Australian-based trials were used wherever possible to maximise relevance to Australia. However there are insufficient high quality Australian trials addressing the four subject risk factors and thus the international literature, notably European and North American trials were also used. In considering likely transferability of results, not only is the country of Trial pertinent, but also patient characteristics (clinical and personal) and aspects of the health service delivery system.

Selection bias and the Hawthorne effect typically associated with trials, and the possibility of a poor match between the comparator used in a trial and current Australian practice can all affect transferability and generalisability of results. However, to fully take into account all such factors is a large research task and one beyond the scope of this analysis. The performance of interventions described in the following chapters derives from the clinical trial setting and transferability to the community or clinical practice setting has not been explored. This is a limitation of the analysis – and common to any study that uses clinical trial evidence to determine performance.

2.4 Estimating the impact on quality of life and mortality

The impact of an intervention on final outcomes such as quality of life and mortality can be estimated either by direct observation, or in the absence of such observed data, indirectly. The techniques that

[3] For example, Gilpin et al (1997) calculated that "the likelihood of remaining continuously abstinent until follow-up was about 95% *for those who had quit for 1 year or longer*" (Gilpin et al, 1997 p572)[3]. In comparison, "only about 12% of the former smokers who had quit for less than 1 month at baseline remained continuously abstinent at the follow-up interview. This percentage increased to 25% for those who had quit from 1 to less than 3 months; it increased again to 52% if the duration of quitting was from 3 to less than 6 months, but it increased only slightly to 59.2% for those who had quit from 6 to less than 12 months" (Gilpin et al, 1997 p572).

can be applied when recourse must be made to indirect means to estimate the health effect are discussed below, after a brief discussion of the direct approach.

The first-best approach is to directly observe any divergence between intervention and control groups with respect to mortality and morbidity. In relation to life style interventions, this first-best approach is available in only a handful of cases where trial participants have been carefully followed over several years and risk of death is sufficiently high for differences to be observed and/or expected impact on quality of life is sufficiently great (for example Mediterranean dietary advice for person after AMI, deLorgeril 1999, included 5 year follow-up in a high risk population, allowing for the observation of significant differences in cardiac events and all-cause mortality). More commonly, direct observation of intervention and control groups is limited to relatively short periods of 6 to 24 months during which time effects on mortality and morbidity are unlikely to manifest.

The second-best approach relies on supporting evidence of the link between intermediate outcomes (such as smoking cessation or increased physical activity levels) that are directly observed in the available trials and final outcomes of quality of life and mortality. A number of approaches could be used. Continuing with the notation from Figure 2.1 above, the link between ΔD and ΔG could be estimated:

i. directly (presuming this encompasses the effect of the intermediate impact on clinical parameters and disease incidence): $\Delta D \rightarrow \Delta G$,
ii. via clinical parameters (presuming this encompasses the intermediate impact on disease incidence): $\Delta D \rightarrow \Delta E \rightarrow \Delta G$,
iii. via disease incidence (presuming this encompasses the intermediate impact on clinical parameters): $\Delta D \rightarrow \Delta F \rightarrow \Delta G$, or
iv. via clinical parameters and then disease incidence: $\Delta D \rightarrow \Delta E \rightarrow \Delta F \rightarrow \Delta G$.

The second approach $\Delta D \rightarrow \Delta E \rightarrow \Delta G$, estimating the impact on health via clinical parameters/life style behaviours is commonly applied in the economic evaluation literature[4] and relies on the application of published risk equations derived from large-scale cohort studies (eg, Anderson et al, 1991; D'Agostino et al, 2000; Knuiman, Vu & Bartholomew, 1998). These published risk equations provide valuable information as to the determinants of disease-specific mortality or morbidity and depending on the format of the link between intermediate and final outcomes may be suitable for direct application to the findings of clinical trials.

However the potential for application of these equations in the current context is limited by the number of lifestyle behaviours included and pertinent clinical/ biochemical parameters. The precise descriptor of behaviour and clinical parameters is important and their match against clinical trial descriptors. (For example how drinking behaviour is defined or diet – where numerous options are possible). An additional step linking trial results with the clinical/biochemical markers included in published risk equations is frequently required before substitution and this additional step often relies on supporting evidence of variable quality (or crude assumptions).

Importantly the majority of published risk equations link intermediate outcomes to only one disease pathway (such as cardiovascular disease (CVD) events or CVD mortality). Such an approach is useful when lifestyle behaviours are causally linked with just one disease but are less useful when considering exposure to risk factors such as diet, exercise, alcohol and tobacco that operate via multiple disease pathways.

For the purposes of our present discussion, the remaining three approaches are classified as direct (option i) and disease-based (options iii and iv). It should be noted that the direct and disease-based

[4]For example NICE in the UK employ rigorous methods and have used published equations to establish relationships such as Framingham. (See reports such as, Sibutramine#31) The Australian PBAC also accepts submissions relying on similar methods, but details are commercial in confidence.

approaches differ both with respect to the complexity of the modelling task and the level and type of supporting evidence required.

To describe the link between intermediate and final outcomes under the direct approach: $\Delta D \rightarrow \Delta G$, we require evidence of the relationship between lifestyle behaviour (such as smoking status or alcohol consumption or physical activity levels) and health-related quality of life (HRQoL) and all-cause mortality. It is then relatively simple to estimate absolute risk of all-cause mortality for each lifestyle category (such as current, never and ex-smokers or problem, dependent and recovered drinkers) by multiplying each relative risk by the absolute risk of all-cause mortality for the reference category.

To delineate the link between intermediate and final outcomes under the disease-based approach: $\Delta D \rightarrow \Delta F \rightarrow \Delta G$, we require two pieces of evidence:

i. population attributable fractions (PAFs) describing the share of the observed disease incidence that can be 'attributed' to one or more lifestyle behaviours: $\Delta D \rightarrow \Delta F$, and
ii. HRQoL and relative risks of disease-specific mortality by disease: $\Delta F \rightarrow \Delta G$.

Where the lifestyle behaviour of interest is causally linked with just one disease, estimation of the impact on final outcomes under the disease-based approach is no more (or less) complex than under the direct approach. Where the lifestyle behaviour of interest is linked to final outcomes via multiple disease pathways, estimating the impact on final outcomes under the disease-based approach requires attributions to be made for each of those disease pathways.

Even if we were to set aside the problem of double-counting and the additional informational requirements, estimation under the disease-based approach entails a considerable increase in complexity when the link to final outcomes operates through multiple disease pathways. A number of authors have seen fit to comment on the use and misuse of PAFs for informing public health policy (eg, Rockhill, Newman & Weinberg, 1998; Greenland & Robins, 1988). In the current context, particular caution is advised when applying PAFs to the relatively narrow populations targeted by specific interventions. Such concerns as to the applicability of supporting data are, of course, much broader and apply at each stage of the causal chain between ΔD and ΔG.

Similarly, a number of general difficulties arise under the headings of confounding, interaction and reverse causation when using observational data to estimate that fraction of the disease burden that could be prevented if exposure to a particular risk factor was avoided (Walter, 1983). Once again, these concerns are not specific to the estimation of PAFs. That said, attributions to one risk factor or another should not be treated as a black-box and policy-makers should be apprised of the methods used to control for confounders, to adjust for the impact of reverse causation and to capture non-linearity in the relationship between risk factors and the particular disease in question.

Given the scope of the research agenda undertaken, differences between the disease-based and direct approach with respect to complexity and informational requirements had an influence on our decision to adopt the direct approach. We were also concerned at the failure of the 'disease approach' to capture health impacts that accrue directly; that is not mediated via disease.

The potential for changes in lifestyle behaviours to directly generate quality of life gains is of potential importance and could only be captured in the 'direct approach'.

To illustrate the data requirements of the direct approach establishing the link: $\Delta D \rightarrow \Delta G$ we consider an example from the smoking cessation interventions. Estimates of the relative risk of all-cause mortality by smoking status were taken from Taylor et al (2002). These estimates are based on data from the Cancer Prevention Study II, a prospective study in a cohort of 1.2 million US adults recruited in late 1982. While the sample is not representative of the target population with respect to education, health status & race, it does have the advantage of controlling for age, sex and time since

smoking cessation in ex-smokers. The Taylor et al (2002) data therefore reflects the age/sex adjusted cumulative effects of each additional cycle as an ex-smoker. The Taylor et al (2002) estimates of all-cause mortality by smoking status imply no reduction in the risk of all-cause mortality during the initial 3 years in the ex-smoker state. “Those who had quit less than 3 years before baseline were combined with current smokers because they have similar mortality rates and because relapse among recent quitters is quite high” (Taylor et al, 2002 p991). We therefore apply the risk of death for current smokers to the initial three cycles in the ex-smoker state. The age/sex adjusted risk of all-cause mortality for ex-smokers is then applied to subsequent cycles in the ‘ex-smoker’ state, after adjusting for the duration of continuous abstinence (3-5 yrs, 5-10 yrs, 11-15 yrs and ≥ 16 yrs).

2.5 Effects that extend beyond the individual

Health benefits can extend beyond the individual, to family members and the wider community. However, it is not common to capture these wider influences in economic evaluation. This is partly because of the sheer complexity of the relationships, but also because such influences may not be quantitatively important relative to the health impact on the individual. Thus a focus entirely on individual benefit will for many health interventions represent an acceptable simplification. It is the adopted base case in all the models. However, in relation to interventions targeted at alcohol, a focus entirely on the individual is clearly incomplete, because a major part of disease burden associated with alcohol misuse is borne by families and others. But, while it is thus desirable to incorporate these wider impacts, the quality of data relating to such issues – for instance the impact on family functioning and how this improves with the adoption of ‘safe drinking behaviour’ is poor. However, if these wider impacts are excluded altogether we know that the potential benefits of these interventions will be understated with performance subsequently also undervalued. What we have done therefore is to develop an alternative family model for alcohol, in which the effect on performance of including impacts on family members is estimated. This work is essentially exploratory given the lack of good quality evidence.

2.6 Key assumptions underlying the economic modelling

For each risk factor and specific intervention, the approach adopted to estimate the impact on quality of life and mortality reflects the quality of trial evidence and access to pertinent epidemiological and other data. As discussed above, we have as first preference used reported impact on health outcomes where these are observed, and secondly used published relationships based on cohort data between lifestyle behaviours and health. Where an intervention is targeted at a specific disease group we have used a disease model.

The specific assumptions adopted are described in the chapters of the Executive report, with more detail contained in the Technical Report. Where possible, consistent assumptions have been used across all interventions. Key assumptions are summarised in Table 2.1 below. Alternative assumed values for uncertain parameters have been explored via univariate sensitivity analysis or where the quality of the data warranted it, using a probabilistic sensitivity analysis.

Table 2.1 Key assumptions underlying the economic modelling

Description	Details
Base Case- common to all models	
Discount rate	5% for costs and benefits.
Cycle length	1 year for all Markov models except the diabetes Gutbusters model of 5 years and the alcohol model where cycles are 3 or 6 months.
Time horizon	Chosen to match the disease process, age of participants and strength of available evidence. Time horizons range between 5 years and full life expectancy.
Evidence of treatment effect	Ideally drawn from meta-analyses or if unavailable from 1 or 2 key RCTs.
Length of intervention benefit	Generally in the base case the length of intervention benefit is not extended beyond the duration of the original trial evidence.
Direct costs of intervention	Estimated in Australian dollars $2003. Based on described resource use or published costs adjusted by health price index and exchange rates.
Indirect costs	Indirect costs such as transportation, waiting times, costs to careers and productivity losses have not been included.
Comparator	Usual care, current practice, placebo or no intervention. If the comparator was inappropriate, comparison was made between intervention group final outcomes and baseline values.
Downstream costs	Excluded in base case analysis, except where trial includes long-term follow-up, cost/event data is collected and significant difference is observed. (All these conditions only apply to the Mediterranean diet post AMI).
Sensitivity analysis- illustrative examples	
Discount rate	0%, 3% and 7%.
Downstream costs	Estimated for disease-based models, scenario analysis for other interventions. See discussion in text.
External effects	Health effects for family members are considered for the alcohol interventions. (chapters 30-34)
Other variables frequently varied	Time horizon, length of intervention benefit, utilities, costs, treatment effect, characteristics of starting population, relapse rates.

SECTION II RESULTS

Chapter 3 Multi-risk factor interventions – Adults*[5]

3.1 Description

A series of interventions seek to modify several harmful lifestyle behaviours of the adult population simultaneously. They commonly target physical activity, nutrition and smoking and sometimes alcohol misuse. As these risk factors jointly influence disease incidence and progression of common chronic diseases, notably of Cardiovascular Disease (CVD) and Type 2 diabetes in a way that is more than additive, there is logic in seeking to address a number of risk factors simultaneously. On the other hand, the more complex the message, perhaps the less easy it is for people to respond.

We attempted to locate good quality studies, that cover the main modalities and settings of i) large scale community interventions involving active use of print and electronic media plus ii)'on-the-ground'; workplace based group programs and iii) enterprise wide; such as primary care. While we identified studies of these three types they are of mixed quality. As shown in Tables 3.1 and 3.2 we analysed five multi-risk factor interventions for adults.

Table 3.1 Study design for multi-risk factor interventions for adults

Intervention *(key references)*	Location, setting and year of intervention	Trial design	Target population
Large Scale media/Community			
Fighting Fit, Fighting Fat (FFFF) *(Wardle et al, 2001)*	UK, mass media + enrolment + substantial supportive materials. 1999	Baseline vs follow up Self report No control	High prevalence of obesity 21 to 45 years Skilled occupations Lower socioeconomic status
Stanford 5 City project. *(Farquhar et al, 1990)*	Northern California, mass media + community elements 1980 to 1990	'Matched control cities' Cohort & random sample Before/after & cf between intervention and control	Multiple target audiences for each component of the intervention, (including children, adults, Spanish language)
Workplace			
GutBusters *(Egger et al, 1996)*	Australia, workplace 1992	Baseline vs follow-up self report + measured, self selected enrolment	Overweight males Blue colour occupations Mean weight 95 kg Mean BMI 31.5
Workplace prevention of heart disease. *(WHO European Collaborative Group, 1980, '82, '83, '86)*	UK, Belgium, Italy, Spain and Poland, workplace, 1971-1974	Matched factory pairs Cf b/w control and intervention factories in change in target parameters	Middle aged men (40 – 59yrs) Employed in recruited workplace units. Focus on those with highest risk for CHD
Primary Care			
Oxcheck- Primary care nurse health checks. *(Imperial Cancer Research Fund, 1991, 1994 and 1995)*	UK, primary care, 1989	RCT, control group delayed receipt of intervention. Change in measured clinical parameters b/w control and intervention	Patients aged 35 to 64 Registered with 5 general practices

Examples of large scale community programs that incorporate a combination of media plus local activities were the UK 'FFFF' campaign - Fighting Fit, Fighting Fat and the USA 'Stanford 5 City'

[5] Interventions exclusively or primarily treating adults.

study). The Australian 'GutBusters' program, initially a group based weight loss program for middle aged over-weight men located in the company setting and the WHO European healthy workplace initiative also targeting middle aged men with high Coronary Heart Disease (CHD) risks were both based in workplaces. The 'WHO Workplace' program together with the UK 'Oxcheck' program was delivered by health care professionals. The 'Stanford 5 City' program while primarily focussing on adults also had a school component.

Table 3.2 Intervention components, including participants

Intervention ***Risk factors targeted***	**Description**	**N Trial participants, mean age % female**
FFFF *Weight* *Physical activity*	▪ Media campaign lasting 7 weeks (TV, radio and print) ▪ Registration scheme including self-help guide; 3 cards to be returned over 5 months charting weight, activity levels, eating habits. Selection of potential goals and advice. Vouchers for FFFF book & exercise video. Voucher for free exercise session, chance to win prizes such as year supply of fruit and veg, home visits by health/exercise specialists ▪ Website; Ceefax pages *BBC teletext service ▪ 192 page FFFF book and a exercise video	33,474 registered 3661 evaluated 58% 35-64 years 88% female No controls
Stanford 5 City *Weight, diet* *Physical activity, Smoking,*	▪ 6 year multi-risk factor, risk education program ▪ Newspapers, TV, radio, print media, classes, contests and correspondence courses ▪ School based programs for grades 4,5,7 and 10 ▪ Estimated average of 527 'educational episodes' for each adult in the intervention sites over 5 years with total exposure estimated as 26 hours over 5 years	Cohort and random sample N= 1188 intervention N= 1176 control 52% female
GutBusters *Weight/nutrition, Physical activity, Alcohol misuse*	▪ 6 week course of 1.5 hours per week, with sessions held in workplace or nearest suitable location ▪ Courses run by trained leader in small groups ▪ Courses included education, tailored reports, measurements, and recommended behaviour change (eat less fat, more fibre, more activity - trade movement for food and drinks) ▪ weight loss guide and fat and fibre counter book	51 participants 2 year follow-up No controls
WHO Workplace *Weight,* *Physical activity* *Smoking*	▪ Screening examination to identify men at highest risk for CHD ▪ Individual and sustained advice from workplace–based doctor ▪ General health education campaign (including posters, brochures, personal letters, progress charts and group discussions) ▪ Program centred on advice to lower cholesterol, cease smoking, weight reduction, daily exercise, treatment of hypertension ▪ Intervention differed in each country: UK- factory doctors & project nurses, Belgium- 2 half time project doctors, Italy- 2 doctors, 1 nurse or dietician working 4 hrs/day at each factory	UK 12 factory pairs, Belgium 15 factory pairs, Italy 2 factory pairs 100% male mean age ~ 49 yr
Oxcheck *All risk factors for CHD and cancer*	▪ Health checks conducted by nurses in the primary care setting 45-60 mins initial, 10-20 min follow up, 30 min annual recheck ▪ Assessment included risk factors for CHD and cancer ▪ Checks consisted of an introduction, information gathering, clinical measurement, target negotiation and education ▪ Follow up from nurses	Intervention N =2776 3 control groups received intervention at years 2 (N=2771), 3 (N=2760) and 4(N=2783) Mean age 49

3.2 Quality of evidence

The quality of the five multi-risk factor intervention studies is summarised in Table 3.3. Only the 'Oxcheck' study had an RCT design and was considered good quality. Each of the other studies has serious potential sources of bias which limits confidence in the results. The main sources of potential bias are lack of control groups (2 studies) and differences between groups at baseline or no measurements made of the control group at baseline (4 studies). This makes it difficult to determine if the intervention had an effect and if any observed changes can be attributed to the intervention. Specifically; the main limitation of the 'FFFF' study was the lack of a control group and the lack of validated outcomes, given the reliance on self report. The 'Stanford 5 City' intervention was mainly limited by baseline differences between the groups and a high drop out rate of 50% by the fourth survey. The 'GutBusters' intervention had a very small sample size and did not include a control group. The WHO study failed to report the baseline characteristics of the control groups which lead to a potential selection bias.

Table 3.3 Summary of quality of the five multifactorial intervention studies

Criteria	FFFF	Stanford 5 City	GutBusters	WHO	Oxcheck
Study included a control group?	X	✔	X	✔	✔
Assignment to treatment groups an adequate method of randomisation?	X	X	X	X	✔
Similarity of Groups at baseline in terms of prognostic factors?	X	X	X	X	?
Report of point estimates and variability for the primary outcome measure?	✔	✔	?	X	✔
Objective and validated outcome measures?	X	✔	X	✔	✔
Were all patients accounted for?	?	?	✔	✔	✔
Was the analysis intention-to-treat?	✔	?	X	?	✔

✔ = yes, X= no, ?= unclear, based on CRD report number 4 (York University)

3.3 Outcomes as reported

The five multi-risk factor studies reported different outcome measures, which are summarised in Table 3.4. A number of studies reported health endpoints (such as CHD events). Four studies measured weight or Body Mass Index (BMI), and the majority of studies also reported smoking behaviour and cholesterol levels. For a detailed report of all outcomes see the relevant chapters in the technical report.

Fighting Fit, Fighting Fat – UK mass media campaign

Behaviour Changes: The 'FFFF' intervention reported on a number of behavioural changes including physical activity levels, nutrition and alcohol. At 6 month follow up 47.8% of evaluation participants were active compared to 29.9% at baseline, an increase in the proportion eating more than 5 serves of fruit and vegetables per day from 20.9% at baseline to 33.9%, and a reduction in units of alcohol consumed by the evaluation participants (Table 3.4). Although these results are based entirely on self report.

Table 3.4 Summary of behaviour change outcomes – FFFF (mean change baseline to follow up)*

Behavioural Change	Outcome definition	Intervention group	Control group	Diff. between groups	P value
Activity levels	% participants active	47.8%	29.9%	16.9%	<0.001
Nutrition	% participants eating >5 fruit & veg/day	33.9%	20.9%	13.0%	<0.001
Alcohol	Mean change in consumption of alcohol units (%)	-0.9%	-	-	<0.001

* 6 month follow up

Clinical Parameters: The 'FFFF' intervention reported on the mean change in BMI (Table 3.5). At 6 month follow up the average loss in BMI for the evaluation participants was -0.88kg/m^2, however these results were not statistically significant. The 'FFFF' intervention also reported results by categories of weight, which revealed a -6.0% reduction of participants who were obese (BMI≥ 30).

Mortality: The 'FFFF' intervention did not report any outcomes on mortality.

Table 3.5 Mean change in BMI (kg/m2) from baseline to follow up*

Clinical Parameter	Outcome definition	Intervention group	Control group	Diff. between groups	P value
BMI	Mean change BMI (kg/m^2) (Self reported height & weight)	-0.88kg	-	-	NS

* 6 month follow up NS – not statistically significant

Stanford 5 City Project – Northern California mass media campaign

Behaviour Changes: The 'Stanford 5 City' intervention reported the smoking mean change from baseline to 5 years follow up as -9.02% for the intervention group compared with -10.24% for the control group. The difference between the groups is 1.22% however these results were not significant (Table 3.6).

Table 3.6 Behaviour change outcomes – Stanford 5 City (mean change from baseline to follow up)*

Behavioural Change	Outcome definition	Intervention group	Control group	Diff. between groups	P value
Smoking	% smokers	-9.02%	-10.24%	1.22%	NS

* 5 years follow up NS – not statistically significant

Clinical Parameters: The 'Stanford 5 City' intervention reported a number of clinical parameter changes including cholesterol levels and BMI (Table 3.7). There was a reduction in cholesterol levels in the intervention group, which was not statistically significant. The 'Stanford 5 City' intervention reported statistically significant benefit for the intervention group in terms of mean change in BMI.

Table 3.7 Clinical outcomes – Stanford 5 City (mean change baseline to follow up)*

Clinical Parameter	Outcome definition	Intervention group	Control group	Diff. between groups	P value
Cholesterol	Total cholesterol level (mmol/L)	-0.13	-0.04	0.09	NS
BMI	Mean change BMI (kg/m^2)	+0.49kg	+1.12kg	0.63kg	<0.05

* 5 years follow up NS – not statistically significant

Mortality: The 'Stanford 5 City' intervention reported an average decrease in the estimated 1-year mortality risk score of 1.78 deaths per 1000 persons per year in the intervention cities and 0.73 in the control cities (<0.02, one tailed sign.). During the trial there was no statistically significant difference reported in actual cardiovascular morbidity and mortality for the intervention cities compared to control.

GutBusters – Australian workplace intervention

Behaviour Change: The 'GutBusters' intervention reported that all evaluation participants reduced waist size by at least 7% and 70% of participants maintained or increased these losses over a 1 year period.

Clinical Parameters: 'GutBusters' reported mean change in BMI (Table 3.8) at 2 years follow up of -2.6kg for participants relative t baseline values, which is statistically significant.

Mortality: The 'GutBusters' intervention did not report any outcomes on mortality.

Table 3.8 Mean change in BMI (kg/m2) from baseline to follow up*

Clinical Parameter	Outcome definition	Intervention group	Control group	Diff. between groups	P value
BMI	Mean change BMI (kg/m^2)	-2.6kg	-	-	<0.001

* 2 years follow up

WHO – Workplace prevention of heart disease (UK, Belgium, Italy, Spain, Poland)

Behaviour Changes: The WHO intervention reported the smoking mean change from baseline to 4 years follow up. The results varied in each location, with 1.4% and 1.9% less smokers in the intervention group in UK and Belgium respectively, and 7.5% more smokers in the intervention group in Italy (Table 3.9).

Table 3.9 Summary of Behaviour change outcomes – WHO (mean change baseline to follow up)*

Behavioural Change	Outcome definition	Intervention group	Control group
Smoking	% smokers	UK: -1.4%; Italy:+ 7.5% Belgium: -1.9%	-

* 4 years follow up

Clinical Parameters: The WHO intervention reported on cholesterol levels as a clinical parameter (Table 3.10). At 4 years follow up there was a reduction in cholesterol levels in the intervention group in 2 countries, significance was not reported. The WHO study also reported mean change in weight (kg) for each centre over 4 years. The changes were +0.1kg for the UK, +0.5kg for Belgium and -2.9kg for Italy.

Table 3.10 Cholesterol outcomes WHO intervention trial (mean change baseline to follow up)*

Clinical Parameter	Outcome definition	Intervention group	Control group
Cholesterol	Cholesterol level(mg/dl)	UK: -4.1; Italy: -4.2 Belgium +2.0	-

* 4 years follow up

Mortality: The WHO study reported in the UK arm of the trial a greater increase in the 6 year cumulative mortality rate in the intervention group (4.8%) compared to the control group (4.2%). The other two centres reported lower mortality rates in the intervention group compared to control (Belgium: intervention 3.3%, control 4%; Italy; intervention 4.2%, control 4.5%,).

Oxcheck – Primary care nurse health checks (UK)

Behaviour Changes: The 'Oxcheck' intervention reported on smoking and alcohol behavioural changes. The smoking results reveal that the intervention group did better than the control group although the difference was not statistically significant. In relation to alcohol misuse there was a reported improvement for the intervention group compared to the control group (Table 3.11).

Table 3.11 Summary of Behaviour change outcomes – Oxcheck (mean change baseline to follow up)*

Behavioural Change	Outcome definition	Intervention group	Control group	Diff. between groups	P value
Smoking	% smokers	-	-	1.4%	NS
Alcohol	Reported weekly intake >21 units for men and >14 units for women	-	-	0.6%	-

* 4 years follow up
NS – not statistically significant

Clinical Parameters: The 'Oxcheck' intervention reported a number of clinical parameter changes including cholesterol levels and BMI. There was a reduction in cholesterol levels in the intervention group however significance was not reported (Table 3.12). The 'Oxcheck' intervention also reported results by categories of weight, which revealed a -1.6% reduction of participants who were obese (BMI≥30).

Table 3.12 Cholesterol outcomes reported by 'Oxcheck' (mean change baseline to follow up)*

Clinical Parameter	Outcome definition	Intervention group	Control group	Diff. between groups	P value
Cholesterol	% with elevated cholesterol (≥ 8mmol/L)	-	-	3.9%	-

* 4 years follow up

Mortality: The 'Oxcheck' intervention did not report any outcomes on mortality.

3.4 Program costs

Program costs have been estimated in 2003 Australian dollars based on the description of the intervention contained in the study publications ('FFFF', 'Stanford 5 City' and 'Oxcheck'), published costs translated into Australian dollars for the WHO workplace interventions and advertised price (for 'GutBusters'). Costs per person are summarised in Table 3.13. Detailed cost components are described in the Technical Report.

Table 3.13 Average cost per person for each of the study groups

Intervention	Intervention group $	Control group $	Incremental cost rel to control group/person $
FFFF	324 (per registrant) 0.56 (per person in the region)	na	308
Stanford 5 City*	103	0	103
GutBusters**	299	na	299
WHO†	UK : 90 Belgium: 224 Italy: 461	0	UK : 90 Belgium: 224 Italy: 461
Oxcheck	100	36	64

* cost is as reported by the Trial
** based on price of the program
† costs are in Australian dollars based on the description of the program run in each of these countries

3.5 Cost-effectiveness analysis

Economic performance is firstly described in terms of cost per person to change behaviour based purely on trial results, for three of the interventions – as reported in Table 3.14 where incremental cost effectiveness ratio (ICER) is defined as cost of intervention less cost of control / additional

person adopting less harmful behaviour. In addition two studies report costs per reduction in CHD event or mortality risks which leads to the cost effectiveness estimates reported in Table 3.15.

Table 3.14 Cost effectiveness: Cost/person to adopt less harmful behaviour

Intervention	Length of follow up	Outcome changed	Incremental cost per 'changer' $
FFFF*	6 months	Eating > 5 serves fruit/veg per day	7,513
		Person classified active	5,779
		Person not obese	16,277
GutBusters*	2 years	Weight reduction goal achieved	426
		Person maintaining any weight loss	318
Oxcheck	4 years	Person smoking	5,560
		Person misusing alcohol	12,830
		Cholesterol>8mmol/L	1,853
		BMI>30kg/m^2 (obese)	4,068

*intervention group is compared to own baseline values

Table 3.15 Preliminary cost effectiveness: Intervention group compared to control group. Cost/death averted or CHD event verted, $

Intervention	Length of follow up	Outcome	Incremental cost per changer $
Stanford 5 City	5 years	Change in all-cause mortality risk score	7,816
		Death averted	14,664
WHO	4 years	Reduction in one predicted CHD event	UK: 30,523
			Belgium: 70,075
			Italy: 197,587

3.6 Cost-utility analysis

Economic models are developed for three of the five multidisciplinary interventions. For the 'Stanford 5 City' intervention there is already a published model estimating 'deaths averted' from 10 year all-cause mortality rates based on Framingham equations; incorporating key clinical parameters for control and intervention samples. We have not been able to complete a model for the WHO intervention due to resource/time constraints.

Stanford 5 City

The 'Stanford 5 City' published report (Farquhar et al, 1990) already reports modelled risk equations for 10 year mortality based on Framingham equations. These give results of $14,664, which in effect assumes no quality of life gain. We have not provided additional modelling as the approach used, based on the Framingham risk equation, is precisely the approach we would have adopted. Our concern arises more from lack of clarity in the clinical/behavioural results, which we cannot address. Firstly, the results for the cohort and random sample are inconsistent, with only one analysis showing a statistically significant reduction in the mortality risk score, secondly results from the risk score analysis were not confirmed by actual results which showed no difference in cardiovascular morbidity or mortality over 14 years.

FFFF and Oxcheck

The 'FFFF' intervention and 'Oxcheck' have both been modelled using a weight/BMI Markov model. The Gustbusters intervention was unable to be modelled using this approach as data regarding overweight and obese were not presented in the necessary format (see below for 'GutBusters' approach). Two separate economic evaluations were performed for the 'FFFF' and 'Oxcheck' interventions. We determined the progression, costs and utilities of a cohort of 1000 people receiving the interventions compared with 'usual care'. Individuals were allocated initially into one of three

discrete health states: normal weight, overweight, obese. A notional intervention and control cohort is cycled through these states and death, with a cycle length of 1 year. The model is run for a period of 20 years.

The starting probabilities for each intervention for each of the health states are presented in Table 3.16. Over the 20 years of the model, death is time dependent and is different for each category of weight. The model was developed in 'DATA' and estimates mortality from actual and projected proportion of cohort who are normal weight (BMI<25kg/m^2), overweight (BMI 25-29 kg/m^2) and obese (BMI>30 kg/m^2). Progression between BMI categories per 1 year cycle reflects evidence from the clinical trials and assumptions about retention of weight change as summarised in Table 3.17 below.

Probabilities of death for each year are determined by fitting a Weibull curve to survival curves (for normal weight, overweight and obese, by gender and smoking status) in the paper by Peeters et al (2003)**.** The probabilities of death are weighted for a population that is 50.7% female (ABS 2002), and where 27.3% of males and 21.4% females are smokers (ABS National Health Survey 2001). To simplify the model the cohort is assumed to be 40 years at the commencement of the model. (While we recognise that this is a simplification, it was not possible given the number of analyses to be completed, to take an age distribution equivalent to the Australian adult population.)

A quality of life weight is assigned to each BMI state using utilities derived from the SA Health Omnibus survey results for the AQoL, (McNeil & Segal, 1999) giving a mean utility of 0.82 for persons who are overweight and 0.78 for those obese, compared with 0.85 for normal weight.
Costs and benefits have been discounted at 5% per annum. Other key assumptions in the model are listed in Table 3.18. Further details are provided in the Technical Report.

Table 3.16 Starting probabilities for each of the economic models

Intervention	Normal	Overweight	Obese	Source
FFFF	9%	33%	58%	Miles et al, 2001
Oxcheck	49%	38%	13%	Imperial Cancer Research Fund, 1991

Table 3.17 Transition probabilities

Intervention	% of obese becoming normal	% obese becoming overweight	% overweight becoming obese	Length of intervention benefit
FFFF	4.2	1.8	-	1 year
Oxcheck	-	-	I= 3.7 C=4.2	4 years

Applying this model the cost/QALY for the 'FFFF' and 'Oxcheck' programs have been calculated. Table 3.19 presents the economic performance of the 'FFFF' intervention at an incremental cost utility ratio of $5,642 per QALY gained, and the economic performance of the 'Oxcheck' program at an incremental cost utility ratio of $12,613 per QALY gained.

Table 3.18 Additional assumptions

FFFF	Oxcheck
Control group have same weight as baseline measures in intervention group and do not change	Control group do not change their weight
Intervention effect assumed to last for 1 year after which relapse rate of 50% is applied in the 2nd year	Intervention effect assumed to last for 4 years after which no additional weight gain occurs

Table 3.19 Modelled cost utility FFFF and Oxcheck base case per person

	FFFF media campaign			Oxcheck		
	Intervention group	'Control'	Difference	Intervention group	Control group	Difference
Total costs	$308.00*	$0.00	$308.00	$89.10**	$32.20	$56.90
Total life years	12.2134	12.2016	0.0118	12.2792	12.2778	0.0014
Total QALYs	9.8119	9.7572	0.0546	10.1599	10.1554	0.0045
$/LY gained			$26,071			$41,459
$/QALY gained			$5,642			$12,613

* Costs are not exactly the same as Table 3.10 due to discounting

**costs from Table 3.10 are divided by 4 for each of the intervention years and discounted

Extensive one way sensitivity analyses were performed giving results ranging from $10 per QALY to $20,231 per QALY (Figure 3.1) for the 'FFFF' intervention, with results most sensitive to the time horizon of the model and the costs of the intervention. It should be noted that the key estimates of effectiveness have not been varied in these sensitivity analysis. There were no sensible values to use aside from randomly inserting figures. We would suggest that due to the quality issues discussed in Section 3.2 the most conservative lower limit of effectiveness would be that both groups are equally as effective and therefore the intervention would be dominated by the control group. The 'Oxcheck' intervention gave results ranging from $6,829 per QALY to $65,224 per QALY (Figure 3.2), with results most sensitive to the cost of the intervention and the time horizon of the model.

Figure 3.1 Results of one-way sensitivity analyses FFFF

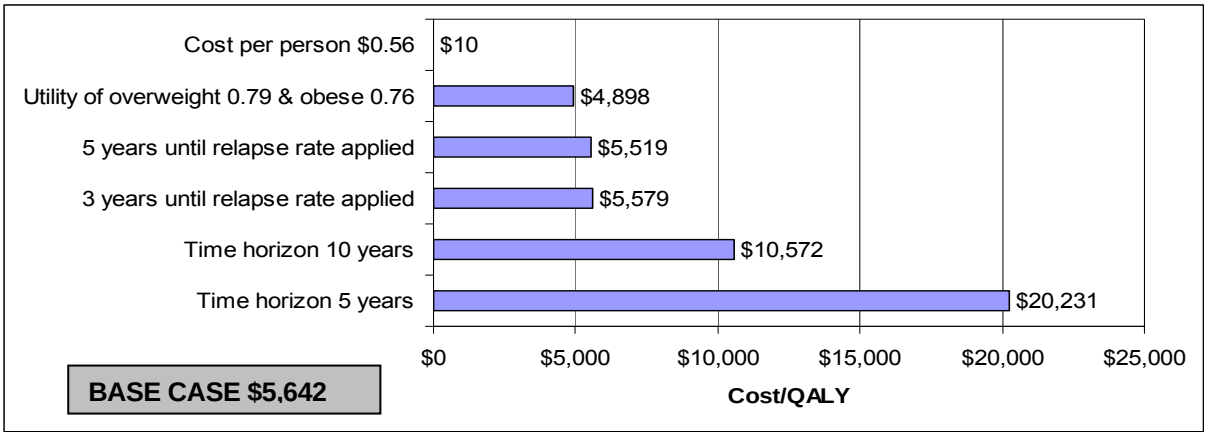
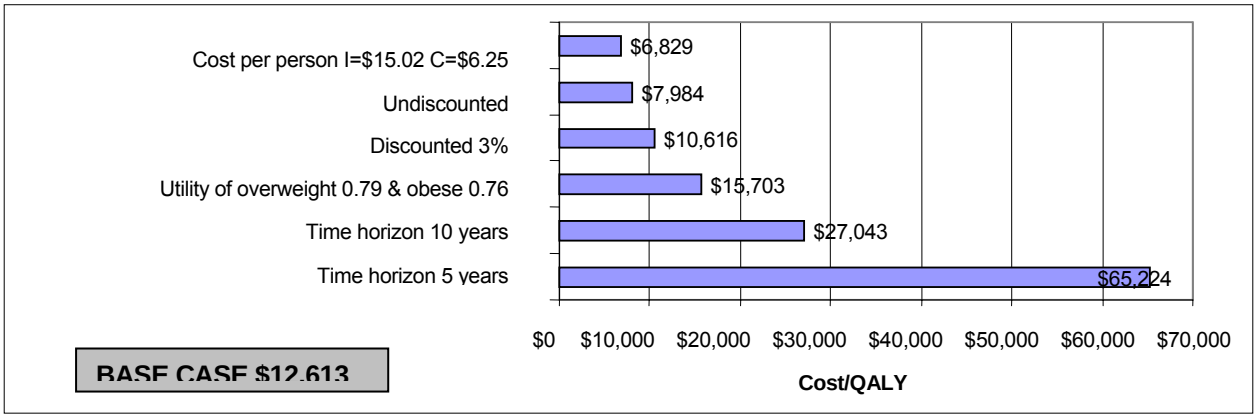


Figure 3.2 Results of one-way sensitivity analyses Oxcheck



Diabetes model (GutBusters)

The 'GutBusters' intervention was originally devised with a view to reducing the incidence of diabetes as a major objective, therefore we have analysed using a diabetes model. A modelling approach was used to enable the surrogate or intermediate outcome measures of weight loss reported by Egger et al., 1996 to be linked to life-years saved and QALYs gained. A Markov process structure was developed comprising three 5-year cycles.

Results were simulated over 15 years. Given the importance of Type 2 diabetes in overweight and obese subjects to health prognosis, the model provides for transitions between three different metabolic states (Type 2 diabetes, Impaired Glucose Tolerance (IGT) and Normal Glucose Tolerance (NGT)) and death.

The baseline prevalence of Type 2 diabetes, IGT and NGT is estimated from Dunstan et al., 2002. The transition probabilities were derived from Eriksson et al., 1991 as the population of males was similar to that of the 'GutBusters' study group. The values for the transition matrix were held constant in the model over each of the three cycles and are shown in Figure 3.3.

Figure 3.3 Metabolic Transition Matrix Probabilities Applied in Model (assumed values in italics)

Control Metabolic Transition Matrix

	NIDDM	IGT	NGT
NIDDM	*0.950*	*0.040*	*0.010*
IGT	0.214	0.428	0.358
NGT	0.010	0.070	0.920

Intervention Metabolic Transition Matrix

	NIDDM	IGT	NGT
NIDDM	0.462	0.307	0.231
IGT	0.106	0.372	0.522
NGT	*0.010*	*0.040*	*0.950*

The 5-year cumulative mortality rates of the Australian population (Australian Bureau of Statistics, 2000) were used to inform the transition to death in the model. A relative risk of 1.1 was applied to mortality rates to adjust for the increased risk of mortality imposed by changes in metabolic state (Balkau et al 1993 and Rockwood et al 2000) and a relative risk of 1.2 for degree of excess weight (Manson, 1987; Rissanen et al., 1990). For further details refer to the technical report. The utility values in Table 3.20 (Colagiuri et al., 2003) were used to provide an estimate of the QALYs over time.

Table 3.20 Quality of Life (Utility Values) DiabCost Study (Colagiuri et al 2003)

Age	**General Population**	**Complications**			
		None	Microvascular	Macrovascular	Both
All ages		0.79	0.69	0.65	0.65
36-50	0.88	0.83	0.71	0.84	0.72
51-65	0.84	0.80	0.71	0.64	0.65
66+	0.79	0.78	0.67	0.64	0.59

Costs and benefits are discounted at 5% per year. Results are presented in Table 3.21. The base case analysis assumes that health benefits are conservatively realised over only years 0-5.

The cost per life year saved was $40,511 ($356/0.01) and the cost per QALY gained was $19,796 ($356/0.02).

Results of one-way sensitivity analyses are presented in Table 3.21.

Table 3.21 Sensitivity analysis results

Parameter	Cost per life year saved	Cost per QALY gained
Including downstream costs of $2508 per patient per year for Type 2 diabetes	Intervention dominates	Intervention dominates
Discount rate 0% and including downstream costs	Intervention dominates	Intervention dominates
Excluding downstream and health benefits maintained for 15 years	$3,317	$2,836

The model is sensitive to the inclusion of downstream costs and the length of time that benefits are maintained.

3.7 Overview multiple risk factor - Adult

An overall comparison of modelling results is presented in Table 3.23. The 'FFFF' intervention is the cheapest although the 'Oxcheck' and 'Stanford 5 City' estimates are the most certain, based on the quality of inputs. All interventions are likely to dominate when downstream costs are included. The 'FFFF' intervention dominates with the inclusion of costs associated with being obese that are greater than an average of $265 per person per year and the 'Oxcheck' intervention dominates if these costs are greater than $405. 'GutBusters' dominates with the inclusion of a downstream cost of Type 2 diabetes of $2,508 per person per year.

Table 3.23 Comparison of cost utility results

Intervention	Key assumptions in base case (a)	Cost per QALY	Range from sensitivity analyses ($/QALY)	Quality of evidence (b) Behav.	L-T B	H =f(B)
FFFF	▪ BMI/weight Markov model ▪ 20 year time horizon ▪ 50% relapse rate in year 2	$5,642	$10 to $20,231	#	☐	##
Oxcheck	▪ BMI/weight Markov model ▪ 20 year time horizon ▪ No additional weight gain permitted after intervention period (4 years)	$12,613	$6,829 to $65,224	##	☐	##
GutBusters	▪ Diabetes Markov model ▪ 15 year time frame, benefits maintained for 5 years	$19,796	Intervention dominates to $19,796	☐	☐	##
Stanford 5 City	▪ Published result of Stanford team (adjusted for Austn. costs). All-cause risk score used to estimate death averted based on all-cause mortality risk score ▪ Assumes no change in quality of life	$14,664	-	#	☐	#

Notes

(a) Also 5% discount of costs and benefits and potential downstream cost offsets excluded

(b) *Behav*.: Evidence of behaviour change during trial; *L-T B* :Evidence of long term behaviour change ie maintenance of behaviour change; *H =f(B)* : Evidence of relationship between behaviour and health

Good quality of published data

Poor quality of published data

☐ No data identified

Chapter 4 School based multi-risk factor interventions

4.1 Description

This chapter includes a series of interventions seeking to modify multiple harmful lifestyle behaviours simultaneously in school children. The interventions commonly target physical activity, nutrition and smoking. It is thought that by targeting school children there is a chance of preventing the formation of unhealthy habits and addictions. The risk factors targeted all jointly influence incidence and progression of common diseases such as heart disease and diabetes in a greater than additive way, therefore, there is logic in seeking to address a number of risk factors simultaneously. On the other hand, the more complex the message presented to children, perhaps the less easy it is for them to respond.

We attempted to locate good quality studies of interventions that targeted smoking, nutrition, physical activity or alcohol misuse across a number of settings. The search and inclusion process described at the beginning of Chapter 2 resulted in a number of interventions being selected that were specifically targeting school children. As this is a unique population and setting we decided to summarise and report the findings for children in a separate chapter. We identified four Randomised Controlled Trials (RCTs) in this population of mixed quality (Tables 4.1 and 4.2). The interventions were published between 1988 and 1999 in the United States.

Table 4.1 Study design for school based multi-risk factor interventions

Intervention	Location, setting and year of intervention	Trial design	Target population	Chapter in technical report
TV Viewing and Obesity *(Robinson, 1999)*	California 2 public elementary schools 1996	RCT	All 3rd and 4th grade students (with parental consent)	3
Interdisciplinary intervention and obesity *(Gortmaker et al 1999)*	Massachusetts 10 schools 1995	RCT results reported for completers only	All 6th and 7th grade students (with parental consent)	4
Cardiovascular disease risk factors *(Harrell et al, 1996)*	North Carolina 12 schools year not reported	RCT	Schools were selected if they were clearly urban or rural. All 3rd and 4th grade students (with parental consent)	5
Cardiovascular disease risk reduction *(Killen et al, 1988)*	North Carolina 4 schools year not reported	RCT Analysis of completers only	All 10th grade students	6

Two studies specifically aimed to reduce or prevent obesity, the 'TV Viewing & Obesity' intervention and the 'Planet health' a Massachusetts based intervention located at 10-schools. The other two studies aimed to reduce risk factors for cardiovascular disease (CVD). The studies targeted different aged children: grade 3-4, 6-7 and 10 and were all conducted in the United States. The sample sizes varied from 192 to 1295. Specific details of each intervention are presented in Table 4.2.

The 'TV Viewing & Obesity' intervention focussed on television and video game use. This intervention used classroom teaching, a TV budgeting device, and a TV turn off period. The other three interventions focussed on a range of risk factors such as TV viewing, activity, nutrition and smoking. These three interventions all included classroom teaching components as well as physical activity sessions. In all studies the control schools appeared to receive no additional treatment aside from assessment.

Table 4.2 Details of interventions and participants

Intervention	Description	N trial participants Mean age % female	
		Intervention	Control
TV Viewing and Obesity *(Robinson, 1999)*	▪ 18 lessons of 30-50 min on TV viewing and video game use. Final lessons made children advocates for reducing media. ▪ 10 day television turn-off followed by 7 hour per week limit ▪ Television managers budgeted viewing by controlling the power use of a power socket ▪ Newsletters providing advice to parents about reducing viewing and video game use	92 9.5 yrs 44.6%	100 8.92 yrs 48.5%
Massachusetts 10-school intervention 'Planet Health' *(Gortmaker et al, 1999)*	▪ Goals to reduce television to less than 2 hours a day, increase moderate and vigorous physical activity, decrease consumption of high fat foods and consume 5+ fruit and vegetables per day ▪ 16 lessons per year (32 total) lasting one or two 45 minute periods in language, maths, arts and social studies subjects, as well as physical education ▪ Physical activity lessons were goal based. Fitness-Funds of $400-$600 were available for proposals at intervention schools ▪ Two week campaign to reduce television viewing (Power Down)	641 11.7 yrs 48%	654 11.7 yrs 48%
CVD Risk Factor *(Harrell et al, 1996)*	▪ Classroom lessons twice a week. Topics included: 'heart healthy foods', the importance of physical exercise, the dangers of smoking, and how to resist pressure to smoke. ▪ Physical activity lessons three times a week. Fun aerobic lessons, with warm up and cool down. Activities included: 'jumping rope to music, "endless relay", parachute and other small-group games, and aerobic dance.'	588 46% 9 yrs 52%	686 48% 9 yrs 51%
CVD Risk Reduction *(Killen et al, 1988)*	▪ Special physical activity sessions 3 x per week for 7 weeks ▪ 20 classroom sessions lasting 50 minutes focussing on physical activity, nutrition, smoking, stress and personal problem solving (taught by 8 teachers from research group) ▪ Session design based on Bandura's social cognitive theory ▪ Each student carried out a self-change project	622 70% 15 yrs 44.5%	508 70% 15 yrs 47.5%

4.2 Quality of evidence

The quality of the four school based intervention studies is summarised in Table 4.3. All four intervention studies adequately randomised participants to groups, specified clear study inclusion criteria and presented point estimates and measures of variability. Each of the studies had potentials for bias. Overall the main sources of potential bias included the lack of concealment and blinding (providers of care, outcome assessors and participants), the lack of comparability of groups at baseline and the failure to analyse results on an intention to treat basis. All studies were limited by the relatively short follow up periods ranging from 4 to 21 months. This restricts the conclusions that can be made about how long the effects of the intervention persist. The best quality study was the 'TV Viewing & Obesity' intervention reported by Robinson.

The suitability of reported outcomes for economic evaluation is another important issue. The most suitable outcomes are measures of activity, and clinical measures such as Body Mass Index (BMI). If behavioural outcomes such as activity and clinical outcomes such as BMI or weight are both changed then it adds further weight to the likelihood that the intervention had an effect and that this may lead to long term health gains. Even with behavioural and clinical outcomes there is considerable difficulty translating into longer term mortality and quality of life. Ideally a cohort study showing the effects of activity or BMI on long term outcomes would be required. There is a lack of quality data such as this showing links between children's behaviour and their long term well being.

Table 4.3 Summary of quality of the four school based intervention studies

Criteria	TV Viewing & Obesity	Massachusetts 10-school intervention	CVD Risk Factors (Harrell et al, 1996)	CVD Risk Reduction (Killen et al, 1998)
Was the assignment to treatment groups an adequate method of randomisation?	✔	✔	✔	✔
Was the treatment allocation concealed?	?	?	?	?
Were the groups similar at baseline in terms of prognostic factors?	✔	✔	✔	X
Were the eligibility criteria specified?	✔	✔	✔	✔
Were the outcome assessors blinded to the treatment allocation?	?	?	?	?
Was the care provided blinded?	?	?	?	?
Was the patient blinded?	?	?	?	?
Were point estimates and measure of variability presented for the primary outcome measure?	✔	✔	✔	✔
Was a power calculation performed at study design?	X	X	X	?
Were all patients accounted for?	✔	✔	X	✔
Was the analysis intention-to-treat?	✔	X	X	X

✔ = yes, X= no, ?= unclear, based on CRD report number 4 (York University)

The main specific limitation of the 'TV Viewing & Obesity' intervention was the small sample size and lack of power calculations performed. The quality of the 'Planet Health' intervention was compromised by the relatively low participation rate (65%) especially given the failure to report results on an 'intention to treat' basis, rather than only for students who completed the trial. Similarly for the 'CVD Risk Factor' intervention (Harrell et al, 1996) quality was compromised by the low participation rate and the fact of missing data from some analyses. The CVD Risk Reduction study (Killen et al, 1988) had group differences at baseline (for education of parents, body mass index, body fat, heart rates, blood pressure and exercise) and also failed to include those who dropped out of the study in the analysis.

4.3 Outcomes reported

Each of the four school based intervention studies reported slightly different outcome measures. These have been summarised using the following broad categories: behaviour change and clinical parameters. None of the four studies reported service utilisation, morbidity (including quality of life) or mortality. All four studies included some measure of physical activity, BMI and skin fold measurement. The majority of studies also reported diet and fitness, for instance as described by number undertaking at least 20 mins exercise at least 3 times per week (Killen), or daily serves of high fat food, and meals eaten in form of TV (Robinson).

For a detailed report of all outcomes see the technical reports. The following sections summarise key outcomes.

Behaviour change - physical activity and nutrition

Physical activity: The 'TV Viewing & Obesity' intervention as well as the 'Massachusetts 10-school' intervention did not show statistically significant increases in physical activity for the intervention group. The 'CVD Risk Factor' intervention (Harrell et al, 1996) reported an increase in the physical activity score on the 'know your own body health habits survey' although statistical significance was not reported. The 'CVD Risk Reduction' intervention (Killen et al, 1988) did show a statistically

significant increase in the proportion of people becoming regular exercisers for the intervention group compared to control.

Table 4.4 Summary of physical activity outcomes (mean change from baseline to follow up)

Intervention	Outcome definition	Follow up interval (trial end)	Intervention group	Control group	Difference# between groups (95% CI)	P value
TV Viewing & Obesity (Robinson, 1999)	Physical activity metabolic equivalent (mins/week)	7 months	-34.5	+27.8	16.7	0.6
'Planet Health' Massachusetts 10-school intervention (Gortmaker et al, '99)	Moderate/vigorous physical activity (≥ 3.5 hours/day met. equiv.)	21 months	Girls +0.11 Boys –0.10	+0.07 –0.03	+0.36 (-0.63 to 1.35) –0.40 (-1.0 to 0.2)	Girls 0.43 Boys 0.16
CVD Risk Factor (Harrell et al, 1996)	Know Your Own Body Health Habits Survey scores	10 weeks	+1.89	-0.76	2.65	Not reported
CVD Risk Reduction (Killen et al, 1988)	% non-regular exercisers at baseline who became regular exercisers	4 months	30%	20%	10 percentage points or 50% more	<0.0003

#the difference between intervention group and control group adjusted for differences at baseline in age and sex

Nutrition: The 'CVD Risk Factor' intervention (Harrell et al, 1996) did not report any nutrition outcomes. The 'TV Viewing & Obesity' intervention did not find statistically significant differences between groups for the consumption of high fat foods. There was a statistically significant increase in the number of servings per day of fruit and vegetables and a significantly lower total energy intake for the intervention group compared to control in the 'Planet Health' intervention. There was also a statistically significant increase in the number of healthy foods chosen in the food pairs choice in the 'CVD Risk Reduction' intervention (Killen et al, 1988).

Table 4.5 Summary of nutrition outcomes (mean change from baseline to follow up)

Intervention	Outcome definition	Follow up	Intervention group	Control group	Adj.# difference b/w groups (95% confidence interval)	P value
TV Viewing & Obesity (Robinson '99)	Daily servings of high fat food	7 months	-1.01	-0.45	-0.82 (1.87 to 0.23)	0.12
'Planet Health' Massachusetts 10-school (Gortmaker et al, '99)	Servings fruit & veg Total energy intake (j/day)	21 months	Girls +0.2 Boys -0.2 Girls +630 Boys +453.6	Girls -0.2 Boys -0.5 Girls +886.2 Boys +701.4	+0.32 (0.14 to 0.50) 0.18 (-0.21 to 0.56) -575.4 (-1155 to 0) -466 (-1094 to 164)	0.003 0.31 0.05 0.13
CVD Risk Reduction (Killen et al, 1988)	Food pairs choice test → number of healthy foods chosen	4 months	Not reported	Not reported	F[1,850]=56.6	<0.0001

adjusted for differences in demographics at baseline

Clinical parameters (BMI, obesity, skin folds, fitness)

The 'Planet Health' intervention only used BMI to estimate obesity and did not report it separately. BMI was statistically significantly reduced in the intervention group compared to control in the 'TV Viewing & Obesity' intervention and the 'CVD Risk Reduction' intervention (Killen et al, 1988).

Table 4.6 Mean change in BMI (kg/m^2) from baseline to follow up

Intervention	Follow up	Intervention group	Control group	Adj.# difference b/w groups (95% confidence interval)	P value
TV Viewing & Obesity (Robinson, '99)	7 months	+0.29	+0.71	-0.45 (-0.73 to 0.17)	0.002
CVD Risk Factor (Harrell et al, 1996)	10 weeks	+0.24	+0.18	0.05 (-0.07 to 0.18)	NS
CVD Risk Reduction (Killen et al, 1988)	4 months	Girls –0.2 Boys +0.1	Girls 0 Boys +0.4	Girls -0.2 Boys -0.3	0.05

adjusted for differences in demographics at baselines
NS – not statistically significant

'Planet Health' (Massachusetts 10-school) reported obesity prevalence as a primary outcome. The prevalence of obesity between baseline and follow up increased for girls in the control group (21.5% to 23.7%) but fell for girls in the intervention group (23.6% to 20.3%), a statistically significant difference. For boys the prevalence of obesity fell in both groups between baseline and follow up (control 34.7% to 31.8% and intervention 29.3% to 27.8%), with no significant difference between groups. The lack of consistency in results across the various clinical parameters as well as between girls and boys suggests the need for caution in interpreting results. The 'CVD Risk Factor' intervention (Harrell et al, 1996) reported cholesterol levels as a key outcome and found a mean reduction of 6.79mmol/l for the intervention group compared to a reduction of 1.4 mmol/l for the control group (no statistically significant difference).

Three studies reported triceps skin fold measures (Table 4.7). The 'Planet Health' intervention noted triceps skin fold measurement and used this to estimate obesity prevalence. The 'TV Viewing & Obesity' intervention and the 'CVD Risk Reduction' intervention reported statistically significant results in favour of the intervention group, however the 'CVD Risk Factor' intervention (Harrell et al, 1996) failed to detect a significant difference.

Table 4.7 Mean change in triceps skin fold (mms) from baseline to follow up

Intervention	Follow up	Intervention group	Control group	Adj.# difference b/w groups (95% CI)	P value
TV Viewing & Obesity (Robinson, '99)	7 months	+0.92	+2.49	-1.47 (-2.41 to –0.54)	0.002
CVD Risk Factor (Harrell et al, 1996)	10 weeks	-0.90	+0.25	-0.04 (-0.11 to 0.03)	NS
CVD Risk Reduction (Killen et al, 1988)	4 months	Boys –0.1 Girls –0.4	Boys –0.52 Girls +1.5	Boys 0.42 Girls 1.9	0.004

the difference between intervention group and control group adjusted for demographics at baseline
NS – not statistically significant

Fitness was reported for three studies but defined differently by each (Table 4.8). The only study to report a statistically significant difference was the 'CVD Risk Reduction' intervention (Killen et al. 1988), which reports a decrease in resting heart rate for the intervention group compared to an increase in the control group.

Table 4.8 Mean change in assessment of fitness from baseline to follow up

Intervention	Definition of fitness	Intervention group	Control group	Adj.# difference b/w groups (95% CI)	P value
TV Viewing & Obesity (Robinson, 1999)	20-m shuttle test (number of laps)	+4.51	+3.38	0.87 (-1.41 to 3.15)	0.45
CVD Risk Factor (Harrell et al, 1996)	Predicted aerobic power (PVO_2 ml/kg/min)	+2.66	+1.34	1.76 (–0.70 to 4.22)	NS
CVD Risk Reduction (Killen et al, 1988)	Heart rate (beats/min)	Boys -2.3 Girls -4.1	Boys +0.4 Girls +0.4	Boys 2.7 Girls 4.5	0.0001

the difference between intervention group and control group adjusted for demographics at baseline
NS – not statistically significant

4.4 Program costs

Program costs for the school based intervention studies have been estimated in Australian dollars (2003) based on the description of the intervention contained in the study publications (Table 4.9). For further details of cost components refer to the technical report. In estimating the cost of school based programs the main component is teacher time costed at the standard salary rate. However the opportunity cost is the time no longer available on the curriculum for other studies. It is not clear how this should be handled. Some resource inputs such as parent involvement, a central component of some interventions have not been costed.

Table 4.9 Mean cost per person for each of the study groups

Intervention	Length of follow up	Intervention group	Control group	Incremental cost per person
TV Viewing & Obesity (Robinson, 1999)	7 months	$757.25	$590.26	$166.99
'Planet Health' (Gortmaker et al, 1999)	2 years	$68.63	$0.00	$68.63
CVD Risk Factor (Harrell et al, 1996)	8 weeks	$323.12	$29.61	$293.51
CVD Risk Reduction (Killen et al, 1988)	4 months	$86.60	$0.00	$86.60

4.5 Cost-effectiveness analysis

Economic performance is firstly described based on the results and time frame reported in the trials.

BMI

Three of the school based studies reported BMI. ('Planet Health' measured BMI but it was not reported). The control group dominated the intervention group (no change in BMI and cheaper) in the 'CVD Risk Factor' study by Harrell et al (1996).

Obesity

For 'Planet Health' the Incremental Cost Effectiveness Ratio (ICER) was $3,384 per additional case of obesity prevented for girls, but for boys the intervention was dominated by the control group (no difference in outcome but additional cost). Change in time spent viewing television was for girls, an important predictor of likelihood of becoming/remaining obese.

Table 4.10 Cost effectiveness of intervention group compared to control group

Intervention	Length of follow up	Incremental cost per BMI point reduction
TV Viewing & Obesity (Robinson, 1999)	7 months	$371
'Planet Health' Massachusetts 10-school (Gortmaker et al, 1999)	2 years	-
CVD Risk Factor (Harrell et al, 1996)	8 weeks	Control group dominates
CVD Risk Reduction (Killen et al, 1988)	4 months	$289 for boys $433 for girls

Television viewing

An ICER of $30 per hour reduction in TV viewing per week for the intervention group compared to control is found for the 'TV Viewing & Obesity' intervention; and for 'Planet Health', $118 per person hour reduction/in TV viewing per day for girls and $172 for boys.

Physical activity

The 'CVD Risk Factor' intervention (Harrell et al, 1996) gives an ICER of $79 per point reduction in physical activity score. An ICER of $866 per additional non regular exerciser at baseline who became an exerciser was found for the 'CVD Risk Reduction' intervention (Killen et al, 1988).

Cholesterol

An ICER of $2,097 per percentage point reduction in cholesterol level was estimated for the 'CVD Risk Factor' intervention (Harrell et al, 1996).

4.6 Cost-utility analysis

A published economic evaluation of the 'Planet Health Massachusetts 10-school' intervention was identified (Wang et al 2003). We have used the structure of this model as the basis for the cost-utility analyses of the school-based interventions. The model relates childhood weight for girls only (average age 11 years in the trial) to adult weight 40+ years. The key assumptions in the Wang model are that weight loss reported at trial end (2 years) is retained for the entire model and the exclusion of boys from the model. The model takes a two step approach firstly using published literature to link overweight as a child (aged 1 to 17 years) to overweight as a young adult (21 to 29 years). The authors then calculate, using an existing database, the risk of an overweight young adult becoming an overweight person aged over 40 to 65 years and link this to medical costs averted (US$2,737). The model also incorporates quality of life and mortality gain for those aged 40 to 65 years. Given the assumptions underpinning their analysis they report a cost per QALY of US$4,305. While it is traditional to adopt conservative assumptions in modelling for cost-utility analysis, Wang and colleagues have rather chosen a more optimistic scenario. Most important is the expectation of maintenance of weight change for children and the relationship between outcomes in children and adult weight. The latter is established from cohort studies which cannot be reliably used to predict an intervention effect. (In fact the observed relationship between childhood and adult obesity might suggest that weight is quite resistant to any short-term changes). Thus the relationship between weight change in school children and mortality and quality of life more than forty years into the future is little more than conjecture. Long term intervention data is needed. Further, as noted Wang et al (2003), in applying the model to the 'Planet Health Massachusetts 10-school' intervention, use the results for females only. This post hoc selection, excluding the results for males (in which results were worse for the intervention group compared to controls) is an important source of bias.

Given the great interest in school based interventions, we have replicated the model by Wang et al (2003) to incorporate Australian costs and discount rates, additional sensitivity analyses, specifically to explore the implication of adopting a more conservative set of assumptions. The model has also been applied to other school based interventions, (although not the 'CVD Risk Factor' intervention by Harrell et al (1996) as the intervention is dominated when outcomes is measured by change in BMI.)

Planet Health - Massachusetts 10-school intervention, (Gortmaker et al, 1999)

A new base case was developed incorporating what were considered more realistic and certainly a more conservative set of assumptions:

- Results of boys and girls combined
- Downstream cost impacts excluded
- Cost of intervention Australian $68.63 per person (based on described resource use)
- 5% discount rate
- Relapse rate of 50% by seven years after trial end (50% of those who became normal weight, relapse to be overweight again by year 7). This is not really a conservative assumption, as there is no evidence that the effect is maintained at all.

This set of assumptions is broadly consistent with assumptions else-where in this report, and makes comparison more reasonable. The cost per QALY gained for the 'Planet Health Massachusetts 10-school' intervention under this set of assumptions is A$50,091 (compared with US$4,305).

TV viewing and obesity (Robinson et al, 1999) – hypothetical scenarios

The 'Wang model structure' was applied to the population of 9 year olds as was the case in the 'TV Viewing & Obesity' study by Robinson et al (1999). It was assumed that 19% were overweight or obese at baseline (AIHW, 2003). Costs are as reported in Table 4.9. As Robinson et al (1999) does not report the proportion overweight or becoming normal weight, a number of hypothetical scenarios are presented in Table 4.11 (excluding downstream costs) and in Table 4.12 (including downstream costs) converted to Australian 2002 dollars.

Table 4.11 Cost per QALY assuming reduction in overweight/obese children 5 to 20% with 0% relapse (change in weight maintained into adulthood) or 50% relapse

% reduction in those overweight/obese	% overweight/obese at end of intervention	Resulting cost/QALY No relapse $	Resulting cost/QALY 50% relapse $
5%	18.05%	$149,217	$298,630
10%	17.1%	$74,609	$149,745
15%	16.15%	$49,739	$103,153
20%	15.2%	$37,304	$74,591

These scenarios are only intended to provide a guide as to what cost/QALYs may be likely if certain results were to be obtained.

Table 4.12 Cost per QALY assuming reduction in overweight/obese children 5 to 20% and 0 or 50% relapse and allowing downstream cost savings attributable to obesity

% reduction in those overweight/obese	% overweight/obese at end of intervention	Resulting cost/QALY No relapse	Resulting cost/QALY 50% relapse
5%	18.05%	$136,032	$285,445
10%	17.1%	$61,424	$136,561
15%	16.15%	$36,554	$89,968
20%	15.2%	$24,119	$61,405

CVD risk reduction (Killen et al, 1988) - hypothetical scenarios

The 'Wang model' was applied to the population of average age 15 years as was reported in the 'CVD Risk Reduction' study by Killen et al (1988). It was assumed that 20% were overweight or obese at baseline (AIHW, 2003) and that the intervention cost $86.60 per person. The publication by Killen et al (1988) does not report the proportion overweight or becoming normal weight so a number of hypothetical scenarios are presented in Table 4.13 (excluding downstream costs) and in Table 4.14 (including downstream costs converted to Australian 2002 dollars). These scenarios are only intended to provide a guide as to what cost/QALYs may be likely if certain results were to be obtained.

Table 4.13 Cost per QALY assuming reduction in overweight/obese children 5 to 20% and 0 or 50% relapse

% reduction in overweight/obese	Proportion overweight/obese at end of intervention	Resulting cost/QALY No relapse	Resulting cost/QALY 50% relapse
5%	0.19	$73,514	$147,678
10%	0.18	$36,757	$72,356
15%	0.17	$24,505	$48,814
20%	0.16	$18,379	$37,053

Table 4.14 Cost per QALY for various scenarios of reductions in overweight/obese children including downstream costs of obesity (CVD Risk Reduction)

% reduction in overweight/obese	Proportion overweight/obese at end of intervention	Resulting cost/QALY No relapse	Resulting cost/QALY 50% relapse
5%	0.19	$60,329	$134,493
10%	0.18	$23,572	$59,171
15%	0.17	$11,320	$35,629
20%	0.16	$5,194	$23,869

4.7 Discussion

Overview of results: obesity as primary outcome

Cost/QALY of the 'Planet Health Massachusetts 10-school' intervention result of A$50,091 based on the multivariate analysis reported above. For the other 2 interventions (not dominated by the control group), based on hypothetical scenarios, as the effect on obesity increased from 5%-20% cost/QALY ranged from A$74,591 to $298,630 for 'TV Viewing & Obesity' intervention, and A$37,053 to $147,678 for 'CVD Risk Reduction' intervention (Killen et al, 1988).

Thus under what might be considered plausible sets of assumptions, but focusing only on obesity, none of the school based interventions perform well. There are several major components to modelling the cost utility of these school based interventions; the cost of the interventions, quality of life improvement and gains in survival. The interventions enrolled children with average ages ranging from 9 to 15 years and length of follow up ranging from 8 weeks to 2 years.

In these populations modelling mortality gains is problematic for a number of reasons:

- There is a lack of evidence that the difference in behaviour/outcomes would be maintained beyond the period of the trial, which is essential for mortality gain only realisable many years into the future;
- There is a lack of quality evidence of the relationship between being overweight as a child and overweight as an adult and specifically how this is affected by an intervention designed to change childhood weight;
- There is a lack of quality evidence relating changes in BMI of a child to differences in mortality of adults

Given the uncertainty in long term mortality, impact on current quality of life could have an important potential contribution to QALY gain. However, none of the school based interventions measured quality of life. If some weight reduction is maintained and some improvement in fitness and the reduction in TV viewing, this might be associated with significant quality of life gains in the short and longer term. However, we have no evidence on this. The published literature does not report utilities for obese or overweight children, although there is some literature, that suggest children who are obese or overweight have lower quality of life scores (Friendlander et al, 2003; Schwimmer et al, 2003). For severely obese children inpatient rehabilitation has been shown to increase quality of life, although, how this relates to weight loss is not clear, nor the persistence of the gain, (Ravens-Sieberer et al, 2001).

Further research is critical in this area. The first requirement is to investigate how long behaviour change or outcomes are maintained following interventions such as this. Other useful research relates to impact on quality of life associated with weight loss in children and other impacts of these school-based programs. Specific research into the downstream impacts on morbidity and mortality of weight loss in children is also needed.

The Department of Human Services, Victoria is conducting an economic evaluation of a number of school-based interventions for obesity. Their results are to become available over the next year or so. Their work will also face the same issues.

Chapter 5 Physical activity interventions

5.1 Description

In recent decades the population has become increasingly sedentary. This relates in large part to the changing nature of society such that physical activity is no longer an integral part of daily life for the majority of people. A sedentary life style is identified as a risk factor for a range of chronic conditions, including heart disease, hypertension and thus stroke, type 2 diabetes and some cancers. For this study, physical activity is considered as a means to promote cardiovascular fitness. We are not looking at physical activity as part of disease management – as in strength training for falls prevention, or to treat depression or in managing knee osteoarthritis. The role in those contexts is established elsewhere (eg Segal et al, 2004) and resource allocation to such activities is in many cases already justified.

There are many plausible ways to address sedentary behaviour; many of which sit outside the health sector. These include changes to the urban environment (eg building cycling/walking/jogging tracks), creating an attractive public transport system, working through schools and other community groups to provide opportunities for physical activity, finding opportunities in the work place/public places for incidental physical activity (eg by ensuring stairs are prominent). Within the health sector, the main opportunities to promote physical activity for cardiovascular fitness behaviours are through public health campaigns, or provision of advice/other support to physical activity in the primary care or other clinical settings. Physical activity interventions can be introduced in isolation or as part of a multiple risk factor strategy. The multiple risk factor strategies discussed in Chapters 3 and 4 all include physical activity as one of the objectives. In addition a few of the interventions analysed under Nutrition (see Chapter 6), also include advice about physical activity advice as a secondary element.

In this chapter we focus on interventions to address sedentary behaviour that fall within the health sector, and where the focus is physical activity. We analysed five physical activity interventions that had a broad fitness focus, all in the general practice setting (Table 5.1). This project only included physical activity interventions with a broad fitness focus. All the studies on which our analysis is based were conducted between 1995 and 2001 in Australia, New Zealand and the UK. Details of each intervention are presented in Table 5.2.

Two studies targeted older populations ('Exercise Sessions for the Elderly' by Munro et al, 2002 and 'Individualised Exercise Advice for the Elderly' by Halbert et al, 1999), both of which targeted the most sedentary. One study targeted adults with Coronary Heart Disease (CHD) risk factors (Taylor et al, 1998). The 'New Zealand Active Script' intervention targeted most adults, only excluding those who exercised less than 30 minutes per day, 5 days per week (Elley et al 2003). The definitions of less physically active, which was used to define eligible populations, varied substantially. Sample sizes varied from 142 to 6420. Two interventions focussed on tailoring physical activity advice provided by the general practitioner ('NZ Active Script' and 'Individualised Exercise Referrals for the Elderly'). 'GP Exercise Referral for CHD Risk' and 'Exercise Sessions for the Elderly' involved specific elements to support access to activity programs through subsidised (or free) sessions, and 'NZ Active Script' involved proactive contact of patients by activity specialists at the exercise centre. In three of the interventions the control group also received some instruction and follow up ('NZ Active Script', 'GP Exercise Referral for CHD Risk' and 'Individualised Exercise Referral for the Elderly').

Table 5.1 Description of setting, population, and numbers for five Physical Activity interventions

Intervention	Location, setting, year of intervention	N trial participants, Mean age, % female		Target population	Chapter in technical report
		Intervention	Control		
GP Active Script (AUST) *(Nacerrella & Huang, 2001)*	Australian general practice, 2000	Not known*	none	General practitioners* and via them 'sedentary' patients	11
GP Active Script (NZ) plus leisure centre follow-up. *(Elley et al, 2003)*	New Zealand general practice 2000 to 2001	451 57.2 years 67%	427 58.6 years 66%	Adults aged 40-79 not exercising 30 mins per day, 5 days per week	11
GP Exercise Referral for CHD Risk Factors. *(Taylor et al, 1998)*	England primary care 1996 to 1997	97 - -	45 - -	Adults 40-70 with risk factors for CHD (smokers, BMI>25 or hypertensive)	12
Community based exercise program for persons 65 + *(Munro et al, 2002)*	UK general practice 1995 to 1997	2283 76 years 67%	4137 75 years 60%	Adults aged over 65 who were in the top 20% most sedentary	13
Physical activity program and individualised advice for persons 60+ *(Halbert et al, 1999)*	Australian general practice 1996	149 67.3 years 52%	150 67.8 years 56%	Community dwelling 'healthy' adults aged over 60 years	14

*no information was provided on patient involvement, but 670 GPs were 'enrolled' in the trial and their views sought

The Australian active script intervention (Nacerrella & Huang 2001) is excluded from further consideration due to the lack of a control group and absence of data on patient outcomes – specifically behaviour, clinical parameters and health. The Australian Active Script intervention was focused on training and provision of physical activity advice by GPs and thus data collection was predominantly through GP survey, plus 54 in-depth interviews with patients selected by five GPs[6]. The analysis in this Chapter thus draws on just four physical activity interventions.

5.2 Quality of evidence

The quality of the four physical activity intervention studies is summarised in Table 5.3.

The sample size for the 'Exercise for CHD Risks' program (involving information re CHD risk information plus referral to supervised and subsidised exercise sessions) was small, with only 97 persons in the intervention group and 45 in the control. Furthermore results were only reported for study completers, who are likely to differ from all those enrolled.

The 'Exercise Sessions for the Elderly' program reported by Munro et al (2002) is generally of high quality, except that the study fails to report exercise levels for the control group. Poor attendance at any exercises session in the intervention group; with only 26% attending any exercises sessions, is an important outcome of this trial, but also confusing when interpreting health endpoints.

Three studies report physical activity and selected clinical parameters (see Section 5.3). The 'Exercise Sessions for the Elderly' intervention also reported final health outcomes; death rates both all-cause and for specific causes. In order to model the impact of physical activity interventions, additional published information was required, specifically on the impact of physical activity on mortality. Several studies report a relationship between physical activity and death, after allowing for potential confounders. We have used the study by Andersen and colleagues (2000) who report the relative risks of mortality for different categories of exercisers. We have some confidence in the

[6] Despite the absence of patient data, Nancy Huang (from VicFit) and colleagues have published a 'cost-effectiveness' analysis of the Victorian Active Script Program (Huang, et al, 2004). However, because of the complete lack of patient data the analysis is viewed as seriously flawed and is not therefore drawn upon.

robustness of the published relative risks, given similarity with other published studies (notably with D'Agostino et al, 2000). Where the impact on clinical parameters is reported, the effect on all-cause mortality could be derived from a suitable published risk equation such as Framingham.

Table 5.2 Details of intervention and care received by control groups

Intervention	Activities for experimental group	Care received by control group
NZ Active Script *(Elley et al, 2003)*	▪ Identification of less active patients by the research team ▪ Patients trained concerning 'stages of change' and being given a prompt card to give to their GP to initiate activity advice by their GP ▪ GP training in motivational interviewing techniques ▪ GPs helped patients set appropriate tailored physical activity goals which were written on a green prescription card for the patient ▪ Exercise specialists received faxed copies of the prescriptions and followed up with patients over the phone and via newsletters	Standard physical activity advise from their GP during usual consults
GP Exercise Referral for CHD Risk (*Taylor et al, 1998)*	▪ Participants encouraged to perform moderate to vigorous semi supervised exercise twice a week at a leisure centre and were given 20 half price vouchers for use over 10 weeks ▪ Receipt of a Health Education Authority leaflet on preventing CHD ▪ Initial physical assessment including information on preventing CHD ▪ Further assessments at 8, 16, 26 and 37 weeks ▪ Introductory session at leisure centre - use of equipment, exercise perceptions and goals, measurement of BP, height and weight.	Minimal advice on preventing CHD (via leaflet). May have received some clinical input through their ongoing assessments
Exercise Sessions for the Elderly (*Munro et al, 2002)*	▪ A range of locally available exercise sessions conducted regularly each week, most free of charge; conducted by qualified exercise instructors. Included standard exercise, gentle mobility, swimming, tai chi, dancing. ▪ Additional activities were organised including bowling, walking and social events which were held less regularly ▪ Participants were invited to attend 2 sessions per week but could drop out and rejoin the intervention as they wished	No organised sessions
Individualised Exercise Advice for the Elderly *(Halbert et al, 1999)*	▪ 20 min interview with exercise physiologist to receive individualised advice about the benefits of physical activity and a pamphlet containing a plan for physical activity over the next 3 months ▪ The plan involved activity of moderate intensity 3 times per week for 20 mins with self-monitoring of heart rate ▪ Focus on incorporating activity into usual activities and recommended preferred, familiar activities to the participant ▪ Discussion of potential barriers to exercise and strategies to overcome ▪ Participants were followed up by interview at 3, 6 and 12 months	A pamphlet promoting good nutrition for older adults which was discussed for 20 minutes. Follow up by questionnaire.

Table 5.3 Summary of quality of the four physical activity intervention studies

Criteria	NZ Active Script	Exercise for CHD Risk	Exercise Sessions for the Elderly	Exercise Advice for the Elderly
Assignment to treatment groups an adequate method of randomisation	✔	✔	✔	✔
Treatment allocation concealed?	✔	?	?	?
Groups similar at baseline in terms of prognostic factors?	✔	X	X	✔
Eligibility criteria specified?	✔	✔	✔	✔
Outcome assessors blinded to treatment allocation?	?	?	?	?
Providers blinded to care provided?	X	X	X	X
Patient blinded?	✔	?	?	?
Were point estimates and measure of variability presented for the primary outcome measure?	✔	✔	X	✔
Was a power calculation performed at study design?	✔	✔	X	✔
Were all patients accounted for?	✔	✔	✔	✔
Was the analysis intention-to-treat?	✔	X	X	✔
Those enrolled in the trial represent an unbiased sample of those eligible. Self-selection bias not an issue.	X	X	X	X

✔ = yes, X= no, ?= unclear, based on CRD report number 4 (York University)

5.3 Outcomes as reported

Each of the four physical activity intervention studies report slightly different outcome measures. All studies report exercise levels, but using different measures. Most studies also report blood pressure and SF-36 scores. For a detailed report of outcomes see the technical report.

Physical activity levels

The 'NZ Active Script' intervention and the 'Exercise Advice for the Elderly' intervention both reported greater increases in physical activity for the intervention group compared to the control group at 1 year (Table 5.4). Whilst the 'Exercise for CHD Risk' intervention reported no difference in the mean time spent on moderate or vigorous physical activity in the intervention group compared to the control group by week 26 week (mean 239 minutes in the exercise group compared with 240 minutes in the control group), despite a significant difference at week 8 (296 vs 166 minutes).
At latest follow-up, 37 weeks there was also no significant difference in time spent on exercise. Taylor and colleagues (1998) report that 'at 26 weeks 15% more patients in the intervention group did at least some weekly moderate/vigorous activity', compared with no increase in the control group (Taylor et al, 1998, p.597). But results are reported for study completers only, a biased sample of 41% of enrolled intervention patients, and only 69% of control patients demonstrating substantial and important differences in characteristics from the enrolled sample.

In the 'Exercise Sessions for the Elderly' intervention activity/attendance was only reported for the intervention group. However, 74% of intervention participants attend none of the scheduled exercise sessions over the 2 year trial period, 5% attend between 50 and 100 sessions (0.5 to 1.0 per week over 2 years), and 4% more than 100 sessions (> 1/week over 2 years). The mean attendance across all exercise sessions was observed to fall over the 2 year study period from 24 persons per class in 1995 to 15.5 persons per class by early 1996, 12 per class by late 1996, and 10.6 per class by mid 1997. However the trend in numbers of persons involved in exercise over time is not reported.

Clinical parameters (blood pressure, BMI, cholesterol)

None of the studies showed a significant improvement in the clinical parameters of BMI, blood pressure or cholesterol, for the intervention group compared to control. Non-significant differences in clinical parameters between the intervention and control groups were observed in the 'NZ Active Script' program. The 'Exercise for CHD Risk' program also reported non-significant differences in mean change in BMI and mean change in blood pressure between the control and intervention groups. The 'Exercise Advice for the Elderly' program also reported no statistically significant differences in change in clinical parameters between study groups. Refer to Table 5.5.

Quality of life: SF-36

The 'NZ Active Script' intervention reported a statistically significant difference in mean change from baseline for SF-36 role physical, bodily pain, general health and vitality scores for the intervention compared to control group. The 'Exercise for CHD Risk' intervention did not report SF-36 quality of life scores. The 'Exercise Sessions for the Elderly' reported a statistically significant improvement on the vitality dimension score and a significant 0.01 utility gain – based on the Brazier transformation of the SF-36 (Brazier et al, 1998). This is interesting with only 9% of the intervention group participating in at least an average of 0.5 exercise session per week over the 2 years of the trial. The 'Exercise Advice for the Elderly' intervention reported a significant decrease in SF-36 scores for bodily pain, physical functioning, general health, vitality and role physical dimensions for both groups compared to baseline and failed to show a significant difference between groups.

Table 5.4 Summary of main physical activity outcomes for the four interventions

Intervention	Outcome definition	Follow up	Intervention group	Control group	Difference between groups	P value
NZ Active Script (Elley et al, 2003)	Leisure exercise - mean increase, (mins/week)	1 yr	54.6 (95%CI: 41.4 to 68.4)	16.8 (95%CI: 6.0 to 32.4)	33.6 (95%CI: 2.4 to 64.2)	0.04
Exercise for CHD Risk (Taylor et al, 1998)	Moderate exercise (mins/week)*	Wk 8 Wk 16 Wk 26 Wk 37	247 226 183 158	145 160 206 162	102 66 -23 -4	0.02 NS NS NS
Exercise Sessions for the Elderly (Munro et al, 2002)	% attending exercise sessions more than once per week on average (100 sessions)	2 yrs	4% (89/2283)	-	-	-
Exercise Advice for the Elderly (Halbert et al, 1999)	Proportion increasing frequency of walking from baseline	1 yr	75% (111/149)	62% (93/150)	13%	0.067

* 'completers only'
NS – not statistically significant

Table 5.5 Mean change in clinical parameters for three of the physical activity interventions

		Clinical Parameter		
Intervention	**Study Group**	**BMI (kg/m^2)**	**Blood pressure (Diastolic mmHg)**	**Cholesterol (mmol/L)**
NZ Active Script (Elley et al, 2003)	Intervention	-0.11 (95%CI: -0.25 to 0.02)	-2.62 (95%CI: 3.62 to 1.61)	-0.019 (95%CI: –0.08 to 0.05)
	Control	-0.05 (95%CI: –0.18 to 0.07)	-0.81 (95%CI: –1.77 to 0.16)	0.01 (95%CI: –0.05 to 0.06)
Exercise for CHD Risk (Taylor et al, 1998)	Intervention	-1.2	-2.1	-
	Control	0.9	-5.1	-
Exercise Advice for the Elderly (Halbert et al, 1999)	Intervention	-	0.5	-0.22
	Control	-	0.6	-0.18

Morbidity and mortality

No change in hospital admission rates is found in the two studies that report this outcome ('NZ Active Script' and 'Exercise Sessions for the Elderly', see Technical Report). However, only the 'Exercise Sessions for the Elderly' intervention was powered to observe a change in mortality. Similarly these studies do not report any significant difference in death rates between study groups (Table 5.6). The 'NZ Active Script' intervention reported a non-significant 20% lower 4-year CHD risk in the intervention group compared with control.

Table 5.6 Number/proportion of deaths from all causes

Intervention	Length of follow up	Intervention group	Control group
NZ Active Script (Elley et al, 2003)	1 year	3/451 (0.7%)	6/427 (1.4%)
Exercise Sessions for the Elderly (Munro et al, 2002)	3 years	15%	15%

5.4 Program costs

Program costs for the 'NZ Active Script' program, 'Exercises for CHD risk' and 'Exercise Advice for the Elderly' have been estimated in Australian dollars (2003) from the description of the intervention contained in study publications (Table 5.7). Costs of 'Exercise Sessions for the Elderly' are as

reported by Munro et al (2002), converted to AU$ and inflated to AU$2003 using the CPI health deflator. Further details of cost are in the Technical Report.

Table 5.7 Average cost per person (AU$2003) based on resource use described in the studies

Intervention	Intervention group	Control group	Difference
NZ Active Script (Elley et al, 2003)	$563	$122	$441
Exercise for CHD Risk (Taylor et al, 1998)	$491	$258	$233
Exercise Sessions for the Elderly (Munro et al, 2002)	$144	$0	$144
Exercise Advice for the Elderly (Halbert et al, 1999)	$126	$0	$126

As the control group in the 'Exercise Advice for the Elderly' program was a diet group rather than 'usual care', for the cost-effectiveness and cost-utility analyses we compare the intervention group to their own baseline scores and assume a control group cost of $0.

5.5 Cost-effectiveness (cost per person to change behaviour)

Economic performance is described in this section in terms of cost per additional person that becomes active. Cost per additional active person is found to be ~$4500 for the 'NZ Active Script' program and possibly $3,750 for 'Exercise Sessions for the Elderly' program (based on numbers attending more than 1 trial exercises session per week over 2 years). This may understate the cost per exerciser as exercises rates for the control group are not reported (and assumed to be zero), nor are exercises levels at baseline reported. The 'Exercise for CHD Risks' program was dominated with fewer people exercising in the intervention group (58% in the intervention group engaging in moderate or intensive exercise at trial end of 26 weeks compared with 62% in the control group). Although at 16 weeks the exercise group on average spent more time exercising. The 'Exercise Advice for the Elderly' intervention reported a cost effectiveness ratio of $168 per person to increase walking frequency from baseline.

5.6 Cost-utility analysis

GP exercise referral for CHD risk (Taylor et al, 1998)

It was not appropriate to undertake a cost-utility analysis for this intervention. Primarily because the trial was subject to some serious potential biases which lead to uncertainty when interpreting results. The trial only reports results for study completers who are unlikely to have results that are typical of the exercise group as a whole – confirmed in a comparison with baseline characteristics. Secondly, even on selected patients – those completing all assessments, the trial does not demonstrate maintenance of an effect in key physical activity outcomes by 26 weeks. The failure to maintain an effect is an important finding in the area of physical activity for other lifestyle interventions, especially in the face of a lack of published evidence to suggest that long term behaviour change can be obtained. If physical activity interventions are only able to produce short term behaviour change then it is unlikely that these interventions will yield significant or substantial health gain.

In order to model the cost utility of interventions such as this, further research is required regarding the maintenance of behaviour change. Other research into the impact of physical activity on quality of life over the short and long term and on mortality is also needed.

Table 5.8 Cost/person to change behaviour

Intervention	Length of follow up	Costs	Outcomes	Incremental cost effectiveness ratio (ICER)
NZ Active Script (Elley et al, 2003)	1 year	I =$563 C=$122	Additional number of active people I = 66/451 (14.6%) C= 21/427 (4.9%)	$4,546 per additional active person
Exercise for CHD Risk (Taylor et al, 1998)	37 weeks	I =$491 C=$258	No data for group as a whole. Even for 'study completers' no difference in exercise levels b/w control and intervention group by wk 26.	Not able to be calculated
Exercise Sessions for the Elderly (Munro et al, 2002)	2 years	I =$144 C=$0	Session attendance* >100: I = 89/2283 (4%) > 50 sessions I = 212 (9%)	$3,767/ person attending >100 sessions $1,600/person attending >50 sessions
Exercise Advice for the Elderly (Halbert et al, 1999)	1 year	I =$126 C=$0	Increase in walking frequency from baseline (responder) I=111/149 (75%)	$168 per person to increase 'walking frequency'

I= intervention group, C= control group

** It assumed that the control group do not change their exercise attendance.

Exercise sessions for the elderly (Munro et al, 2002)

Munro et al (2002) reports a statistically significant increase in utility of 0.01 for the intervention group compared to the control group using the Brazier transformation of SF-36 scores (Brazier et al, 1998).

What is not reported, is comparative levels of exercises in control and intervention group clients, or how exercise levels in the intervention group changed over the trial period. What was reported was numbers attending the organised activity sessions, 4% attending on average at least 1/week over the 2 year trial period and a further 5% attending at least 1 session per fortnight. In order to model downstream mortality, actual activity levels for intervention and control groups are required. At 3 years, no difference in death rates was observed. (This is despite 684 deaths recorded equal to 15% of both control and intervention group participants, whose mean age was 75 years at enrolment).

A cost/QALY has been calculated based on the reported difference in utility score between intervention and control participants of 0.010:

- If this applied for the 2 years of the trial, and on average across all intervention participants cost/QALY gain =$7,200; (cost of $144/person divided by QALY gain of 0.02).
- If however the gain only applied to those completing the surveys (1,052 of 2,283 intervention participants), that is assuming no change in those for whom follow-up data was not collected, but still assuming 2 years of benefit, cost/QALY = $15,650; (cost of $144/person divided by 1052/2283 x 0.02).
- If the gain applied for a mean 12 months the cost/QALY = $31,300.

Even if no mortality gain (or loss) is assumed and a quality of life gain is presumed to accrue only to those actually surveyed and occurs across a 2 year period, the cost per QALY for the 'Exercise Sessions for the Elderly' intervention is $15,650/QALY.

NZ active script (Elley et al, 2003)

A state transition (Markov) model was developed in Microsoft Excel to estimate mortality and quality of life (utility) from the actual and projected proportion of the cohort who are physically active and inactive.

Utility scores were based on the Brazier transformation (Brazier et al, 1998) of SF-36 scores for all active and inactive patients across the control and intervention groups. The calculated scores were 0.7635 for the active state and 0.7380 for the inactive state. Progression between the states of physically active and inactive and dead, and associated utilities and accumulated life years were calculated for a cohort of 1000 people receiving the 'NZ Active Script' programme compared with 'usual care'. The model used a cycle length of 1 year and a time horizon of 5 years. Costs and benefits were discounted at 5% per annum. The model commences with 19.5% of people active at baseline (average for the study). The additional proportion of people active at the end of year 1 was 4.9% for the control group and 14.4% for the intervention group. This was assumed to reduce in both groups at an even rate until the proportion of active people returned to baseline (19.5%) in each group by year 4.

It is assumed that people die at the same rate as all-cause mortality for the Australian population (ABS, 2002) adjusted for active/inactive status (relative risks from Andersen et al, 2000 and prevalence of activity from ABS 1995).

Table 5.9 presents the results of the cost-utility analysis for the base case, (assumptions as defined above), yielding an incremental cost utility ratio of $29,022 per QALY gained.

Table 5.9 Modelled cost utility base case results

	'Active Script' group	'Usual care' group	Difference
Total costs	$533*	$116*	417
Total life years	4.90854	4.90496	0.00358
Total QALYs	3.16602	3.15163	0.01439
Discounted $/QALY gained			**$29,000****

* Note these costs are slightly lower than in Table 5.7 due to discounting
** Rounded to nearest '000.

Extensive univariate sensitivity analyses were performed (See technical report for details of the assumptions and values) and gave results ranging from $14,511 per QALY to $ 58,045 per QALY as shown in Figure 5.1.

The cost per QALY gained was most sensitive to the costs, change in level of activity and the time horizon of the model. We also conducted simultaneous multivariate stochastic sensitivity analysis (see technical report for details) with 1000 Monte Carlo trials run to obtain a distribution of incremental cost-effectiveness ratios (ICER). The mean value is shown in Table 5.10. Results have also been presented as a 'cost-effectiveness acceptability curve' which shows the likelihood that the cost/QALY will be less than any designated value (Figure 5.2). Reading directly from this curve, there is a 50% chance that the 'NZ Active Script' programme has a cost/QALY less than (or greater than) $29,000, or a 75% chance that the cost/QALY is less than $75 000, but only a 30% chance it is less than $20,000/QALY.

Table 5.10 Results of probabilistic sensitivity analysis – Mean value

	'Active Script' group	'Usual care' group	Difference
Total costs	$533*	$115*	$418
Total QALYs	3.16473	3.14526	0.01947
Discounted $/QALY gained			**$21,450****

* Note these costs are slightly lower than in Table 5.7 due to discounting
** Note that calculation doesn't add up correctly due to rounding

Figure 5.1 Results of one-way sensitivity analyses

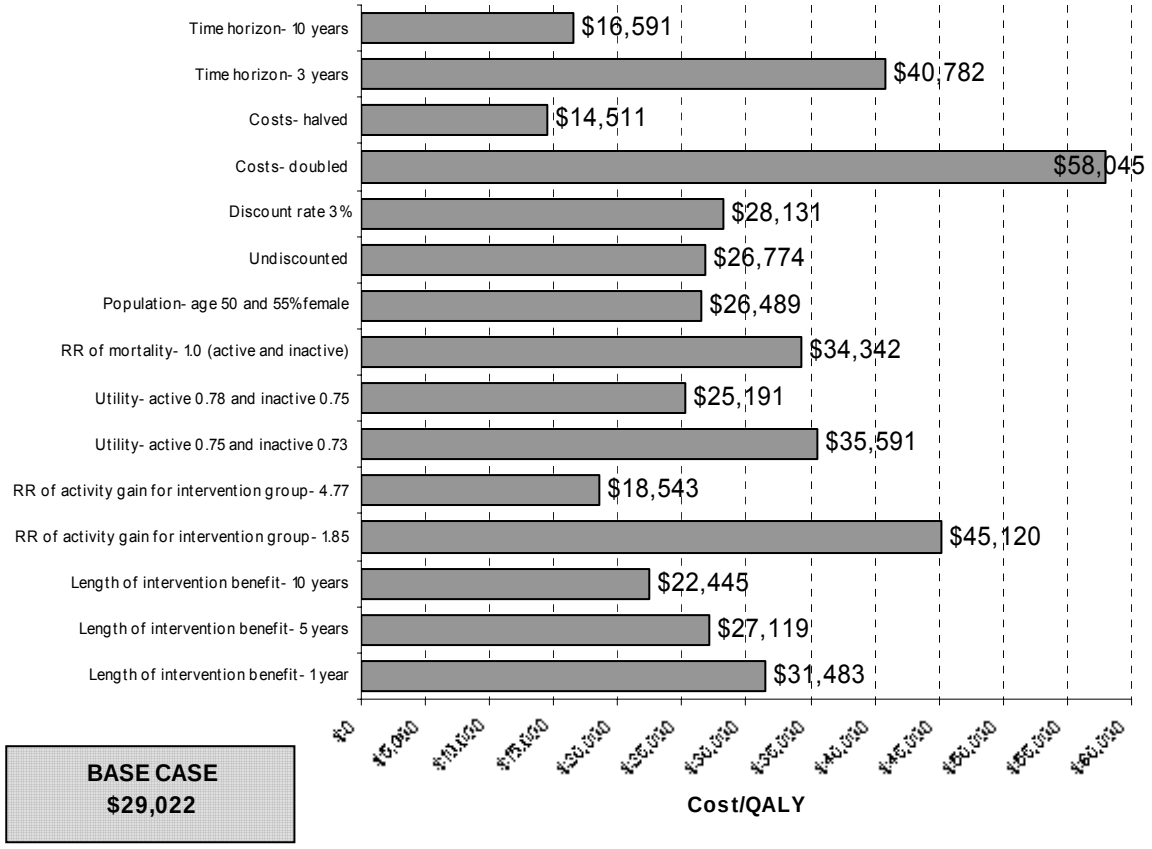
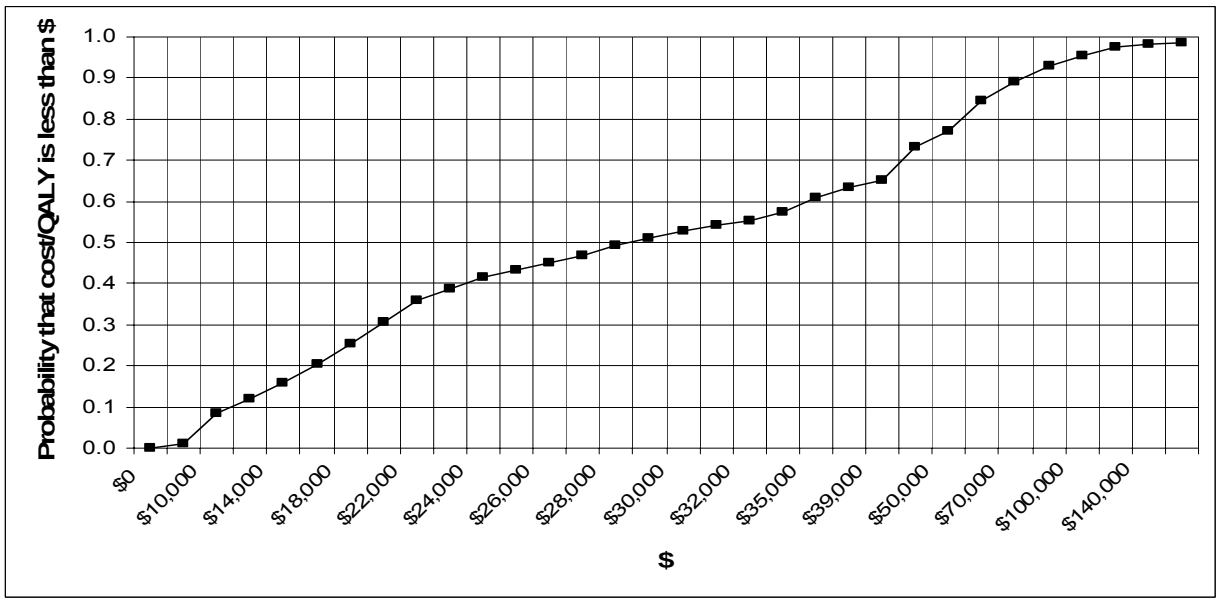


Figure 5.2 Probability that $/QALY gain is less than $X (Cost effectiveness acceptability curve)



Individualised exercise advice for the elderly (Halbert et al, 1999)

While SF-36 scores were measured, scores fell between baseline and follow-up in both groups, with no significant difference between control and intervention groups observed. Whilst significant differences were not observed between control and intervention groups in relation to clinical parameters, as control clients received a nutrition intervention, the significant difference in total cholesterol from base line observed in the intervention group could plausibly reflect a real

improvement. Thus cost/QALY was developed using the difference compared to baseline (of just under 10%) reported for total cholesterol levels for its projected effect on cardiovascular disease. We thus modelled the following:

- Expected prevalence of CVD disease, to capture attributable morbidity reductions;
- Expected cumulative deaths attributable to CVD (coronary heart disease, myocardial infarction, stroke and peripheral vascular disease) to capture the impact upon life-expectancy.
- These outcomes are then converted to QALYs to determine performance.

The model relied on the 4 published equations derived from the Framingham Heart Study along with derived coefficients for each variable to estimate the prevalence of CVD disease and CVD attributive deaths (see technical report for details). A 15 year modelling time frame is assumed. Results are modelled with reduction in cholesterol maintained for 1 year, 5 years and 15 years. We have also modelled results with and without realisation of downstream cost savings.

In adapting the equations to the available data reported by the 'Exercise Advice for the Elderly' intervention, the development of the model required some assumptions:

- None of the patients had Left Ventricular Hypertrophy (LVH)
- None had developed type 2 diabetes
- The residual risk carried by previous smokers (39% and 37% respectively) gave them the same risk as present smokers, and that these proportions were the same for males and females.

The model was run separately for female non smokers, female smokers, male non smokers and male smokers. A weighted average of these four sub-populations was obtained for the control and intervention groups. The cumulative mortality difference, discounted over 15 years (area under curve) is estimated to be 0.005 years per patient (Table 5.11). In Table 5.12 we report the cumulative probability of a CVD event.

Total QALYs were estimated as the sum of years alive and without CVD (utility = 1.0) plus years as a survivor with CVD with a utility of 0.8, being the utility of coronary heart disease (Tengs and Wallace, 2000). Total QALYs are shown in Table 5.13. This will of course over-state the quality of life gain, as people 'without CVD' cannot be assumed to be in full health.

Table 5.11 Estimated Life-Years Saved over 15 years

Cohort	Undiscounted	Discounted
Control Group (years lost)	0.1264	0.074
Exercise Groups (years lost)	0.1183	0.069
Difference in Life-Years (years saved)	0.0081	0.005

Table 5.12 Estimated Probability of a CVD Event

Cohort	Undiscounted	Discounted
Control Group	0.2779	1.432
Exercise Group	0.2676	1.369
Difference in Probability of a CVD event	0.0103	0.063

Table 5.13 Estimated QALYs over 15 years

Category	Undiscounted	Discounted
Control	14.4283	10.538
Intervention	14.4556	10.555
Total QALYs	0.0273	0.0174

Base-case result

Assuming cholesterol reduction is maintained for 12 months (as observed), no cost offsets and gains in mortality and quality of life then the 'Exercise Advice for the Elderly' intervention costs $575,000/QALY gained.

Sensitivity analysis

Cost/QALY has also been calculated assuming cholesterol benefits are maintained for up to 15 years, there is a quality of life gain of 0.2 associated with avoiding CVD and downstream cost savings are realised of $1,090 for each CVD event avoided. If cholesterol benefits are maintained for 15 years, this would yield a cost saving of $69/person, (See Table 5.14). The results of the sensitivity analysis are presented in Table 5.15, which also includes an estimate for downstream cost savings, calculated by multiplying the proportion of patients each year with a CVD event by $1,090.

Table 5.14 Estimated Savings from Exercising per Patient (over 15 years)

Category	Undiscounted	Discounted
Control	$2,427	$1,561
Intervention	$2,323	$1,492
Total Savings	$104	$69

Table 5.15 Results and sensitivity analysis

	Cost/QALY assuming only mortality benefits	Cost per QALY assuming mortality & quality of life benefits
Base case: No cost offsets, Benefits maintained for 1 year	***$47,632,000***	***$573,300***
Benefits maintained for 10 years	$54,500	$9,600
Benefits maintained for 5 years	$522,800	$40,000
Benefits maintained for 15 years	$26,255	$7,252
Benefits maintained for 15 years Downstream cost savings accrue	$11,972	$3,307

5.7 Overview

In this chapter we have evaluated four studies of reasonably robust design and highlighted the need for further research, especially regarding the maintenance of physical activity behaviours.

All four physical activity interventions were randomised controlled studies, a robust study design. All interventions had the limitation of enrolling a small proportion of those eligible, suggesting possible selection bias, and an expectation of a greater chance of achieving a positive result. The 'Exercise Sessions for the Elderly' and 'Exercise for CHD Risk' programs were the only interventions to follow patients beyond the length of the intervention with both finding poor retention of behaviours. In the 'Exercise for CHD Risk' intervention the time spent in moderate or vigorous activity was not significantly different between the control and intervention groups by 26 weeks, and in the 'Exercise Sessions for the Elderly' intervention, attendance at exercise sessions fell over the course of the study from an average of 24 per class to 11.

Studies report a lack of improvement in clinical parameters within the intervention period. This may mean behaviour was not changed sufficiently to induce clinical changes, or that behaviour was not retained long enough to induce clinical changes or a combination of both. This is an important finding in itself and highlights a critical gap in the literature. If physical activity behaviour is not able to be changed beyond a short period of time (6 months to 1 year) then interventions are unlikely to yield significant or substantial health gains and downstream benefits. If physical activity interventions are not able to yield downstream benefits then it is unlikely that they will be cost-effective.

A comparison of performance of the interventions in terms of cost/QALY is presented in Table 5.16. While, the 'Exercise Sessions for the Elderly' intervention appears to be cost effective, it is based on a small but significant improvement in utility, but this is not consistent with the very low attendance at exercise sessions and lack of change in other clinical parameters.

Table 5.16 Comparison of cost utility results

Study	Key assumptions in base case*	Cost per QALY	Range from sensitivity analyses ($/QALY)
NZ Active Script (Elley et al, 2003)	▪ Markov model ▪ 5 year time horizon ▪ Behaviour change a 1 year reverts to control group by year 5 ▪ Mortality differential starts year 1 with no lag	$29,022	$14,511 to $ 58,045
Exercise for CVD Risks, (Taylor 98)	▪ No evidence of behaviour change	∞ dominated	
Exercise Sessions for the Elderly (Munro et al, 2002)	▪ QoL utility gain of 0.02 applies for 2 years ▪ Mean QoL gain applies only to those surveyed (ie no change in other participants) ▪ No mortality gain	$15,650#	$7,200 to $31,300 to ∞ #
Exercise Advice for the Elderly (Halbert et al, 1999)	▪ Life years based on Framingham equations ▪ 15 year time horizon ▪ Benefits maintained for 1 year ▪ QoL for non-fatal CHD events of 0.8	$575,000	$33,097 to ∞ dominated

*all discounted at 5% pa

but not consistent with lack of participation in exercise

Annex: Comment on the published cost-utility analysis on the Victorian Active Script Program

We note that N Huang, J Simms, J Pietsch and L Naccarella, have published a paper on the Victorian Active Script Program, 'The Victorian Active Script Program: promising signs for general practitioners, population health and the promotion of physical activity', Br J Sports Medicine, 2004 38: 19-25.

The authors note the aim of the Active Script Program was to 'increase the number of general practitioners in Victoria who deliver appropriate, consistent and effective advice on physical activity to patients' and that the program focused on training and supporting GPs in advising sedentary patients and developing resource tools to assist them. The primary outcome was thus change in GP knowledge and behaviour and up-take of the program by GPs.

Data collection was through GP surveys of GP attitudes, behaviour, skills and knowledge. A small patient sample was subject to in-depth telephone interview (54 patients, nominated by 5 GPs who undertook the programs clinical audit) to establish patient views of role of GPs in promoting physical activity, and impact of advice on their activity levels. Even in this highly selected group the authors report that only 37% recalled receiving any written physical activity advice from their GP.

As the Active Script Program did not systematically collect data on patient behaviour, other evidence was sought by Huang and colleagues for their cost-effectiveness analysis of the Victorian Active Script Programme. For the crucial evidence on patient physical activity levels, the authors draw on the results of a different physical activity intervention reported in a non-peer reviewed, unpublished conference presentation by Bull (1999), which on inspection reports a just significant 20% difference in activity levels between control and intervention group at 6 months, which had fallen to a small (<5%) non significant difference in the percent active between intervention and control groups at 12

months. The assumption in the model of a 20% increase in physical activity levels associated with the Active Script Program is thus surprising. This key input is not varied in sensitivity analysis. Fifty percent of this group is presumed to maintain their activity levels long enough to accrue a health benefit, which is unreferenced, and not consistent with the data by Bull (1999), which shows that by 12 months there has been 75% reduction in the difference observed at 6 months. Thus the assumptions included in this cost-utility analysis are neither drawn from the Active Script trial nor inconsistent with their own cited reference.

A more intensive active script type intervention, which measured impact on life style behaviours, demonstrated an increase in the proportion of people physically active from baseline of <10% for the intervention group compared to control (Elley et al, 2002), which is considerably less than that assumed in the Huang et al (2004) evaluation.

The key effectiveness figure is thus almost certain to be overstated in the Huang et al (2004) model and therefore lead to results that are not 'persuasive'. The leap taken in the economic analysis from GP awareness, knowledge and behaviour (which were measured) to patient behaviour (which was not measured) is unwarranted. Thus, the conclusion that the Australian Active Script intervention 'is a highly successful program and one suitable for wider adoption' is not supported by the available evidence.

Chapter 6 Nutrition interventions

6.1 Description

Nutrition can potentially be influenced through a broad range of program types; including clinical programs of various intensities, delivered in a variety of settings (primary care, hospital – in-patient or out-patient); via differing delivery models (multi-disciplinary, single clinician, one-on-one or group sessions). Programs can address all citizens or be targeted at those that fall in various high risk categories (persons who are currently overweight, or obese), persons with specific health conditions for which nutrition is part of management (diabetes, coronary heart disease (CHD), renal failure etc.), or people in particular occupational/life stage categories (such as elite athletes, elderly, pregnant women/nursing mothers). Besides clinical approaches, nutrition can be influenced by media-based strategies - the electronic and print media, supported by on-the-ground initiatives, with content of message varied to reflect the particular purpose. A wide range of settings can be employed including not just clinical settings, but also schools and other community locations. Nutrition can also be addressed by programs outside the health sector, such as strategies to modify the food supply and food retailing and the regulation/control of advertising and sale of less nutritious foods.

For this project we have focused on initiatives which fall broadly within the ambit of health agencies, and cover a range of modalities, settings and target groups. In addition to the 8 specific nutrition interventions, nutrition is an element of all the multi-risk factors interventions described in chapters 3 and 4. The specific nutrition interventions selected cover:

- 1:1 nutrition counselling by GP and dietician (or GP alone) in the general practice setting, for high risk middle- aged adults (overweight and/or hypertensive and/or diabetic) (Pritchard et al, 1999);
- 1 hour nutrition counselling by dietician and cardiologist for survivors of Acute Myocardial Infarction (AMI), < 70 years, recruited as in-patient - plus free rapeseed margarine (de Lorgeril et al 1999);
- Comprehensive, diet/behaviour change education to reduce fat, (including use of food diary etc). delivered through small group sessions; in primary care (Swinburn et al 2001);
- Pharmacotherapy (orlistat) + diet for persons who are overweight (Padwal et al 2003)
- Intensive dietary advice for persons with Impaired Glucose Intolerance (IGT) by physician plus nutritionist (initial consult) + 6 individualised session with dietician, + group sessions + very low calorie diet (VLCD) if weight targets not achieved. Diet aimed to reduce saturated fat, increase dietary fibre and reduce weight (Eriksson et al 1999).
- Technical solution through a ‘talking computer’ to monitor diet and suggest strategies in the patients home, for sedentary persons 25yrs+ and poor diet (Delichatsois et al 2001);
- Nurse counselling in general practice (Steptoe et al 2003);
- Multi media “2 fruit 5 veg” campaign (Dixon 1998).

Details of the eight interventions are provided in Tables 6.1 and 6.2. Four interventions target persons who are overweight or those with a suboptimal diet, four target persons from specific disease categories (3 targeted glucose intolerance, 1 targeted persons who have been hospitalised from a myocardial infarction (MI)) and two interventions address the population at large. All except the multi-media ‘2 fruit 5 veg’ intervention are random controlled trials (RCTs). All control groups receive some form of intervention, which is not necessarily equivalent to usual care.

Interventions consist of different intensity of dietary counselling, varying from a single counselling session to several sessions supported by extensive materials, dietary diaries etc. Five interventions consist of advice that is individualised (‘Nutritional Counselling in GP’, ‘Mediterranean Diet’, ‘Lifestyle

Change to Prevent Type 2 Diabetes', 'Talking Computer for Nutrition' and 'Nurse Counselling in GP'). Two are based on social learning theory ('Talking Computer for Nutrition' and 'Nurse Counselling in GP'). The content of dietary advice varies considerably - depending in part whether weight loss is the primary objective. One set of studies looked at the use of a pharmaceutical (Orlistat) in addition to dietary advice. Sample sizes varied from 136 to 6021 (the latter combined n across 11 trials), while the target population for the 'Multi-media 2 fruit 5 veg' intervention could be considered the entire population of Victoria of over 4 million persons.

Table 6.1 Description of setting, study population, study design: Nutrition interventions

Intervention	Location, setting, year of intervention	Study design and N trial participants Mean age % female	Target population	Chapter in technical report
Nutritional Counselling in general practice *(Pritchard et al, 1999)*	W. A. General practice 1992 to 1994	RCT 3 arms ▪ Counselling by GP + dietician N= 131 ▪ Counselling by GP N=123 ▪ Control N= 130 73% female	Adults aged 25-65 yrs who are overweight, hypertensive or diabetic.	15
Mediterranean Diet *(deLorgeril et al, 1999)*	France Hospital and outpatient 1988 to 1992	RCT I = 303, mean age 53.5, F: 7.9% C= 302, mean age 53.5, F: 10.6%	Adults aged < 70 yrs surviving an MI in previous 6 months.	16
Reduced Fat Diet for IGT (*Swinburn et al 2001)*	Auckland N. Z. Community setting intervention ~1993 follow-up to ~1998	RCT I = 66, mean age 52.5, F: 32% C=70, mean age 52, F: 20%	Participants identified from Workforce Diabetes Survey with IGT.	17
Orlistat + Diet for Obesity (*Padwal et al, 2003)*	US and Europe Multicentre trials 1998 to 2002	11 RCTs N=6021 mean 49 years, F:71%	Overweight participants with BMI>30 or >27 with other risk factors	18
Lifestyle Change to Prevent Type 2 Diabetes (*Eriksson et al, 1999)*	Finland Research centres 1993 to 1998	RCT I = 265, mean age 55, F: 66% C=257, mean age 55, F: 68%	Overweight subjects aged 40-64 yrs with IGT	19
Talking Computer for Nutrition (*Delichatsios et al, 2001)*	Massachusetts Home based	RCT I =148, mean age 46.2, F: 72% C=150, mean age 45.7 F: 72%	People over 25 years who were sedentary and had a suboptimal diet	20
Nurse Counselling in general practice (*Steptoe et al, 2003)*	UK General practice 1999 to 2001	RCT I = 136, mean age 43.3, F: 60% C= 135, mean age 43.2, F: 62%	People registered at a primary health centre	21
Multi-Media '2 fruit 5 veg' Campaign (*Dixon et al, 1998)*	Multi-media Victoria: 1992 to 1994 WA: 2001 to 2003	Victorian study: sample survey at each wave of the intervention. No control, F: 50% 1992 sample 515, 1993 sample 509 1994 samples 511 & 509, WA study but no published data	Women with children, young to middle-aged adults	22

Table 6.2 Details of intervention received by Experimental and Control Groups

Intervention	Experimental Group	Control group
Nutritional Counselling in GP *(Pritchard et al, 1999)*	Dietician group ▪ 6 one-on-one counselling sessions within 12 months; Initial consult 45 mins, 15 mins for follow-up consults ▪ Sessions focussed on good nutrition and exercise with individualised advice provided ▪ Measurement of clinical parameters Doctor + dietician group ▪ above + GP record flagged with progress measurements ▪ initial consult with GP + 2 other visits in 12 months of 5 mins ea	Received results on initial measurements and were advised to follow up with GP with any questions
Mediterranean Diet *(deLorgeril et al, 1999)*	▪ 1 hour session with cardiologist and dietician ▪ Advised to follow Mediterranean diet; More bread, root, green vegetables (no day w/out fruit), legumes, fish. Less red meat. Olive or rapeseed oil only fat, rapeseed margarine provided. Moderate alcohol consumption encouraged. ▪ Personalised instructions were given	Advised by attending physicians or hospital dieticians to follow a prudent Western diet of the American Health Association
Reduced Fat Diet for IGT (*Swinburn et al 2001)*	▪ 1 year structured program aimed to reduce fat intake through intensive education involving personalised goal setting, why reduce fat, how to count fat in food, strategies to reduce fat intake, fat counter book. Participants asked to complete regular food diaries and attend monthly small group sessions	General dietary advice about healthy food choices on entering the trial.
Orlistat + Diet for Obesity (*Padwal et al, 2003)*	▪ Orlistat dose 120mg, three times daily with meals ▪ advice to adopt well balanced diet rich in fruit & veg, + mean 30% calories from fat, calorie restriction ▪ advised to increase physical activity	Placebo plus equivalent diet intervention
Lifestyle Change to Prevent Type 2 Diabetes (*Eriksson et al, 1999)*	▪ Physician and nutritionist advice about risk factors for diabetes and establish a weight loss goal ▪ Tailored dietary advice, but broad message ↑ fibre (vegetables, fruit), ↓ foods high in fat (use low fat meats, low fat dairy etc.) ▪ Study visits in weeks 1-2, 5-6, and in 3, 4, 6 months and then every 3 months (7 visits in first year and 4 thereafter) ▪ Complete a 3-day food diary every 3 months ▪ Very low calorie diet (VLCD) if weight loss not achieved in first 6 months ▪ Supervised and tailored exercise sessions	Dietary advice from nutritionist at start of study to reduce BMI below 25kg/m^2, diet with <30% fat, reduce alcohol and stop smoking. Routine advice at annual visits. Completing of 3-day food diaries at baseline and follow up
Talking Computer for Nutrition (*Delichatsios et al, 2001)*	▪ Interactive computer based system linked to home telephone at initial home visit ▪ System aimed to monitor, educate and counsel individuals over telephone with respondents answering questions by pressing key pad ▪ Nutrition advice based on social cognitive theory, goals negotiated ▪ Calls to system 1/week for 6 months, each call 5 to 7 mins. People received reminder calls if they forgot to call system	Same intervention with a physical activity program installed rather than a nutrition program
Nurse Counselling in GP (*Steptoe et al, 2003)*	▪ Two 15 minute individual consults by research nurses, one at baseline and one at 12 weeks ▪ Founded on social learning theory and stage of change model ▪ Interventions tailored to individual with personalised advice and goal setting	Same sessions, education about importance of fruit and vegetables emphasising '5 a day' 'message
Multi-Media 2 fruit 5 veg Campaign (*Dixon et al, 1998)*	▪ Multi media campaign "2 fruit and 5 veg every day"- TV advertising over 3 week periods in 1992, 1993 and 1994 ▪ Other purchased promotional activities- print advertising, transit advertising, sport/art sponsorships and point of sale promotions	No control group

6.2 Quality of evidence

The quality of the seven nutrition RCTs, including the systematic review and meta-analysis for the 'Orlistat + Diet for Obesity' by Padwal et al (2003) is summarised in Table 6.3. The 'Multi-media 2 fruit 5 veg' intervention had a loose pre post study design and is discussed separately below.

All RCTs had an adequate randomisation process, specified clear study inclusion criteria, provided point estimates and measures of variability and accounted for all patients. The best quality interventions according to study reports were the 'Lifestyle Change to Prevent Type 2 Diabetes', the 'Mediterranean Diet', the 'Nurse Counselling in GP', and the 'Orlistat + Diet for Obesity'. The main potentials for bias were lack of concealment of randomisation, lack of blinding (providers of care, outcome assessors and participants) and the failure to analyse results on an intention to treat basis. The 'Orlistat + Diet for Obesity' study was a Cochrane systematic review and meta-analysis of high quality that used a clear search strategy and precise inclusion criteria. It systematically assessed the quality of the included trials and used appropriate data synthesis techniques. In the 'Nutritional Counselling in GP' intervention treatment contamination is possible due to the same doctors treating control and intervention patients, and with the 'Reduced Fat Diet for IGT' intervention the ~24% loss to follow up and lack of 'intention to treat' analysis are potential sources of bias. In the 'Nurse Counselling in GP' and 'Lifestyle Change to Prevent Type 2 Diabetes' interventions the control group also received dietary/other advice at a level perhaps more than would be expected under 'usual care'. This will tend to under-state the effect of the intervention. Limitations in relation to the 'Talking Computer for Nutrition' intervention include high loss to follow up at 6 months.

Table 6.3 Summary of quality of the six nutrition RCTs (plus meta analysis)

Criteria	Nutritional Counselling in GP	Mediterranean Diet	Reduced Fat Diet for IGT	Lifestyle Change to Prevent Type 2 Diabetes	Orlistat + Diet for Obesity	Talking Computer for Nutrition	Nurse Counselling in GP
Was objective and pertinent outcome information gathered	✔	✔	✔	✔	✔	✔	✔
Was the assignment to treatment groups an adequate method of randomisation?	✔	✔	✔	✔	✔	✔	✔
Was the treatment allocation concealed?	?	?	?	?	✔	?	X
Were the groups similar at baseline in terms of prognostic factors?	?	✔	✔	✔	✔	✔	✔
Were the eligibility criteria specified?	✔	✔	✔	✔	✔	✔	✔
Were the outcome assessors blinded to treatment allocation?	?	?	?	✔	?	?	?
Was the care provided blinded?	?	✔	?	?	✔	?	?
Was the patient blinded?	?	✔	?	?	✔	?	?
Were point estimates + measure of variability presented for the primary outcome measure?	✔	✔	✔	✔	✔	✔	✔
Was a power calculation performed at study design?	✔	✔	?	✔	?	?	?
Were all patients accounted for?	✔	✔	✔	✔	✔	✔	✔
Was analysis intention-to-treat?	X	✔	X	✔	✔	?	✔

✔ = yes, X= no, ?= unclear, based on CRD report number 4 (York University)

The 'Multi-media 2 fruit 5 veg' intervention reported by Dixon et al (1998) was a single arm pre-post study. This study has some serious sources of potential for bias and error. These include, a lack of true baseline measurement, reliance on self report which is potentially unreliable, and low response rates which suggest possible selection bias, lack of precision in the main outcome measure (serves of fruit and veg), and lack of control group. This limits the capacity to describe the effect of the campaign and to attribute any change to the intervention. The results derived for this intervention cannot therefore be considered reliable.

Two trials report 5 year follow-up, which is valuable for under-standing the maintenance of behaviour change and observing health effects. However for other trials, short follow-up is problematic, as potential benefits are largely downstream in a postulated reduction in morbidity and mortality. This gap in the clinical trial evidence, can only partly be addressed by obtaining published information on the long term causative relationship between nutrition, mortality and quality of life.

6.3 Study outcomes

Each of the nutrition intervention studies report slightly different outcome measures. Outcomes reported by most studies, include blood pressure and weight. Only the 'Mediterranean Diet' intervention followed up participants for a sufficient period of time to observe final health endpoints, including all-cause and cardiac specific mortality and other cardiac end-points. Other trials do not report final health endpoints – largely reflecting insufficient period of follow-up relative to risk profile.

Behaviour change

Reported change in some of the behaviour outcome measures is summarised below. More details are provided in Technical Report Chapters 15 to 22.

Nutrient Intake: The 'Reduced Fat Diet for IGT' and the 'Mediterranean Diet' interventions both report detailed nutrition intake, based on an analysis of food diaries. Both report significant changes/differences between control and intervention participants in nutrient intake, consistent with the dietary advice given (See Table 6.4). In the 'Mediterranean Diet' intervention, nutrient intake is both significantly and substantially highly in relation to ω-9 (oleic), and ω-3 (linolenic) and fibre; but significantly lower in relation to ω-6 (linoleic), total lipids, saturated fats, polyunsaturated fats and total cholesterol. No change is reported in consumption of alcohol or protein. This is consistent with dietary advice to increase consumption of fish and fruit and vegetables and to use olive oil or rapeseed oil/margarine and reduce consumption of red meat.

For the 'Reduced Fat Diet for IGT' intervention, the focus was reduction in dietary fat. This is consistent with the reported significant reduction in fat as a percentage of energy intake and an increase in carbohydrates.

The 'Talking Computer for Nutrition' intervention also reported increase in dietary fibre and reduction in saturated fat and trend to increase in folate levels. Changes in other nutrients were non-significant.

Fruit and vegetable consumption (and other key food groups): The 'Mediterranean Diet', 'Lifestyle Change to Prevent Type 2 Diabetes', 'Nurse Counselling in GP', and 'Talking Computer for Nutrition' interventions all report statistically significant increases in the consumption of fruit and/or vegetables over the study period. The 'Mediterranean Diet' intervention also reports a statistically significant reduction in consumption of red meat, butter and cream. The 'Multi-media 2 fruit 5 veg' intervention reported by Dixon et al (1998) failed to find a statistically significant increase in daily serves of fruit and vegetables (Table 6.5). The 'Nutrition Counselling in GP' and 'Orlistat + Diet for Obesity' interventions provide no information about food intake.

Table 6.4 Differences in nutrient intake in three Nutrition interventions

Intervention	Nutrition component	Change		P value
		Control	Experimental	
		Nutrient intake record at final visit (12+ months)		
Mediterranean Diet (deLorgeril et al, 1999)	Total calories	2088	1947	0.033
	% calories			
	Lipids	33.6	30.4	0.002
	Saturated fats	11.7	8.0	0.0001
	Polyunsat fats	6.10	4.6	0.0001
	18:1 (ω-9 oleic)	10.8	12.9	0.0001
	18:2 (ω-6 linoleic)	5.3	3.6	0.0001
	18:3(ω-3 linolenic)	0.29	0.84	0.0001
	Alcohol	5.98	5.93	0.8
	Protein g	16.6	16.2	0.3
	Fibre g	15.5	18.6	0.004
	Cholesterol mg.	312.0	203	0.0001
		Change from baseline at 12 months		
Reduced Fat Diet for IGT (Swinburn et al 2001) Change at 1 year	Energy (kcal)	-59	-363	0.016
	Fat (% energy)	-2.3	-8.7	< 0.0001
	Carbohydrate (% energy)	+0.6	+8.3	< 0.0001
	Protein (% energy)	-0.2	+1.7	0.025
	Alcohol (% energy)	+1.3	- 0.9	0.19
	Fibre g/1,000 cals	+0.1	+1.3	0.061
		Change from baseline at 6 months		
Talking Computer for Nutrition * (Delichatsios et al, 2001)	Dietary fibre (g)	+0.2	+1.1	< 0.05
	Saturated fat (% energy)	-0.7	-1.9	< 0.05
	Folate (µg)	+1.0	+19.0	< 0.05

*adjusted for sex, age, ethnicity, income, smoking and baseline stage of change

Table 6.5 Change/differences in consumption of fruit and vegetables (and other key foodstuffs) of five nutrition interventions

Intervention	Length of follow up	Food group	Control Group	Experimental Group	P value
Mediterranean Diet (deLorgeril et al, 1999)	4 years	Mean grams per day			
		▪ fruit	203	251	0.007
		▪ vegetables	288	316	0.07
		▪ legumes	9.9	19.9	0.07
		▪ red meat	60.4	40.8	0.009
		▪ butter/cream	16.6	2.8	<0.001
		▪ margarine	5.1	19.0	<0.001
		▪ fish	39.5	46.5	0.16
Lifestyle Change to Prevent Type 2 Diabetes (Eriksson et al, 1999)	1 year	Consumption of vegetables (% who increased)	62%	72%	0.01
Talking Computer for Nutrition * (Delichatsios et al, 2001)	6 months	Mean serves per day			
		▪ fruit	2.0	3.2	<0.05
		▪ vegetables	3.6	4.5	
		▪ red/processes meats	0.6	0.5	
		▪ whole fat dairy	1.1	1.0	
Nurse Counselling in GP * (Steptoe et al, 2003)	12 months	Mean increase in portions/day ▪ fruit and veg	0.87	1.49	0.021
Multi-Media 2 fruit 5 veg Campaign (Dixon et al, 1998)	3 years	Mean serves per day** ▪ fruit + vegetables	-	0.49	NS

*adjusted for sex, age, ethnicity, income, smoking and baseline stage of change
**compared to Phase 1 of study
NS - not statistically significant

Clinical parameters

A full description of changes in clinical parameters can be found in the Technical Report. Key results are summarised in Table 6.6. The 'Talking Computer for Nutrition' intervention and the 'Multi-media 2 fruit 5 veg' intervention did not report results for any clinical parameters.

Weight: Four interventions ('Nutritional Counselling in GP', 'Orlistat + Diet for Obesity', 'Lifestyle Change to Prevent Type 2 Diabetes', and 'Reduced Fat Diet for IGT') reported mean weight changes. The 'Reduced Fat Diet for IGT' intervention reported that the difference disappears at 5 years. None of the three studies that report BMI ('Mediterranean Diet', 'Reduced Fat Diet for IGT', and 'Nurse Counselling in GP') demonstrate a statistically significant difference between groups at final follow up. However, large improvements in other clinical end points could still be observed for instance with the 'Mediterranean Diet', associated with dietary change that did not result in weight loss.

Blood pressure: Blood pressure was statistically significantly reduced in the intervention group compared to the control group in both the 'Orlistat + Diet for Obesity' and the 'Lifestyle Change to Prevent Type 2 Diabetes' interventions. Three studies failed to demonstrate a statistically significant difference between groups ('Nutritional Counselling in GP', 'Mediterranean Diet', and 'Nurse Counselling in GP').

Cholesterol: Of the five studies reporting cholesterol only the 'Orlistat + Diet for Obesity' intervention reported a statistically significant benefit for the intervention group compared to control (Table 6.6), although the 'Mediterranean Diet' did report a lower use of lipid lowering drugs.

Blood glucose: Several studies report a range of measures of blood glucose such as fasting plasma, 2hr serum insulin, fasting serum insulin, 2hr plasma glucose, HbA1c (specific type of haemoglobin) and glucose status. Significant improvement in these measures has been reported for the 'Orlistat + Diet for Obesity' and the 'Lifestyle Change to Prevent Type 2 Diabetes' interventions, but for the 'Reduced Fat Diet for IGT' intervention the results, while significant at 12 months, show no difference at 5 years.

Table 6.6 Mean change in clinical parameters for six Nutrition interventions

Intervention	Weight (kgs)		Blood pressure (Diastolic mmHG)		Cholesterol (mmol/L)		BMI (kg/m^2	
	Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control
Nutritional Counselling in GP (Pritchard et al, 1999)	-6.13	+0.58*	+12**	0**	-	-	-	-
Mediterranean Diet (deLorgeril et al, 1999)	-	-	78	79	6.20	6.18	26.3	26.9
Reduced Fat Diet for IGT (Swinburn et al 2001)	-3.32* +1.06*	0.59* +0.26*	-	-	-	-	-1.09* +0.72*	+0.22* +0.59*
Orlistat + Diet for Obesity (Padwal et al, 2003)	Weighted mean difference -2.70*		Weighted mean difference 1.6*		Weighted mean difference 0.27*		Not reported	
Lifestyle Change to Prevent Type 2 Diabetes (Eriksson et al, '99)	-3.5*	-0.8*	-5	-3	-4	0	-	-
Nurse counselling in GP (Steptoe et al, 2003)	-	-	-0.13	0.03	-0.09	-0.07	0.01	-0.04

*p<0.00001
**Study reports mean difference between groups ie. Intervention group has a fall in blood pressure of 12mmHg relative to control group

Morbidity and mortality

The 'Mediterranean Diet' intervention resulted in a large and significant reduction in all primary and secondary health endpoints at 4 year follow-up, including all-cause and cardiac morality as summarised in table 6.7. Cumulative survival without cardiac event was also substantially and significantly improved (80% to 65%) in the experimental group (p <0.0002). (Non-cardiac deaths were higher in the intervention group – presumably reflecting the obverse of the intervening opportunities effect. If people aren't dying of heart diseases they are more likely to die of something else).

The 'Lifestyle Change to Prevent Type 2 Diabetes' intervention reported that diabetes was diagnosed in 27 people in the intervention group and 59 in the control group. This is equivalent to halving the incidence of diabetes of persons with IGT from a mean 6% per year in the control group to a mean 3% per year in the intervention group.

Table 6.7 Key health outcomes 5 year follow-up Mediterranean diet (de Lorgeril et al 1999)

Health end point	control	Experimental	Risk ratio (95% CI)	p
Primary endpoints				
Cardiac deaths	19	6	0.35 (0.15 to 0.83)	0.01
Non-fatal AMI	25	8	0.83	
Combined cardiac deaths/ and non-fatal AMI	44	14	0.28 (0.15 to 0.53)	0.0001
Non-cardiac deaths	5	8	1.50	
All-cause deaths	24	14	0.44 (0.21 to 0.94)	0.03
Major secondary endpoints. Major CVD events*	46	13	0.27	
Combined primary and major secondary endpoints	90	27	0.33 (0.21 to 0.52)	0.0001
*Minor secondary endpoints***	90	68	0.73	
Total major and minor endpoints	180	95	0.53(0.38 to 0.74)	0.0002

* Unstable angina, heart failure, stroke, pulmonary and peripheral embolism
** stable angina, elective MI revascularisation, post PTCA restenosis

6.4 Program costs

Program costs for all interventions except the 'Talking Computer for Nutrition' intervention are summarised in Table 6.8. These have been developed by allocating unit costs to inputs drawn from description of interventions contained in the study publications. For the 'Talking Computer for Nutrition' intervention, we have been unable to derive costs and have had no success in obtaining these from the trial research team. For the Australian 'Nutritional Counselling in GP' intervention, costs as reported have been adjusted to 2003 values, using the CPI heath price deflator. For details of cost components refer to the Technical Report.

6.5 Cost- effectiveness analysis

Cost-effectiveness estimates have been developed based on behavioural and clinical outcomes reported for each trial (Table 6.9). Because we have been unable to obtain a cost for the 'Talking Computer for Nutrition' intervention it is not included in either the cost-effectiveness or cost-utility analysis. This is not to say this type of intervention might not be cost-effective, we just were not in a position to take the analysis further.

Table 6.8 Estimated mean cost per person[#] (AU$2003)

Intervention	Intervention group	Control group	Difference
Nutritional Counselling in GP (Pritchard et al, 1999)	$119.31	$31.13	$88
Mediterranean Diet (deLorgeril et al, 1999)	$652.68	$365.83	$287
Reduced Fat Diet for IGT (Swinburn et al 2001)	$937.93	$697.11	$241
Orlistat + Diet for Obesity (Padwal et al, 2003)	$1,492.05	$152.25	$1,340
Lifestyle Change to Prevent Type 2 Diabetes (Eriksson et al, 1999)	$949.62	$142.55	$807
Nurse Counselling in GP (Steptoe et al, 2003)	$964	$0	$1,203
Multi-Media 2 fruit 5 veg Campaign (Dixon et al, 1998)	$690,000 for Victoria*	$0	$690,000

Applying unit costs to inputs derived from description of interventions, except for 'Nutritional Counselling in GP' intervention which is based on costs reported in the 1999 study publication, inflated to AU$2003 using health CPI inflator

* Cost is for entire campaign across a large population of > 5million people. Cost/head depends on how the target group is defined.

Table 6.9 Cost-effectiveness analysis of nutrition interventions

Intervention	Length of follow up	Differential cost $ I–C	Outcomes	Incremental cost effectiveness ratio
Nutritional Counselling in GP (Pritchard et al, 1999)	12 months	$88	Weight loss (kg) I= -6.13 C= 0.58	$13.14 per extra kg lost
Mediterranean Diet (deLorgeril et al, 1999)	4 years	$287	Non-fatal MIs averted: 8.6/100 Deaths 'averted' 5.4/100 (5 year follow-up)[#]	$ 3,335 per non-fatal MI averted $5,310 per death averted
Reduced Fat Diet for IGT (Swinburn et al 2001)	5 years	$2401	Weight loss (kg): I = 1.06 C=0.26 BMI: I=0.72 C=0.59	Control group dominates at 5 years
Orlistat + Diet for Obesity (Padwal et al, 2003)	various	$1340	Weight loss (kgs): Pooled weighted mean difference of 2.7kg greater loss in I vs C	$496.22 per additional kg lost
Lifestyle Change to Prevent Type 2 Diabetes (Eriksson et al, 1999)	6 years	$807	Incidence of diabetes I=20.0 C=42.6	$9,463.46 per incident case of diabetes prevented
Nurse Counselling in GP (Steptoe et al, 2003)	12 months	$1,203	N change to recommended diet (>5 serves of fruit + veg/day) I = 42.2% C = 26.8%	$5,754 per person adopting recommended diet
Multi-Media 2 fruit 5 veg Campaign (Dixon et al, 1998)	4 years	$689,961 for Victoria	Increase in % of popn eating >5 serves fruit + 2 serves veg/day I = 1.9 % C = 0%	$12.19 per extra person eating 2 fruit + 5 veg

I= intervention group, C= control group

based on non fatal AMI of 8/219 (3.7%) and 14/219 (6.4%) deaths in the 'Mediterranean diet' group and 25/204 (12.3%) non-fatal AMI and 24/204 (11.8%) deaths in the 'western diet' group.

6.6 Cost-utility analysis

We have not developed cost-utility estimates for two interventions, the 'Talking Computer for Nutrition' and the 'Nutrition Counselling in GP' interventions. The former has been excluded because

of difficulty in developing a cost estimate, whilst the latter is excluded, because of a number of problems with the study design, where patients were grouped according to three conditions (hypertensive, overweight and diabetic), but with patients able to be allocated to more than one group interpretation of outcomes is difficult. Other issues included potential group differences at baseline, the same doctors caring for patients in the control and intervention groups, loss to follow up and lack of intention to treat analysis.

We have used 4 types of models for determining cost/QALYs that are pertinent to the interventions studied.

1. A cardiovascular disease (CVD) model has been applied to the 'Mediterranean Diet' intervention, as the intervention was offered to persons surviving an MI and CVD events are the primary outcome and are reported in the study.
2. A diabetes model for the two interventions addressed at persons with IGT ('Reduced Fat Diet for IGT' and 'Lifestyle Change to Prevent Type 2 Diabetes') which have both reported outcomes suitable for a diabetes model.
3. A fruit and veg model has been applied to the 'Multi-media 2 fruit 5 veg' intervention and the 'Nurse Counselling in GP' intervention. The key element of this model is the relationship between the consumption of the recommended number of serves per day of fruit and vegetables and mortality and quality of life.
4. For the 'Orlistat + Diet for Obesity' intervention, a cost-utility analysis reported by Foxcroft and Milne, 2000 prepared for NICE (the British National Institute of Clinical Effectiveness) has formed the basis of our cost-utility estimate. Specifically we have used their estimated QALY gain of 0.016 per patient year of treatment and related this to our cost estimate (which incorporates Australian unit costs).

All models are described below, but for more detail refer to the Technical Report.

CVD model – mediterranean diet

A Markov model was used to predict the health states of the intervention and control group over time. Each person starts the trial post AMI, and then moves between 5 health states as listed below. Each of these health states attracts a quality of life value, a risk of death and costs of management. Transition probabilities were derived from the clinical trial and relevant literature for the 2 cohorts; a) the experimental Mediterranean diet group and b) the control 'prudent' western diet group.

The model cycle was 1 year and the time horizon of the model was 10 years. The model included five health states, i) free of events after initial AMI; ii) minor event, such as stable angina; iii) subsequent AMI; iv) major event, such as unstable angina or pulmonary embolism; v) Stroke; plus death.

The transition probabilities for the experimental and control group are shown in Table 6.10. Details of data source for these are provided in the Technical Report (Table 16.2). Key references include Peltonen (2000), Antiplatelet Trialists' Collaboration (1994), Heit et al (1999), Tanne et al (2002), and Petty (1998). The model commences with all people 'Alive free of events' (post an initial AMI according to initial indication). The model is driven by the substantial reported reduction in mortality and increase in numbers free of major or minor events in the intervention group compared with the control group, 17 % free of events in the intervention group, compared with 33% in the control group. The other important drivers of the model are the transitions seen in the first lines of Table 6.10 which are the transitions from 'alive free of events' to the other health states. These transitions were derived directly from the study data by deLorgeril et al (1999).

Table 6.10a Transition matrix for Intervention (Experimental) group

	Alive free of events	Alive after minor event	Alive after AMI	Alive after major event	Alive after stroke	Dead
Alive free of events	#	0.091	0.010	0.016	0.000	0.017
Alive after minor event	▫	#	0.014	0.03	0.011	0.033
Alive after AMI	▫	▫	#	0.183	0.055	0.159
Alive after major event	▫	▫	▫	#	0.015	0.170
Alive after stroke	▫	▫	▫	▫	#	0.22
Dead	▫	▫	▫	▫	▫	1

residual value
▫ no transition permitted

Table 6.10b Transition matrix for Control group

	Alive free of events	Alive after minor event	Alive after AMI	Alive after major event	Alive after stroke	Dead
Alive free of events	#	0.144	0.034	0.136	0.005	0.033
Alive after minor event	▫	#	0.002	0.03	0.011	0.033
Alive after AMI	▫	▫	#	0.183	0.055	0.159
Alive after major event	▫	▫	▫	#	0.015	0.170
Alive after stroke	▫	▫	▫	▫	#	0.22
Dead	▫	▫	▫	▫	▫	1

residual value
▫ no transition permitted

The costs for year 1 were $433.40 for the intervention group and $36.71 for the control group. An additional cost of $32.70 is also assigned to the intervention group each year for years 2 to 5 for ongoing assessment costs. A conservative set of utility values were used which will tend to understate the benefit of the intervention. These were derived from several sources:

- AMI at 0.88 (Lee et al 1997),
- CVD but event free at 0.93 (Kunz, 1996)
- Major events at 0.78 (Kunz, 1996)
- Minor events at 0.89 (Kunz, 1996)
- Stroke at 0.54 (Derdeyn, 1996)

As elsewhere, costs and benefits have been discounted at 5% per annum.

Based on the above model and data inputs, advising persons post AMI to adopt a Mediterranean diet is estimated to cost $339 per QALY gained, best estimate, as shown in Table 6.11. Extensive univariate sensitivity analyses were also performed with the results summarised in Figure 6.1. This shows a very narrow plausible range of $244 to $ 697 per QALY gained. The narrow range reflects the high quality data and certainty around data inputs. The intervention is highly cost effective under all scenarios.

Because CVD events are reduced in the experimental group costs of management will be lower. We have estimated the cost differential from the differential event rate reported in the clinical trial (see Table 6.7), at the unit cost of events using Australian data sources:

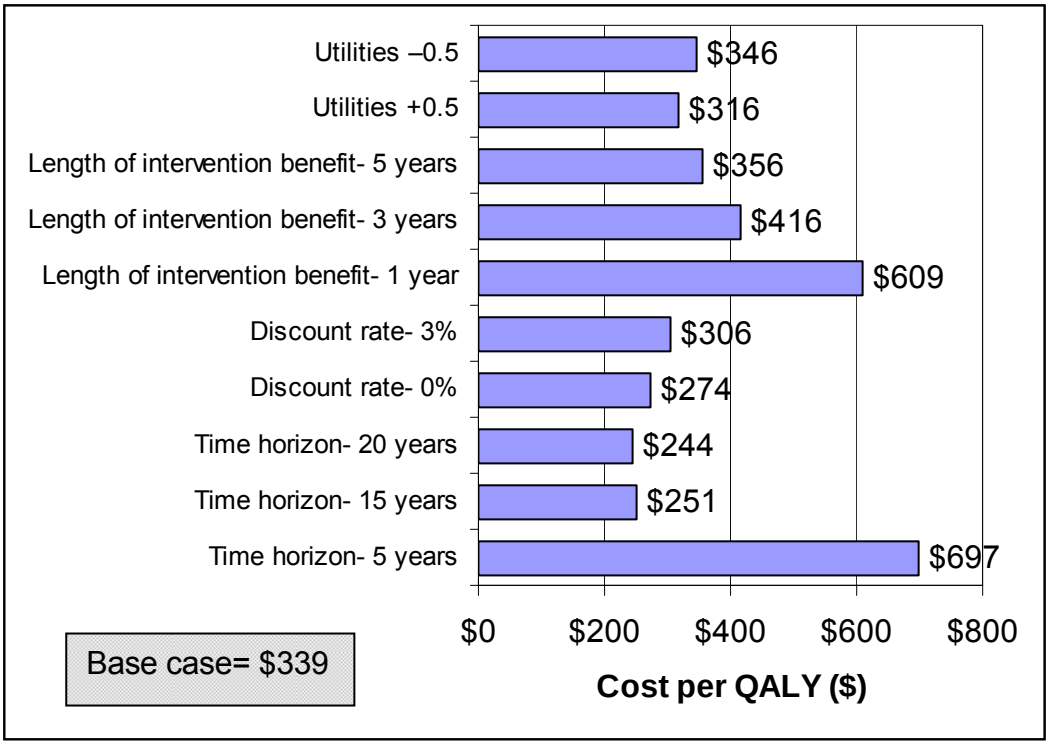
- AMI at $3,712 (AIHW National Hospital Cost Data Collection and National Hospital Morbidity Database)
- Minor events at $3,430 (ACE Heart Disease Study based on Victorian Admitted Episodes Database (VAED) and AIHW hospital statistics)
- Major events at $9,764 (ACE Heart Disease Study based on VAED and AIHW hospital statistics)
- Stroke at $10,000 (ACE Heart Disease study based on NEMSIS and average survival from DisModII).

When the differential costs of managing CVD are included in the analysis the Mediterranean diet dominates - being both cost saving and improving health outcomes. The Mediterranean diet still dominates even if downstream costs are one tenth of that listed above.

Table 6.11 Modelled cost utility base case results/person

	Mediterranean diet	Western diet	Difference
Total costs	$523.20	$35.00	$488.20
Total life years (QoL = 1)	6.78	5.46	1.32
Total QALYs	6.12	4.68	1.44
Discounted $/LY gained			**$369.00**
Discounted $/QALY gained			**$339.00**

Figure 6.1 Results of sensitivity analyses



Diabetes model – lifestyle change to prevent type 2 diabetes

A modelling approach was used to enable the surrogate or intermediate outcome measures of diabetes incidence (reported by Eriksson et al, 1999) to be linked to life-years saved and QALYs gained. A Markov process structure was developed comprising 1 year cycles. The time horizon of the model was 20 years. The model includes the health states impaired glucose tolerance (IGT), non insulin dependent diabetes mellitus (NIDDM) and death.

We determined the progression, costs and utilities of a cohort of 1000 people receiving the lifestyle program compared with 'usual care'. In accordance with the trial data, the economic model assumes the cohort is 67% female with an average age of 55 years.

The cohort progressed annually between health states over a 20-year time horizon with 0.037 who were IGT becoming NIDDM per year in the intervention group compared to 0.088 in the control group (Lindstrom et al, 2003). The model commences with all people in the IGT health state as was the case in the 'Lifestyle Change to Prevent Type 2 Diabetes' study.

Transition probabilities vary by cycle for all-cause mortality which was estimated using life tables for the Australian population (ABS, 2002) for adults aged 55 years to 75 years. These mortality rates were adjusted for the proportion female and the relative risk of morality for those with IGT and NIDDM (adjusted for the prevalence of IGT and NIDDM in the population). The resulting relative risks were 1.5 for IGT and 1.9 for NIDDM.

The costs for each of the study groups for year 1 were $949.62 for the intervention group and $142.55. In addition a cost of $16.92 per year for 6 years is allocated to both groups for an hour follow up consultation with a dietician. Utilities of 0.84 for IGT and 0.701 for NIDDM were incorporated. Costs and benefits are discounted at 5% per annum.

Table 6.12 presents the economic performance of the lifestyle program, at an incremental cost utility ratio of $1,879 per QALY gained.

Table 6.12 Modelled cost utility base case results

	Lifestyle program	'Usual care' group	Difference
Total costs	$974.20	$205.50	$768.60
Total life years	11.36	11.30	0.06
Total QALYs	9.14	8.73	0.41
Discounted $/LY gained			**$13,693**
Discounted $/QALY gained			**$1,879**

Extensive univariate sensitivity analyses were performed (See technical report for details of the assumptions and values) and gave results ranging from $1,127 per QALY to $9,958 per QALY as shown in Figure 6.2. The cost per QALY gained was most sensitive to the time horizon of the model and the utility assigned to diabetes. When a downstream cost associated with NIDDM is included of $5,540 the intervention group dominates the control group. Threshold analysis shows that the intervention group will dominate if downstream costs of NIDDM exceed $175 per person per year.

Diabetes model – reduced fat diet for IGT

As the intervention subjects had all regained weight by the fifth year of follow-up, modelling was not taken beyond year 5, as health outcomes (and costs) would have been no better. Any benefits, and incremental costs of the intervention, would be entirely captured within the first five years. An economic model was constructed with three health states of Type 2 Diabetes, glucose intolerance, and normal glucose tolerance (NGT) with the distribution of patients over the model shown in Table 6.13.

Figure 6.2 Results of sensitivity analyses

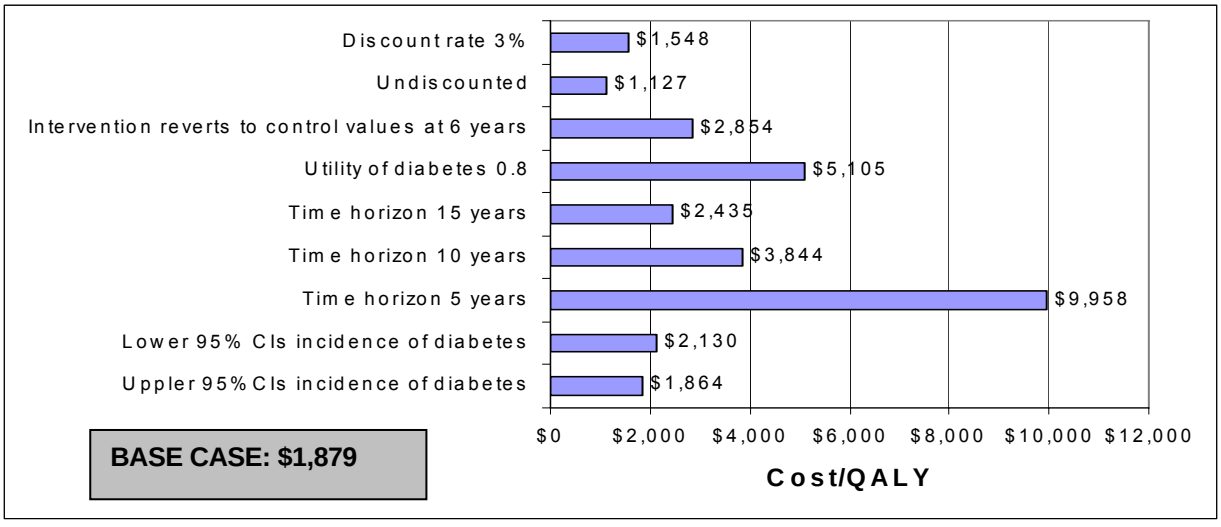


Table 6.13 Health State Distribution of Patients over 5 years

Health State	Baseline	Yr 1	Yr 2	Yr 3	Yr 4	Yr 5
Type 2 Diabetes	0.33	0.26	0.31	0.15	0.27	0.38
Glucose Intolerance	0.32	0.49	0.50	0.31	0.27	0.23
NGT	0.35	0.25	0.19	0.54	0.47	0.39
TOTAL	**1.00**	**1.00**	**1.00**	**1.00**	**1.00**	**1.00**

The 5-year cumulative mortality rates of the Australian population (ABS, 2000) were used to inform the transition to death in the model. A relative risk of 1.1 was applied to mortality rates to adjust for the increased risk of mortality imposed by changes in metabolic state (Balkau et al, 1993 and Rockwood et al, 2000) and a relative risk of 1.2 for increased risk of mortality imposed by excess weight (Manson, 1987 and Rissanen et al, 1990). For further details refer to the technical report. Utility values from the DiabCost Study were applied to the survival figures generated.

This resulted in QALYs as shown in Table 6.14. Costs and outcomes are brought together in table 6.15, to yield a cost/QALY gain of just over $10,000. Including estimated cost savings from reduced costs of management of $1,380 per patient (Table 17.15 of Technical Report), the intervention becomes dominant with both improved health outcomes and resource savings, as shown in Table 6.16.

Table 6.14 Estimated QALYs from Model

Time from Baseline	Fat-Reduced	Control	Increment
Year 1	0.825	0.821	0.005
Year 2	0.819	0.815	0.004
Year 3	0.821	0.815	0.006
Year 4	0.813	0.807	0.006
Year 5	0.804	0.798	0.006
Total (years)	**4.082**	**4.056**	**0.027**
Discounted at 5% p.a. (years)	**3.714**	**3.690**	**0.024**

Table 6.15 Cost/QALY base case

	Low fat group	'Usual care' group	Difference
Total costs	$937.93	$697.11	$241
Total QALYs (disc @ 5%)	3.714	3.690	0.024
Disc $/QALY gained			**$10,049**

Table 6.16 One-way sensitivity analysis results

Parameter	Cost per life year saved	Cost per QALY gained
Downstream cost savings included	Intervention dominates	Intervention dominates
Discount rate 0%	$88,463	$9,064
Downstream costs ignored	$103,486	$10,049

Fruit and vegetable model

A modelling approach was used to link the surrogate/intermediate outcome measure of fruit and vegetable consumption (reported by Steptoe et al, 2003 and Dixon et al, 1998) to life-years saved and QALYs gained. A Markov process structure was developed comprising 1 year cycles. The time horizon of the model was 20 years. The model includes the following health states:

- Success (eating at least 5 serves of vegetables and 2 serves of fruit per day)
- Failure (not eating 5 serves of vegetables and 2 serves of fruit per day)
- Death

We determined the progression, costs and utilities of a cohort of 1000 people receiving the '2 fruit 5 veg' intervention compared with a control group who were assumed to receive no intervention (and who are assigned baseline values reported by Steptoe et al, 2003 or Dixon et al, 1998 as

appropriate). The economic model assumes the cohort is 50% female with an average age of 40 years. The cohort was progressed annually between health states over a 20-year time horizon.

'Nurse counselling in GP' (Steptoe et al 2003)

The transition probabilities are based on the publication by Steptoe et al (2003), which reported 20.9% of people in the intervention group progress from failure to success in the first year of the model. It is assumed that the new food habits are retained for the period of the model, while there is no change in the control group. The model commences with 21.3% of each group in the success state (eating at leat 2 fruit + 5 veg) as was reported by Steptoe et al (2003).

Transition probabilities to death vary by cycle and have been estimated from Australian life tables (ABS, 2002) for adults aged 40 to 60 years. Mortality rates were adjusted for gender and relative risk of death associated with consuming fruit and vegetables at recommended levels of 0.68, relative to persons with low fruit and veg consumption. Adjusting for the prevalence of people in the Australian population consuming recommended amounts of fruit and vegetables <10 % (Dept Health WA), gives a relative risk of 0.94 for those consuming more than recommended and 1.38 for those consuming less.

A utility of 0.777 was assigned to those consuming the recommended amounts of fruit and vegetables per day with 0.7573 assigned to those not consuming recommended amounts (a difference of 0.02). These values were obtained by performing a Brazier transformation (Brazier, 1998) on data from the National Nutrition survey (1995).

The costs for the intervention group as reported in Table 6.7 were estimated at $964 per person for the first year of the model, whilst the control group is assumed to incur zero costs. Costs and benefits are discounted at 5% per annum.

The results are summarised in Table 6.17 and show an estimated incremental cost utility ratio of $10,555 per QALY gained. The results of univariate sensitivity analyses ranged from $6,503 to $39,023 per QALY gained, with results being most sensitive to the time horizon of the model (Figure 6.3). This also means if the behaviour change is not retained and the differential between control and intervention group diminishes the cost/QALY will increase substantially. It is also interesting to observe that performance is not sensitive to the relative risk of death, and in fact moves in the 'opposite direction' to expectations. This seems to be driven by the dominant role of quality of life in the differential QALYs, such that a lower death rate in the control group means a greater QoL tally. There are many uncertainties in the inputs to the model, notably the presumed relationship between fruit and vegetable consumption and all-cause mortality and its application to the cohort, as a dichotomous model.

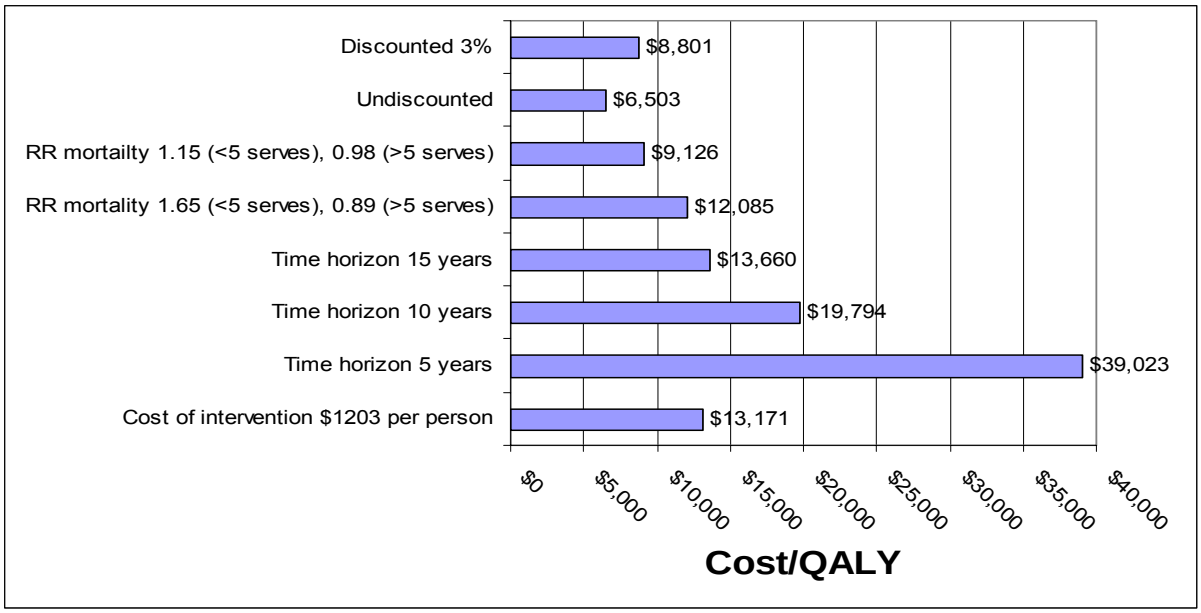
Whether behaviour change is maintained and the differential between the intervention and control group is also highly contentious given the study provides data up to 12 months only.

In fact the results for the 5 year model at **$38,440/QALY** might well be more valid, certainly as a more conservative estimate of performance.

Table 6.17 Modelled cost utility 'base case' results 20 years

	Intervention group	Control group	Difference
Total costs	$916.60	$0	$916.60
Total life years (QoL set = 1)	12.217	12.193	0.024
Total QALYs	9.372	9.285	0.087
Discounted $/LY gained			**$38,441**
Discounted $/QALY gained			**$10,555**

Figure 6.3 Results of univariate sensitivity analyses



Results suggest if the downstream costs associated with failing to consume 5 serves of fruit and vegetables per day is greater than an average of $265 per person per year (over a 20 year time period) then the intervention will dominate the control (greater benefits for lower costs).

‘Multi-media 2 fruit 5 veg campaign’ (Dixon et al 1998)

The basic model as described above has also been applied to the ‘Multi-media 2 fruit 5 veg’ intervention. Based on the paper by Dixon et al (1998), 6% of people in the intervention group progress from failure to success (an average of 3% in each of the first two years). It is assumed that all success is maintained and that there is no success in the control group. The model commences with 24.3% of each group in the success state as reported by Dixon et al (1998).

Transition probabilities and utility values are as described above. The costs for the intervention group are estimated at $0.20 per person, assuming a program targeted at the entire adult population (Table 6.6). Costs and benefits are discounted at 5% per annum.

Table 6.18 presents the economic performance of the ‘Multi-media 2 fruit 5 veg’ intervention, at an incremental cost utility ratio of **$46 per QALY** gained. The results of univariate sensitivity analyses are presented in Figure 6.4. Estimated cost/QALY gained ranges from $24 to $2,523 (with cost at 30 x base case). Even if the cost of the intervention were 10 times that identified and the benefits were modelled for only 5 years, the ‘2 fruit 5 veg’ intervention would still come in at <$2,000/QALY gained.

Table 6.18 Modelled cost utility base case results

	‘2 fruit 5 veg’ campaign	Control group	Difference
Total costs $/head	0.204	0	0.2040
Total life years	12.201	12.196	0.0050
Total QALYs	9.746	9.741	0.0048
Discounted $/LY gained			**$40**
Discounted $/QALY gained			**$46**

However, there are some major concerns with the data inputs to this model, in addition to the uncertainty about the relationship between fruit and vegetable consumption and health as noted above, is the actual behaviour change associated with the campaign. The estimate of behaviour change is based entirely on self report, with no proper base line and no control group. Further, the

reported difference from baseline in mean number of serves of fruit and vegetables was not statistically significant. It therefore should be noted that if there was in actual fact no change in fruit and vegetable consumption then the intervention would be dominated (same effect, higher costs).

The size of downstream cost savings that would mean the intervention was dominant is shown in table 6.19. This of course assumes the potential health gains are realised. The 'break-even' cost saving figure for the '2 fruit 5 vege' campaign is very small due to the low cost of that campaign.

Figure 6.4 Results of univariate sensitivity analyses

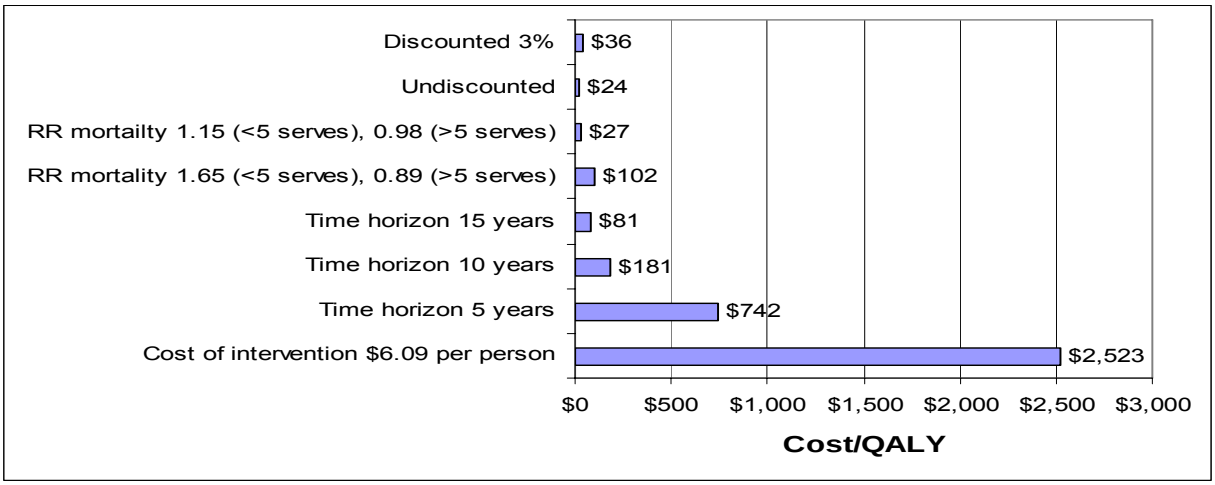


Table 6.19 Results of threshold analysis for downstream costs (Fruit and veg interventions)

Intervention	Downstream cost saving per person per year associated with consuming recommended serves of fruit and vegetables/day that results in intervention dominance
Nurse Counselling in GP (Steptoe et al, 2003)	>$265
Multi-Media 2 fruit 5 veg Campaign (Dixon et al, 1998)	>$0.30

Published model – 'orlistat + diet for obesity'

The cost utility of orlistat treatment for obesity is reported in the review by Foxcroft and Milne (2000). Foxcroft and Milne (2000) calculated utility benefit for 100 patients treated with orlistat for 1 year of 1.601 (or 0.016 per person). They calculated cost utility over 2 years using costs in £ for the year 2000, which we have exchanged into Australian dollars and inflated to 2003 figures (shown in brackets). This leads to an incremental cost utility for 100 patients over 2 years of £45,881 ($154,227) per QALY gained with figures ranging from £19,452 to £55,391 ($65,387 to $186,194) per QALY gained in multi way sensitivity analyses. We have used the utilities reported by Foxcroft and Milne (2000) as reported above and applied our estimated costs based on Australian resource use of $1339.80 per person (as shown in Table 6.7).

This gives estimates of $83,685 per additional QALY gained per person. All the above calculations exclude possible benefits beyond the trial, or any mortality gain. They are based on a 2 year time horizon and can be considered conservative.

6. 7 Comparative performance of nutrition interventions

A comparison of the cost-utility analysis for six interventions is presented in Table 6.17. The upper estimate of the sensitivity analysis from the 'Reduced Fat Diet for IGT' intervention is presented as this is most comparable to the other modelling assumptions. The 'Multi-media 2 fruit 5 veg'

intervention appears highly cost effective, although it must be noted that this is solely due to a very low cost rather than large benefits. The results for the 'Mediterranean Diet' intervention are highly cost effective and relatively certain. The 'Mediterranean Diet' intervention dominates the control group (less costly and more effective) if downstream costs are included. This intervention still dominates if downstream costs of 1/10 that estimated are included.

The 'Reduced Fat Diet for IGT' and the 'Lifestyle Change to Prevent Type 2 Diabetes' interventions also dominate when downstream costs for diabetes are included. For the fruit and vegetable interventions threshold analyses have been performed and are summarised in Table 6.19.

Table 6.19 Comparison of cost utility results

Intervention	Key assumptions in base case (a)	Cost per QALY (base case)	Range from sensitivity analyses ($/QALY)	Quality of evidence (b) Behav.	L-T B	H =f(B)
Orlistat + Diet for Obesity (Padwal et al, 2003)	▪ Published model for QALY gain of 0.016 per person per year ▪ 2 year time horizon ▪ Downstream costs excluded ▪ undiscounted	**$83,685 (Australian inputs)**	Base case £45,881 (range £19,452 to £55,391) (UK inputs)	# #	☐	#
Mediterranean Diet (deLorgeril et al, 1999)	▪ CVD Markov model ▪ 10 year time horizon ▪ Length of benefit 10 years ▪ Downstream costs excluded ▪ Discount rate 5%	**$339**	$244 to $697	# #	##	##
Lifestyle Change to Prevent Type 2 Diabetes (Eriksson et al, 1999)	▪ Diabetes Markov model ▪ 20 year time frame, ▪ Benefits maintained for 20 years ▪ Downstream costs excluded ▪ Discounted 5%	**$1,879**	$1,127 to $9,958	# #	##	##
Reduced Fat Diet for IGT (Swinburn et al 2001)	▪ Diabetes Markov model ▪ 5 year time horizon ▪ Benefits maintained for 5 years ▪ Discounted 5%	**$10,049**	Intervention dominates to $10,049	##	#	##
Nurse Counselling in GP (Steptoe et al, 2003)	▪ Fruit and vegetable consumption Markov model ▪ 20 year time horizon ▪ Benefits maintained 20 years ▪ Downstream costs excluded ▪ Discounted 5%	**$10,555**	$6,503 to $39,023	#	#	#
Multi-Media 2 fruit 5 veg Campaign (Dixon et al, 1998)	▪ The reported 0.49 extra serves of fruit & veg is real and difference is maintained for 20 years ▪ 20 year time horizon ▪ Excluding downstream costs ▪ Discounted 5%	**$46**	$24 to $2,523 (intervention will be dominated if there is no change in fruit and vegetable consumption)	☐	☐	#

(a) Base case for all interventions excludes downstream costs
(b) Quality of Evidence;

Behav -Evidence concerning change in behaviour during intervention,

LT-B Evidence concerning maintenance of behaviour change;

H=f(B) Evidence concerning relationship between behaviour and Health (mortality and quality of life as a function of nutrition), ## Good quality of published data identified,

Poor quality of published data identified,

☐ No data identified

Chapter 7 Tobacco smoking interventions

7.1 Description

In this chapter, four broad approaches to smoking cessation are evaluated (plus several variations): mass media campaigns in a community setting, GP advice to current smokers (of varying intensity), phone counselling plus NRT and pharmacotherapy for addicted smokers (bupropion) (Table 7.1).

For evidence we draw on reports of specific interventions (for the media-based and phone counselling – Biener et al 2000 and Rigotti et al 2000, Wakefiled et al 1999 and Zhu et al 2000), but large meta-analyses for the other intervention types (Silagy et al 2004, and Hughes et al 2004). The latter allowing various features to be analysed. A meta-analysis conducted by Baille et al (1994) of 86 trials comparing brief interventions, NRT and various behavioural techniques for smoking cessation interventions, alone and in combination, is used primarily for background information. Findings are summarised in the Technical Report (chapter 26), but no attempt has been made to perform cost effectiveness or cost utility analyses primarily due to the availability of more recent data.

Table 7.1 Description of setting, population target and key references for Tobacco interventions subject to analysis

Intervention	Location, setting, year of intervention	N trial participants Mean age % female		Target population	Chapt in tech report
		Intervention	Control		
Mass media					
US mass media campaign: MTCP *(Biener et al, 2000 & Rigotti et al, 2002)*	Massachusetts *vs* Rest of US. Community setting 1993 to 1999	Sample drawn from pop^{n} of Massachusetts≅ 6million	Sample drawn from pop^{n} of Rest of US	General population	23
AUS mass media campaign: Phase 1 National Tobacco Campaign *(Wakefield et al, 1999)*	Australia Community setting 6/1997 to 11/1998	Sample for evaluation 4,197	Sample for evaluation 1,192	Current smokers aged 18-40 years	24
Physician advice					
Meta-analysis of 34 trials evaluating minimal to intensive physician advice. *(Silagy et al, 2004)*	Various incl. US, UK, AUS Primary care setting 1974 to 2000	1,832 to 7,705 depending on comparison	1,941 to 5,870 depending on comparison	Smokers aged ≥ 11 years	25
Counselling + NRT					
Phone counselling as adjuvant therapy for NRT *(Zhu et al, 2000)*	California, USA Community setting 7/1995 to 11/1996	524 for >1 session group - -	140 for 1 session group - -	Smokers aged ≥ 18 years	27
Pharmacotherapy					
Meta-analysis of 16 Bupropion SR trials *(Hughes et al, 2004)*	Various but mostly US Primary care 1974 to 2000	3147 - -	2227 - -	Adult smokers without current depression	28

MTCP: Massachusetts Tobacco Control Program

Further details of the studied interventions are presented in Table 7.2.

The two mass media campaigns included differ significantly in their intensity, scope and duration. The Massachusetts Tobacco Control Program (MTCP) operated over a period of seven years and included mass media delivery of over 100 adverts in concert with local education/intervention and tighter tobacco control regulation. Phase 1 of Australia's National Tobacco Campaign operated over 12 months and emphasised mass media delivery of the message: 'Every cigarette is doing you damage' through three television advertisements. Both campaigns included among their objectives increased propensity to quit of current smokers.

The physician advice interventions brought together in the Silagy et al (2004) meta-analysis were of varying levels of intensity involving from 1 to several consultations delivered largely by a general practitioner to message to smokers who were potentially resistant to change.

Phone Counselling + NRT as evaluated by Zhu et al, 2000 and the 'Bupropion SR' trials reported by Hughes et al 2004 were directed at subjects who had actively sought assistance with quitting smoking on entry to the relevant trial or study sample.

For the majority of available comparisons, the control group received some intervention or follow-up that was likely to increase the rate of smoking cessation. For example, comparison in the MTCP studies was against controls drawn from other states in the USA that may have been subject to anti-tobacco advertising, tobacco control legislation or physician advice with a stop smoking message. Similarly, comparison in the Australian 'National Tobacco Campaign' intervention was against a benchmark survey conducted in a sample that had been exposed to a raft of existing tobacco control measures and in the same month as World No Tobacco Day. The control group for the minimal versus control comparison for the 'Physician Advice for Smoking Cessation' meta-analysis comes closest in approximating the absence of intervention. The no intervention arm from this meta-analysis is included as a comparator when evaluating the performance of active interventions, 'Phone Counselling + NRT' and 'Bupropion SR'.

Table 7.2 Details of interventions and care received by control groups

Intervention	Activities for Experimental Group	Care received by the control group
MTCP *(Biener et al, 2000: Adults)* *(Rigotti et al, 2002: Youth)*	▪ aimed at entire population: 3 objectives: (1) change community norms re tobacco use, (2) prevent first use, (3) help current smokers quit. ▪ November 1992: 25 cent/pack increase in state tobacco taxes. ▪ 1993 to 1999: (1) mass media campaign via TV, radio and print media, > 100 adverts, (2) local education and intervention services such as school-based prevention programs, telephone counselling, free NRT patches or gum, educational materials, etc (3) various public policy initiatives such as extra regulation and stronger enforcement of existing regulation.	▪ For adults, the comparison group was 41 mainland US states. California was excluded because an intensive anti-smoking program was already in place. ▪ For youths, the comparison group was defined as those who had attended out-of-state high schools. ▪ Tobacco control measures in the comparison groups are not described in any detail.
National Tobacco Campaign NTC (AUST) *(Wakefield et al, 1999)*	▪ First phase of Australia's National Tobacco Campaign aimed at current smokers 18-40 yrs. ▪ Mass media campaign via a series of three TV adverts promoting the message: 'Every cigarette is doing you damage' (depicting damage to lung tissue, fatty deposits being squeezed from an aorta etc.). ▪ TV adverts reinforced through other media. ▪ All advertising urged smokers to contact Quitline to obtain information, assistance and support. ▪ Campaign ran from June 1997. 4-week period of intensive advertising, which gradually decreased until the campaign ended in November 1998.	▪ Comparison against a benchmark survey conducted in a sample that had been exposed to a raft of existing tobacco control measures. ▪ World No Tobacco Day also fell in the same month as the benchmark survey.

Intervention	Activities for Experimental Group	Care received by the control group
Physician Advice for Smoking Cessation *(Silagy et al, 2004)*	▪ Minimal advice entailed a single consultation lasting less than 20 minutes with or without a leaflet plus one follow-up visit. ▪ Intensive advice was any intervention that required a greater time commitment or if materials additional to a leaflet were provided ▪ Advice was defined as verbal instructions from a physician with a 'stop smoking' message irrespective of whether information was provided about the harmful effects of smoking. ▪ In addition to being of different intensities, the interventions were quite different in kind. In one intervention, patients were asked whether they smoked and were simply handed a leaflet if they wanted to stop. Another intervention encouraged smokers to sign a contract to quit. A third intervention offered a free phone card to quitters.	▪ Meta-analysis of 34 trials comparing (1) minimal advice against no advice (16 trials), (2) intensive advice against no advice (5 trials), (3) intensive advice against minimal advice (14 trials). (4) One further trial compared two interventions that provided intensive advice.
Phone Counselling +NRT *(Zhu et al, 2000)*	▪ Observational study of smokers who called the California Smokers' Helpline between January 1994 and June 1998. ▪ Study sample included 664 callers who had used one form of NRT (either gum or patches but not both) and counseling during quit attempts, with some overlap between NRT and counseling.	▪ Compared groups based on Medical coverage, whether smoked >25 cigarettes/day, whether had one or multiple counseling sessions, NRT via patch or gum.
Bupropion SR *(Hughes et al, 2004)*	▪ Meta-analysis of trials to assess the effect of anti-depressants plus counseling in aiding long-term smoking cessation. ▪ Included 16 trials comparing buproprion SR plus counseling against placebo plus counseling. ▪ Mechanism of action probably relates to a capacity to block re-uptake of dopamine and nor-adrenaline, although other mechanisms may also be involved. ▪ Dose regimen in the trials varied but was most commonly 300mg once daily dose for 7 to 12 weeks with adjuvant psych therapy.	▪ Placebo plus some form of counselling or motivational therapy.

7.2 Quality of evidence

The quality of the smoking cessation trials/studies is summarised in Table 7.3 below.

The quality of evidence for the smoking cessation interventions varied widely. The best quality studies were for trials of 'Physician Advice for Smoking Cessation' and 'Buproprion SR' interventions. For these studies, the main areas of concern relate to (1) within-study variation in the quality of included trials and (2) incomplete reporting of the characteristics of included trials. The quality of the 'Physician Advice for Smoking Cessation' meta-analysis is also reduced by the potential for measurement error in the main outcome measure. Smoking status was typically self-reported with confirmation from lab or sponsor in only 13 out of 34 trials. In addition, the advantages of Level 1 evidence from the 'Bupropion SR' intervention are largely forfeited because we are forced to rely on controls from the 'Physician Advice for Smoking Cessation' meta-analysis to evaluate the performance of bupropion SR plus counselling against no intervention.

Table 7.3 Summary of quality of the smoking cessation studies

Intervention type	Mass media		Physician advice	Counselling and NRT	Pharmaco-therapy
Criteria	MTCP	National Tobacco Campaign	Brief to intensive	Phone Counselling +NRT	Bupropion SR
Was the assignment to treatment groups an adequate method of randomisation?	x	x	✓	x	✓
Was the treatment allocation concealed?	x	x	x	x	?
Were the groups similar at baseline in terms of prognostic factors?	x	x	?	x	?
Were the eligibility criteria specified?	x	x	✓	x	✓
Were the outcome assessors blinded to the treatment allocation?	x	x	?	x	?
Was the care provided blinded?	x	x	x	x	?
Was the patient blinded?	x	x	x	x	✓
Were point estimates and measure of variability presented for the primary outcome measure?	✓	✓	✓	✓	✓
Was a power calculation performed at study design?	?	✓	?	?	?
Were all patients accounted for?	x	x	?	✓	?
Was the analysis intention-to-treat?	x	x	?	x	✓

✓ = yes, X= no, ?= unclear, based on CRD report number 4 (York University)

For the remaining interventions, the evidence was drawn from observational studies with no baseline comparison between groups with respect to known confounders. The checklist in Table 7.3 above provides an indication of the potential for bias when we are forced to rely on observational studies instead of Level 1 evidence from RCTs. The MTCP intervention as reported by Biener et al (2000) and Rigotti et al (2002) suffer from a number of other limitations that further reduced their quality. For example, Biener et al (2000) pooled data from two population-based surveys: the Behaviour Risk Factor Surveillance System (BRFSS) and the Massachusetts Tobacco Survey. The Massachusetts Tobacco Survey in 1993-4 was a base line survey of adults *and youths* even though the study and the remainder of the dataset, was specifically aimed at adult smoking prevalence. Outcomes for the control group were estimated based on data for 41 mainland US states from the BRFSS whereas outcomes for the intervention group were based on data from the BRFSS from 1989 to 1993 and then on pooled data from the BRFSS and the Massachusetts Tobacco Survey from 1994 to 1998.

Each year of the BRFSS and the Massachusetts Tobacco Survey was effectively a new cross-section with sample sizes ranging from 1,221 to 4,944 for the Massachusetts sub-sample of the BRFSS. Finally, the definition of a smoker was also changed during the BRFSS series resulting in a correction of the trend in 1996. As a consequence, the estimate of treatment effect from the Biener et al (2000) might be partly or wholly attributable to bias or confounding.

In short, the study reports of the MTCP by Rigotti et al (2002) and Biener et al (2000), of the Australian 'National Tobacco Campaign' by Wakefield et al (1999), and the 'Phone Counselling +NRT' by Zhu et al (2000) are subject to serious threats to validity. Estimates of treatment effect derived from these studies should be interpreted with caution. Further details are provided in the relevant chapters of the Technical Report.

Finally, the main outcomes for the smoking cessation interventions were typically quit rates or continuous abstinence rates at 6 or 12 months. The MTCP study by Biener et al (2000) reported the trend in the point prevalence of current smokers in a pooled dataset spanning 10 years. Despite the length of the evaluation period, the Biener study provides no guidance as to the

persistence of treatment effect with respect to behaviour change or as to the impact on final outcomes.

In order to model these smoking interventions, additional published information is therefore required regarding the persistence of behaviour change and its impact on mortality and health-related quality of life. For the former we rely on primarily on estimates of long-term relapse rates as a function of duration of abstinence by Gilpin Pierce and Farkas (1997). For the latter, we rely on estimates of relative risk of all-cause mortality as a function of duration of abstinence by Taylor et al (2002) and on Brazier transformed SF-36 scores by smoking status derived from the ABS National Nutrition Survey 1995.

7.3 Outcomes as reported

Each of the studies evaluating smoking cessation interventions report slightly different measures of behaviour change. Only one study reported on final outcomes with respect to morbidity or mortality but no statistically significant effects were identified and the data was drawn from just one of 34 trials (Rose, 1992) included in the 'Physician Advice for Smoking Cessation' meta-analysis.

Smoking cessation

Table 7.4 summarises key results from the trials with respect to smoking cessation. For a detailed report of all outcomes see the Technical Report.

Table 7.4 Smoking cessation

Study	Outcome definition	Comparison	Control (95%CI)	Intervention (95%CI) OR Intervention vs control
Mass media				
MTCP (Adults) (Biener et al, 2000)	% point change in prevalence 1993 to 1999	MTCP *vs* Rest of US: Adults	0.03% per year (-0.06% to 0.12%)	-0.43% per year (-0.66% to -0.21%)
MTCP (Youths) (Rigotti et al, 2002)	point prevalence at follow-up	MTCP *vs* Rest of US: Youth	38.3%	27.5% Adj OR=0.58 (0.40 to 0.87)
NTC (Wakefield et al, 1999)	%quit during last 12 months	Baseline *vs* 6-month follow-up	8.0%	11.0%
Physician advice				
Physician Advice for Sr Cessation (Silagy et al, 2004)	%quit at final follow-up	Minimal *vs* Nil Intensive *vs* Nil Intensive vs minimal	4.1% 6.3% 7.6%	5.9% OR=1.69 (1.45, 1.98) 12.3% OR=2.11 (1.74, 2.54) 10.8% OR=1.82 (1.24, 1.66)
Counselling and NRT				
Phone Counselling +NRT (Zhu et al, 2000)	%quit at 12 mnths	All *vs* single session *vs* multiple sessions	Baseline	*vs single* 16.1% *vs Multiple* 25.6% *vs All 24%*
Pharmacotherapy				
Bupropion SR (Hughes et al, 2004)	%quit at final (6-12 months) follow-up	Bupropion SR plus counseling *vs* placebo plus counseling	Baseline	*Placebo + Counselling* 10.2% *Bupropion + Counselling* 19.3% OR = 1.97 (1.67 to 2.34)

Other behaviour change

Two interventions reported data on propensity to quit or quitting activity: 'National Tobacco Campaign' and 'Phone Counselling +NRT'. The differences in quitting attempts between benchmark and follow-up in the 'National Tobacco Campaign' is summarised in Table 7.5a. At follow-up, significantly more participants report having tried to quit at anytime, in the past month or in the past two weeks, compared with the benchmark survey. Differences of quitting attempt between groups in the 'Phone Counselling +NRT' intervention are reported in Table 7.5b. Those who received multiple counselling sessions were significantly more likely to have tried to quit than those receiving only a single counselling session, 84.4% versus 77.1% ($p<0.05$). Those who used nicotine patches were more likely to make a quit attempt than those subjects who used the gum, 85.2% versus 66.3% ($p<0.01$).

Table 7.5a Quitting activity: 'National Tobacco Campaign'

	Benchmark (n = 1,192)	Follow-up (n = 2,981)
Ever tried to quit smoking	76%	78%
Tried to quit in the last month	7%	10%
Tried to quit in the last 2 weeks	4%	6%

Source Wakefield, 1999 p44

Table 7.5b Quit attempt 'Phone Counselling +NRT' by medical insurance status, smoking rate, counselling intensity and type of NRT

		Quit for 24 hours (%)	*P*-value
Covered by Medi-Cal	Yes	85.0	0.07
	No	79.6	
Smoked ≥ 25 cigarettes per day	Yes	82.9	0.96
	No	82.7	
Counselling Sessions	Single session	77.1	<0.05
	Multiple session	84.4	
NRT Usage	Nicotine patch	85.2	<0.01
	Nicotine gum	66.3	

Source Zhu et al, 2000 p360

Service utilisation

Only one study reported differential rates of service utilisation either between groups or between benchmark and follow-up. Comparisons between service use at benchmark and follow-up from the 'National Tobacco Campaign' intervention are summarised in Table 7.6 below.

Table 7.6 Service utilisation: 'National Tobacco Campaign'

	Benchmark (n = 1,192)	Follow-up (n = 2,981)
Rung the Quitline	2%	4%
Asked doctor for help to quit	9%	10%

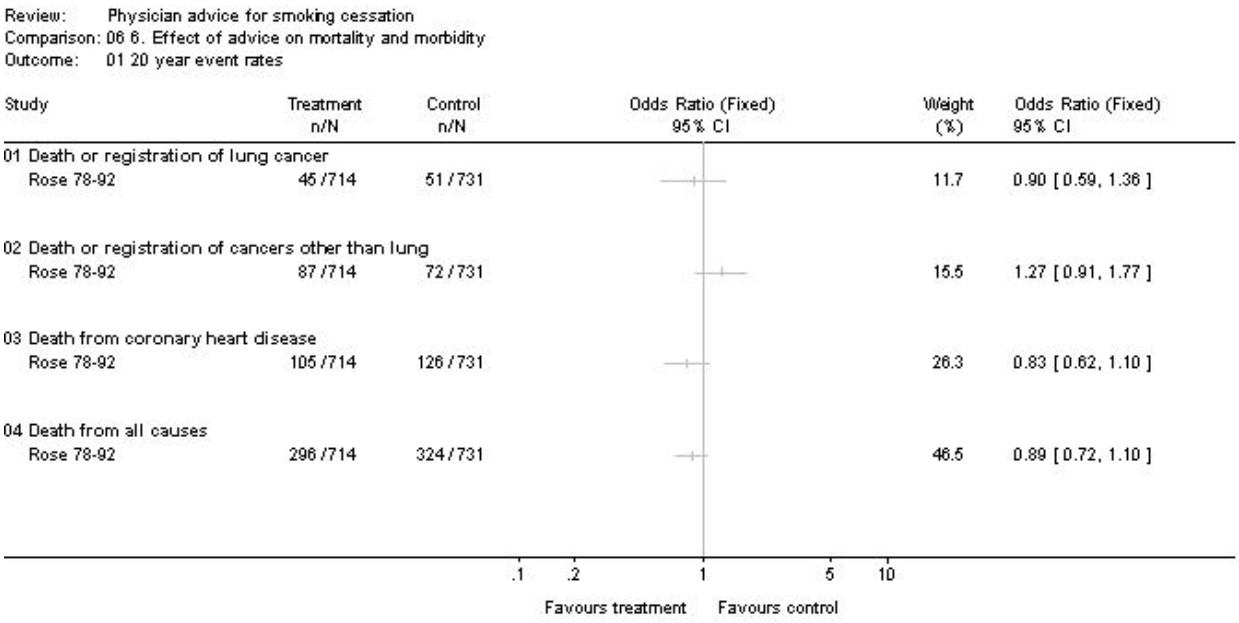
Source Wakefield, 1999 p44

Mortality and morbidity

Only the 'Physician Advice for Smoking Cessation' intervention reported the relative effect of the intervention and comparator on final outcomes of mortality and morbidity. Odds ratios for the effect of advice were reported for death or registration of lung cancer, death or registration of cancers other than lung, death from coronary heart disease and death from all causes. Data were drawn from just one of 34 included trials (Rose, 1992). Results are summarised in Figure 7.1 below. No statistically

significant effects were identified. Moreover, the inclusion criteria for this trial were atypical in that the all-male sample was drawn from the UK Civil Service and participants were required to be at high risk of cardiorespiratory disease.

Figure 7.1 Odds ratios for effect of advice on mortality and morbidity



Source: Silagy, 2004

7.4 Program costs

Program costs for the 'Physician Advice for Smoking Cessation', the 'Phone Counselling +NRT', and the 'Bupropion SR' interventions have been estimated in Australian dollars (2003) based on the description of the intervention contained in the study publications (Table 7.7). Average cost per person for the two mass media campaigns was derived by dividing the total program cost by the number of persons in the relevant target population. For further details of cost components refer to the Technical Report.

7.5 Performance

Economic performance is firstly described based on the results and time frame reported on the trial. This will lead to conservative estimates as few assumptions are required. The incremental cost effectiveness ratio (ICER) is calculated as incremental cost per additional quitter (smoking cessation in the intervention group minus smoking cessation in the control or comparison group).

7.6 Cost-utility analysis

MTCP (Biener et al, 2000; Rigotti et al, 2002)

A Markov model with 19 non-absorbing (never smoked, current smoker & a tunnel sequence of ex-smoker1 to ex-smoker17) and one absorbing state (dead) was used to estimate QALYs gained per person for the MTCP as compared to tobacco control measures in place (or lack thereof) during the trial period for the rest of the US. All analyses were split by age/sex band and then recombined to reflect the demographic characteristics of the Australian population in 2001. Based on the quit rates given in Table 7.4 above, the MTCP is estimated to deliver 0.0211 QALYs gained per person if it was implemented in the 2001 Australian population. The QALY gain in men is slightly above the average at 0.0303/person and slightly lower in women 0.0121/person.

Table 7.7 Average cost per person (AU$2003) based on resource use described in the studies

Intervention	Intervention group	Control group	Difference
Mass media			
MTCP (Biener et al, 2000; Rigotti et al, 2002)	$47.00	$0	$47.00
National Tobacco Campaign (Wakefield et al, 1999)	$0.71	$0	$0.71
Physician advice			
Physician Advice for Smoking Cessation (Silagy et al, 2004) Minimal *vs* Nil Intensive *vs* Nil Minimal *vs* Intensive	 $14.30 $61.06 $61.06	 $0 $0 $14.30	 $14.30 $61.06 $46.76
Counselling and NRT			
Phone Counselling +NRT (Zhu et al, 2000) NRT+ Counselling *vs* Nil NRT+ Counselling *vs* NRT alone Multiple *vs* Single session	 $501.00 $501.00 $500.86	 $0 $176.00 $263.31	 $501.00 $325.00 $237.55
Pharmacotherapy			
Bupropion SR (Hughes et al, 2004) ZybanSR+ Counselling *vs* Nil ZybanSR+ Counselling *vs* Counselling	 $570.00 $570.00	 $0 $214.00	 $570.00 $356.00

Table 7.8 Effectiveness and cost-effectiveness smoking interventions: Cost per additional quitter.

Intervention	Effectiveness	Cost effectiveness (rounded)
	Differential Quit rate*	ICER $/person to quit smoking
MTCP vs rest of USA Follow-up 6 years; (Beiner et al 2000)	4.0%	Adults $1,700 Adults and youth $1,100
National Tobacco Campaign (Wakefield et al 1999 , Tan et al 2000)	3.0%	$ 100
Clinician advice (Silagy et al 2004) ▪ Minimal vs Nil ▪ Intensive vs nil ▪ Intensive vs Minimal	 1.8% 6.0% 3.2%	 $ 800 $1,020 $1,460
NRT + telephone counselling. (Zhu et al 2000) ▪ Vs nil	24.0%	$2,090
Pharmacotherapy (Hughes et al 2004) ▪ Bupropion + counselling v nil ▪ Bupropion + counselling v counselling alone	 15.3% 10.2%	 $3,750 $3,500

*Where no placebo, adjusted for background quit rate of 4%

The cost of the project was approximately $200m US dollars ($282m AUS dollars[7]). This equates to a cost per person of $32.83 US dollars (A$46.29) based on the Massachusetts population of 6,091,639 in which the MTCP was implemented. It is assumed that the costs of the intervention are spread evenly over the intervention period, with costs and benefits discounted at 5% per annum, and the per person cost is $43.60. The base case does not include downstream cost offsets, but a threshold analysis has been undertaken to calculate the minimum downstream cost offset that would be required for the MTCP to dominate its comparator (see Table 7.19).

For the base case, the cost per QALY gain is estimated at $2,100, if the MTCP were implemented in the 2001 Australian population. Estimates of cost per QALY for age/sex bands have also been calculated and are reported in the Technical Report.

[7] Average exchange rate over length of program, 1.410352 (www.x-rates.com)

Table 7.9 Cost/QALY gain base case

Group	QALYs gained/person	Incremental cost/person	Cost/QALY gained (rounded)
Males, aged ≥ 10 years	0.0303	$43.60	**$1,400**
Females, aged ≥ 10 years	0.0121	$43.60	**$3,600**
All, aged ≥ 10 years	0.0211	$43.60	**$2,100**

National Tobacco Campaign (Wakefield et al, 1999)

A Markov model with 19 non-absorbing (never smoked, current smoker & a tunnel sequence of ex-smoker1 to ex-smoker17) and one absorbing state (dead) was used to estimate QALYs gained per person for Phase 1 of the National Tobacco Campaign compared to baseline. All analyses were split by age/sex band and then recombined to reflect the demographic characteristics of the Australian population in 2001. Based on the quit rate for adults aged 18-40 years of age, Phase 1 of the National Tobacco Campaign is estimated to deliver a very small 0.0006 QALYs gained per person if it was implemented in the 2001 Despite the small benefit per head, the intervention is still cost-effective because cost per head is low, being spread across the entire adult population. Total Commonwealth and State expenditure on Phase 1 of the National Tobacco Campaign was $8.95million in 1997 dollars or $9.81million in 2002 dollars[8]. This equates to a cost per person of $0.64 in 1997 dollars or $0.71 in 2002 dollars, based on an adult Australian population of 13.8 million in 1997/98 (ABS, 1998). We make the conservative assumption that the entire cost of the intervention falls in the first 12 months, although in reality the Quit campaign ran for just under 18 months.

Taking the QALY gains discounted at 5%/an., with program cost, yields a cost per QALY gain for Phase 1 of the National Tobacco Campaign of $1,220, (based on the 2001 Australian population aged 10 years and over). If the campaign were targeted only at persons aged 18-40 years, the performance is virtually unchanged at an estimated cost/QALY of $1140. Estimates of cost per QALY for individual age/sex bands are provided in the Technical Report.

Downstream cost offsets are not included in this base case (but would only serve to reduce the cost/QALY ratio, further enhancing performance). We have however performed a threshold analysis to calculate the minimum downstream cost offset that would be required for the intervention to be cost saving (see Table 7.19).

Table 7.10 Cost/QALY gain; base case by key subgroups

Comparison	QALYs gained/person	Incremental cost/person	Cost/QALY gained (rounded0
Males, aged ≥ 10 years	0.0007	$0.71	**$960**
Females, aged ≥ 10 years	0.0004	$0.71	**$1,640**
All, aged ≥ 10 years	0.0006	$0.71	**$1,220**
Males, aged 18 -40 years	0.0008	$0.71	**$880**
Females, aged 18-40 years	0.0004	$0.71	**$1,620**
All, aged 18-40 years	0.0006	$0.71	**$1,140**

Physician advice for smoking cessation (Silagy et al, 2004)

A Markov model with 18 non-absorbing (current smoker plus ex-smoker1 to ex-smoker17) and one absorbing state (dead) was used to estimate QALYs gained per person for the minimal intervention as compared to no intervention and for the intensive intervention as compared to both the minimal intervention and no intervention. All analyses were split by gender due to uncertainty as to the proportion of males and females in the target populations for minimal and intensive interventions.

[8] Based on 10% health inflator (ABS, 2004).

The comparison between the intensive and minimal interventions was also conducted in two subgroups: unrestricted populations and high risk populations.

Based on the quit rates from the meta-analysis together with supporting data and various assumptions described in the technical report, brief intervention is estimated to deliver between 0.0017 and 0.0093 QALYs gained per person depending on the characteristics of the specific intervention and of the target population. The comparison between the intensive intervention and no intervention in males (see Table 7.11) delivered the greatest QALY gain per person. The comparison between the minimal intervention and no intervention in females (see Table 7.12) delivered the lowest QALY gain per person. The cost per QALY gained is estimated at between $5,271 and $34,560; depending on the choice of treatment and comparator and the population subgroup targeted.

Table 7.11 Summary of cost utility according to the model (discount rate= 5%), males

Comparison	QALYs gained/person	Incremental cost/person	Cost/QALY gained
Minimal vs background	0.0027	$14.30	$5,270
Intensive vs background	0.0093	$61.06	$6,570
Intensive v Minimal	0.0050	$46.76	$9,320
Unselected populations	0.0029	$46.76	$16,170
High risk populations	0.0080	$46.76	$5,820

Table 7.12 Summary of cost utility according to the model (discount rate= 5%), females

Comparison	QALYs gained/person	Incremental cost/person	Cost/QALY gained
Minimal *Vs* Control	0.0017	$14.30	$8,620
Intensive *Vs* Control	0.0057	$61.06	$10,750
Intensive *Vs* Minimal	0.0031	$46.76	$19,910
Unselected populations	0.0018	$46.76	$34,560
High risk populations	0.0049	$46.76	$12,450

Downstream cost offsets are not included in the base case, but a threshold analysis has been used to calculate the minimum downstream cost offset that would be required for brief interventions to become cost saving (see Table 7.19).

Phone counselling +NRT (Zhu et al, 2000)

A Markov model with 18 non-absorbing (current smoker plus ex-smoker1 to ex-smoker17) and one absorbing state (dead) was used to estimate QALYs gained per person for NRT plus counselling as compared to both no intervention and NRT alone. A comparison was also conducted between two subgroups: patients receiving multiple counselling sessions in addition to NRT versus patients receiving a single counselling session in addition to NRT. All analyses were split by gender due to uncertainty as to the proportion of males and females in the relevant target populations.

Based on the quit rates from the trial, an increase from a single counselling session to multiple counselling sessions is estimated to deliver approximately 0.53 QALYs gained per person. Based on the average quit rates from the trial and from the no intervention arm of Silagy & Stead et al (2004), the NRT+counselling intervention is estimated to deliver up to 0.04 QALYs gained per person for males as compared to no intervention and just over half that gain in females. Based on the average quit rates from the trial and quit rates for NRT alone from Silagy & Lancaster et al (2004), the NRT+counselling intervention is estimated to deliver 0.015 QALYs gained per person in males as compared to NRT alone and just over half that gain in females. The incremental cost of multiple counselling sessions over single counselling sessions is just the average per person cost of subsequent counselling sessions and consumables. The difference in per person direct treatment

costs is assumed in the first instance to reflect the incremental cost over the entire evaluation period. Downstream cost offsets have not been included in the modelled cost-utility analysis, but threshold analysis has been used to calculate the minimum downstream cost offset that would be required for each intervention to dominate its comparator (see Table 7.19).

Table 7.13 Summary of cost/QALY results derived from the model (discount rate= 5%), males

Comparison	QALYs gained/person	Incremental cost/person	Cost/QALY gained (rounded)
NRT+Counselling *vs* Nil	0.0426	$501.00	$11,770
NRT+Counselling *vs* NRT alone	0.0150	$325.00	$21,700
Multiple *vs* Single Sessions	0.0203	$237.55	$11,680

Table 7.14 Summary of cost/QALY results derived from the model (discount rate= 5%), females

Comparison	QALYs gained/person	Incremental cost/person	Cost/QALY gained
NRT+Counselling *vs* Nil	0.0251	$501.00	$19,930
NRT+Counselling *vs* NRT alone	0.0088	$325.00	$36,750
Multiple *vs* Single Sessions	0.0120	$237.55	$19,790

In males, the cost per QALY gained is estimated at $11,800 for the NRT+counselling intervention compared to no intervention and $21,700 for the NRT+counselling intervention compared to NRT alone. In females, the cost per QALY gained is estimated at $19,900 for the NRT+counselling intervention compared to no intervention and $36,700 for the NRT+counselling intervention compared to NRT alone.

Bupropion SR (Hughes et al, 2004)

A Markov model with 18 non-absorbing (current smoker plus ex-smoker1 to ex-smoker17) and one absorbing state (dead) was used to estimate QALYs gained per person for bupropion SR plus counselling as compared to both no intervention and placebo plus counselling. Based on the quit rates from the Hughes et al (2004) meta-analysis and from the no intervention arm of the Silagy & Stead et al (2004) meta-analysis, the bupropion SR+counselling intervention is estimated to deliver 0.0544 QALYs gained per person as compared to no intervention in males and 0.0407 in females. Based on the average quit rates from the Hughes et al (2004) meta-analysis, the bupropion SR+counselling intervention is estimated to deliver 0.0326 QALYs gained per person as compared to placebo+counselling in males and 0.0244 in females. The difference in per person direct treatment costs is assumed to reflect the incremental cost over the entire evaluation period. Downstream cost offsets have not been included in the modelled cost-utility analysis, but a threshold analysis has been undertaken to calculate the minimum downstream cost offset that would be required for each intervention to dominate its comparator (see Table 7.19).

In males, the cost per QALY gained is estimated at $10,470 for the bupropion SR+counselling intervention compared to no intervention and at $10,920 for the bupropion SR+counselling intervention compared to the placebo+counselling intervention. The cost/QALY ratios are slightly higher for females: $14,010 for the bupropion SR+counselling intervention compared to no intervention and at $14,610 for the bupropion SR+counselling intervention compared to the placebo+counselling intervention.

Table 7.15 Summary of cost utility according to the model (discount rate= 5%), males

Comparison	QALYs gained/person	Incremental cost/person	Cost/QALY gained (rounded)
ZybanSR+Counselling *vs* Nil	0.0544	$570	$10,470
ZybanSR+Counselling *vs* Placebo+Counselling	0.0326	$356	$10,920

Table 7.16 Summary of cost utility according to the model (discount rate= 5%), females

Comparison	QALYs gained/person	Incremental cost/person	Cost/QALY gained
ZybanSR+Counselling *vs* Nil	0.0407	$570	$14,010
ZybanSR+Counselling *vs* Placebo+Counselling	0.0244	$356	$14,610

Summary – all smoking interventions and sensitivity analysis

An overall comparison of modelling results is presented in Table 7.17. The modelled cost-utility analysis for the smoking cessation interventions is based on a common structure, adapted to reflect the characteristics of the target population. The following assumptions are common across all five smoking cessation models:

- Markov model
- Ex-smoker tunnel sequence
- Cycle length=12 months
- Cohort distributed across states as per prevalence of current, never & ex-smokers
- Modelled out to full life-expectancy
- Observed difference in quit rates at trial-end apply to trial period. Beyond trial end, quit rates for all revert to control group levels.
- Quality of Life utility gain directly attributable to smoking cessation =0.01
- Mortality differential commences from 25 years of age
- Mortality differential based on Taylor et al (2002)
- Exclude downstream costs
- Discount rate 5% (base case)

Despite these common elements, the initial relapse rate and within-trial quit rates in each model were specific to the evaluated intervention. A number of other intervention-specific assumptions were also made in order to conform to the characteristics of the relevant target population. In an effort to identify key drivers and to evaluate robustness of estimates as to cost per QALY gained, univariate sensitivity analyses were conducted by varying parameters such as start-age, HRQoL weights in the ex-smoker tunnel sequence, discount rate, initial rate of relapse (in the ex-smoker1 state), the relative risk of death, estimates of treatment effect and estimates of incremental costs.

A full description of the sensitivity analysis is contained in the Technical Report. The resulting cost/QALY range is reported in table 7.17 below. The key parameters varied were:

- starting age,
- quality of life weights,
- discount rate,
- relative risk of death
- incremental cost.

In relation to cost offsets, given the complexity of this calculation, with potential cost savings for each attributable disease varying by age of the person and length of time since smoking cessation, we have instead completed a threshold analysis to identify the mean per person year reduction in health service cost that would need to be achieved for the intervention to cost less (in net terms) than the comparator, so that it becomes dominant. (The net cost/QALY result will be somewhere between the estimate without taking into account any downstream cost offsets, as summarised in table 7.17 and cost saving, depending on the actual cost savings that are achieved.

Table 7.17 Comparison of cost utility results

Intervention	Key assumptions in base case	Cost per QALY (rounded)	Range from sensitivity analyses ($/QALY)	Min downstream cost offset for Intervention to dominate (cost<comparator)
Mass media				
MTCP (Massachusetts Tabbocco Control program (Biener et al, 2000; Rigotti et al, 2002)	▪ Markov with 19 non-absorbing (current, never & ex1 to ex17) & 1 absorbing (dead) ▪ Cohort distributed across states as per prevalence of current, never & ex-smokers ▪ Cohort with demographic characteristics as per 2001 Australian population	**$2,100**	$880 to $188,660 Vary: Age/sex of cohort, Discount rate, Treatment effect	$22/year to $394/year depending on age/sex of the target pop[n]
National Tobacco Campaign (Wakefield et al, 1999)	▪ Markov with 19 non-absorbing (current, never & ex1 to ex17) & 1 absorbing (dead) ▪ Cohort distributed across states as per prevalence of current, never & ex-smokers ▪ Cohort with demographic characteristics as per 2001 Australian population ▪ Self report valid indicator of smoking status	**$1,140**	$632 to $21,515 Vary; Age/sex of cohort, Discount rate, Treatment effect	$14/year to $15/year depending on age/sex of the target pop[n]
Physician advice				
Physician Advice for Smoking Cessation (Silagy et al, 2004)	▪ Markov with 18 non-absorbing states (current & ex1 to ex17) & 1 absorbing (dead) ▪ All commence in 'current' with start-age=30 years ▪ Separate model for men and women	**$5,270 to $34,560** eg Males: $5,271 to $16,200 Females: $8,620 to $34,560 High risk popn: $5,820 to $12,450	$262 to $69,120 As vary: start-age, QoL weights, initial relapse rate, discount rate, relative risk of death, treatment effect, incremental cost.	From $228/year to $912/year depending characteristics of the intervention and comparator
Counselling and NRT				
Phone Counselling +NRT (Zhu et al, 2000)	▪ Markov with 18 non-absorbing states (current & ex1 to ex17) & 1 absorbing (dead) ▪ All commence in 'current' with start-age=30 years ▪ Comparison against NRT alone based on supporting data from Silagy, Lancaster and colleagues (2004). ▪ Separate model for men and women	From **$11,684 to $36,746** depending on characteristics of intervention and target population	$1,480 to dominated when start-age, QoL weights, initial relapse rate, discount rate, relative risk of death, treatment effect, or incremental cost varied	From $484/year to $898/year depending characteristics of the intervention & comparator
Pharmacotherapy				
Bupropion SR (Hughes et al, 2004)	▪ Markov with 18 non-absorbing states (current & ex1 to ex17) & 1 absorbing (dead) ▪ All commence in 'current' with start-age=45 years ▪ Separate model for men and women	From **$10,471 to $14,608** depending on characteristics of Rx and target pop[n]	$2,095 to dominated when start-age, QoL weights, initial relapse rate, discount rate, relative risk of death or incremental cost varied	From $737/year to $794/year depending characteristics of the intervention & comparator

Chapter 8 Alcohol interventions

8.1 Description

This project evaluated six types of interventions for moderation of alcohol consumption, one of which was a mass media campaign in a community setting (Table 8.1); brief clinician based interventions for 'problem drinkers, and heavy drinkers, and various forms of cognitive behavioural therapy (as described below).

A description of the US mass media campaign (Holden & Treno, 1997) is provided primarily as background information and to provide an insight into the range of interventions that have sought to address alcohol problems. However, no attempt has been made to derive estimates of cost effectiveness or cost utility for the US mass media campaign due to an absence of quantifiable outcomes. The results that follow therefore focus on the remaining interventions.

Table 8.1 Description of setting, population and numbers for six interventions for moderation of alcohol consumption

Intervention	Location, setting, year of intervention	N trial participants Mean age, % female		Target population	Chapter in Technical Report
		Intervention	Control		
US mass media campaign *(Holden & Treno, 1997)*	US Community setting			General population	29
Meta-analysis of 8 trials of brief interventions for problem drinking *(Wilk et al, 1997)*	Various incl. Norway & Sweden. Six trials in outpatients, two in inpatients; 1966-95	N=1,632 31.4% F	N=1,130 29.6% F	Heavy drinkers aged ≥ 19 years	30
Brief intervention for heavy drinkers *(Saunders et al, 1991)*	Multi-centre Australian trials; Outpatient setting	N=424, 480, 460 in 3 arms	N=402	Hazardous level of consumption; not physically dependent; aged 17-70 years	31
MOCE & BSCT for moderately dependent drinkers *(Heather et al, 2000)*	North of England Outpatient setting	N=48 40.7 ± 10.5 yr 20% F	N=43 42.3 ± 9.3 yrs 30% F	Patients seeking help for alcohol problems with a preference for moderation rather than abstinence	32
MET *&* NDRL for mildly to moderately dependent drinkers *(Sellman et al, 2001)*	New Zealand Community setting -	*MET:* N=42 38.1 ± 11.5 yrs 45.2% F *NDRL:* N=40. 35.4 ± 8.7 yrs 45.0% F	N=40 33.4 ± 10.3 yrs 37.5% F	Mild to moderately dependent drinkers aged 15-59 years.	33
Meta-analysis of 7 trials evaluating Naltrexone + psych0therapy *(Streeton et al, 2001)*	Various incl. US, UK & Germany Outpatient setting 1976 - 2001	N=406	N=402	Recently detoxified, no significant psychiatric disease & no co-existing substance use	34

MOCE: Moderation-Oriented Cue Exposure. BSCT: Behavioural Self-Control Training.
MET: Motivational Enhancement Therapy. NDRL: Non-directive Reflective Listening.

Specific details of each of the interventions evaluated are presented in Table 8.2. Despite differences in approach and target population, four out of five approaches emphasise moderation of alcohol consumption rather than abstinence. The Brief Interventions summarised by Wilk et al (1997) covered interventions of varying intensities for heavy drinkers aged 17-70 years who were not physically dependent. At the lowest level of intensity, brief intervention amounted to simple advice lasting 5 minutes. Higher intensity interventions included simple advice followed by brief counselling and problem solving strategies totalling 20 minutes or simple advice and counselling followed by two booster sessions including feedback of lab results totalling 120-150 minutes. Each of the brief interventions emphasised moderation rather than total abstinence (irrespective of intensity). The brief interventions included in the meta-analysis reported by Saunders et al (2000) were defined as being "motivational with a self-help orientation" and the objective of moderation rather than abstinence.

In contrast, the 'MET and NDRL' intervention reported by Sellman (2001), trialled Motivational Enhancement Therapy (MET) and Non-Directive Reflective Listening (NRDL) in a sample of physically dependent drinkers aged 15-59 years. MET is a brief, psychotherapeutic intervention based on 5 key principles of motivational interviewing: i) expressing empathy, ii) deploying discrepancy, iii) avoiding argument, iv) rolling with resistance to change, v) supporting self-efficacy. The aim is to first build motivation to change and then strengthen commitment to change. NDRL allows subjects to talk about anything they want, with no attempt to steer the session towards issues with alcohol. Despite targeting patients at the more severe end of the spectrum and (perhaps necessarily) employing a more intensive intervention, the 'MET and NDRL' intervention retained the emphasis on moderation (in this case, drinking within New Zealand National Guidelines) rather than on abstinence.

The 'MOCE and BSCT' intervention reported by Heather et al 2000, emphasised controlled drinking and excluded patients with a preference for abstinence rather than moderation. In contrast, the meta-analysis prepared by Streeton (2001) compares Naltrexone plus psychosocial therapy against placebo plus psychosocial therapy in patients with severe alcohol dependence who had already completed detoxification. Abstinence was included as an outcome in 5 of the 7 included trials suggesting that moderation was either less than ideal or less than realistic in patients with severe physical dependence.

For a number of studies, the control group received active intervention or follow-up that was likely to increase the likelihood of a moderation or cessation of alcohol consumption. For example, both active and control arms of the 'Naltrexone +psych therapy' intervention received detoxification and counselling as the agreed minimum standard of care for severely dependant patients. Similarly, the 'MET and NDRL' and the 'MOCE and BSCT' interventions received alcohol-related treatment that could be considered the minimum acceptable care for mild to moderately dependent drinkers. Specifically, participants in the 'MET and NDRL' intervention attended a feedback/education session that provided details of personal drinking history over the baseline 6 months. The significant other of the participant was also encouraged to attend this session. All participants in the 'MET and NDRL' intervention were then given pamphlets and information booklets on responsible drinking and encouraged to drink within national guidelines. MOCE was compared against BSCT a commonly used active intervention. The Brief Interventions targeted heavy drinkers at a lower level of severity than the dependent drinkers selected for the more intensive cognitive behavioural interventions and pharmacotherapy; (MET, MOCE and Naltrexone). Controls in the Brief Interventions received no alcohol-related treatment.

Table 8.2 Details of interventions and care received by control groups

Intervention	Activities for Experimental Group	Care received by the control group
Brief Interventions for Problem Drinking *(Wilk et al, 1997)*	▪ Various brief interventions (BIs) characterised as "motivational with a self-help orientation" and the objective of moderation rather than abstinence. ▪ Intensity differed with some BIs involving just one session, whereas others had up to 4. ▪ No more than 1 hour total counselling time but some BIs included just 5 minutes counselling time.	▪ No alcohol-related treatment
Brief Interventions for Heavy Drinkers *(Saunders et al, 1991)*	▪ Three brief interventions (BIs) of differing intensity. ▪ BIs were: i) simple advice of 5 mins, ii) simple advice + brief counselling and problem solving strategies for 20 mins, or iii) simple advice + counselling + 2 booster sessions incl. feedback of lab results total time 120-150 minutes.	▪ Initial 20 min. interview on general health, nutrition, stress, smoking, sleep patterns. ▪ No alcohol-related treatment
MOCE and BSCT *(Heather et al, 2000)*	▪ Pre-trial assessment including Severity of Alcohol Dependence Questionnaire and Alcohol Problem Questionnaire ▪ MOCE is a form of extinction procedure where patients are given a priming dose of alcohol, and then asked to resist the cravings that the first couple of drinks will usually elicit. ▪ Emphasis on controlled drinking and aimed at moderation rather than abstinence. ▪ Average length of MOCE intervention was 88 minutes over 7.67 sessions.	▪ Pre-trial assessment including Severity of Alcohol Dependence Q'aire and Alcohol Problem Q'aire ▪ Behavioural Self Control Training (BSCT) ▪ Emphasis on controlled drinking, aimed at moderation rather than abstinence. ▪ Mean length of BSCT 63.49 mins over 6.56 sessions.
MET and NDRL *(Sellman et al, 2001)*	▪ Allocated randomly to MET or NDRL. ▪ MET is a brief, psychotherapeutic intervention based on 5 key principles of motivational interviewing: i) expressing empathy, ii) deploying discrepancy, iii) avoiding argument, iv rolling with resistance to change, v) supporting self-efficacy. The aim is to first build motivation to change and then strengthen commitment to change. ▪ NDRL allows subjects to talk about anything they wanted, with no attempt to steer the session towards issues with alcohol. ▪ Both MET and NDRL entailed four sessions over a 6 week period.	▪ No further counselling after an initial comprehensive assessment and feedback/education session.
Naltrexone +psych Therapy *(Streeton et al, 2001)*	▪ Naltrexone plus psychotherapy ▪ Psychotherapy ranged from weekly group therapy to weekly one-to-one Cognitive & Behavioural Therapy (CBT) to intensive inpatient treatment. ▪ Naltrexone is an opioid receptor antagonist that acts to reduce the pleasurable effects of alcohol thereby masking the cue for further consumption. ▪ Dose regimen of 50mg/day over 12 weeks	▪ Placebo plus psych therapy. ▪ Psych therapy ranged from weekly group therapy to weekly one-to-one CBT to intensive inpatient treatment.

8.2 Quality of evidence

The quality of the alcohol trials/studies is summarised in Table 8.3 below.

Table 8.3 Summary of quality of the alcohol studies

Criteria	Brief Interventions for problem or heavy drinkers		Cognitive behavioural therapy		Naltrexone +psycho therapy
	Wilk 1997	Saunders 1991	MOCE and BSCT	MET and NDRL	
Was the assignment to treatment groups an adequate method of randomisation?	x	✓	✓	?	✓
Was the treatment allocation concealed?	x	?	?	?	?
Were the groups similar at baseline in terms of prognostic factors?	?	✓	x	x	✓
Were the eligibility criteria specified?	✓	✓	✓	✓	✓
Were the outcome assessors blinded to the treatment allocation?	x	?	x	?	✓
Was the care provided blinded?	x	x	x	x	✓
Was the patient blinded?	x	x	x	x	✓
Were point estimates and measure of variability presented for the primary outcome measure?	✓	✓	✓	✓	✓
Was a power calculation performed at study design?	x	?	?	?	?
Were all patients accounted for?	x	x	✓	✓	✓
Was the analysis intention-to-treat?	x	x	x	x	✓

✓ = yes, X= no, ?= unclear, based on CRD report number 4 (York University)

The quality of evidence for the five alcohol interventions varied widely. In the Wilk meta-analysis, for example, trials received Chalmers' Scores for methodological quality ranging from 0.27 to 0.78 on a 0 to 1 scale for a mean of 0.49 (± 0.17). Likewise, the studies included in the Saunders meta-analysis and the two cognitive behavioural studies are also methodologically flawed. The main areas of concern relate to between-group differences in severity and other patient characteristics and adequacy of follow-up. The seven trials in the 'Naltrexone +psych therapy' meta-analysis were generally of higher quality, each receiving a quality rating ranging from 10 to 11 (mean: 10.4) on a 0 to 12 scale[9].

The main outcomes for each of the alcohol interventions were typically the proportion of patients drinking either side of a specified threshold (eg, safe limits, NZ Guidelines, "in moderation") at 6 or 12 months. A 10-year follow-up was reported by Saunders (1991) but the 10-year data is difficult to interpret due to attrition and an established age-gradient in alcohol consumption.

Evidence from Streeton and Whelan (2001) suggests that a degree of pessimism would be advisable with regards to the persistence of any treatment effect. For instance as reported "Study 006 was extended to include a 6-month follow-up period, where, at the end of the 12-week trial, the

[9] "The quality rating score is comprised of seven factors: (1) level of security of the randomisation method (scale: 0, not stated; 0.5, under investigator control eg sealed envelope; 1, by pharmacy, central registry or using blinded drug supply); (2) whether comparable groups were achieved at baseline through randomization (scale: 0, not stated or potentially important between-group differences; 1, comparable groups); (3) the degree of blinding (scale: 0, open; 0.5, single-blind with respect to patient; 1, blinded observer; 2, double-blind); (4) adequacy of follow-up (scale: 0, significant number of drop-outs with no trial assessment and different rates between groups; 1, some drop-outs with no trial assessment and equivalent rates between groups; 2, assessment in all patients who were not lost to follow-up); (5) adequacy in describing the inclusion/exclusion criteria and concomitant therapy (scale: 0, no; 0.5, partially; 1, fully); (6) the reliability of outcomes assessment (scale: 0, method not stated ; 1, sub-optimal but acceptable ; 2, highly accurate method such as antibody titre); and (7) the comprehensiveness of the data analysis, specifically whether follow-up of drop-outs (withdrawals and lost to follow-up of drop-outs was sufficient to allow ITT analysis as well as per protocol analysis (scale: 0, per protocol only; 1, per protocol for key efficacy criteria and ITT for safety; 3, ITT for efficacy and safety)" (Streeton and Whelan, 2001 p545).

study medication was discontinued, but the outcomes were re-evaluated after 6 months. The results of the study indicated that the benefit of a 12-week treatment of naltrexone appears to be lost within 6 months of discontinuing pharmacotherapy" (p544). In another meta-analysis of brief interventions, Moyer et al (2002) noted that effect sizes are largest at the earliest follow-up points "suggesting decay in intervention effects over time".

In order to model alcohol interventions additional published information is therefore required regarding the persistence of behaviour change and its impact on mortality and health-related quality of life. For the latter, we rely on estimates of relative risk of all-cause mortality as a function of current and past alcohol consumption by Rehm, Greenfield and Rogers (2001) and on Dutch disability weights by severity of alcohol problem used in Australian Burden of Disease estimates (AusBODI, 2001). For the former, no suitable data as to the persistence of behaviour change (such as long-term relapse rates) could be identified. Conservative assumptions were therefore derived from the trial evidence. (For example, the differential between 6-month and 12-month effect sizes in the Brief Interventions is taken as an indication of per cycle relapse rates for the second 6 month cycle and all subsequent cycles).

8.3 Outcomes as reported

Each of the studies evaluating alcohol interventions reported slightly different measures of behaviour change. Only the 'Brief Interventions for Heavy Drinkers' intervention reported on final outcomes with respect to morbidity or mortality, however there was no significant difference between the experimental groups on either mortality or morbidity at 10 year follow-up.

Behaviour change

Table 8.4 summarises key results from the trials with respect to behaviour change. For a detailed report of all outcomes see the Technical Report. In Figure 8.1 describes results based on 10 year follow-up reported by Saunders (1991). This shows that those who receive more intensive counselling have a great reduction in problem drinking in the short to medium term, while in the longer term, the entire cohort seems to moderate their drinking behaviour, with no significant difference left after 10 years. This suggests most benefit accrue in the short to medium term (up to ~seven years).

Figure 8.1 Key findings with respect to behaviour change from 'Brief Interventions for Heavy Drinkers' (Saunders et al, 1991)

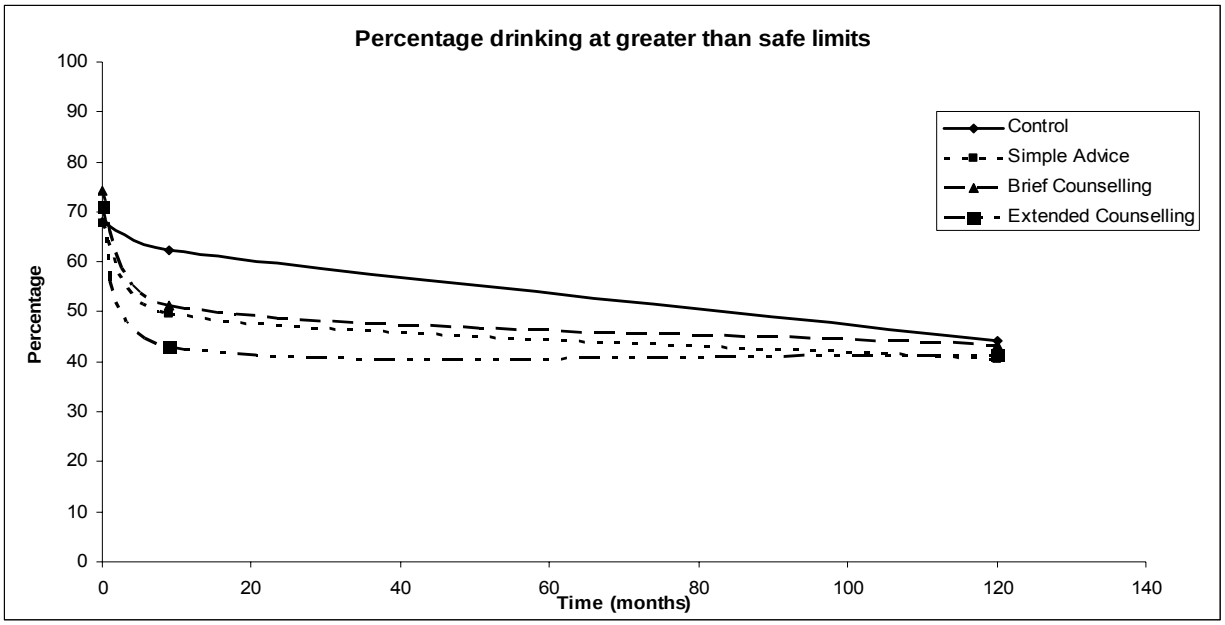


Table 8.4 Behaviour change

Intervention	Comparison	Outcome definition	Control (95%CI)	Treatment1 (95%CI)	Treatment2 (95%CI)	Treatment3 (95%CI)
Primary care Brief Interventions						
Brief Interventions for Problem Drinking (Wilk et al, 1997)	*vs* Nil	%drinking in moderation @ 6 to 12 months	27.8%	43.8% OR=1.95 (1.66, 2.3)	-	-
Brief Intervention via physician advice for Heavy Drinkers (Saunders et al, 1991)	*vs* Nil	% drinking >safe limit		***Simple***	***Brief***	***Extended***
		▪ Baseline	67.9%	67.7%	74.2%	71.0%
		▪ 9 months	62.2%	49.6%	51.2%	43.1%
		▪ 10 years	44.2%	40.5%	43.4%	41.5%
		% intoxicated >mnthly 10yrs	51.0%	53.5%	54.0%	55.9%
		% alcohol dependence syndrome at 10 yrs	10.1%	8.0%	6.9%	10.1%
Cognitive behavioural therapy						
MOCE *vs* BSCT (Heather et al, 2000)	Rel to baseline @ 6 months			***MOCE***	***BSCT***	
		% abstinent		7%	7%	
		%non-problem drinker		17%	17%	
		% much improved		29%	17%	
		%somewhat improved		15%	17%	
		% not improved		32%	42%	
MET and NDRL I (Sellman et al, 2001)	No further counselling @ 6 months			***MET***	***NDRL***	
		% breaking abstinence	92.5%	88.1%	90.0%	
		% >NZ Guide-lines	72.5%	64.3%	77.5%	
		% ≥ 10 drinks > once	79.0%	61.9%	77.5%	
		% ≥ 10 drinks ≥ 6X	65.0%	42.9%	62.5%	
Pharmacotherapy						
Naltrexone +psychotherapy (Streeton et al, 2001)	*vs* placebo +psychological therapy	%continuously abstinent		RR=1.28 (1.08, 1.52)		
		%relapse*	53.0%	40.9% RR=0.72 (0.55,0.94)		

*Relapse defined as ≥ 5 drinks for men or ≥ 4 drinks for women on any day from baseline to follow-up.

Consumption

Three interventions report data on alcohol consumption: 'Brief Interventions for Heavy Drinkers', 'MOCE and BSCT', and 'Naltrexone +psychotherapy'. Table 8.5 summarises key results with respect to alcohol consumption.

Clinical parameters

None of the studies reported the effect of the intervention on clinical parameters. Saunders reported data on biochemical markers for alcohol consumption, but primarily to cross-validate self-report measures of consumption and drinking behaviour.

Service utilisation

Not reported.

Table 8.5 Alcohol consumption

Intervention	Comparison	Outcome definition	Control (95%CI)	Treatment1 (95%CI)	Treatment2 (95%CI)	Treatment3 (95%CI)
Brief Interventions for Heavy Drinkers (Saunders et al, 1991)	*vs* No intervention	median weekly consumption baseline 9 months 10 years	 308.9g 262.9g 158.0g	***Simple*** 282.8g 220.9g 150.1g	***Brief*** 336.3g 230.1g 181.8g	***Extended*** 348.2g 195.6g 204.0g
MOCE and BSCT (Heather et al, 2000)	Baseline	DDD mean (SD) ▪ baseline ▪ 6 months %days abstain mean (SD) ▪ baseline ▪ 6 months		***MOCE*** 20.41 (12.12) 13.06 (8.91) 20.34 (22.66) 40.88 (30.29)	***BSCT*** 17.32 (15.10) 9.17 (9.90) 19.30 (24.27) 33.38 (33.80)	
Naltrexone +psych therapy (Streeton et al, 2001)	y *vs* placebo plus psychological therapy	diff in mean %drinking days difference in mean DDD		risk diff = -3.0 (-5.4,-0.5) risk diff = -1.04 (-2.0,-0.1)		

DDD= drinks per drinking day

Mortality and morbidity

Only Saunders reported the relative effect of the intervention and comparator on final outcomes of mortality and morbidity. No significant differences between the intervention groups and controls were found at 10 year follow-up on either mortality or alcohol-related morbidity. This is important as a health status endpoint, but also in term of expectation of realisation of cost offsets.

8.4 Program costs

Program costs have been estimated in Australian dollars (2003) based on the description of the interventions contained in the study publications (Table 8.6). For further details of cost components refer to the Technical Report. As with other interventions, potential impact on downstream costs is not estimated but dealt with as a threshold analysis.

Table 8.6 Mean cost per person (A$2003) based on resource use described in the studies

Intervention	Intervention group	Control group	Difference
Brief Interventions for Problem Drinking (Wilk et al, 1997)	$60.98	$0	$60.98
Brief Interventions for Heavy Drinkers (Saunders et al, 1991)	Simple: $14.91 Brief: $29.63 Extended: $90.03	Nil: $0 Nil :$0 Nil: $0	$14.91 $29.63 $90.03
MOCE and BSCT (Heather et al, 2000)	MOCE: $679.20	BSCT: $433.17	$246.06
MET and NDRL (Sellman et al, 2001)	MET: $469.25 NDRL:$373.71	NFC: $79.96 NFC: $79.96	$389.29 $293.75
Naltrexone +psych therapy (Streeton et al, 2001)	$684.70 + cost of psychological therapy	$0 + cost of psychological therapy	$684.70

8.5 Performance

Economic performance is firstly described based on the results and time frame reported on the trial. This will lead to conservative estimates as few assumptions are required. The incremental cost effectiveness ratio is calculated as incremental cost per additional person achieving the specified outcome.

Table 8.7 Cost per changer based on the trials

Intervention	Outcome	Treatment1	Treatment2	Treatment3
Brief Interventions for Problem Drinking (Wilk et al, 1997)	person drinking in moderation @ 6-12mnth follow-up	$339		
Brief Interventions for Heavy Drinkers (Saunders et al, 1991)	person drinking within safe limit 9-month follow-up 10-year follow-up	simple $120 $426	brief $171 $417	extended $406 $1,552
MOCE and BSCT (Heather et al, 2000)	person ≥ 'non-problem drinker' 6mnth follow-up	BSCT dominates MOCE		
MET and NDRL (Sellman et al, 2001) MET vs NDRL vs NFC	person within NZ guidelines @ 6 months	MET $4,747	NDRLvsNFC NFC dominates*	
Naltrexone +psych therapy (Streeton et al, 2001)	person abstinent 3-9mnth follow-up	$4,891		

BSCT was as effective & cheaper than MOCE wrt 'full responders'
* NFC was as effective & cheaper than NDRL

8.6 Cost-utility analysis

Brief interventions for problem drinking (Wilk et al 1997)

A Markov model with seven non-absorbing (alcproblem1, alcproblem2, alcproblem3, moderate1, moderate2, moderate3, dependence) and one absorbing state (dead) was used to estimate QALYs gained per person for brief intervention as compared to control.

Due to differences in pooled estimates of treatment effect for men as compared to women and the availability of supporting data by age and sex band, the modelled cost-utility analysis is run for men and women separately. While the magnitude of the treatment effect for men and women differed sufficiently to justify separate models (OR: 1.9 vs OR: 2.42), there were no differences in the direction of effect or statistical significance (95%CI: 1.57-2.31 vs 95%CI: 1.7-3.45).

In men aged 30 years brief intervention is estimated to deliver 0.091 QALYs gained per person if external effects are assumed away, and 0.243 QALYs gained per person if within-family external effects are included. In women aged 30 years brief intervention is estimated to deliver 0.125 QALYs gained per person if external effects are assumed away, and 0.330 QALYs gained per person if within-family external effects are included. Calculation of within-family external effects is described in the corresponding chapters of the Technical Report. The average cost of brief intervention was estimated at $A60.98 and is assumed to reflect the incremental cost over the entire evaluation period. External effects beyond the family unit (such as the cost of alcohol-related road trauma) and downstream healthcare costs have been excluded from the modelled cost-utility analysis. It is likely that the inclusion of these costs will serve to further reduce the cost/QALY ratio. Threshold analysis has calculated the minimum downstream cost offset that would be required for each intervention to dominate its comparator (see Table 8.16). The cost per QALY gained is estimated at less than $A671 in men aged 30 years and less than $A490 in women aged 30 years.

Table 8.8 Summary of cost/QALY according to the modelled cost-utility analysis (discount rate= 5%)

	Male	Male + within-family external effects	Female	Female + within-family external effects
QALYs gained/person	0.091	0.243	0.125	0.330
Extra cost/person A$	$60.98	$60.98	$60.98	$60.98
Cost/QALY gained A$	**$671**	**$251**	**$490**	**$185**

Brief interventions for heavy drinkers (Saunders et al, 1991)

A Markov model with seven non-absorbing (alcproblem1, alcproblem2, alcproblem3, moderate1, moderate2, moderate3, dependence) and one absorbing state (dead) was used to estimate QALYs gained per person for (i) brief intervention of simple advice plus extended counselling, (ii) brief intervention of simple advice plus brief counselling, and (iii) a no intervention control as compared to (iv) brief intervention of simple advice alone. Two versions of the model are presented. Version 1 calculates cost/QALY gains under the assumption that the 9-month treatment effect is evenly distributed over the first two cycles before reverting to the background quit rate calculated from the 10 year follow-up. Version 2 assumes that the 10-year treatment effect is unevenly distributed over a 10-year period, with the 9-month treatment effect distributed over the first two cycles and the remainder of the 10-year treatment effect distributed over the remaining 18 cycles before reverting to the background quit rate calculated from the 10 year follow-up. Further details are given in the corresponding chapters of the Technical Report.

Based on quit rates reported in the trial, the brief intervention of simple advice alone is estimated to deliver up to 0.397 QALYs gained per treated person compared to a no intervention control in an Australian population aged 40 years. More intensive intervention was more effective producing up to 0.757 QALY gains per treated person not including any external effects. These are very substantial health gains. Whilst effects within the family unit have been modelled, broader societal gains - such as that associated with alcohol-related road trauma are not included at all. These would only serve to further increase benefits and improve cost-effectiveness ratios.

Costs are calculated as the difference in per person costs of treatment. Downstream healthcare costs are not included in the modelled cost-utility analysis. The inclusion of these costs would reduce cost/QALY making the interventions even more cost-effective. Threshold analysis has been used to calculate the minimum downstream cost offset that would be required for each intervention to dominate its comparator (see Table 8.16).All costs and benefits discounted at 5% pa.

Cost per QALY gained is estimated at considerably less than $1,000 for all types of brief interventions evaluated in the Australian centre of the WHO multi-centre alcohol reduction trial, as summarised in Tables 8.9 to 8.12.

Table 8.9 Cost/QALY brief alcohol interventions V_1: 1st-person effects only

	QALYs gained/person	Incremental cost/person A$	Cost/QALY gained A$ (rounded)
Advice alone *vs* Nil	0.181	$15	$80
Advice+brief *vs* Nil	0.251	$30	$120
Advice+extended *vs* Nil	0.319	$90	$280
Advice+brief *vs* Advice alone	0.070	$15	$210
Advice+extended *vs* Advice+brief	0.068	$60	$890
Advice+extended *vs* Advice alone	0.138	$75	$540

Table 8.10 Cost/QALY Brief alcohol interventions V_1: 1st-person plus within-family effects

	QALYs gained/person	Incremental cost/person A$	Cost/QALY gained A$
Advice alone *vs* Nil	0.358	$15	$40
Advice+brief *vs* Nil	0.496	$30	$60
Advice+extended *vs* Nil	0.632	$90	$140
Advice+brief *vs* Advice alone	0.138	$15	$110
Advice+extended *vs* Advice+brief	0.135	$60	$450
Advice+extended *vs* Advice alone	0.274	$75	$270

Table 8.11 Cost/QALY Brief alcohol interventions: V2, 1st-person effects only

	QALYs gained/person	Incremental cost/person A$	Cost/QALY gained A$
Advice alone *vs* Nil	0.225	$15	$70
Advice+brief *vs* Nil	0.326	$30	$90
Advice+extended *vs* Nil	0.406	$90	$220
Advice+brief *vs* Advice alone	0.102	$15	$140
Advice+extended *vs* Advice+brief	0.079	$60	$760
Advice+extended *vs* Advice alone	0.181	$75	$420

Table 8.12 Cost/QALY Brief alcohol interventions: V2, 1st-person plus within-family external effects

	QALYs gained/person	Incremental cost/person A$	Cost/QALY gained A$
Advice alone *vs* Nil	0.421	$15	$40
Advice+brief *vs* Nil	0.606	$30	$50
Advice+extended *vs* Nil	0.757	$90	$120
Advice+brief *vs* Advice alone	0.185	$15	$800
Advice+extended *vs* Advice+brief	0.152	$60	$400
Advice+extended *vs* Advice alone	0.336	$75	$220

Cognitive behavioural therapies

Moderation-Oriented Cue Exposure (MOCE), Behavioural Self-Control Training BSCT (Heather et al, 2000)

MOCE is more expensive than BSCT and does not increase the numbers who are abstinent. However, there is a differential effect of + 10% with respect to participants across the categories 'much improved', 'non-problem drinkers' or 'somewhat improved'.

A Markov model with six non-absorbing (dependence1, dependence2, dependence3, recovered1, recovered2, recovered3) and one absorbing state (dead) was used to estimate QALYs gained per person for MOCE as compared to BSCT. In a predominantly male population aged 41 years MOCE is estimated to deliver an additional 0.116 QALYs gained per completer compared to BSCT not including external effects and 0.244 QALYs gained per completer compared to BTSC if within-family external effects are included. The estimated incremental cost per completer of MOCE is $A250.
External effects beyond the family unit (such as the cost of alcohol-related road trauma) and downstream healthcare costs have been excluded from the modelled cost-utility analysis. Their inclusion would reduce cost/QALY enhancing performance. Threshold analysis has been used to calculate the minimum downstream cost offset that would be required for each intervention to dominate its comparator (see Table 8.16).

Cost per QALY gained is estimated at $A2,145 based on 1st-person effects or $A1,020 if within-family external effects are included.

Table 8.13 Cost/QALY gain MOCE *vs* BSCT (discount rate= 5%)

	1st-person effects only	1st-person + within-family external effects
QALYs gained/completer	0.116	0.244
Extra cost/completer A$	$249	$249
Cost/QALY gained A$	$2,145	$1,020

Motivational enhancement therapy and non-directive reflective listening (Sellman et al, 2001)

A Markov model with six non-absorbing (dependence1, dependence2, dependence3, recovered1, recovered2, recovered3) and one absorbing state (dead) was used to estimate QALYs gained per person for MET compared to the 'NFC no further counselling' control. In a predominantly male population aged 35 years MET is estimated to deliver 0.116 QALYs gained per completer compared to NFC excluding all external effects and 0.287 QALYs gained per completer compared to NFC included within-family external effects. The incremental cost per completer of MET compared to NFC is A$389.

External effects beyond the family unit (such as the cost of alcohol-related road trauma) and downstream healthcare costs have been excluded from the modelled cost-utility analysis. Threshold analysis has been used to calculate the minimum downstream cost offset that would be required for each intervention to dominate its comparator (see Table 8.16). The cost per QALY gained is estimated at $A3,370 based on 1st-person effects or $A1,360 if within-family external effects are included. NDRL is inferior to NFC based on the proportion remaining within national guidelines at 6-month follow-up, and also more costly and so NDRL is dominated.

Table 8.14 Cost/QALY MET and NDRL (discount rate= 5%)

1st-person effects only	**QALYs gained/person**	**Incremental cost/person AUD**	**Cost/QALY gained AUD**
MET *vs* NFC	0.1157	$389	$3,370
NDRL *vs* NFC	-0.0705	$294	NFC dominates
1st-person plus within-family external effects			
MET *vs* NFC	0.2865	$389	$1,360
NDRL *vs* NFC	-0.1747	$294	NFC dominates

Pharmacotherapy

Naltrexone +psychotherapy (Streeton et al, 2001)

A Markov model with six non-absorbing (dependence1, dependence2, dependence3, recovered1, recovered2, recovered3) and one absorbing state (dead) was used to estimate QALYs gained per person for naltrexone (+psychotherapy) as compared to placebo (+psychotherapy). In a predominantly male population aged 41 years naltrexone is estimated to deliver 0.0528 QALYs gained per person compared to placebo not including external effects and 0.132 QALYs gained per person compared to placebo including within-family external effects. The incremental cost of naltrexone per person is estimated at $A685. External effects beyond the family unit (such as the cost of alcohol-related road trauma) and downstream healthcare costs have been excluded.

The cost per QALY gained is estimated at $A12,970 based on 1st-person effects or $A5,190 including also within-family external effects.

Table 8.15 Cost/QALY naltrexone+psycotherapy *vs* placebo+psycotherapy (discount rate= 5%)

	1st-person effects only	1st-person + within-family external effects
QALYs gained/person	0.0528	0.132
Extra cost/person A$	$685	$685
Cost/QALY gained A$	$12,970	$5,190

Summary

A comparison of the performance of all the alcohol interventions modelled is presented in Table 8.16. The cost-utility analysis has used a common structure for the alcohol interventions, but adapted to reflect the characteristics of the target population. The following assumptions are common across all five alcohol models:

- Markov model,
- Tunnel sequences used to delay the health effects of moving from one state to another,
- Cycle length of 6mnths (except naltrexone model where cycle length is 3months),
- Modelled out to full life-expectancy,
- Difference in rates of behaviour change at trial-end, revert to control group rate after that (but differential drinking behaviour at that time will continue to generate health gains),
- QoL gain directly attributable to alcohol moderation is selected to reflect severity of alcohol mis-use in target population,
- Mortality differential by age and gender based on Rehm, Greenfield and Rogers (2001),
- Base-case model 1st-person effects only (own HRQoL + mortality),
- Alternative 'Family model' includes 1st-person plus within-family external effects (1st-person effects plus HRQoL impact on family),
- Within-family external effects cease at 45 years of age,
- Other external effects excluded,
- Downstream cost impacts excluded,
- Threshold analysis used to calculate cost saving as which intervention would dominate,
- Discount rate 5%.

In addition a number of intervention-specific assumptions were made in order to reflect the magnitude and persistence of treatment effect that were specifically relevant to each target population.

Univariate sensitivity analyses were conducted by varying parameters such as start-age, HRQoL weights, discount rate, initial rate of relapse, the relative risk of death, estimates of treatment effect and estimates of incremental costs. This highlights key drivers of performance and an understanding of the robustness of estimated cost per QALY gained.

QALY gain per person (base case) is seen to range from 0.05 for Naltrexone up to 0.310 for extended advice for heavy drinkers. The Cost/QALY for the base case ranges between $70 to $500 for brief interventions, slightly higher for the more intensive cognitive behavioural therapies of MOCE at $1,020 and MET at $6,280, with Naltrexone least cost –effective at $nearly $13,000/QALy based on individual effects only. However the latter interventions are targeted at groups with more serious drinking problems, and all fall well within accepted community norms, where interventions up to $50,00/QALy are typically funded (George et al 2003).

Table 8.16 Comparison of performance Interventions to modify Alcohol misuse

Intervention	QALY gain/head (base case)	Cost per QALY		Range from sensitivity analyses (a) $/QALY	Min downstream cost offset for Rx to dominate
		Base case	Including within-family effects		
Brief Interventions in primary care					
Brief Interventions for Problem Drinking (Wilk et al, 1997)	Male 0.09 Female 0.125	Men: $670 Women: $490	Men: $250 Women: $185	$93 to $10,549	From $75/cycle to $104/cycle depending on characteristics of target pop[n]
Brief Interventions for Heavy Drinkers (Saunders et al, 1991)	Simple advice 0.128 Advice + brief interv. 0.251 Advice + extended 0.319	$ 70 to $85(b) $ 90-120 $220-285	$ 35 to $45 (b) $ 50-60 $120-140	$15 to $2,654	From $13/cycle to $45/cycle depending on characteristics of intervention
Cognitive Behavioural Therapies					
MOCE vs BSCT (Heather et al, 2000)	MOCE vs BSCT 0.116	$2,145	$1,020	$510 to $57,391	$301/cycle
MET and NDRL (Sellman et al, 2001)	MET 0.062 NDRL -0.038	MET: $6,280 NDRL dominated	MET $1,850 NDRL dominated	MET $274 to $xxx NDRL dominated	$702/cycle
Pharmacotherapy and psychotherapy					
Naltrexone +psych therapy (Streeton et al, 2001)	Naltrexone 0.0528	$12,970	$5,190	$1,468 to dominated	$752/cycle

Notes

(a) main parameters varied: start-age, QoL weights, initial relapse rate, discount rate, relative risk of death, treatment effect, incremental cost

(b) vs nil intervention, function of target population

SECTION III RELATIVE PERFORMANCE

There are many challenges in seeking to identify how to reduce the burden of harm from physical inactivity, poor nutrition, tobacco smoking and alcohol misuse. Challenges arise from various sources, including:

i. the breadth of the project and consequent extensive nature of the literature of potential interventions and other pertinent evidence;
ii. the inherent complexity of the relationship between an intervention, lifestyle behaviours and health – including the likely maintenance of any behaviour change, relative to the normal pattern, and the lack of evidence to describe these relationships;
iii. the difficulty in describing the lifestyle behaviours in a simple uni-dimensional way, especially for nutrition, physical activity and alcohol misuse;
iv. the need to develop unique models for not just each risk factor but also sub-categories, and that can accommodate interventions addressed at multiple risk factors;

However, there are also benefits of such a comprehensive research program, especially the potential for comparison across risk factors, modalities and target populations. This has created a unique opportunity to learn about the relative performance of interventions and the important gaps in research knowledge.

Despite the challenges, we have been able to compare the performance of interventions which address the four life style behaviours including multiple risk factor interventions, for 29 interventions, through 27 cost-utility analyses, plus 2 interventions identified as dominated (See Table 9.1). These analyses yield insights as to where resources might best be focussed to reduce burden of harm from the nominated lifestyle behaviours; especially with respect to risk factor, type of intervention and modality and population target. Where there is good quality evidence we are able to draw clear conclusions, whilst in other areas additional evidence must be obtained.

We note also that in this research program our focus has been on the technical task of deriving measures of performance expressed in cost/QALY to allow comparison across a wide range of program types. While we recognise that in making decisions about resource allocation, other criteria might be considered, rather than incorporate these other issues, which tend to be subjective and value laden, we have rather reported the technical result. In this way, we identify for policy makers, resource allocation decisions that will maximise QALYs gained and the loss of potential QALY gain if other choices are made.

As noted elsewhere, there is a need for high quality data at three levels;

i. Effectiveness of behaviour change and other outcomes contemporaneous with the intervention;
ii. Maintenance of behaviour/clinical change over time;
iii. Link between behaviour change/clinical parameters and health and wellbeing.

When data is missing at any of these stages, either performance cannot be estimated, or confidence and certainty in the results is reduced. The quality of data has been found to be highly variable, with critical gaps in evidence of effectiveness, even in terms of behaviour change concurrent with the intervention, but with more serious deficiencies in relation to maintenance of behaviour change.

Evidence relating behaviour change to health is also incomplete. Where effectiveness data is of very poor quality, we have performed scenario analyses, based on assumed values for inputs, which not surprisingly gives an extremely wide range of plausible values. The quality of available data across the risk factor areas is highly variable. This is seen in our capacity to complete cost-utility analyses, as summarised in Table 9.1 and also in terms of confidence in results and other data requirements,

as summarised in Table 9.2. As a general rule, evidence related to nutrition interventions, especially those targeted at specific high risk groups is high quality, as is evidence concerning tobacco interventions is also good, especially for clinic-based interventions. In general evidence from which to assess the performance of broad community-wide interventions is both incomplete and what is available is of poor quality. There is strong evidence concerning alcohol programs, in terms of impact on current behaviours, but with less known about maintenance of behaviours, although there is some information from one long-term (10 year trial). Less is known about the impact of change in alcohol consumption on health and wellbeing, both for the individual, but even more so for family members or others. Least satisfactory is the evidence concerning physical activity and multiple risk factor interventions, particularly in relation to retention of any behaviour change. The limited information that is available about physical activity interventions suggests very poor maintenance of behaviour change.

An important contribution of this research is the identification of major gaps in the evidence base relating to these risk factor areas and which gaps are of potentially higher priority. We would strongly support future initiatives to address these important research needs.

Table 9.1 Interventions by Risk Factor and whether performance has been assessed.

	Yes $/QALY *model constructed by research team*	***Yes $/QALY*** *based on published C-U*	***Yes but*** *intervention dominated*	*Sub-Total C-U Analyses completed*	***Scenario*** *analysis only*	***No*** *data absent or outcomes inconsistent*
Multiple risk factor	*3*	*2*	*1*	*6*	*2*	*1*
Physical activity	*2*		*2*	*4*		*1*
Nutrition	*5*	*1*		*6*		*2*
Tobacco	*6*			*6*		*1*
Alcohol	*5*			*5*		*1*
All	***21***	***3***	***3***	***27***	***2***	***6***

The Economic performance of interventions is specified in terms of cost/QALY, the lower the cost to achieve a QALY gain the better. As the steps taken to model each intervention have required data inputs of varying quality, the confidence which can be placed on the estimates of cost/QALY also varies. This is important in interpreting the results. We have therefore classified interventions according to both cost/QALY and confidence in the estimates, with confidence specified according to the schema described in Tables 9.2 i to 9.2 iii, which relate to our confidence in the 3 key sources of evidence:

i. Quality of the primary trial(s) providing estimates of effectiveness, which determines validity and reliability of reported results. Relevant is also whether this evidence is based on a single trial, whether these results have been reproduced, or whether based on a meta-analysis;

ii. Length of follow up of the trial following the delivery of the intervention, which determines how confident we are in the maintenance of change in behavioural/clinical outcomes.

iii. Quality of the data linking behavioural/clinical outcomes with long term health outcomes such as quality of life, disease and mortality.

Table 9.2 i Quality of evidence: Current behaviour change

Rating	Criteria
##	Good quality study (RCT, similar groups, ITT analysis, appropriate outcomes, minimal loss to follow up)
#	Poor quality study (eg lack of similar groups, lack of ITT)
?	Some evidence but poor quality/results inconsistent
□	Unacceptable quality study with significant potentials for bias (eg lack of control group, lack of baseline measures, inappropriate outcomes measured)

Table 9.2 ii Quality of evidence: Maintenance of behaviour change

Rating	Criteria
##	Appropriate length of post intervention follow up (eg ≥ 4 years)
#	Short length of post intervention follow up (<4 years)
□	No post intervention follow up

Table 9.2 iii Quality of Evidence: Relationship between behaviour change and health in the long term

Rating	Criteria
##	Good quality published data identified
#	Poor quality published data identified
□	No data identified

In table 9.3 we identify those interventions that perform extremely well cost/QALY < $5,000 and for which the quality of evidence is good; and others which also perform well, cost/QALY >$5,000 & <$15,000 and where quality of evidence is good. In Table 9.4 we list interventions found to perform less well cost/QALY >$25,000, but also based on acceptable quality evidence. Other interventions may perform well or poorly but the evidence is of insufficient quality, across all dimensions to be confident in the result.

The cost effectiveness of each intervention together with the quality of evidence rating scale is presented in Table 9.5. Base case cost/QALY estimates are derived using conservative assumptions, as is the tradition in health economic evaluation. As noted our base case excludes possible downstream cost savings, except for the Mediterranean diet, where health events were part of the clinical trial evidence.

The most outstanding interventions, in terms of cost/QALY combined with good quality evidence are:

- *Mediterranean diet for persons post AMI,* at $340/QALY or taking account the differential rate of health events (such as subsequent heart attack, stroke), generating substantial health sector cost savings. The estimated cost savings amounted to $14,000 saving per person (present value).
- *Lifestyle modification for persons with IGT,* at $1,900/QAY based on good quality evidence and projected cost savings of over $20,000 per person. Although we have less confidence in estimated downstream costs savings as it is not based on observations.
- *Brief interventions for alcohol* misuse also appear highly cost effective, based on good quality data, at less than $700/QALY.
- Other potentially highly cost-effective interventions are as listed in Table 9.5.

Table 9.3 Interventions there were highly cost-effective with good quality evidence

Intervention	***Estimated Cost/QALY*** *$ (Base case, excluding downstream cost savings)*	***Quality of evidence***
Mediterranean diet in post AMI (deLorgeril et al, 1999)	*340*	# # #
Lifestyle change to prevent type 2 diabetes (Eriksson et al, 1999)	*1,900*	# # #
Brief Interventions in primary care for problem drinking (Wilk et al, 1997)	*< 700*	#
Minimal physician advise to quit smoking (Silagy et al, 2004)	*m = 5,300 f = 8,600*	#
Intensive physician advise to quit smoking (Silagy et al, 2004)	*m = 6,600 f = 10,700*	#
Reduced fat diet for IGT (Swinburn et al, 2001)	*10,000*	#
Nurse nutritional counselling in general practice (Steptoe et al, 2003)	*10,600*	#
Phone counselling + NRT to quit smoking (Zhu et al, 2000)	*m=11,800 f=20,000*	#
Buprorion SR + counselling to quit smoking (Hughes et al, 2004)	*m = 10,500 f=14,000*	# #
Naltrexone + psych therapy for alcohol dependence (Streeton et al, 2001)	*5,200 to 13,000*	#

Table 9.4 Interventions that perform relatively poorly, reasonable quality evidence

Intervention	***Estimated Cost/QALY*** *$ (base case) (Excluding downstream cost savings)*	***Quality of evidence***
Cardiovascular disease risk factors in children (Harrell et al, 1996)	*Control dominates*	#
GP exercise referral for CHD risk factors (Taylor et al, 1998)	*Control dominates*	#
Individualised exercised advice for over 60 year olds (Halbert et al, 1999)	*575,000*	#
Orlistat + diet for obesity (Padwal et al, 2003)	*83,700*	#
Oxcheck – primary care nurse health checks (Imperial Cancer Research Fund, 1995)	*63,000*	# #
School-based interdisciplinary lifestyle (Gortmaker et al, 1999)	*50,000*	#
NZ Active Script (Elley et al, 2003)	*29,000*	#

Table 9.5 Summary of rating scale indicating confidence in results along with cost utility for each intervention modelled

Intervention	Cost/QALY $A	Quality of Evidence of		
		Clinical trial evidence re behaviour change	Maintenance of behaviour change	Link to long term health outcomes
1. Fighting fat, fighting fit media campaign (Wardle et al, 2001)	$5,600	□	□	#
2. Stanford 5 City project (Farquhar et al, 1990)	$14,700	?	?	#
3. Student TV viewing and obesity (Robinson, 1999)	Scenarios: range $74,600 to $298,600	□	□	#
4. Interdisciplinary student intervention and obesity, (Gortmaker et al, 1999)	$50,100	# #	□	#
5.Cardiovascular disease risk factors in children , (Harrell et al, 1996)	Control dominates	#	□	#
6. Cardiovascular disease risk reduction in children, (Killen et al, 1988)	scenarios range $37,100 to $148,000	□	□	#
7. GutBusters workplace program (Egger et al, 1996)	$19,800	□	#	# #
8. Workplace prevention of heart disease (WHO European Collaborative, 1986)	Not modelled	?	?	# #
9. Oxcheck- Primary care nurse health checks (Imperial Cancer Research Fund, 1995)	$12,600	# #	#	# #
10. Australian Active Script (Nacerrella & Huang, 2001)	Not modelled, no outcome data	□	□	□
11. New Zealand Active Script (Elley et al, 2003)	$29,000	# #	?	#
12. GP Exercise referral for CHD risk factors (Taylor et al, 1998)	Control dominates	#	#	#
13. Community based exercise for over 65 year olds (Munro et al, 2002)	$15,650	?	□	#
14. Physical activity program for 60+ year olds (Halbert et al, 1999)	$575,000	# #	#	# #
15. Nutritional counselling in GP (Pritchard et al, 1999)	Not modelled no outcome data	□	□	# #
16. Mediterranean diet in those with previous MI (deLorgeril et al, 1999)	$340	# #	# #	# #
17. Reduced fat diet for IGT (Swinburn et al, 2001)	$10,000	#	#	# #
18. Orlistat and diet for obesity (Padwal et al, 2003)	$83,700	# #	□	#

Intervention	Cost/QALY $A	Quality of Evidence of		
		Clinical trial evidence re behaviour change	Maintenance of behaviour change	Link to long term health outcomes
19. Lifestyle change to prevent type 2 diabetes (Eriksson et al, 1999)	$1,900	# #	# #	# #
20. Talking computer for nutrition (Delichatsios et al, 2001)	Not modelled (no costs)	#	□	#
21. Nurse nutritional counselling in GP (Steptoe et al, 2003)	$10,600	# #	#	#
22. Multi media 2 fruit 5 veg (Dixon et al, 1998)	$50	?	□	#
23. US mass media smoking campaign: MTCP (Beiner et al, 2000; Rigotti et al, 2002)	$2,100	□	□	# #
24. AUS mass media campaign: Phase 1 National Tobacco Campaign (Wakefield et al, 1999)	$1,100	□	□	# #
25a Minimal smoking advice in GP (Silagy et al, 2004)	m=$5,300 f= $8,600	#	□	# #
25b Intensive smoking advice in GP (Silagy et al, 2004)	m=$6,400 f=$10,700	#	□	# #
26. Meta-analysis of 86 trials comparing brief, NRT, and behavioural smoking interventions (Baille et al, 1994)	Not modelled (interventions too diverse)	#	# #	# #
27.Phone counselling + NRT (Zhu et al, 2000)	m=$11,800 f=$20,000	?	#	# #
28. Meta-analysis of 16 Bupropion SR trials (Hughes et al, 2004)	m=$10,500 f=$14,000	# #	#	# #
29.US mass media campaign (Holden and Treno, 1997)	Not modelled	?	?	#
30. Brief interventions in primary care for problem drinking (Wilk et al, 1997)	$185 to $670	# #	#	#
31 Brief interventions for heavy drinkers (Saunders et al, 1991)	$35 to $888	#	#	#
32 MOCE vs BSCT (Heather et al, 2000)	$1,000 to $2,100	#	#	#
33 MET vs NDRL (Sellman et al, 2001)	$1,360 to $3,370	?	?	#
34. Naltrexone + psych therapy (Streeton et al, 2001)	$5,200 to $13,000	# #	#	#

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