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RISK FACTOR STUDY

How to Reduce the Burden of Harm from Poor Nutrition, Tobacco Smoking, Physical Inactivity and Alcohol Misuse: Cost-Utility Analysis of 8 Nutrition Interventions

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

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CHE Research Paper 2005/6	Risk Factor Study: Economic Evaluation of Six Interventions to Promote Safe Use of **Alcohol**

Introduction to Risk Factor Project

The risk factor project was commissioned by the Department of Health and Ageing, Population Health Division 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. The research objective was to establish 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, focused on health, measured by mortality and quality of life as the primary objective of health policy. While there may be other objectives and other issues relevant to policy decisions, these have not been incorporated into the analysis, due largely to their more subjective nature.

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. The interventions selected through this process for economic analysis are listed in Table 1. We identified 35 interventions for assessment and have been able to report 29 cost-utility (C-U) analyses; 22 based on models developed by the research team, 3 based on published models, 2 'scenario analyses', whilst 2 interventions were dominated. The results of these analyses are reported in 6 volumes; an Executive Report, plus 5 technical volumes covering each of the 4 risk factors, plus one for multiple risk factor interventions.

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 then be directly compared, without having to understand the relationship between behaviour and health. This technique is applicable where behaviour is consistently and simply described. 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. The ultimate approach to performance measurement is the *cost-utility analysis* which we have conducted wherever data allowed.

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 have been used for 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 1 Interventions selected for economic evaluation

MULTI-FACTORIAL (Chapter 1-9)

Research Paper 2

Adult Interventions	**School-based Interventions**
▪ Fighting Fit, Fighting Fat Media Campaign	▪ Student TV viewing and obesity
▪ Stanford 5 City media/community Project	▪ Interdisciplinary student intervention and obesity
▪ GutBusters Workplace Program	▪ Cardiovascular disease risk factors in children
▪ Workplace prevention of heart disease *	▪ Cardiovascular disease risk reduction in children
▪ Oxcheck – Primary care nurse health checks	

PHYSICAL ACTIVITY (Chapter 1-4)

Research Paper 3

▪ Australian GP Active Script *	▪ General practice exercise referral for cardiovascular disease risk factors
▪ New Zealand GP Active Script	▪ Physical activity program and individualised advice for over 60 year olds
▪ Community based exercise for over 65 year olds	

NUTRITION (Chapter 1-8)

Research Paper 4

▪ Nutritional counselling in general practice *	▪ Orlistat plus diet for obesity
▪ Mediterranean diet in those with previous myocardial infarction	▪ Lifestyle changes to prevent type 2 diabetes
▪ Reduced fat diet for those with impaired glucose intolerance	▪ Talking computer for nutrition *
	▪ Nurse nutritional counselling in general practice
	▪ Multi-media '2 fruit 5 veg' campaign

SMOKING (Chapter 1-5)

Research Paper 5

▪ US mass media smoking campaign – Massachusetts Tobacco Control Program	▪ Meta-analysis of 34 trials evaluating minimal to intensive advice in general practice
▪ Australian mass media campaign – Phase 1 National Tobacco Campaign	▪ Meta-analysis of 86 trials comparing brief intervs, NRT and behavioural interventions *
▪ Meta-analysis of 16 Bupropion SR trials	▪ Phone counselling as adjuvant therapy for NRT

ALCOHOL (Chapter 1-6)

Research Paper 6

▪ US mass media alcohol campaign *	▪ MOCE and BSCT for moderately dependent drinkers
▪ Meta-analysis of 8 trials evaluating brief interventions in primary care for problem drinking	▪ MET and NDRL for mildly to moderately dependent drinkers
▪ Brief interventions for heavy 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.

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.

1. Nutritional counselling in general practice

1.1 Description

Intervention type

Nutritional counselling in general practice aims to improve lifestyle and dietary patterns. The dietary advice will normally reflect current knowledge. The dietary advice may be provided by a general practitioner and/or a dietician or practice nurse.

References/sources of evidence

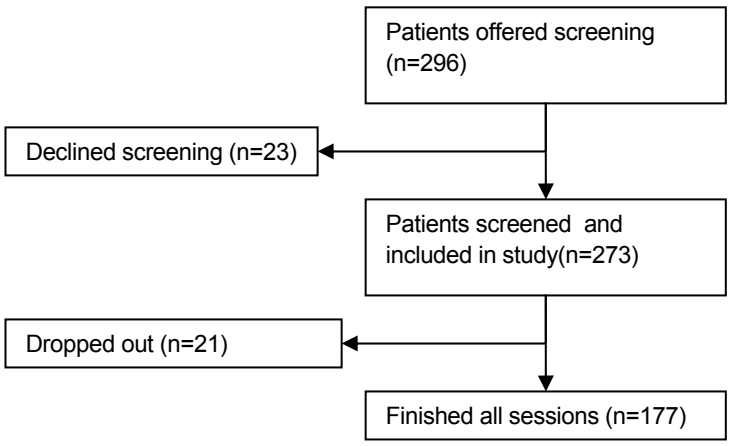
This analysis of the nutritional counselling in general practice is based on the cost effectiveness study by Pritchard et al (1999) conducted in a general practice at Lockridge, near Perth, Western Australia. The intervention targeted patients aged between 25 and 65 years as they attended the practice between November 1992 and May 1994. The advice consisted of restricting total dietary energy, reducing fat, limiting carbohydrates, discouraging smoking and limiting alcohol consumption. In this study counselling was performed by either a dietician in the general practice setting or jointly between a dietician and general practitioner.

The objective of this study was to examine the clinical and cost outcomes of nutritional counselling for patients diagnosed with one or more of the following conditions: overweight/obesity, hypertension or type 2 diabetes.

Recruitment: target population and participants

One university general practice was chosen for the study, the reasons for selection were not specified. The study employed a dietician who screened opportunistically those who attended the practice. Patients aged 25 to 65 with a pre-existing diagnosis of overweight, hypertension or type 2 diabetes were invited to participate in screening. Patients were excluded if they were mentally ill, intellectually handicapped, terminally ill, acutely ill, pregnant or already participating in other health education programs. Of the 296 patients who were offered screening, 273 (92%) were enrolled in the study. One hundred and seventy seven patients completed all sessions. The process of screening, recruitment and follow up is shown in Figure 1.1.

Figure 1.1 Summary of screening, recruitment and follow up for the study



Source (Pritchard et al, 1999 pg. 313)

Table 1.1 shows the average screening measurements of patients in each group by condition.

Table 1.1 Baseline characteristics of the three study groups

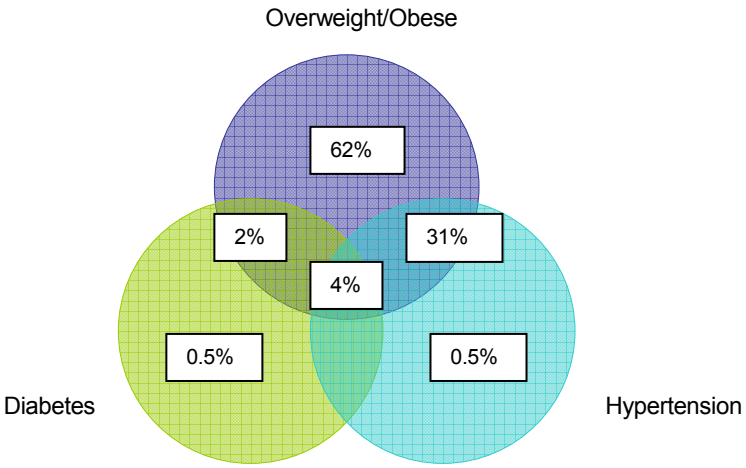
Condition	Control group (n=91)	Doctor/dietitian group (n=93)	Dietitian group (n=89)	Total
Overweight/Obese (kg) mean	89.1 (90)	91.7 (92)	85.5 (88)	270
Hypertension (mm Hg) mean	110 (34)	112 (33)	109 (30)	97
Type 2 diabetes (% glycated haemoglobin) mean	7.7 (6)	8.0 (6)	8.2 (5)	17
Total with risk factors	130	131	123	384*

Source (Pritchard et al, 1999 pg. 313)

*Note that the total number of patients exceeds the number recruited as patients are permitted to be grouped as more than one condition

Overweight alone accounted for 62% of patients. A further 31% were overweight and had hypertension, 2% were overweight and diabetic, and 4% had all three conditions. The other 1% had either diabetes or hypertension alone (Pritchard et al 1999, pg 313). See Figure 1.2.

Figure 1.2 Percentage of patients with nominated risk factors



Details of baseline characteristics are incompletely reported. It is noted that 75 men and 198 women participated and there was no significant difference between groups with respect to sex (Pritchard et al 1999, pg 313). Seventy-three per cent of participants were less than 50 years old and there were no significant differences in age between groups (Prichard et al 1999, pg 313).

There were no significant differences between groups by socio-economic status (SES) or occupation. The greatest proportion of patients were from most or more disadvantaged socio-economic status groups (78%).

Intervention

The trial consisted of three study groups which are described as follows:

Dietician group:

A dietician was hired for the study and conducted six counselling sessions, evenly spaced within 12 months for each patient allocated to this group. The initial session lasted 45 minutes and subsequent sessions for 15 minutes each. The counselling sessions focused on good nutrition and exercise. Lifestyle and dietary patterns were discussed to identify problem areas. Advice was provided on food

shopping, cooking methods, food selection, meal planning, and exercise programs. Advice was individualised with the help of patient kept food records and diet histories.

Based on Pritchard et al 1999, pg 313 the following recommendations were made to patients in this group:

- Restriction of total dietary energy
- Reduction of fat component of total dietary intake to ≤30%
- Reduction of carbohydrate component of total dietary intake to ≤50%
- Protein to contribute the balance of the total dietary intake
- Smoking discouraged
- Alcohol consumption ≤2 standard drinks per day for women and ≤4 for men with at least 2 alcohol free days per week

Doctor/dietician group:

In this group treatment was the same as for the dietician group with the following additions. The dietician also was responsible for flagging the patient record for the GP with progress measurements and coordinating patient follow up appointments with the GP. Patients saw the same GP for an initial visit and two subsequent visits during 12 months. In each case 5 minutes of GP time was allocated.

Control group:

Control patients received the results of the initial measurements (i.e. weight and blood pressure) and were advised to follow these up with their GP should they have any questions. These patients did not see the study dietician but received usual care from their GP.

1.2 Quality of evidence

Recruitment

The study enrolled a total of 273 patients, with 91 allocated to the control group, 93 to the doctor/dietician group and 89 to the dietician group. Patients were randomised to groups using a random number table. It is not reported whether randomisation was secure and whether there was blinding to group allocation.

Results are reported for overweight, hypertension and type 2 diabetes separately within each study group. Interpretation of the results is not straight forward as the categorisation of some patients with multiple risk factors is unclear.

The sample size calculation was based on an expected 5% weight reduction in the dietician group, 10% in the doctor/dietician group and no change in the control group. To detect this change with 90% power and α=0.05, 35 overweight patients were required per group.

Of those patients enrolled a total of 177 (65%) completed all follow up sessions. Significantly fewer patients in the dietician group completed all sessions compared to the other two groups (Pritchard et al 1999, pg 314). It is possible that those who dropped out or were lost to follow up may have differed from those who remained in the study.

Control group

The study was designed so that the control group received the same “usual care” as any patients presenting to the practice. It is of particular concern that these patients saw the same GP’s who were involved in the doctor/dietician group. There is a risk of cross contamination and that these GPs altered how they treated all patients as a result of being involved in the study.

Evaluation method

The study states that analyses were performed on an intention to treat basis (Pritchard et al 1999, pg 314). The study's definition of intention to treat is that a patients measurement is assumed to be unchanged if they drop out of the study. Thus a patient's last measurement was used to populate all subsequent missing data values. This is possibly inappropriate as patients dropping out may do so because of worse outcomes, and because outcomes such as weight and blood pressure generally worsen over time with increasing age.

Simple comparisons between groups were made, with 95% confidence intervals and some chi-squared tests. The comparisons between groups are problematic due to the double counting of some patients. No overall results are presented with each patient only included once.

Outcome measures

Outcomes were measured at baseline and after 12 months and included: weight, blood pressure, medication use and glycated haemoglobin levels. Outcome measurement was standardised where possible to lessen measurement error and variation.

Most outcomes were objective which lessens the possibility of measurement bias. It is unknown if investigators and outcome assessors were blinded to group allocation which may have influenced results.

Bias, confounders, efficacy

The main sources of potential bias are whether the groups were similar at baseline due to the lack of detailed data provided. It is unknown whether patients, doctors, investigators and outcome assessors were blinded to group allocation.

Bias also arises by the same GPs providing care to the doctor/dietician and control groups of the trial with the possibility of cross contamination of care. It is possible that due to involvement in the trial doctors changed how they treated "usual care" and control patients.

There were a number of patients who dropped out of the study and it is not known if these patients differed significantly from those who completed follow up.

Patients were recruited to the study opportunistically so it is not known if patients will be representative of the general population of patients presenting to general practice. The patients in this trial were significantly disadvantaged (according to their SES groupings) which may mean that results are not generalisable to patients of a different socio-economic mix seen in other regions.

1.3 Outcomes – as reported

All analyses compare outcomes between the dietician, doctor/dietician and control groups and Table 1.2 shows the main analyses reported in the study.

Table 1.2 Outcome measures, data sources and analyses reported in the trial

Outcome measures	Data sources	Analyses
BEHAVIOUR CHANGE		
Not reported	-	-
CLINICAL PARAMETERS		
▪ Systolic blood pressure (mm Hg) ▪ Diastolic blood pressure (mm Hg) ▪ Weight (kgs) ▪ Glycated haemoglobin (%)	Blood pressure taken from left arm while sitting using a mercury sphygmomanometer. Body weight measured with patients wearing light clothing and no shoes on digital balance scales to nearest 0.1 kg. Venous blood was taken to measure glycated haemoglobin	Differences between baseline and 12 months and between groups. Confidence intervals and percentages are reported.
MEDICATION USE		
Medication use	Self reported. The defined daily dose as described in the WHO system was calculated. Only medicines included in the ATC grouping C: cardiovascular system were included	Differences between baseline and 12 months and between groups. Confidence intervals and percentages are reported.
MORTALITY		
Not reported	-	-
MORBIDITY		
Not reported	-	-

Clinical parameters

Clinical parameter results as presented in the study report are presented in Table 1.3, for weight, blood pressure and glycated haemoglobin for each group and each of the three conditions.

Table 1.3 Mean final measurement and % change from baseline for each group for patients with each condition

	Control group			Doctor/dietician group			Dietician group		
Condition	**Mean**	**% change**	**n**	**Mean**	**% change**	**n**	**Mean**	**% change**	**n**
Overweight (kg)									
Baseline	89.1			91.7			85.5		
All patients	89.7	-0.7	90	85.5	6.8	92	80.4	6.0	88
Completed	91.7	-2.9	64	82.7	9.8	65	76.6	10.4	48
Drop outs	85.0	4.6	26	89.9	2.0	27	84.9	0.7	40
Hypertension (mm Hg)									
Baseline	110			112			109		
All patients	112	-1.8	34	102	8.9	33	104	4.6	30
Completed	112	-1.8	28	100	10.7	24	98	10.1	14
Drop outs	113	-2.7	6	108	3.6	9	109	0.0	16
Type 2 diabetes (%)									
Baseline	7.7			8.0			8.2		
All patients	7.8	-1.3	6	7.2	10	6	8.2	0.0	5
Completed	7.8	-1.3	6	6.7	16.3	5	6.1	25.6	3
Drop outs	-	-	0	9.2	-15.0	1	10.3	- 25.6	2

Source (Pritchard et al 1999, pg 314)

*Note patient numbers reported for each group do not equal the total number in each group as patients may have more than one condition

The doctor/dietician group lost 6.7kg or 7.3% of screening weight compared with the control group (95%CI 6.5% to 8.5%) while the dietician group lost 5.6kg or 6.6% compared with the control group (95%CI 5.8% to 7.6%).

The doctor/dietician group had a blood pressure fall of 12mm Hg or 12% compared with the control group (95%CI 9% to 15%) and the dietician group had a fall of 7 mm Hg or 7% compared to the control group (95%CI 4% to 10%).

The percentage glycated haemoglobin reduced by 0.8% over the trial period in the doctor/dietician group, did not change in the dietician group and increased by 0.1% in the control group.

Medication use

There was no significant difference in the average defined daily dose of cardiovascular drugs for patients in the three groups at baseline or at final follow up.

1.4 Program costs

As reported by trial

The study dietician recorded time spent on study tasks of screening, making and modifying appointments, drawing patient files, data entry and counselling. All costing was based on 1993/94 Australian values. The cost of the dietician was valued at $20 per hour and the GP was $82 per hour.

Other costs included were the materials used by the dietician, room rental and usual practice overheads (costed and distributed according to number of consults). These costs were recorded for each of the three study groups and a cost effectiveness analysis presented the cost per weight change relative to the control group. The reported costs have also been inflated to 2003 costs as seen in Table 1.4.

Table 1.4 Analysis of cost per weight change

	Control group	**Control group 2003$**	**Doctor/dietician group**	**Doctor/dietician group 2003$**	**Dietician**	**Dietician 2003$**
Total cost per group	$2,103	$2,832	$8,240	$11,096	$5,715	$7,695
Number of patients	91		93		89	
Cost per patient	$23.12	$31.13	$88.61	$119.31	$64.21	$86.47
Additional cost per patient	$0.00	$0.00	$65.49	$88.19	$41.09	$55.34
Weight change per patient (kg)	0.58		-6.13		-5.05	
Additional weight change per patient (kg)	0		-6.71		-5.63	
Additional cost per kg lost	-	-	$9.76	$13.14	$7.30	$9.83

Source (Pritchard et al 1999, pg 314)

The cost per additional kg lost for the doctor/dietician group was $9.76 compared with the control group and for the dietician group it was $7.30 based on 1993/4 figures. The cost per additional kg lost for the doctor/dietician group was $13.14 compared with the control group and for the dietician group it was $9.38 when inflated to June 2003 figures.

1.5 Performance

Further performance figures are not provided for this intervention. An estimate is already provided by the trial (see above). This intervention is not suitable for further estimates of cost effectiveness and cost-utility including economic modelling due to severe potentials for bias. The lack of confidence in the effectiveness results means that further economic analysis is inappropriate. The key problem with the study design is that patients are grouped according to three conditions (hypertension, overweight and diabetes) with significant double counting between groups due to people being included in more than one group. Other issues included potential group differences at baseline, the same doctors caring for patients in each group leading to risk of 'usual care' becoming more like the intervention, loss to follow up and lack of intention to treat analysis.

2. Mediterranean diet and recurrence following first myocardial infarction

2.1 Description

Intervention type

The Mediterranean diet intervention in general terms refers to a diet rich in bread, root and green vegetables, fruit and fish. A Mediterranean diet is low in red meat and saturated fat, with most fat coming from olive oil. Alcohol in moderation is consumed with meals.

Reference

This analysis is centred on randomised controlled trial by de Lorgeril et al (1999), Lorgeril et al (1996) and de Lorgeril et al (1994) conducted in 6 services within Lyon, France. A total of 605 patients aged less than 70 years were recruited to the study between March 1988 and March 1992.

The objective of this study was to assess whether a Mediterranean-type diet reduces recurrence and risk of cardiovascular death after a first myocardial infarction compared to a prudent Western-type diet.

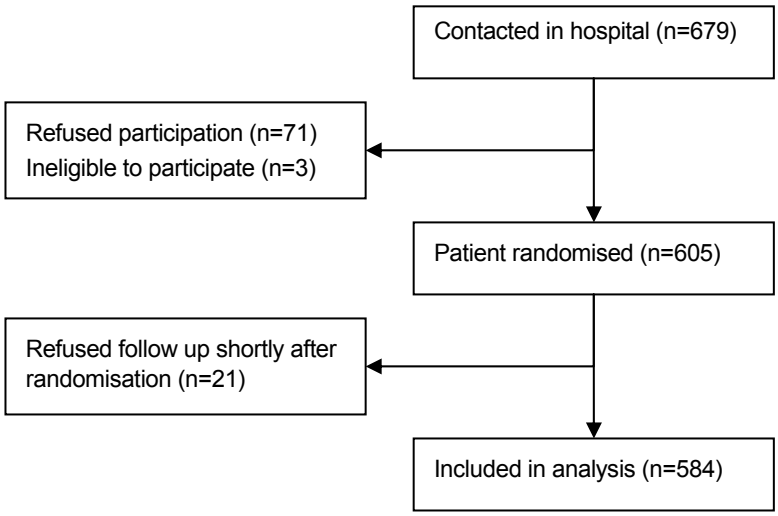
Recruitment: target population and participants

Participants for this study were aged less than 70 years, were clinically stable and had no medical or social conditions that would limit their ability to participate in a long-term dietary trial. Participants all had survived a myocardial infarction within 6 months of enrolment.

During patients hospital stay those eligible were asked to participate in a cohort study with 5 years follow up. They were not fully informed of the study design and were asked to attend an outpatient clinic two weeks after their discharge to be randomised.

A total of 679 patients were contacted in hospital and 584 randomised patients were included in the cardiovascular morbidity and mortality analyses (Figure 2.1).

Figure 2.1 Summary of recruitment to follow up



Source (De Lorgeril et al, 1994, pg 1456)

The distribution of baseline characteristics of the Mediterranean diet (intervention) and Western diet (control) groups are shown in Table 2.1.

Table 2.1 Baseline characteristics of the intervention and control groups

Variable	Control (n=303)	Intervention (n=302)
Age (years)	53.5 (10)	53.5 (10)
Sex ration M/F (%)	92.1/7.9	89.4/10.6
Current smokers (%)	4.9	7.6
Infarction history		
Primary ventricular fibrillation (%)	4.3	4.0
Thrombolytic therapy (%)	45.9	49.7
Highest serum creatine kinase (IU/L)	1972 (1581)	2067 (1789)
Non-Q wave infarction (%)	18.9	20.8
Infarct location (%)		
Anterior	33.3	42.4
Lateral	5.2	5.7
Inferoposterior	61.5	51.9
Positive exercise test (%)	17.6	19.3
Coronary angiography (%)	38.7	44.7
Coronary angioplasty (%)	15.6	14.7
Medication at randomisation (%)		
Anticoagulant agents	26.4	29.4
Antiplatelet agents	64.8	62.6
Beta-blocking agents	63.4	60.2
Calcium-channel blockers	21.7	20.4
Angiotensin-converting-enzyme inhibitors	6.1	9.3
Haematocrit (%)	41.9 (3.4)	41.3 (3.9)
Haemoglobin (g/L)	139 (11)	141 (51)
Leucocyte count (10^8/L)	6.61 (1.7)	6.62 (1.8)
Granulocyte count (10^8/L)	3.93 (1.3)	3.96 (1.3)
Lymphocyte count (10^9/L)	1.87 (0.6)	1.85 (0.7)
Platelet aggregation (%)		
Thrombin-induced	13.9 (8.7)	14.1 (8.1)
ADP-induced		
First wave	34.4 (8.6)	34.5 (8.7)
Secondary wave	21.4 (16.3)	19.9 (14.1)

Source (de Lorgeril et al, 1994 pg. 1455)

Intervention

Patients assigned to the intervention group were asked to comply with a Mediterranean-type diet and were required to sign a consent form agreeing to modify their diet. Advice was provided by the research cardiologist and dietician during a one hour session. Patients were advised to eat more bread, more root and green vegetables, more fish, less meat (beef, lamb and pork to be replaced with poultry), not a day without fruit, and butter and cream to be replaced with margarine supplied by the study. Because patients would not accept olive oil as the only fat, a rapeseed (canola) oil-based margarine was supplied to study participants and their families. This margarine has a comparable composition to olive oil. Olive oil and rapeseed oil were recommended for all salads and food preparation. Moderate alcohol consumption (wine) was permitted with meals. The aim of the diet was to supply 35% of energy as fat, <10% of energy as saturated fat, <4% of energy as linolenic acid and >0.6% of energy as alpha-linolenic acid. The dietary instructions were detailed and customised to each patient. Diet change was suggested in two stages. The first stage involved preparation to accept the detailed instructions given in stage 2. Stage 2 consisted of the dietician

assisting patients and their families to adapt their usual diet to the Mediterranean type. Factors such as preferences, geographic origin, occupations, number in family, resources and community setting were all taken into account when forming detailed, personalised instructions.

Patients in the control group received no dietary advice from the study investigators but were advised by their attending physicians or hospital dieticians to follow a prudent diet of the American Health Association.

Patients in both groups were enrolled at an outpatient appointment 2 weeks following their discharge from hospital. They were then seen again by investigators after two months and then annually. These visits were in addition to their regular appointments to their attending physicians who were responsible for all aspects of their treatment, including medications, invasive diagnostic and therapeutic procedures.

For the first 4 years dietary habits were evaluated at follow up only in the intervention group so as to not prompt the behaviour of controls. The dietary habits of a subset of controls were evaluated at the end of the trial. This difference in evaluation should be considered as part of the intervention itself.

2.2 Quality of evidence

Recruitment

The study recruited 605 patients (89% of those who were contacted). 584 (97%) patients who were recruited were analysed in the study (the other 21 patients refused participation shortly after recruitment). It is not known if those who declined participation differed significantly from those who agreed to participate in the trial, although patient numbers are sufficiently small as to not bias the results.

Originally a sample size of 250 patients was required (ά=0.05, power=90%) to detect a difference in the annual recurrence rate for myocardial infarction of 8% in the control group and 4% in the intervention group (assuming 4% annual attrition). After one year of follow up the calculation was repeated assuming a recurrence rate of 5.3% in the control group and 2.65% in the intervention group and 300 patients were required in each group over 4 years (ά=0.05, power=90%).

Randomisation was secure and the baseline characteristics of the two groups were similar.

The cohort study was designed with 5 year follow up. The Scientific Committed proposed an intermediate analysis after 1 year minimum follow up for each patient. A statistically significant result led to the stopping of the trial.

Table 2.2 shows the withdrawal from follow up at various time points through out the trial. Data was collected past the stopping of the trial as it took some time to schedule individual final assessments for each of the participants.

Table 2.2 Withdrawal from follow up

Weeks	Control group n=303(%)	Intervention group n=302 (%)
0	8 (2)	13 (4)
8	3 (1)	9 (3)
52	13 (4)	10 (3)
104	6 (2)	6 (2)
156	0 (0)	1 (0.04)

Source (de Lorgeril et al, 1994 pg 1455)

Loss to follow up was similar in both groups and was sufficiently small so as to be unlikely to bias the results.

Control group

Patients were unaware of the comparison between two diets and were not fully informed of the study design. Physicians and those performing data analysis were blinded to group allocation. The study blinding reduces the possibility of performance bias or the two groups being treated differently. An independently designed and administered questionnaire found that there were no significant differences in the two groups in their perceptions of clinic visits.

There may have been variation within the control group as to the extent of dietary advice for a prudent Western-type diet that was received. This was dependent on the attending physicians and dieticians responsible for their normal care.

Evaluation method

The study states that all outcome analyses were performed on an intention to treat basis (de Lorgeril et al, 1994). Chi-square tests, unpaired students t-tests, Kaplan Meier survival analysis and cox proportional hazards methods were used to analyse the data.

Outcome measures

Outcomes were measured at baseline, 8 weeks and then annually through a systematic interview and included: hospital admissions, drug treatment changes, invasive and non-invasive cardiac investigations, exercise tolerance, angina, and arrhythmia. In addition the following parameters were also measured: blood pressure, platelet aggregation, plasma total lipid fatty acids, plasma vitamin C, vitamins A and E.

For the first 4 years dietary habits were evaluated at follow up only in the intervention group.

Many outcomes were objective which lessens the possibility of measurement bias. The study report does not state whether outcome assessors were blinded to group allocation.

Bias, confounders, efficacy

The trial has taken a number of measures to lessen the possibility of bias. Randomisation was secure. Patients were unaware of the study design and comparison of diets and physicians were blinded to group allocation. The baseline characteristics of the two groups were similar and analyses were performed on an intention to treat basis.

The main sources of potential bias include whether the two groups were treated equally in all ways except the intervention. The trial does not provide detail of what “usual” dietary advice for the control group entailed.

The impact of potential confounders including independent risk factors such as aspirin use, age, sex, smoking, cholesterol, blood pressure and leukocyte count were investigated using a multivariate Cox proportional-hazards model.

It is possible that the results are not generalisable to those without a first recurrence of myocardial infarction. It is likely that patients would have been motivated to change diet following a recent significant event such as a myocardial infarction.

2.3 Outcomes – as reported

Table 2.3 shows the main analyses reported in the study.

Table 2.3 Outcome measures, data sources and analyses reported in the trial

Outcome measures	Data sources	Analyses
BEHAVIOUR CHANGE		
▪ Intake of the main food stuffs after 1-4 years ▪ Dietary habit	De Lorgeril et al, 1994 Systematic interview	Comparison of groups
BIOLOGICAL PARAMETERS		
Body mass index Blood pressure Cholesterol Triglycerides Lipoprotein Albumin Haemoglobin Creatine Uric acid Leukocyte count	De Lorgeril et al, 1999 Some outcomes were measured using routine blood tests. The method of measurement for other outcomes was not reported.	Comparison of groups at final visit
CLINICAL ENPOINTS		
Non fatal acute myocardial infarction Periprocedural infarction Unstable angina Heart failure Stroke Pulmonary embolism Peripheral embolism Stable angina Elective myocardial revascularization Post-PCTA restenosis Thrombophlebitis Composite scores	De Lorgeril et al, 1999 All endpoints were ascertained at annual and final visits. Detailed information was obtained from the family and medical/hospital records.	Comparison of groups at final visit (number , rate per 100 patients per year of follow up, risk ratio, 95%CI and p value)
MEDICATION USE		
Medication	De Lorgeril et al, 1996 Some information was obtained in interviews held with the patients. The study does not report if other sources of data were also used.	Comparison of groups at baseline and 12 months
MORTALITY		
Cardiac deaths Non cardiac deaths All cause deaths	De Lorgeril et al, 1999 Data for patients withdrawn from follow up was obtained by contacts with the family or birth place city halls	Comparison of groups (number , rate per 100 patients per year of follow up, risk ratio, 95%CI and p value). Kaplan Meier survival curves,
MORBIDITY		
Not reported	-	-

Behaviour change

The intake of the main foodstuffs comprising both types of diet (Mediterranean and Western) after 1-4 years follow up in the two groups is shown in Table 2.4. During the first 4 years of the study dietary habits were only measured in the intervention group. The diet of 192 (52%) consecutive controls was evaluated once, starting in June 1992 (3 months after the last recruitment). There was significantly more intake of bread, fruits and margarine in the intervention group compared to the control group and significantly less intake of delicatessen, meat, butter and cream (assuming p value <0.05 indicates statistical significance).

Table 2.4 Intake of main foodstuffs for intervention versus control groups after 1-4 years of follow up

Food	Control mean g/day (SE) n=192	Intervention mean g/day (SE) n=219	P value
Bread	145 (7)	167 (6)	0.01
Cereals	99.4 (11)	94.0 (10)	0.22
Legumes	9.9 (3.0)	19.9 (4.3)	0.07
Vegetables	288 (12)	316 (10)	0.07
Fruits	203 (12)	251 (12)	0.007
Delicatessen (ham, sausage and offal)	13.4 (2.4)	6.4 (1.5)	0.01
Meat	60.4 (5.5)	40.8 (5.0)	0.009
Poultry	52.8 (6.0)	57.8 (5.0)	0.42
Cheese	35.0 (2.6)	32.2 (2.0)	0.25
Butter and cream	16.6 (1.6)	2.8 (0.6)	<0.001
Margarine	5.1 (0.6)	19.0 (1.0)	<0.001
Oil	16.5 (0.9)	15.7 (0.8)	0.65
Fish	39.5 (5.7)	46.5 (5.6)	0.16

Source (de Lorgeril et al, 1994 pg 1456)

The mean daily nutrient intake recorded on the final study visit is shown in Table 2.5. This analysis was performed on a sub sample of consecutive, non-selected patients.

Table 2.5 Daily nutrient intake at final visit for intervention and control patients

	Control group mean (SD)	Intervention group mean (SD)	P value
Total calories	2088 (490)	1947 (468)	0.033
% calories			
Total lipids	33.6 (7.80)	30.4 (7.00)	0.002
Saturated fats	11.7 (3.90)	8.0 (3.70)	0.0001
Polyunsaturated fats	6.10 (2.90)	4.60 (1.70)	0.0001
18:1 (ω-9) (oleic)	10.8 (4.10)	12.9 (3.20)	0.0001
18:2 (ω-6) (linoleic)	5.30 (2.80)	3.60 (1.20)	0.0001
18:3 (ω-3) (linolenic)	0.29 (0.19)	0.84 (0.46)	0.0001
alcohol	5.98 (6.90)	5.83 (5.80)	0.80
Proteins, grams	16.6 (3.80)	16.2 (3.10)	0.30
Fibre, grams	15.5 (6.80)	18.6 (8.10)	0.004
Cholesterol, mg	312 (180)	203 (145)	0.0001

Source (de Lorgeril et al, 1999 pg 782)

The intervention group had significantly lower levels for total lipids, saturated fats, polyunsaturated fats, linoleic acid and cholesterol compared to the control group and significantly higher levels for oleic acid, linolenic acid and fibre (assuming a p value of <0.05 is statistically significant).

Biological parameters

Biological outcomes were collected for many of the main risks thought to be associated with coronary events. Results at the final study visit for the intervention and control groups are shown in Table 2.6.

Table 2.6 Main risk factors and selected biological parameters for the intervention and control groups at final follow up

	Control group mean (SD) n=204	Intervention group mean (SD) n=219
Body mass index, $kg.m^2$	26.9 (3.4)	26.3 (3.7)
Systolic blood pressure, mm Hg	128 (16)	128 (17)
Diastolic blood pressure, mm Hg	79 (10)	78 (11)
Total cholesterol, mmol/L	6.18 (1.04)	6.20 (1.06)
Triglycerides, mmol/L	1.75 (0.83)	1.94 (0.85)
HDL-cholesterol, mmol/L	1.28 (0.34)	0.29 (0.34)
LDL-cholesterol, mmol/L	4.23 (0.98)	4.17 (0.93)
Lipoprotein (a), g/L	0.35 (0.49)	0.33 (0.35)
Albumin, g/L	47.10 (2.88)	47.28 (3.07)
Glycated haemoglobin, %	4.61 (1.23)	4.66 (1.52)
Creatine, µmol/L	116 (20)	115 (21)
Uric acid, µmol/L	348 (81)	338 (87)
Leukocyte count, $x10^9/L$	6.00 (1.69)	5.99 (1.68)

Source (de Lorgeril et al, 1999 pg 782)

All biological parameters appear very similar for both groups at final follow up.

Medication use

The use of medication at baseline and 1 year was reported by de Lorgeril et al, 1996 (Table 2.7). The two groups were similar at baseline. The data at 12 months show a parallel course in the two groups suggesting that participation in the trial did not influence the current practice of attending physicians in either group (de Lorgeril et al, 1996).

Table 2.7 Use of anti-ischemic and major cardiac drugs at baseline and 12 months

Medication	Intervention group		Control group	
	Baseline %	12 months %	Baseline %	12 months %
Oral anticoagulant agents	29.4	21.8	26.4	18.7
Aspirin	64.8	65.3	62.6	60.9
Beta-blocking agents	60.2	47.6	63.4	47.4
Calcium channel blockers	20.4	25.8	21.7	29.5
ACE inhibitors	9.3	15.2	6.1	9.2

Source (de Lorgeril et al, 1996 pg 1105)

The latest publication by de Lorgeril et al, 1999 reports medication use at the final patient visit, although the categories of drugs vary slightly from earlier reports (Table 2.8).

Table 2.8 Medication use at final visit for intervention and control groups

Medication	Intervention group % (n=204)	Control group % (n=219)
Anticoagulant agents	11.4	16.1
Antiplatelet agents	75.8	69.7
B-Blocking agents	47.5	47.3
Calcium channel blockers	25.6	28.4
ACE inhibitors	18.3	17.4
Lipid-lowering drugs	26.5	34.0

Source (de Lorgeril et al, 1999 pg 782)

Clinical endpoints and mortality

The mean follow up for survival was 44.9 months in the control group and 46.7 months in the intervention group. Clinical endpoints, including a number of composite outcomes for the two groups are presented in Table 2.9.

Table 2.9 Clinical endpoints and risk ratios for the intervention and control groups, calculated using a Cox Proportional-Hazards Model

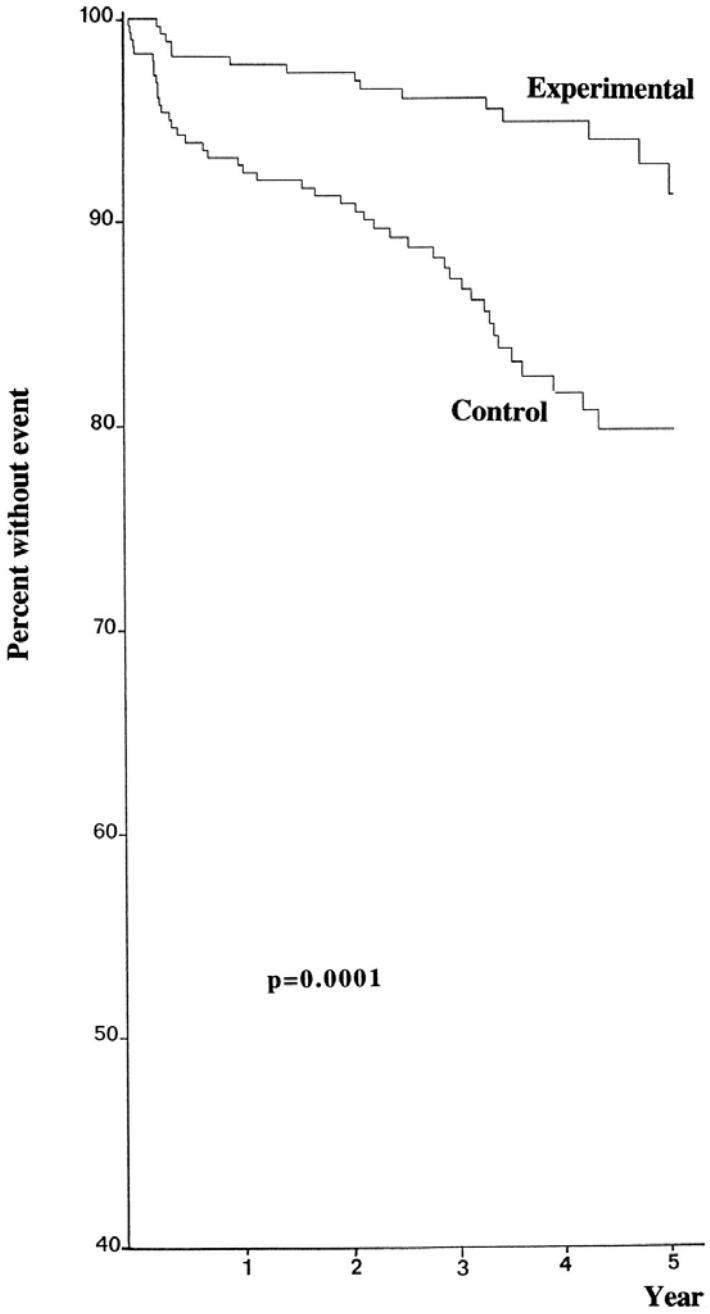
	Control group		Intervention group		Risk ratio (95% CI)	P value
	Number	Rate per 100 patients/year of follow up	Number	Rate per 100 patients/year of follow up		
Major primary endpoints						
Cardiac deaths	19	1.37	6	0.41	0.35 (0.15 to 0.83)	0.01
Non fatal AMI	25	2.70	8	0.83		
Total primary end points (composite outcome 1)	**44**	**4.07**	**14**	**0.24**	**0.28 (0.15 to 0.53)**	**0.0001**
Non cardiac deaths	5	0.36	8	0.54		
All cause deaths	24	1.74	14	0.95	0.44 (0.21 to 0.94)	0.03
Major secondary endpoints						
Periprocedural infarction	2		0			
Unstable angina	24		6			
Heart failure	11		6			
Stroke	4		0			
Pulmonary embolism	3		0			
Peripheral embolism	2		1			
Total secondary endpoints	46	4.96	13	1.35		
Total primary + secondary endpoints (composite outcome 2)	**90**	**9.03**	**27**	**2.59**	**0.33 (0.21 to 0.52)**	**0.0001**
Minor secondary endpoints						
Stable angina	29		21			
Elective myocardial revascularisation	45		37			
Post-PTCA restenosis	15		9			
Thrombophlebitis	1		2			
Total minor endpoints	90	9.71	68	7.04		
Total major and minor endpoints (composite outcome 3)	**180**	**18.74**	**95**	**9.63**	**0.53 (0.38 to 0.74)**	**0.0002**

Source (de Lorgeril et al, 1999 pg 780)

All cause and cardiovascular mortality and the combination of recurrent myocardial infarction and cardiac death (composite outcome 1) were statistically significantly reduced in the intervention compared to control group at final follow up. The combined major primary and secondary endpoints (composite outcome 2) were also reduced for the intervention group (de Lorgeril et al, 1999).

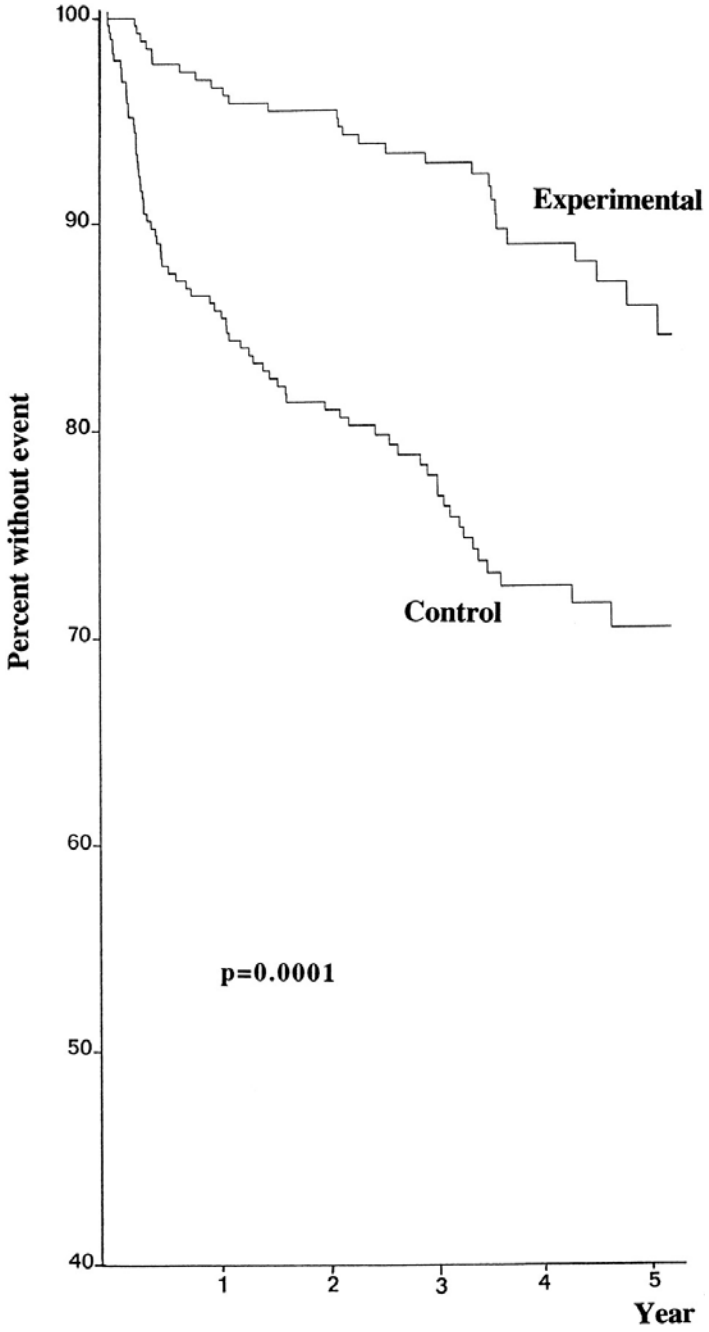
The event free survival curves are shown in Figure 2.2, Figure 2.3 and Figure 2.4.

Figure 2.2 Cumulative survival without nonfatal myocardial infarction (composite outcome 1) among experimental (Mediterranean group) patients and control subjects



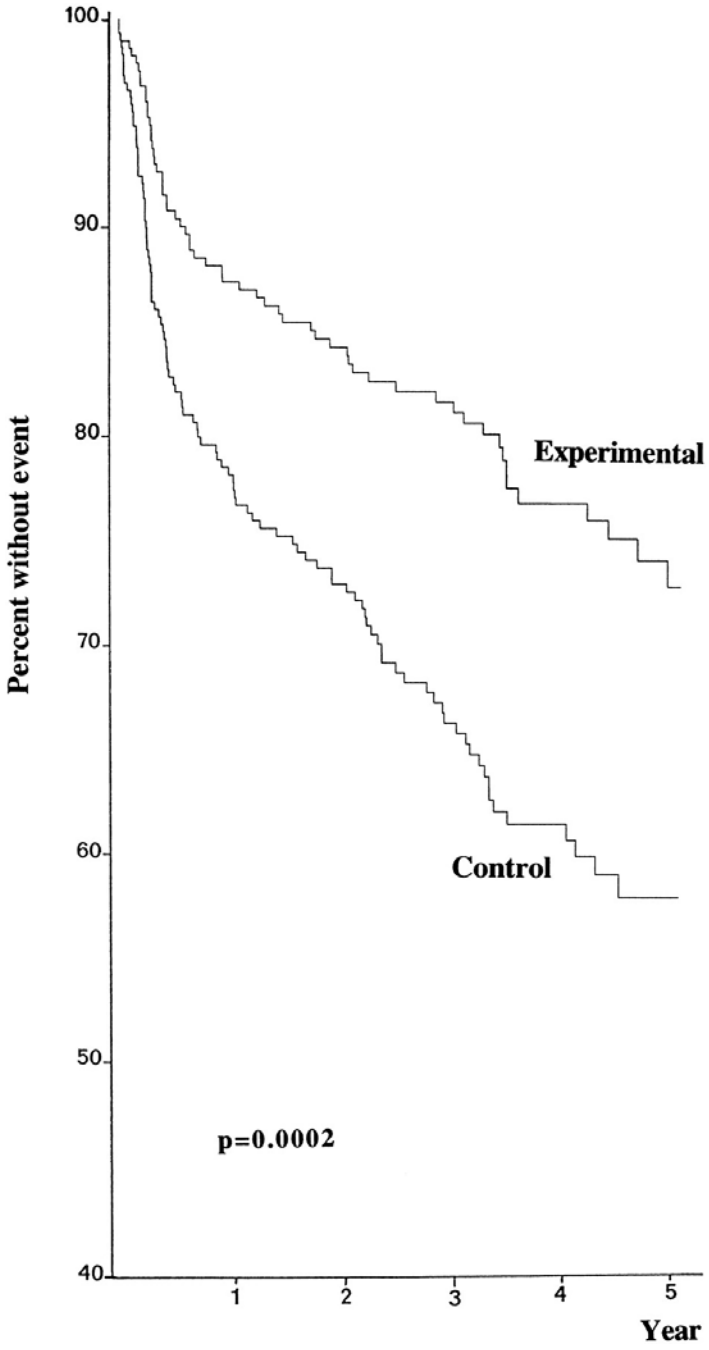
Source (de Lorgeril et al, 1999 pg 781)

Figure 2.3 Cumulative survival without nonfatal infarction and without major secondary end points (composite outcome 2)



Source (de Lorgeril et al, 1999 pg 781)

Figure 2.4 Cumulative survival without nonfatal infarction, without major secondary end points, and without minor secondary end points (composite outcome 3)



Source (de Lorgeril et al, 1999 pg 782)

Event free survival was statistically significantly longer in the intervention group compared to the control group over the 5 years in all three analyses using different classifications of "event free".

Morbidity

No morbidity outcomes were reported.

2.4 Program costs

As reported by trial

The study reports (de Lorgeril et al 1994; de Lorgeril et al 1996 and de Lorgeril et al 1999) do not report any costs associated with the Mediterranean diet intervention.

Based on resource use

Screening, recruitment and research:

The following costs were estimated for the overall study including both the intervention and the control groups.

Table 2.10 Costs of screening, recruitment, study design and set up

	Number	Time	Unit cost	Cost for entire study	Average cost per person
Screening interview	679	10 minutes	$122.15 per hour	$13,823.31	$22.85

The following assumptions were made when estimating the costs of screening, recruitment, study design and set up:

- The screening interview is performed by a physician at a cost of $122.15 per hour (AMA, 2003)
- 679 people are screened to enrol 605 (deLorgeril et al, 1994)
- A screening visit lasts an average of 10 minutes

Mediterranean diet group:

Consultation costs, administration costs, assessment costs and the cost associated with treatment of AMI are relevant for the Mediterranean diet intervention arm (Table 2.11 and Table 2.12). The intervention is assumed to last one year (with annual follow up until year 4) and affect 302 people.

Table 2.11 Consultation costs incurred based on resource use for the Mediterranean diet group

Item	Number required per person (n=605)	Cost per hour	Cost for intervention arm	Average cost per person
Initial consult with attending physician	1	$122.15	$6,148.22	$20.36
Initial consult with dietician	0.25	$65.40	$4,937.70	$16.35
Consultation with cardiologist	1	$168.50	$50,887.00	$168.50
Consultation with dietician	1	$32.70	$17,281.95	$57.23
Annual follow up visit	4	$32.70	$39,501.60	$130.80

The following assumptions regarding consultation costs were made:

- Only a quarter of people will receive a consultation in hospital with a dietician
- All consults are assumed to take one hour except initial consult with physician which is assumed to last 10 minutes
- A hospital physician is assumed to cost $122.15 per hour (AMA, 2003)
- A dietician is assumed to cost $63.85 for an initial consult and $31.90 for a subsequent consult (Dept of Veteran Affairs, 2003)
- A cardiologist is assumed to cost $168.50 (AMA visiting specialist rate in NSW, 2003)

Table 2.12 Administration and program costs incurred based on resource use for the Mediterranean diet

Item	Number required per person	Cost per item	Cost for intervention arm	Average cost per person
Margarine	4x500grams per year	$2.76	$3,334.08	$11.04
Written instructions	1	$1.27	$383.54	$1.27

The following assumptions regarding administration costs were made:

- Margarine costs $2.76 per 500grams (Coles online, 2004) and 4 items are required per year for those in the Mediterranean diet group
- Each person in the Mediterranean diet group receives written instructions (Based on quote for A4 booklet of 8 pages of 300 for $345 (ex GST) from Melbourne University Design and Print Centre 2003 +GST10%= $1.27)
- The cost of consuming a Mediterranean diet is assumed to be similar to a prudent Western diet and is therefore excluded

Table 2.13 Assessment costs

	Number required	Unit cost	Cost for intervention arm	Average cost per person
Outpatient clinic visit	1 per person	$122.15	$36,889.30	$122.15
Questionnaires	3 per person	$1.27	$1,150.62	$3.81

Table 2.14 Costs of treating AMI in intervention group

	Number of AMIs	Cost per AMI	Cost for intervention arm	Average cost per person
Mediterranean group	8 per 302 patients	$3,712.02	$29,696.16	$98.33

The following assumptions were made when estimating the costs of treating AMI:

- The cost of treating AMI is $3.712.02 per episode (AR-DRG F60B, Australian Hospital Statistics 2000-01 for public hospitals, AIHW 2003)

Western diet group:

The western diet group also are assumed to receive an initial consult with a physician and one follow up visit in total (compared to 4 for the intervention group). Control patients are assumed to incur assessment costs. The number and cost of AMIs for the control group is summarised in Table 2.15.

Table 2.15 Costs of treating AMI in control group

	Number of AMIs	Cost per AMI	Cost for intervention arm	Average cost per person
Western group	25 per 303 patients	$3,712.02	$92,800.50	$306.27

Total costs:

Table 2.16 summarises the total costs for each study arm and the costs per person for the study period.

Table 2.16 Total costs per person

Type of cost	Mediterranean diet		Western diet	
	Cost for study arm	Average cost per person	Cost for study arm	Average cost per person
Screening and recruitment	$6,911.65	$22.85	$6,911.65	$22.85
Consultation	$118,756.47	$393.23	$11,085.92	$36.71
Administration	$3,717.62	$12.31	$0.00	$0.00
Assessment	$38,039.92	$125.96	$0.00	$0.00
AMI treatment	$29,696.16	$98.33	$92,800.50	$306.27
Total	$197,121.82	$652.68	$110,798.07	$365.83

2.5 Performance

Cost effectiveness

Costs associated with the Mediterranean and western diet groups were summarised in Table 2.16.

The total number of life years lost and the number of myocardial infarctions for the intervention and control groups is summarised in Table 2.17.

Table 2.17 Number of deaths and myocardial infarctions during the trial

	Mediterranean diet group (%)	Western diet group (%)
Non fatal acute myocardial infarction	8/219 (3.7)	25/204 (12.3)
All cause mortality	14/219 (6.4)	24/204 (11.8)

This leads to the following ICERs:

Myocardial infarctions averted:

=($652.68-$365.83)/(0.123-0.037)
=$286.85/0.086
=$3,335.47 per myocardial infarction averted for the Mediterranean compared to western diet groups during the 4 year period of the trial

Deaths averted:

=($652.68-$365.83)/(0.118-0.064)
=$286.85/0.054
=$5,312.04 per death averted for the Mediterranean compared to western diet groups during the 4 year period of the trial

Cost utility

The published literature indicates a utility of 0.88 for the health state post-myocardial infarction using the time trade off method with patients (Lee et al, 1997). This compares to a utility of 1.0 for perfect health or “no event” and a utility of zero for death.

Table 2.18 reports the utilities associated with the myocardial infarctions reported in the study by de Lorgeril et al (1999).

Table 2.18 Utilities associated with health states reported in the study by de Lorgeril et al (1999)

	Mediterranean diet group n=219		**Western diet group n=204**	
	No. people (%)	Utility	No. people (%)	Utility
Non fatal acute myocardial infarction	8 (3.7)	0.03256	25 (12.3)	0.10824
All cause mortality	14 (6.4)	0	24 (11.8)	0
No event	197 (89.9)	0.898	155 (75.9)	0.759
Total		0.93056		0.86724
Difference				**0.06332**

This translates into the following incremental cost utility for Mediterranean diet compared to western diet for the 4 year period of the trial:
ICER=($652.68-$365.83)/(0.93056-0.86724)
=$286.85/0.06332
=$4,530.16 per additional QALY gained per person during the 4 year period of the trial.

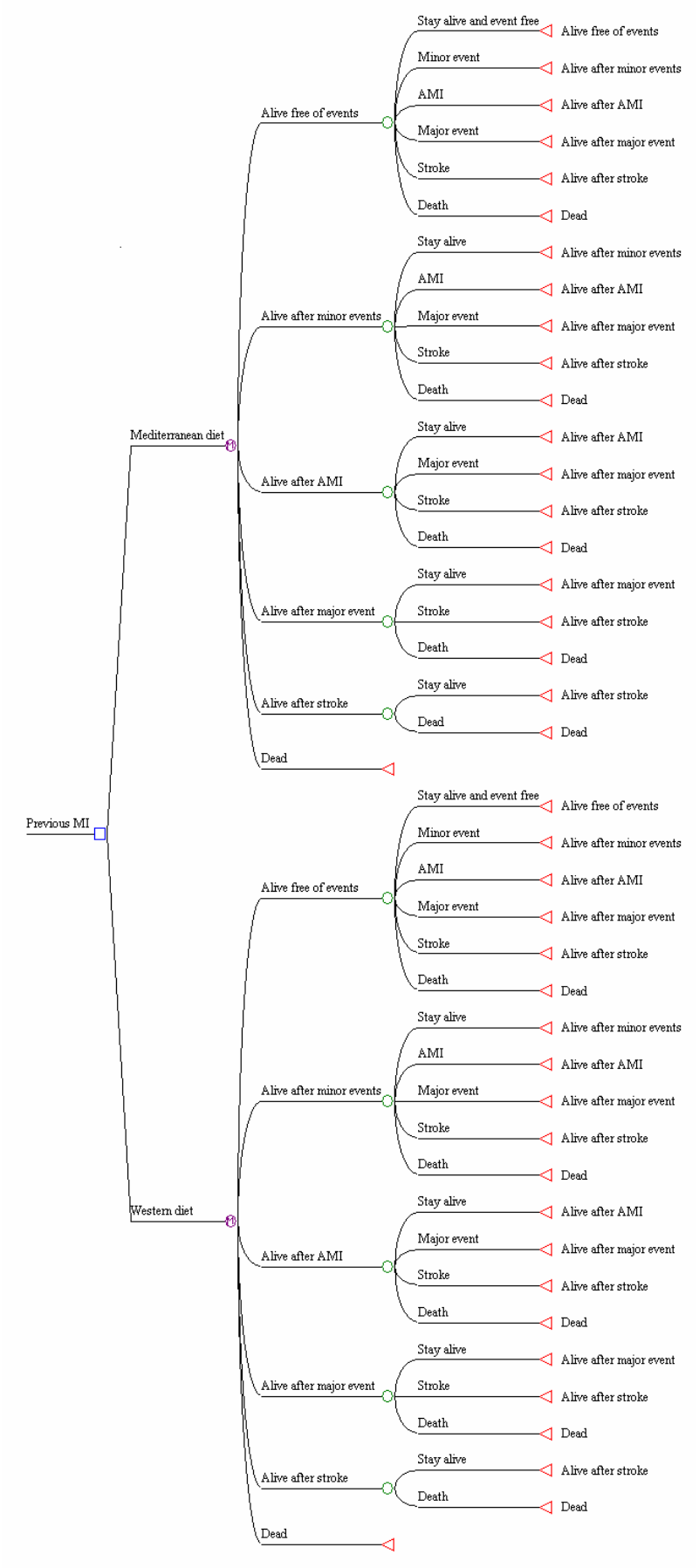
This however, excludes possible benefits beyond the trial. Longer term projection is modelled below.

2.6 Modelling

Methods

A modelling approach was used to enable the short term outcomes (reported by deLorgeril et al, 1999) to extrapolated longer term and translated into life-years saved and QALYs gained. A Markov process structure was developed comprising 1 year cycles. The time horizon of the model was 10 years. The model includes the health states alive free of events, alive after minor events (such as stable angina), alive after AMI, alive after major events (such as unstable angina or pulmonary embolism), alive after stroke and death. The transitions that are permitted are illustrated in Figure 2.5.

Figure 2.5 Representation of states and permitted transitions in Markov model



We determined the progression, costs and utilities of a cohort of 1000 people receiving the Mediterranean diet compared with a prudent western diet.

The cohort progressed annually between health states over an 11-year time horizon according to transition probabilities derived from the published literature (Table 2.19). The model commences with all people in the alive free of events health state. It is assumed that transitions from alive free of events will continue at the probabilities described below for the length of the model. It is also assumed that transitions from states other than alive free of events are permitted from years 2 onwards.

Table 2.19 Transition matrix for each study group

Intervention group	Alive free of events	Alive after minor event	Alive after AMI	Alive after major events	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 events	-	-	-	#	0.015	0.170
Alive after stroke	-	-	-	-	#	0.22
Dead	-	-	-	-	-	1

Control group	Alive free of events	Alive after minor event	Alive after AMI	Alive after major events	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 events	-	-	-	#	0.015	0.170
Alive after stroke	-	-	-	-	#	0.22
Dead	-	-	-	-	-	1

residual value, - no transition permitted

The costs for each of the study groups for year 1 were taken from Table 2.16. The cost of AMI was excluded from the base case analysis with down stream costs associated with each health state included in sensitivity analysis. The cost of the annual follow up visit was not included in year 1 but was included each year for years 2-5.

Costs and benefits are discounted at 5% per annum. The transition probabilities, costs and utilities along with their sources are shown in Table 2.20.

Table 2.20 Description of transition probabilities, costs and utilities along with values and sources

Description	Value	Source
Transition probabilities		
Alive after AMI to dead	0.159	Peltonen 2000 (combined M/F for yr 93-94)
Alive after AMI to alive after major events	0.183	AMI to PE, Antiplatelet Trialists' Collaboration 1994 ref41
Alive after AMI to alive after stroke	0.055	AMI to non-fatal stroke (Antiplatelet Trialists' Collaboration 1994) App1 ref#43
Alive free of events to alive after AMI Mediterranean diet group	0.010*	Fig 16.1 + death
Alive free of events to alive after AMI western diet group	0.034*	Fig 16.1 + death
Alive free of events to dead Mediterranean diet group	0.017*	de lorgeril et al 1999, rate converted to probability
Alive free of events to dead western diet group	0.033*	de lorgeril et al 1999, rate converted to probability
Alive free of events to alive after major event Mediterranean diet group	0.016*	de lorgeril et al 1999, rate converted to probability
Alive free of events to alive after major event western diet group	0.136*	de lorgeril et al 1999, rate converted to probability
Alive free of events to alive after minor event Mediterranean diet group	0.091*	Difference between fig 16.2 and 16.3, deLorgeril et al, 1999 pg 781
Alive free of events to alive after minor event western diet group	0.144*	Difference between fig 16.2 and 16.3, deLorgeril et al, 1999 pg 782
Alive free of events to alive after stroke Mediterranean diet group	0.000*	deLorgeril et al 1999, rate converted to probability
Alive free of events to alive after stroke western diet group	0.005	de lorgeril et al 1999, rate converted to probability
Alive after major events to dead	0.170	5 year survival for all PE table 1 Heit et al 1999
Alive after major events to alive after stroke	0.015	Non fatal stroke in those with unstable angina (Antiplatelet Trialists Collaboration, 1994) App1 Ref#83
Alive after minor events to alive after AMI	0.014	MI following stable angina (Antiplatelet Trialists' Collaboration 1996) App1 Ref#130
Alive after minor events to dead	0.033	Alive free of events to dead control group (deLorgeril et al,1999)
Alive after minor events to alive after major events	0.03	Researcher judgment
Alive after minor events to stroke	0.011	Tanne et al 2002, cumulative incidence of ischemic stroke in patients with angina class 2
Alive after stroke to dead	0.220	Probability of survival 5 years after stroke (Table 2) X RR of already having CHF 2.28 (Petty 1998) adjusted for prevalence of CHF in original population
Costs		
Cost of Mediterranean Diet- Year 1	$433.40	($32.70 for years 2-5) See cost section of report
Cost of Western Diet- Year 1	$36.71	See cost section of report

Description	Value	Source
Quality of life adjustments		
Utility AMI	0.88	AMI ref 182 (Lee et al 1997)
Utility of event free	0.93	Post MI with no angina, no CHF ref 147 (Kunz, Tsevat, Goldman in Circulation 1996)
Utility major events	0.78	Post AMI with severe angina (Kunz, 1996)
Utility minor events	0.89	Post MI with mild angina and no CHF (Kunz, 1996)
Utility stroke	0.54	After stroke post MI ref 134 (Derdeyn, 1996)
Other parameters		
Discount rate for outcomes	0.05	Australian Treasury
Discount rate for costs	0.05	Australian Treasury

*estimated assuming that events roughly translate to people

Extensive univariate sensitivity analyses were performed for the assumptions and values described in Table 2.21.

Table 2.21 Sensitivity analysis: Attributes, base case and alternative assumed values

Assumptions	Base case	Alternative Values	Source
Downstream costs			
- AMI	$0	$3,712.02	AR-DRG F60B, Australian Hospital Statistics 2000-2 for public hospitals, AIHW 2003
- minor events	$0	$3,430.00	ACE Heart Disease Study based on Victorian Admitted Episodes Database (VAED) and Cos MIC study for first ever acute coronary syndrome (ACS) comprising hospitalising angina or AMI, cost for subsequent years
-major events	$0	$9,764.00	ACE Heart Disease Study based on Victorian Admitted Episodes Database (VAED) and Cos MIC study for first ever acute coronary syndrome (ACS) comprising hospitalising angina or AMI, cost for first year
-stroke	$0	$10,000	Approximated using lifetime cost of $41,706 from the ACE Heart Disease study based on NEMSIS and average survival from DisModII.
Time horizon	10 years	5, 15 and 20 years	Researcher judgment
Discount rate	5%	0% and 3%	Researcher judgment
Length of intervention benefit	10 years	1, 3 and 5 years	Researcher judgment
Utilities	See table 16.20	+0.5 and -0.5	Researcher judgment

Results

Table 2.22 presents the economic performance of the Mediterranean diet, and an incremental cost utility ratio of $339 per QALY gained (for base case assumptions, see Table 2.20).

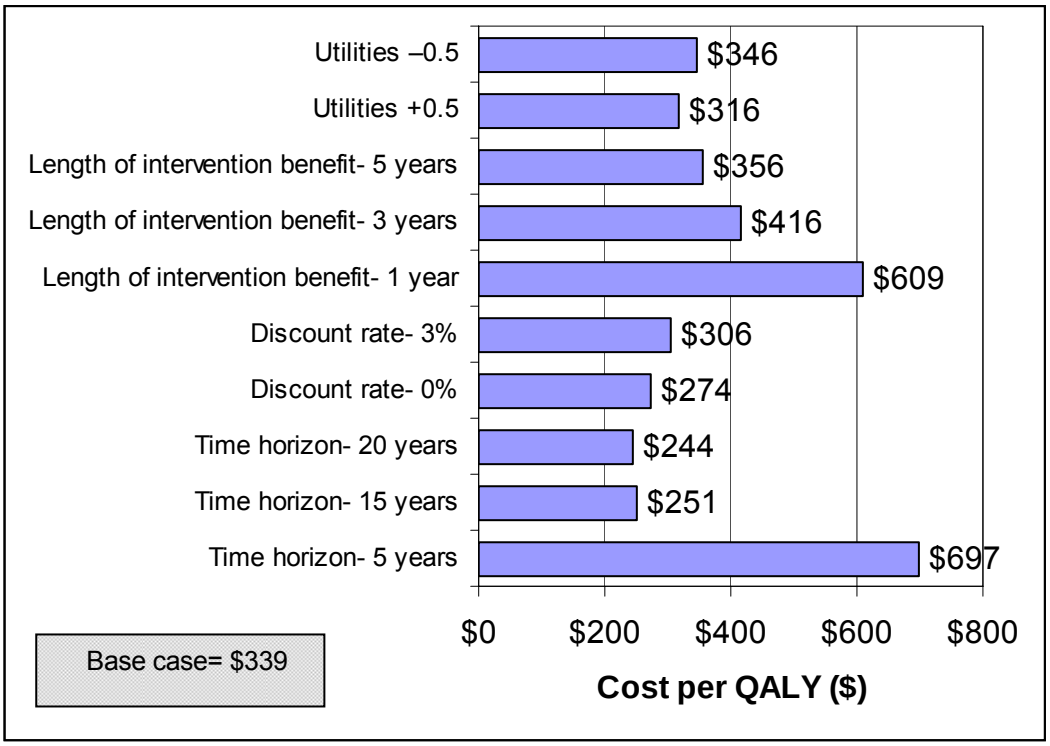
Table 2.22 Modelled cost utility base case results

	Mediterranean diet	Western diet	Difference
Total costs	$523.20	$35.00	$488.20
Total life years	6.78	5.46	1.32
Total QALYs	6.12	4.68	1.44
Discounted $/LY gained			$369
Discounted $/QALY gained			$339

Sensitivity analyses

Sensitivity analyses ranged from $244 per QALY to $697 per QALY (Figure 2.6). Results were most sensitive to the time horizon of the model, although remain highly cost effective under all scenarios.

Figure 2.6 Results of sensitivity analyses



Inclusion of downstream costs

When downstream costs are included for the first year following each event (from Table 2.21) the Mediterranean diet intervention dominates the control group as it is cheaper and more effective (Table 2.23).

Table 2.23 Modelled cost utility- inclusion of downstream costs

	Mediterranean diet	Western diet	Difference
Total costs	$18,000	$32,000	-$14,000
Total life years	6.78	5.46	1.32
Total QALYs	6.12	4.68	1.44
Discounted $/LY gained			Mediterranean diet dominates
Discounted $/QALY gained			Mediterranean diet dominates

The Mediterranean diet will prove even further cost saving if state costs are also included, or in other words the ongoing management costs associated with caring for a person each year for the rest of their life once they have experienced an event. These state costs would be particularly important for a debilitating event such as a stroke.

3. Effects of a reduced fat diet in those with impaired glucose tolerance

3.1 Description

Intervention type

A nutrition intervention with the aim of reducing the total amount of fat in the diet can be achieved via education, goal setting and evaluation. Monthly group sessions are the means of translating the intervention into practice.

Reference

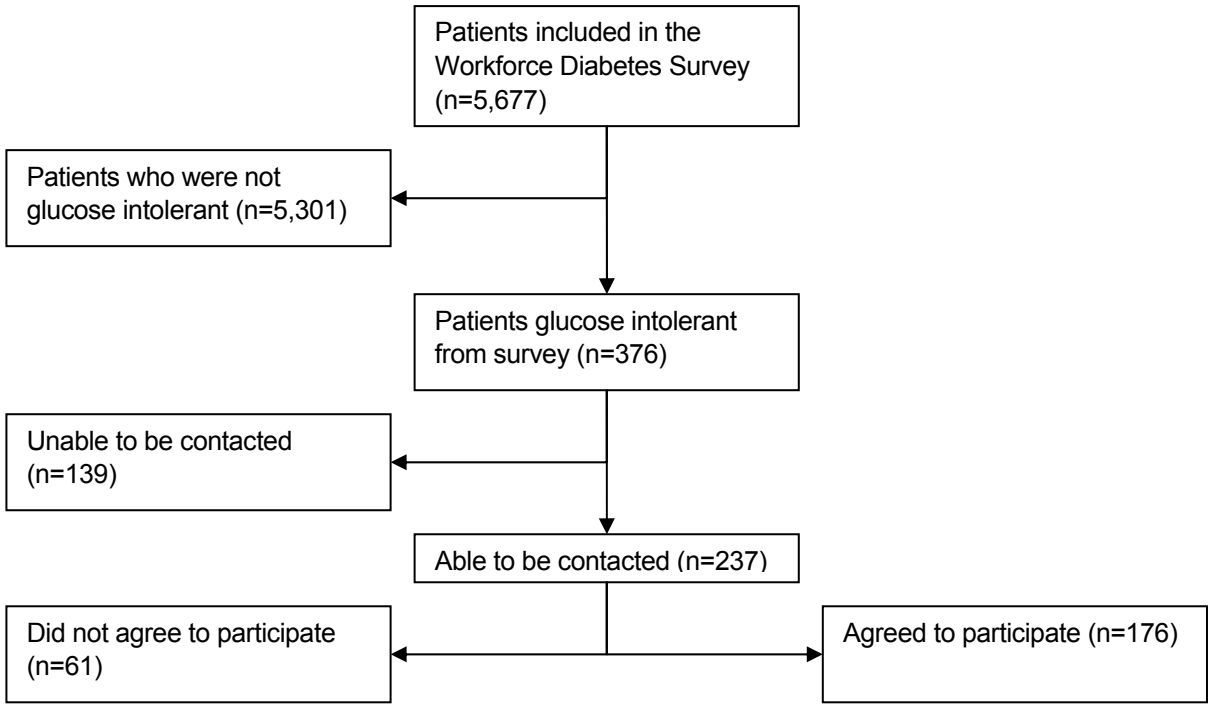
This analysis of the effects of a reduced fat diet on those with glucose intolerance is based on studies by Swinburn et al (2001) and Swinburn et al (1999) conducted in Auckland, New Zealand. The intervention targeted patients with impaired glucose tolerance, age over 40 years, selected from a previous Workforce Diabetes Survey between 1988 and 1990.

The objective of this study was to examine the long-term impact of the reduced-fat-diet program on body weight, glucose tolerance, and development of type 2 diabetes.

Recruitment: target population and participants

Participants were selected from a previous Workforce Diabetes Survey in which oral glucose tolerance tests were performed on 5,677 workers from 41 sites around Auckland, New Zealand. A total of 162 (2.8%) participants from the previous survey were classified as having impaired glucose tolerance (IGT) defined as 2 hour blood glucose 7.8 to 11.0 mmol/l. A further 114 (2%) workers from the previous survey were classified as having high normal blood glucose concentrations (7.0 to 7.8 mmol/l). This gave a combined "glucose intolerant" group of 376 of whom 237 (63%) were able to be contacted and 176 (74%) entered the study (Figure 3.1).

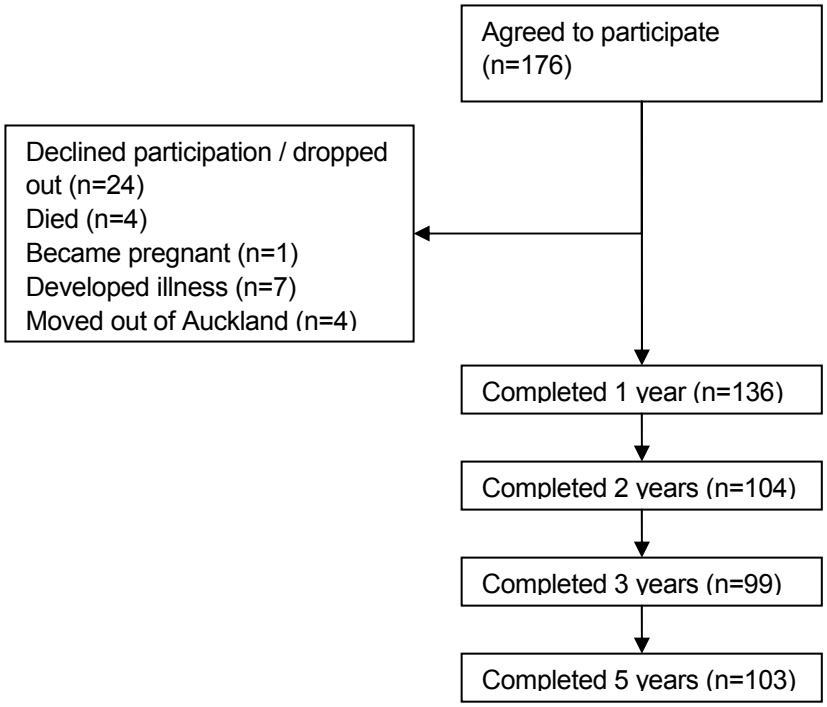
Figure 3.1 Summary of screening and recruitment



Source (Swinburn et al 1999, pg 1401)

Of the 176 individuals who agreed to participate in the study 136 (77%) completed 1 year of follow up and 103 (59%) completed 5 year follow up (Figure 3.2).

Figure 3.2 Summary of follow up



Source (Swinburn et al, 2001 pg. 619 & Swinburn et al 1999, pg 1401)

The demographic data for those in the intervention and control groups who completed the 1 year intervention are shown in Table 3.1.

Table 3.1 Baseline characteristics of the reduced-fat diet and usual diet groups

Variable	Reduced-fat diet group mean (±SEM) or n (%)	Usual diet group mean (±SEM) or n (%)
Number of participants	66	70
Age (years)	52.5 ±0.8	52.0 ±0.8
Sex (M:F)	45:21	56:14
Ethnicity		
European	44 (66.7)	53 (75.7)
Maori	7 (10.6)	5 (7.1)
Pacific Islander	13 (19.7)	9 (12.9)
Other	2 (3.0)	3 (4.3)
Anthropometry		
Weight (kg)	85.46 ±1.80	84.33 ±1.55
Body mass index (kg/m2)	29.08 ±0.55	29.17 ±0.48)
Waist circumference (cm)	100.48 ±1.42	101.60 ±1.28
Waist to hip ratio	0.944 ±0.008	0.954 ±0.008
Glucose tolerance test		
Fasting glucose (mmol/l)	6.7 ±0.2	6.6 ±0.2
2-h glucose (mmol/l)	7.5 ±0.3	7.9 ±0.3
fasting insulin (mIU/l)	16.0 ±1.1	15.8 ±0.9
2-h insulin (mIU/l)	50.2 ±4.2	47.0 ±3.8
Glucose tolerance status		
Normal	24 (36.4)	23 (32.9)
Impaired fasting glucose	11 (16.6)	15 (21.4)
Impaired glucose tolerance	10 (15.1)	9 (12.9)
Diabetes	21 (31.8)	23 (32.9)

Source (Swinburn et al 2001 pg. 621)

The study report states that there were no significant differences of baseline characteristics between the two groups (Swinburn et al 2001, pg 620).

Intervention

The reduced-fat dietary group entered a structured program aimed solely at reducing the amount of fat in their diet. The program consisted of monthly small group sessions with the following components:

- General education of reducing dietary fat
- Reasons for reducing fat
- Identification of high fat foods
- Identification of strategies to reduce fat intake
- Personal goal setting
- Self monitoring and evaluation

Participants were required to complete shorthand food diaries 2 days per weeks on a rotating basis. Participants were also required to calculate the fat content of their food using a simple fat-counter book.

3.2 Quality of trial

Recruitment

The study enrolled a total of 176 participants (74% of those contacted). It is not known if those who were unable to be contacted or declined participation differed significantly from those who agreed to participate in the trial.

The study does not report sample size calculations and it is possible that it did not enrol sufficient participants to demonstrate a statistically significant difference between the study groups.

Participants were randomly assigned to the reduced-fat diet or usual diet groups. The study report states that an unmarked envelope system was used although the precise method of randomisation is not described and no details of security and concealment are provided. Six participants (Pacific Island women) who all worked at the same worksite were cluster randomised to the intervention group to avoid contamination.

Of those patients enrolled a total of 136 (77%) completed the trial at 12 months. The follow up rates were similar in both groups.

Control group

The control or usual diet group continued their usual diet. They were given nutrition advice at the start of the trial, which was about healthy eating in general in accordance with the New Zealand Food and Nutrition Guidelines. Those with nutrition related problems such as high cholesterol or obesity received standard general information about these problems.

Evaluation method

The study does not state whether or not the results were analysed on an intention to treat basis. On inspection it appears that participants with incomplete data are excluded from the analysis. This may to lead to an overestimation of study effect as participants with incomplete data may be less likely to perform well.

Mean and standard errors are adjusted for age, sex, ethnicity and baseline measurement. A repeated measures model was used and analyses were performed using random coefficients models. Comparisons of the groups were made using chi-squared and t-tests.

Subgroup analysis was performed for compliance. It is not known if the study had sufficient power to detect differences in a subgroup. The subgroup analysis was not specified a priori. There are potential differences other than their compliance between the two subgroups (eg general health, other conditions, weight or race) which may also influence the outcomes.

Outcome measures

At baseline and 12 months participants completed a 3-day food diary. Foods were measured using standard cups, spoons and weight approximation diagrams. The diaries were analysed for the following components: energy, fat, % of energy as fat, carbohydrate, % of energy as carbohydrate, protein, % energy as protein, alcohol, % energy as alcohol and fiber.

Weight, body mass index, fasting glucose and 2 hour glucose were measured at baseline, 6 months, 1, 2, 3 and 5 years. Fasting insulin and 2 hour insulin measurements were taken at baseline, 6 months and 1 year.

The main potential for bias is the 3-day self report food diaries. It is possible that because participants were recording diet for these 3 days that they would alter their diet from normal for this period only. Or it is also possible that participants would report a more favourable diet than was actually consumed. This may lead to inaccurate measurements of nutritional intake at each time point for both groups. The study does not state if patients, investigators and outcome assessors were blinded to group allocation.

Bias, confounders, efficacy

The study was randomised and the baseline characteristics of the two groups were similar which lessens the chance of bias.

The study does not state if allocation was concealed from patients, investigators and outcome assessors. It is unclear if the groups were treated equally in all ways other than the intervention, very little detail is provided of doctor visits and ongoing medical treatment.

By year 5 of follow up 58% of participants were assessed. There is some indication that those dropping out of the trial had different characteristics and results to those remaining. Further strengthening the possibility of bias was the lack of intention to treat analysis and the omission of patients not completing assessment from the analysis.

The high proportion of Maori and Pacific Islanders in the study is due to the selection of industries with higher numbers of Polynesian employees for the original Workforce Diabetes Survey. This may affect the generalisability of the results to other groups.

3.3 Outcomes – as reported

The analyses compare outcomes between the intervention and control groups and Table 3.2 shows the main analyses reported in the study.

Table 3.2 Outcome measures, data sources and analyses reported in the trial

Outcome measures	Data sources	Analyses
BEHAVIOUR CHANGE		
Dietary changes	Changes in energy, macronutrients and fibre intake recorded from 3 day self-reported food diaries	Comparison between groups with mean, mean change, SEM and p values presented.
Changes in exercise	Increases in recreational exercise measured annually for 4 years. Method of measurement is not stated.	Proportion in each group increasing exercise and proportion exercising to lose weight.
Smoking	Proportion of each group ceasing smoking at 12 months. Method of measurement is not stated.	Proportion ceasing in each group.
CLINICAL PARAMETERS		
Weight	Weight was recorded wearing lightweight clothing and no shoes on a Seca 2000 scale	Comparison between groups annual for 5 years using mean, SEM and p values.
BMI	Weight calculated as above. Height measured with a stadiometer attached to the Seca 2000 scale. BMI= kg/m^2	Comparison between groups annual for 5 years using mean, SEM and p values.
Glucose tolerance • Diabetes • IGT • Impaired fasting glucose • Insulin	A standard oral glucose tolerance test (OGTT) was performed at each review. Diabetes, IGT and impaired fasting glucose were classified using the revised WHO criteria.	Comparison between groups annual for 5 years using mean, SEM and p values (except insulin reported for 12 months only)
Subgroup analysis by compliance • Weight • Fasting glucose • 2-hour glucose	Compliance score was equal to the % of monthly meetings attended and the % of diet diary completed. Those above the median were classified as compliers.	Subgroup analysis was performed for compliers and non-compliers.
SERVICE UTILISATION		
Not reported		
MORTALITY		
Not reported		
MORBIDITY		
Not reported		

Behaviour change

Table 3.3 shows the mean change in energy, macronutrient and fiber intake for the intervention and control groups at 12 months compared to baseline.

Table 3.3 Mean change in energy, macronutrient and fiber intake for the reduced fat diet and control diet groups at 12 months

	Reduced-fat diet group (n=49)			Control diet group (n=61)			
	Baseline mean (±SD)	**1 year mean (±SD)**	**Change mean (±SD)**	**Baseline mean (±SD)**	**1 year mean (±SD)**	**Change mean (±SD)**	**P value**
Energy (kcal)	2,195 (610)	1,832 (481)	-362 (92)	2,366 (693)	2,307 (856)	-59 (93)	0.016
Fat (g)	86.1 (32.6)	52.1 (24.5)	-34.0 (4.8)	96.5 (35.7)	90.0 (43.6)	-6.6 (4.5)	<0.0001
Fat % energy	34.6 (6.5)	25.9 (8.8)	-8.7 (1.3)	36.1 (6.6)	33.8 (7.2)	-2.3 (1.0)	<0.0001
Carbohydrate (g)	250 (74)	251 (90)	1.0 (14)	261 (80)	250 (73)	-11 (9)	0.49
Carbohydrate % energy	46.2 (8.3)	54.5 (11.7)	8.3 (1.5)	45.0 (9.1)	45.6 (10.1)	0.6 (1.2)	<0.0001
Protein (g)	91.3 (27.3)	83.6 (25.6)	-7.7 (3.7)	96.1 (31.1)	95.1 (45.3)	-1.0 (4.3)	0.25
Protein % energy	16.9 (3.3)	18.6 (4.1)	1.7 (0.6)	16.7 (4.1)	16.5 (3.8)	-0.2 (0.6)	0.025
Alcohol	14.6 (21.1)	10.0 (14.4)	-4.6 (20.5)	17.5 (29.2)	22.1 (34.0)	4.6 (25.8)	0.21
Alcohol % energy	4.4 (6.2)	3.5 (4.7)	-0.9 (0.8)	4.5 (6.7)	5.8 (7.9)	1.3 (0.7)	0.19
Fiber (g)	20.9 (8.1)	20.5 (10.1)	-0.4 (1.3)	19.4 (7.8)	18.4 (6.6)	-1.0 (1.2)	0.73
Fiber (g) g/1,000kcal	9.9 (3.9)	11.2 (4.8)	1.3 (0.6)	8.7 (3.7)	8.8 (3.2)	0.1 (0.5)	0.061

Source (Swinburn et al 2001, pg 621)

The total intake of energy in the reduced-fat diet group statistically significantly reduced compared to the control diet group. The amount of fat reduced in the reduced-fat diet group as did fat as a proportion of total energy. The reduced-fat diet group had a statistically significant increase compared to the control diet group in carbohydrates and protein as a proportion of total energy.

At the 12 month evaluation 20% of the reduced-fat diet group reported that they had increased their recreational physical activity compared with 9% in the control group (p=0.002). At 2 year follow up 21% of the reduced-fat diet group and 12% of the control group reported that they were exercising as way of losing weight (p=0.087). At 3 year follow up 13% of the reduced-fat diet group and 21% of the control group reported exercising (p=0.13).

At the 12 month evaluation 4 participants in the reduced-fat diet group and 2 in the control-diet group had quit smoking.

Clinical parameters

Weight, glucose and insulin:

Results for clinical parameters are presented in Table 3.4, for weight, BMI, fasting glucose, 2-h glucose, fasting insulin and 2-h insulin. Results for weight, BMI and glucose tolerance at all time points have been adjusted for age, sex, ethnicity and baseline measurements.

Table 3.4 Clinical parameter results for the reduced-fat diet (RF) and control diet (CD) groups assessed annually for 5 years as mean change from baseline (±SEM)

	Time (years)					
	Intervention period					
	0.5	**1.0**	**2.0**	**3.0**	**5.0**	**Overall effect of diet (p value)**
n (RF/CD)	66/70	66/70	47/57	48/51	51/52	-
Weight (kg)						
RF	-2.97 ±0.54	-3.32 ±0.68	-3.15 ±0.78	-1.60 ±0.78	1.06 ±0.64	<0.0001
CD	-0.08 ±0.43	0.59 ±1.61	1.06 ±0.46	2.13 ±0.70	0.26 ±0.68	
BMI (kg/m^2)						
RF	-0.99 ±0.18	-1.09 ±0.24	-1.01 ±0.28	-0.46 ±0.28	0.72 ±0.28	<0.0001
CD	-0.01 ±0.15	0.22 ±0.15	0.38 ±0.15	0.75 ±0.24	0.59 ±0.27	
Fasting glucose (mmol/l)						
RF	0.04 ±0.17	0.08 ±0.16	-0.17 ±0.26	-0.04 ±0.18	0.02 ±0.18	NS
CD	0.11 ±0.16	0.17 ±0.13	0.05 ±0.24	0.09 ±0.22	0.29 ±0.30	
2-h glucose (mmol/l)						
RF	-0.36 ±0.36	0.01 ±0.33	-0.76 ±0.42	0.20 ±0.37	1.02 ±0.40	<0.0001
CD	0.13 ±0.37	0.74 ±0.35	0.01 ±0.49	0.48 ±0.45	2.30 ±0.54	
Fasting insulin (mIU/l)						
RF	-3.71 ±1.58	-4.87 ±1.09	-	-	-	<0.0001
CD	-4.31 ±0.86	-3.80 ±0.83	-	-	-	
2-h insulin (mIU/l)						
RF	-12.02 ±6.16	-14.94 ±4.20	-	-	-	0.0103
CD	-6.20 ±3.64	-1.90 ±3.75	-	-	-	

Source (Swinburn et al, 2001 pg 622)

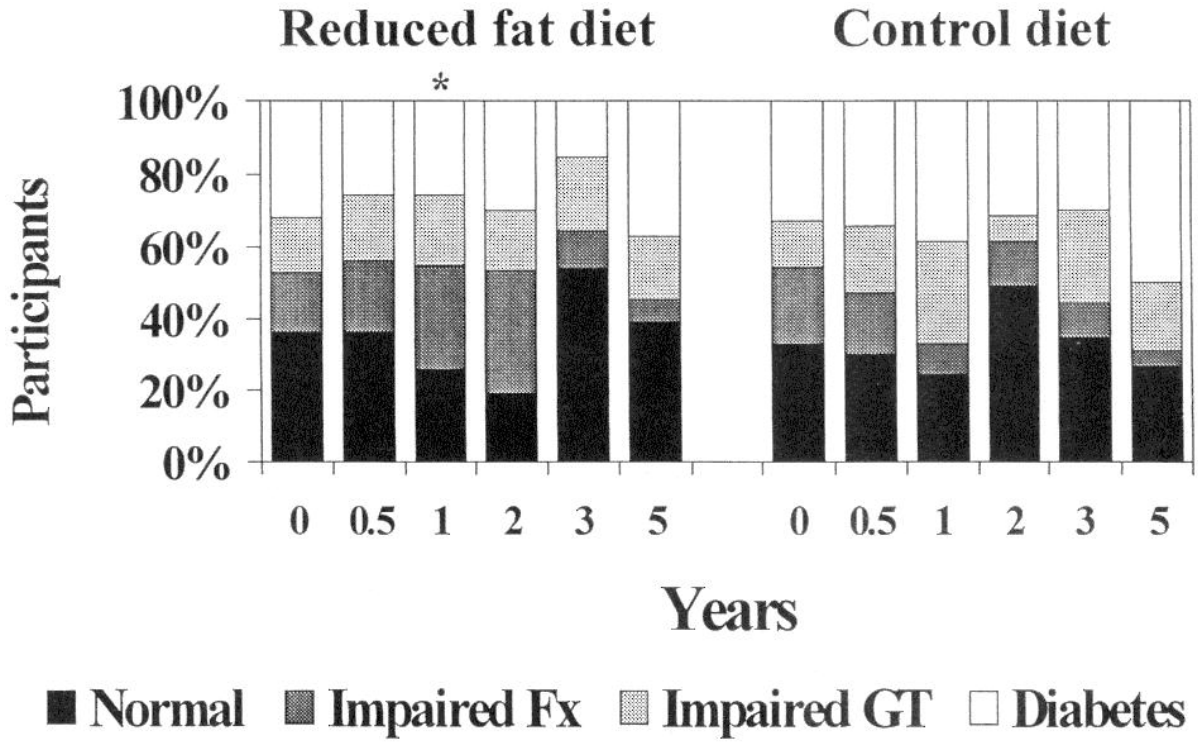
There were statistically significant changes over the 5 year follow up period for weight, BMI and 2-h glucose. There were also statistically significant changes over the 12 month follow up period for fasting insulin and 2-h insulin.

There were statistically significant differences between the groups for weight and BMI at all time points except 5 years, with more favourable outcomes reported for the reduced-fat diet group. Two hour insulin was statistically significantly lower at 12 months for the reduced-fat diet group compared to the control diet group.

Glucose tolerance:

Changes in glucose tolerance status over the 5 years follow up are shown in Figure 3.3.

Figure 3.3 Results over 5 years for glucose tolerance status for the reduced-fat diet and control diet groups



* statistically significant p<0.015

Source (Swinburn et al 2001, pg 622)

Glucose tolerance status was statistically significantly different at 12 months in the low-fat diet group compared to the control diet group. There was less impaired glucose tolerance or diabetes in the intervention group (47% compared to 67% in control group).

Subgroup analyses by compliance:

Compliance was measured only for the low-fat diet group. Those with compliance above the median were classified as “compliers”. Compliers had a significantly lower blood glucose level at fasting and 2 hour insulin levels at 5 years compared with the control-diet group whereas non-compliers showed no significant differences. The compliers had significantly lower weight in the first 3 years but not at 5 years. Compliers also showed lower fasting and 2 hour insulin levels at 1 year compared with the control-diet group.

Service utilisation

Not reported.

Mortality

Not reported.

Morbidity

Not reported.

3.4 Program costs

As reported by trial

The trial reports by Swinburn et al (2001) and Swinburn et al (1999) do not report any costs associated with the fat-reduced diet.

Based on resource use

The trial does not report how many of the 176 patients who agreed to participate were allocated to each group. We therefore assumed that half (n=88) were in each of the reduced fat diet and usual diet groups.

Intervention group (reduced fat diet) costs:

The costs associated with implementing a reduced-fat diet program would include consultation costs with a GP, education/training costs and monitoring costs to feedback progress to participants. The relevant costs are summarised in Table 3.5, Table 3.6 and Table 3.7 respectively.

Table 3.5 Consultation costs

	Number required	Length of consult	Cost per hour	Cost for study	Average cost per person
Screening interview	5,677	10	$122.15	$115,574.26	$656.67
Initial consultation	88	15	$122.15	$2,687.30	$30.54
Follow up consultation	88	15	$122.15	$2,687.30	$30.54

The following assumptions were made in estimating the consultation costs

- The cost of a GP is $122.15 per hour (AMA, 2003)
- 5677 screening interviews are required to enrol 176 people (Swinburn 1999)
- Each person requires one initial and one follow up consultation

Table 3.6 Education/training costs

	Number required	Unit cost	Items/sessions per year	Cost for group	Average cost per person
Trainer (dietician)	8.8	$63.85	12	$6,742.56	$76.62
Room rental	8.8	$25.00	12	$2,640.00	$30.00
Food diaries	1 per person	$4.95	1	$435.60	$4.95
Fat counter book	1 per person	$4.95	1	$435.60	$4.95

The following assumptions were made when estimating the eduction/training costs:

- Trainers would be required to run 12 sessions per year with a group size of 10
- A trainer would be a dietician who would cost $63.85 per hour (Dept of Veteran Affairs, 2003)
- Room rental would cost $25.00/ hour for each of the required group sessions (Australian Counselling Service, 2003)
- Patients would require 1 food diary and 1 fat counter book each

Table 3.7 Monitoring costs

	Number required	Rate	Cost for study	Average cost per person
Nutritionist III software	1	$873.01	$873.01	$4.96
Glucose tolerance test	88	$18.70	$1,645.60	$18.70
Insulin test	88	$80.00	$7,040.00	$80.00

The following assumptions were made when calculating the monitoring costs:

- The software is the Nutritionist Pro plus postage which costs US$610.50 (www.firstbank.com). This is converted into $AU on 27th Oct 2003 at a rate of 0.699302
- A glucose tolerance test costs $18.70 (MBS item number 66542, Nov 2002)
- An insulin test cost $80 (MBS item number 66689, Nov 2002)

Control group (usual diet) costs:

The control group would also incur screening costs and would require an initial consultation. The control group would also require costs associated with the food diary and fat counter books.

Total costs:

The total cost and the average cost per person for each group is presented in Table 3.8.

Table 3.8 Total cost and average cost per person for the two study groups

	LOW FAT DIET GROUP		USUAL DIET GROUP	
Type of cost	**Cost for group**	**Average cost per person**	**Cost for group**	**Average cost per person**
Consultation	$63,161.73	$717.75	$60,474.43	$687.21
Education/training	$10,253.76	$116.52	$871.20	$9.90
Monitoring	$9,122.11	$103.66	$0.00	$0.00
Total	$82,537.60	$937.93	$61,345.63	$697.11

3.5 Cost-effectiveness analysis

Data from the trial results alone are again used first to analyse economic performance. A successful health outcome is attributed to the reduced fat diet. The base case analysis provided therefore only captures health benefits over the five year follow-up period reported.

Outcomes

The results for weight and BMI at baseline 12 months and 5 years are presented in Table 3.9.

Table 3.9 BMI and weight at baseline, 1 year and 5 years

	Baseline	1 year	5 years
Weight (kg)			
Low fat diet	85.46	82.14	86.52
Usual diet	84.33	84.92	84.59
BMI (kg/m^2)			
Low fat diet	29.08	27.99	29.80
Usual diet	29.17	29.39	29.76

The costs of treatment for the two groups were summarised in Table 3.8.

Weight loss:

At 12 months the ICER for the low fat diet group compared to the usual diet group was as follows:
ICER= ($937.93-$697.11)/(2.97-0.08)= $240.82/2.89= $83.33 per additional kg lost over 12 months

At 5 years the usual diet dominates the low fat diet group as it is associated with less weight gain and a lower cost.

BMI:

At 12 months the ICER for the low fat diet group compared to the usual diet group was as follows:
ICER= ($937.93-$697.11)/(-1.09-0.22)= $240.82/1.31= $183.83 per additional BMI point reduction over 12 months

At 5 years the usual diet dominates the low fat diet group as it is associated with a smaller BMI increase and a lower cost.

Low fat diet compared to no control:

It is possible that the usual diet group received more than would occur in the clinical setting through involvement in the trial. For this reason we also compare the low fat diet group to a "no control" group which is assigned baseline values and no costs. This is also not ideal as all patients may change over time and we are unable to account for the possible effects of other confounders.

Cost-effectiveness results

The ICERs for the low fat diet group compared to "no control" are as follows:

Weight loss:

ICER= ($937.93-$0.00)/(2.97-0.0)= $937.93/2.97= $315.80 per additional kg lost over 12 months

BMI:

ICER= ($937.93-$0.00)/(1.09-0.0)= $937.93/1.09= $860.49 per additional BMI point reduction over 12 months

When the estimated 'downstream' cost savings are considered, the ICER is dominated by the reduced fat diet with both lower costs and improved health outcomes (refer Table 3.15).

3.6 Cost-utility analysis

From Figure 3.3, the approximate distribution of patients between the three health states of diabetes mellitus, glucose intolerance, and normal glucose tolerance can be derived. These have been estimated in Table 3.10 and expressed as probabilities. In the absence of data for the fourth year from baseline, an arbitrary assumption was made that the distribution comprised the mid-points between years 3 and 5.

As the intervention subjects had all regained weight by the fifth year of follow-up, modelling was not taken beyond year 5 as the health outcomes (and therefore costs) would have been no better. Any benefits, and incremental costs of the intervention, would be entirely captured within the first five years.

Table 3.10 Health State distribution of patients over 5 years

Health State	Baseline	Yr 1	Yr 2	Yr 3	Yr 4	Yr 5
TYPE 2	0.33	0.26	0.31	0.15	0.27	0.38
GL INTOL	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 sample size was not large enough to detect differences in the small number of deaths amongst those lost to follow-up. Modelling was therefore used to predict the number of deaths between the two groups.

Estimation of all-cause mortality

The approach used to estimate mortality in Chapter 7 was again used for this evaluation. Mortality estimates for each of the three health states of diabetes mellitus Type 2, Glucose Intolerance, and NGT were modelled from Australian Bureau of Statistics data. In Table 2.11, the 5-year cumulative mortality rates of the Australian population are shown by age group in Column 1 for the age group of interest, namely 50-54 year olds (Australian Bureau of Statistics, 2000). The mortality rates for the general population of 50-54 year olds was then adjusted to reflect the increased risk of mortality imposed by changes in metabolic state, and for degree of excess weight. The basis for the adjustment of risk was:

- *Adjustment for Metabolic State:* Balkau et al., 1993 reported that, compared with NGT, the relative risk of premature mortality was 2.1 for people with diabetes mellitus Type 2 and 1.6 for people with glucose intolerance (defined as impaired glucose intolerance). More recent evidence (Rockwood et al., 2000) report a relative risk of 1.9. For this evaluation, the mid-point of 2.0 was used to represent the relative of premature mortality due to diabetes mellitus Type 2. These relative risks for diabetes mellitus Type 2 and impaired glucose intolerance were used to adjust the mortality rates for the Australian general population to determine mortality rates by metabolic state Column 3. The general approach to this calculation was by solving for '*X*' in the following formula:

$$ABS = [2.0 \times X \times PType2] + [1.6 \times X \times PGI] + [X \times PNGT]$$

  Where:

  X is the (unknown) mortality rate for subjects with NGT

  ABS is the 5-year cumulative mortality rates of the Australian population (Source: ABS, 2000)

  PType2 is the prevalence of diabetes mellitus Type 2 in the Australian population (Dunstan et al., 2002).

  PGI is the prevalence of Glucose Intolerance in the Australian population, approximated from Dunstan et al., 2002.

  PNGT is the prevalence of NGT in the Australian population (Dunstan et al., 2002).

- *Adjustment for Degree of Overweight:* In order to reflect the study population who were all overweight, further adjustment of the mortality probabilities was necessary. A literature review was used to examine the relationship of weight to mortality. Under the assumption that the risk gradient for mortality from increasing levels of overweight is linear, the relative risk for the control group was conservatively estimated to be 1.2 (Manson, 1987; Rissanen et al., 1990) and the resulting mortality rates are shown in Column 5. For the intervention group, who achieved minor weight loss, a minimal reduction of 0.1 to an overall relative risk of mortality of 1.1 was assumed for the model (shown in Column 4).

Table 3.11 Estimation of mortality rates

1		2	3	4	5
Age Group	**ABS Mortality Rates (Cat No. 3302.0)**	**Metabolic Status**	**ABS Rates for General Population Adjusted for Metabolic Status #**	**Relative Risk of 1.1 (for Overweight)**	**Relative Risk of 1.2 (for Overweight)**
				Intervention Cohort	**Control Analysis**
50 – 54	0.0200	Type 2 D	0.0338	0.0371	0.0405
		Gluc Intol	0.0270	0.0297	0.0324
		NGT	0.0169	0.0186	0.0203

Adjustment assumes relative risk of 1.6 for Gluc Intol, and 2.0 for Type 2 D.

Overall health outcomes

The application of the mortality rates (Table 3.11) to the health state probabilities (Table 3.10) resulted in the following estimates of health outcomes.

Table 3.12 Estimated probability of survival from model (5-years)

Time from Baseline	Control	Fat-Reduced	Increment
Year 1	0.995	0.995	0.0000
Year 2	0.989	0.990	0.0002
Year 3	0.984	0.984	0.0003
Year 4	0.979	0.980	0.0009
Year 5	0.974	0.975	0.0014
Total (years)	**4.921**	**4.924**	**0.0027**
Discounted at 5% p.a. (years)	**4.476**	**4.479**	**0.0023**

The difference between 5.000 (years) and the total years is the all-cause mortality. The difference between the total years of the two groups is the life-years saved from the intervention.

Applying the utility values of the DiabCost study to the results in Table 3.12 generates Table 3.13.

Table 3.13 Estimated QALYs from model

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

From Table 3.13, the difference between 4.546 (5 years discounted) and the total QALYs is attributable to both differences in the various health states, with a greater proportion of control patients progressing to diabetes mellitus Type 2 relative to intervention patients, and of all-cause mortality. The difference between the total QALYs of the two groups is the QALYs gained from the intervention.

Downstream costs

The DiabCost study is a joint publication of the Australian Diabetes Society and the Australian Diabetes Educators Association. The results were published in September, 2002. The publication focuses specifically upon Type 2 diabetes mellitus in providing estimates of:

- Direct health costs to the health system.
- Out-of-pocket expenses borne by people with Type 2 diabetes mellitus.
- Community resources used by people with Type 2 diabetes mellitus.
- The impact of Type 2 diabetes mellitus upon quality of life.

Summary results of the DiabCost study are provided in Table 3.14 (for further detail on this study, refer Chapter 3 of this report).

Table 3.14 Health costs; DiabCost study; 2002

Cost Category	Overall Respondents	Complications			
		None	Microvascular	Macrovascular	Both
Health costs:					
Direct	$5325	$3990	$6990	$8985	$9610
Indirect	$351	$35	$35	$70	$35
Total	$5360	$4025	$7025	$9055	$9645
Govt Subsidies	$55402	$5075	$6200	$6120	$6240

[1] Comprises productivity losses due to ill-health or premature death. These costs are not incurred by the health sector directly.

[2] Includes welfare payments, referred to in economics as 'transfer payments'.

The DiabCost study estimates the average cost of treating a person with diabetes mellitus Type 2 is $5,325 per annum, being the average health care cost per patient with diabetes mellitus Type 2 from all people responding to the survey. Importantly, people in 'normal' health still use health care for a range of conditions and illnesses unrelated to overweight. The Australian Institute of Health and Welfare have estimated the average cost per person in Australia to be $2,817 per annum (AIWH, 2002).

Thus, the incremental cost attributable to diabetes mellitus Type 2 may be considered the difference between these two figures, or **$2,508** per patient per annum. These costs were applied to the time spent with diabetes mellitus Type 2 (Table 3.15).

Table 3.15 Estimated health costs attributable to diabetes mellitus Type 2

Year from Baseline	Control	Fat-Reduced	Savings
Year 1	$947.45	$646.49	$300.96
Year 2	$991.21	$767.52	$223.69
Year 3	$733.72	$361.06	$372.66
Year 4	$979.56	$647.04	$332.52
Year 5	$1,223.74	$931.09	$292.65
Totals	**$4875.68**	**$3353.20**	**$1522.48**
Discounted at 5% p.a	**$4409.92**	**$3029.90**	**$1380.01**

Cost-Utility Results

If the estimated savings from reduced health care management costs of $1,380 per patient (Table 3.15) are considered, the intervention becomes dominant with both improved health outcomes and resource savings (Table 3.15).

3.7 Sensitivity analysis

Undiscounted results

If cost-offsets and health outcomes are not discounted at 5% per annum, the results become:

- $88,463 per life-year saved.
- $9,064 per QALY gained.

Ignoring cost-offsets (savings)

Using the net incremental cost of $240.82 per patient (Table 3.8), and an average of 0.002 life-years saved (Table 3.12), the cost-effectiveness is:

- $103,486 per life-year saved.

Again using the net incremental cost of $240.82 per patient (Table 3.8), and an average of 0.024 QALYs gained (Table 3.12), the cost utility may be estimated as:

- $10,049 per QALY gained.

3.8 Discussion

The results are supportive of the value of this intervention. Inclusion of the estimated downstream savings from reduced health care management costs provides a particularly compelling argument.

However, even without the inclusion of those savings, at a cost of approximately $10,000 per QALY, the intervention remains attractive relative to other health care interventions receiving funding support. It is noted though that this conclusion remains reliant upon the utility estimate to generate the estimated QALY gain as, at cost of over $100,000 per life-year saved, this argument alone would be insufficient to justify support.

4. Orlistat and diet for treatment of obesity

4.1 Description

Intervention type

Orlistat acts by inhibiting intestinal fat absorption and is the only drug currently available in this class. It works by inhibiting pancreatic lipases; enzymes involved in the breakdown and thus absorption of fat. Orlistat should be used in conjunction with non pharmacological therapy in order to assist with weight loss.

References/ sources of evidence

The analysis of orlistat in conjunction with diet for obesity is based on a Cochrane review by Padwal et al (2003). The Cochrane review included 11 double blind, randomised controlled trials of orlistat used for overweight or obese adult patients.

The objective of the systematic review was to assess and compare the effects and safety of approved anti-obesity medications in clinical trials of at least one-year duration.

In addition a Health Technology Assessment (HTA) has been conducted which reports the cost-effectiveness of orlistat in the management of obesity (Foxcroft and Milne 2000).

The Cochrane review is the most recent, comprehensive analysis of the evidence and forms the evidence base for this chapter. The HTA is referred to in the cost-effectiveness section of this chapter only.

Participants and study characteristics

The Cochrane review by Padwal et al (2003) included 11 orlistat trials. These trials included a total of 6021 participants with an average BMI of 35.7kg/m^2, average weight of 100kg and average age of 49 years. The majority of participants (71%) were female and 80% were Caucasian. The number of participants in each trial ranged from 218 to 982. All of the included studies were multicentre trials, 6 were conducted in the US and 5 in Europe.

Three included studies specifically recruited patients with type 2 diabetes and another 3 enrolled patients with at least one cardiovascular risk factor.

A summary of the included trials is shown in Table 4.1.

Table 4.1 Summary of included trials

Author (year)	Study design	Country	Number of patients	Patient characteristics	Intervention
Bakris (2002)	RCT	USA	278 orlistat 276 placebo	Mean age 53 years Sex 61% female Mean BMI 35.6kg/m^2 Patients with treated hypertension	Orlistat 120mg 3x daily plus 600kcal/d deficit diet, dietician counselling and lifestyle modification literature
Broom (2002)	RCT	UK	265 orlistat 266 placebo	Mean age 46 years Sex 72% female Mean BMI 37.1kg/m^2 At least one CV risk factor	Orlistat 120mg 3x daily plus 600kcal/d deficit diet for 6 months then 900kcal/d deficit and food intake diary
Davidson (1999)	RCT	USA	668 orlistat 224 placebo	Mean age 44 years Sex 84% female Mean BMI 36.3kg/m^2	Orlistat 120mg 3x daily plus 500 to 800 kcal/d deficit diet, dietician led behaviour modification seminars, food intake diary and encouraged exercise
Finer (2000)	RCT	UK	114 orlistat 114 placebo	Mean age 41 years Sex 89% female Mean BMI 36.8kg/m^2	Orlistat 120mg 3x daily plus a 600 kcal/day deficient diet for 6 months then a 900k/cal/day deficit
Hauptman (2000)	RCT	USA	210 orlistat 120mg 213 orlistat 60 mg 212 placebo	Mean age 42 years Sex 78% female Mean BMI 36.0 kg/m^2	Orlistate120mg 3x daily or orlistat 60 mg 3x daily plus 1200k/cal per day deficit diet if <90kg and 1500k/cal per day deficit diet if >90kg. Educational videos, food intake record, and encouraged physical activity
Hollander (1998)	RCT	USA	163 orlistat 159 placebo	Mean age 55 years Sex 50% female Mean BMI 34.3kg/m^2 Higher CV risk population	Orlistat 120mg 3x daily plus a 500 k/cal/day deficient diet
Kelley (2002)	RCT	USA	274 orlistat 276 placebo	Mean age 58 years Sex 56% female Mean BMI 35.7 kg/m^2 Patients had type 2 diabetes	Orlistat 120 mg 3x daily plus 600kcal deficient diet adjusted to 800kcal deficit at 6 months, dietary counselling, encouraged exercise and daily multivitamin
Lindgarde (2000)	RCT	Sweden	190 orlistat 186 placebo	Mean age 53 years Sex 64% female Mean BMI 33.2 kg/m^2 Patients had at least 1 CV risk factor	Orlistat 120 mg 3x daily plus 600kcal/day deficit diet for 6 months then 900kcal/day deficit thereafter, nurse led dietary counselling sessions, encouraged exercise and self-help educational package
Miles (2002)	RCT	North America	255 orlistat 261 placebo	Mean age 53 years Sex 48% female Mean BMI 35.4kg/m^2 Higher CV risk population	Orlistat 120mg 3x daily plus 600kcal deficit diet adjusted to 800kcal deficit at 6 months, dietary counselling, encouraged exercise and daily multivitamin
Rossner (2000)	RCT	Europe	244 orlistat 120 mg 242 orlistat 60 mg 243 placebo	Mean age 44 years Sex 82% female Mean BMI 35.1 kg/m^2	Orlistat 120 mg 3x daily or orlistat 60mg 3x daily plus 600kcal/day deficit diet and food intake diary
Sjostrom (1998)	RCT	Europe	345 orlistat 343 placebo	Mean age 45 years Sex 83% female Mean BMI 36.1 kg/m^2	Orlistat 3x daily plus a 600kcal/day deficit diet for 6 months followed by a 900kcal/day deficit

Source (Padwal et al, 2003)

Intervention

In Australia Orlistat has TGA authority to treat overweight or obesity; defined by BMI >30kg/m^2 or >27kg/m^2 with other risk factors (eg hypertension, diabetes, hyperlipidaemia). The TGA recommended dose is 120mg 3x daily with major meals with no additional benefit gained by increasing the dose. Orlistat should be taken with a well balanced diet that is rich in fruit and vegetables and contains an average of 30% of calories from fat. Caloric restriction, increased physical activity and eating behaviour modification should accompany treatment (Australian Medicines Handbook, Jan 2003 and XENICAL consumer medicine information, 2003). Orlistat is not currently listed with the PBS in Australia.

Orlistat was used in accordance with the TGA recommendations in all 11 trials included in the systematic review. All trials used a 120mg dose 3x daily and were accompanied with diet intervention. Two trials also included a 3rd trial arm of orlistat at a lower dose (60mg 3x daily). All 11 orlistat trials were weight loss trials in which orlistat was used in conjunction with a weight loss diet for 1 year. Four of the 11 trials also contained a 2nd year of follow up which was aimed at weight maintenance (orlistat plus a weight maintenance diet). The low fat, low caloric diet was introduced during a run in period in 8 studies (ranging from 2-5 weeks) and at the point of randomisation in 3 studies.

The extent of the diet intervention varied between trials. All trials used a calorie deficient diet ranging from 500kcal/day to 1500kcal/day (median 600kcal/day). Six of the 11 trials increased the calorie deficiency after 6 months (median 850kcal/day). Eight of the 11 trials also included further dietary interventions (other than calorie deficient diet) such as exercise advice (5 trials), counselling (4 trials), food intake diaries (4 trials), vitamin supplements (2 trials), seminars (1 trial), videos (1 trial), and self-help packs (1 trial). See Table 3.1 for further details.

4.2 Quality of evidence

Selection of studies

A clear and comprehensive search strategy was used to identify relevant studies including an effort to identify unpublished studies. The systematic review had clear inclusion criteria for studies: double blind RCTs, anti obesity drugs, minimum follow up of 1 year from randomisation and full text publication. The review only included studies where participants were overweight or obese adults with BMI>30kg/m^2 or >27kg/m^2 plus one or more obesity related co-morbidities. Two reviewers independently assessed all potentially relevant studies for inclusion and disagreements were resolved by consensus.

Control group

The systematic review did not limit the possible control groups of included studies. All 11 orlistat trials, however, compared to a placebo plus diet intervention. It is not possible from the information provided to separate the effect attributable to diet alone from the effect of placebo. The effect of placebo for obesity has been described in a systematic review (Hrobjartsson et al 2001) and corresponded to a reduction in mean weight of 3.2% (95%CI 7.4% to -1.2%), although the overall difference compared to no treatment was not significant.

Variations in treatment effect between studies could be due to any number of variations between trials (such as methodological rigour, length of follow up, loss to follow up, type of patients as well as intensity of the diet intervention).

Quality assessment of included trials

The systematic review assessed the quality of the included trials by using the Verhagen Delphi list (Verhagen 1998, cited by Padwal et al 2003). Two reviewers independently assessed quality and disagreements were resolved by consensus. The following quality criteria were assessed and described for each study:

- Method of randomisation
- Concealment of treatment allocation
- Groups similar at baseline
- Eligibility criteria specified
- Blinded outcome assessment
- Blinded care provider
- Blinded patient
- Presentation of point estimates and measures of variability
- Intention to treat analysis

Method of data synthesis

The risk difference was calculated for dichotomous outcomes and the weighted mean difference for continuous outcomes. All analyses were based on an intention to treat basis. Meta analysis was performed using random effects models. Tests of heterogeneity were performed. Results were not pooled where there was significant heterogeneity. Values such as means and variance were calculated from original data where possible if missing in study reports.

Subgroup analyses were performed stratifying for cardiovascular risk, or particular conditions such as diabetes. Sensitivity analyses were also performed for the type of meta-analysis, the correlation coefficient, and stratification of studies according to whether they had a study run in period.

Outcomes reported

The main outcome measures of the systematic review were weight loss at one year, total and cardiovascular mortality and change in cardiovascular risk factors i.e. cholesterol and blood pressure. Other outcome measures included change in anthropometric indices, medication adverse effects and treatment adherence.

Bias, confounders, efficacy

The systematic review has taken a number of measures to minimise bias including transparency of reporting, clear study selection, thorough search strategy, inclusion by two independent reviewers, double data extraction, clear quality assessment of included studies and appropriate quantitative techniques for pooling results.

4.3 Outcomes – as reported

All analyses compare outcomes between the orlistat/diet and placebo/diet groups and Table 4.2 shows the main analyses reported in the review.

Table 4.2 Outcome measures, data sources and analyses reported in the trial

Outcome measures	Data sources	Analyses
BEHAVIOUR CHANGE		
Not reported		
CLINICAL PARAMETERS		
Weight loss	11 RCTs reported absolute number of kgs lost and 10 RCTs reported % weight loss	Random effects meta analysis
Waist circumference	5 RCTs reported waist circumference in cms	Results reported descriptively due to significant heterogeneity
Lipid parameters	10 RCTs reported reduction in total cholesterol and low density lipoprotein cholesterol. 8 RCTs reported high density lipoprotein cholesterol and 7 reported triglyceride levels	Random effects meta analysis
Blood pressure control	9 RCTs reported systolic blood pressure reduction and 8 reported diastolic blood pressure reduction	Random effects meta analysis
Metabolic parameters	9 RCTs reported fasting plasma glucose and 4 RCTs reported changes in HbA1c in high risk patients.	Fasting plasma glucose was reported descriptively due to significant heterogeneity and HbA1c was pooled using random effects meta analysis
Weight maintenance	4 RCTs reported the % of initial weight loss regained	Results reported descriptively due to significant heterogeneity
SERVICE UTILISATION		
Not reported		
MORTALITY		
Not reported		
MORBIDITY		
Adverse effects	All events reported in the 11 RCTs are described	Incidence reported descriptively for all conditions reported

Behaviour change

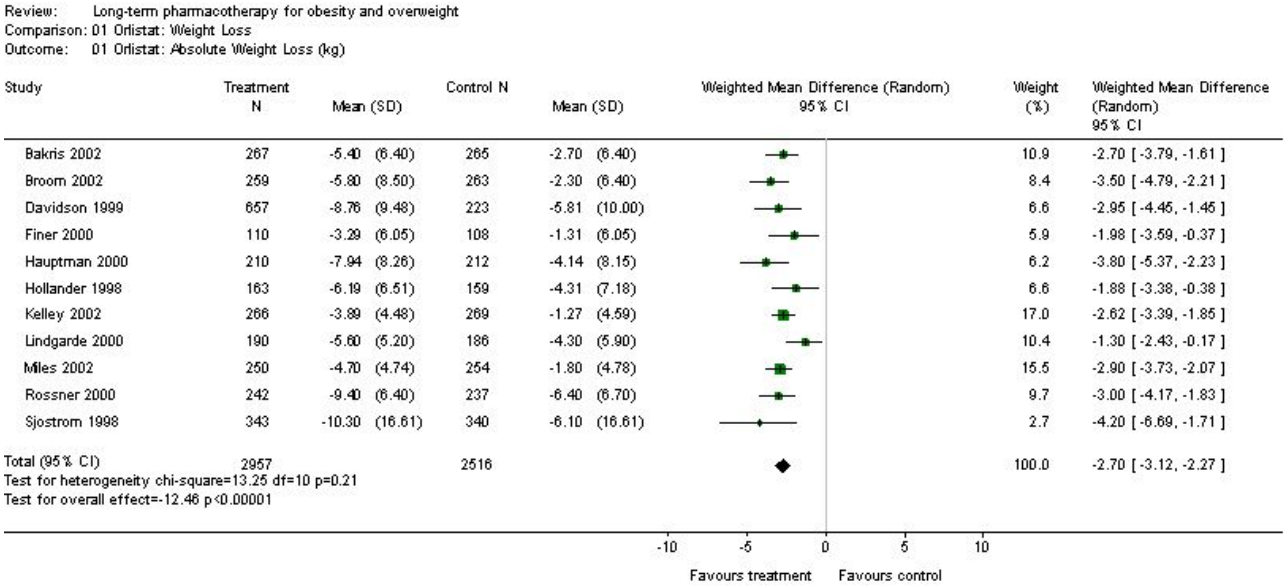
Not reported.

Clinical parameters

Weight loss:

All of the 11 RCTs reported greater weight loss in the orlistat group compared to placebo. Figure 4.1 shows a pooled weighted mean difference of 2.7kg (95%CI 2.3kg to 3.1kg) greater loss in the orlistat/diet group compared to placebo/diet.

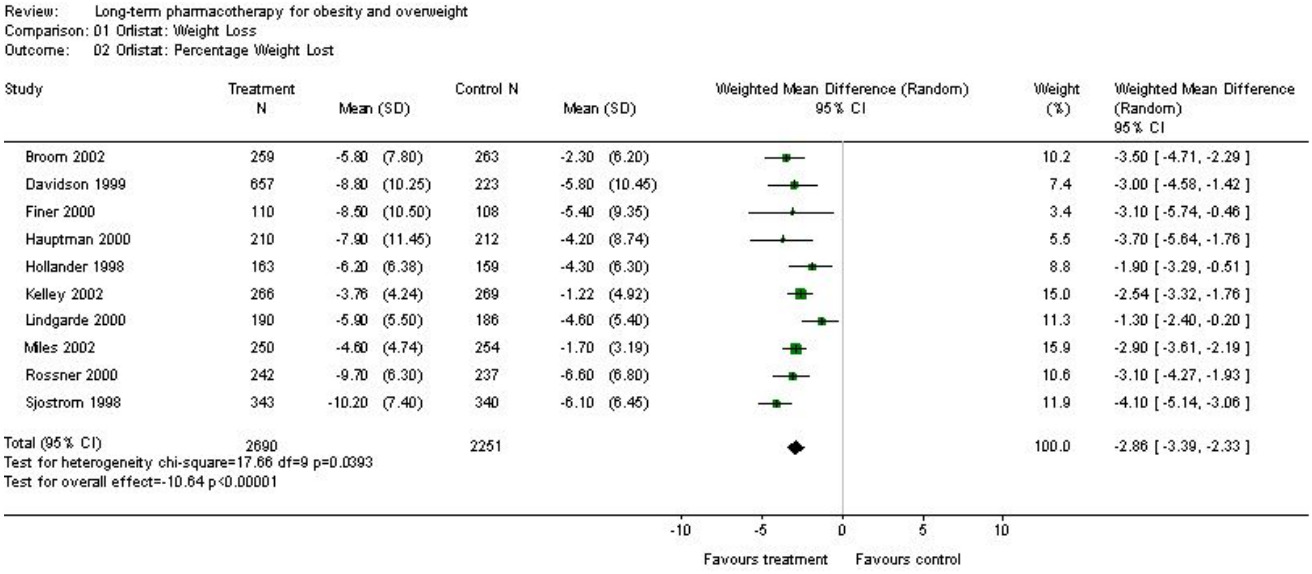
Figure 4.1 Meta-analysis (random effects)- weighted mean difference between orlistat and placebo for absolute weight loss in kilograms



(Source: Padwal et al, 2003)

In addition 10 RCTs reported the percentage weight loss achieved in each group and demonstrated 2.9% greater weight loss when data were pooled in the orlistat group compared to placebo (Figure 4.2).

Figure 4.2 Meta-analysis (random effects)- weighted mean difference between orlistat and placebo for percentage weight loss



(Source: Padwal et al, 2003)

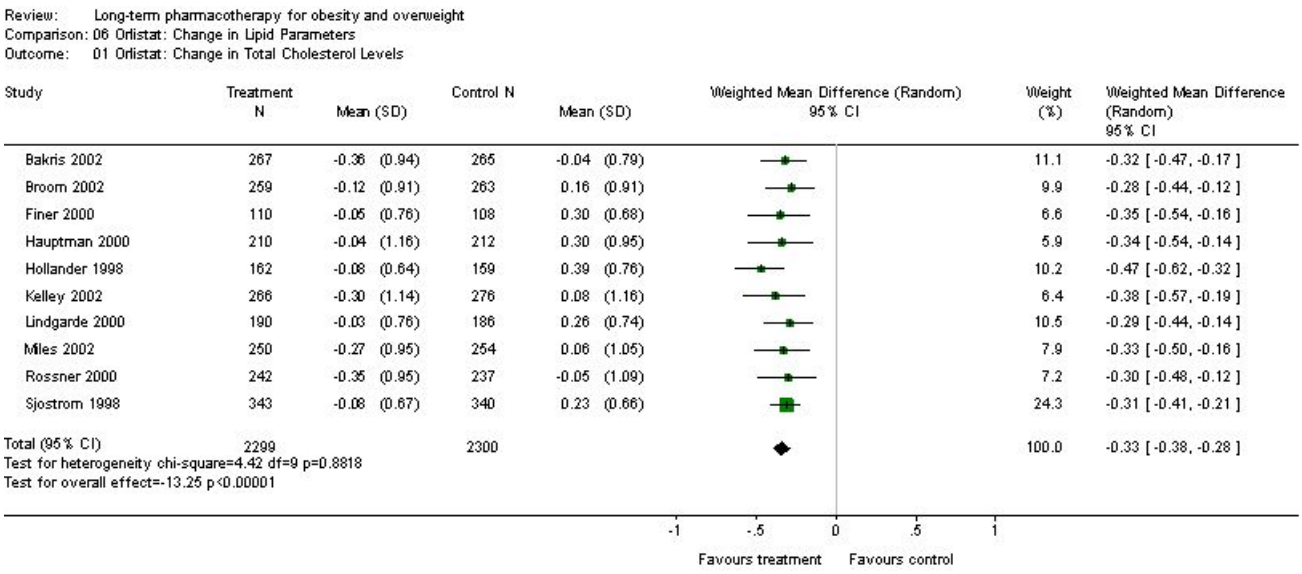
Waist circumference:

Greater reductions in waist circumference were reported for the orlisat/diet group compared to placebo/diet. Effect sizes ranged from 0.7 to 3.4cms and were statistically significant in 4 of 5 RCTs reporting this outcome (Padwal et al, 2003).

Lipid parameters:

Ten RCTs showed that patients in the orlistat/diet groups had greater reduction in their total cholesterol levels by 0.33mmol/L (95%CI 0.28 to 0.38) compared to the placebo/diet group when data were pooled (Figure 4.3).

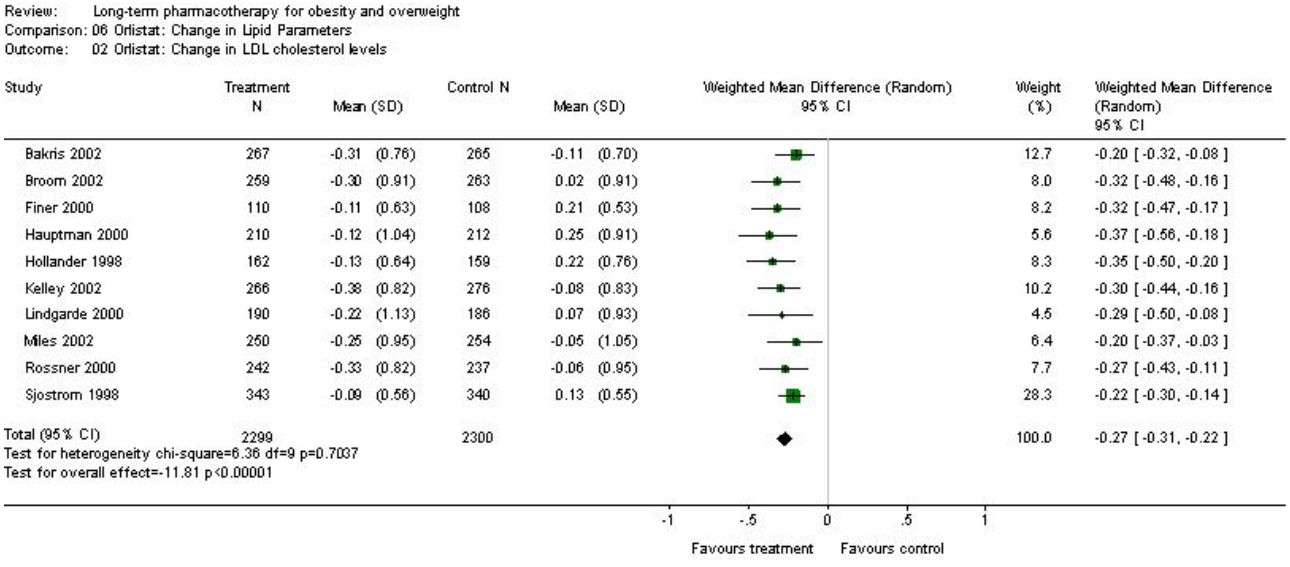
Figure 4.3 Meta-analysis (random effects)- weighted mean difference between orlistat and placebo for change in total cholesterol levels



(Source: Padwal et al, 2003)

Low density lipoprotein cholesterol levels reduced by a pooled mean of 0.27 mmol/L (95%CI 0.22 to 0.31) in the orlistat/diet group compared to placebo/diet in 10 RCTs (Figure 4.4).

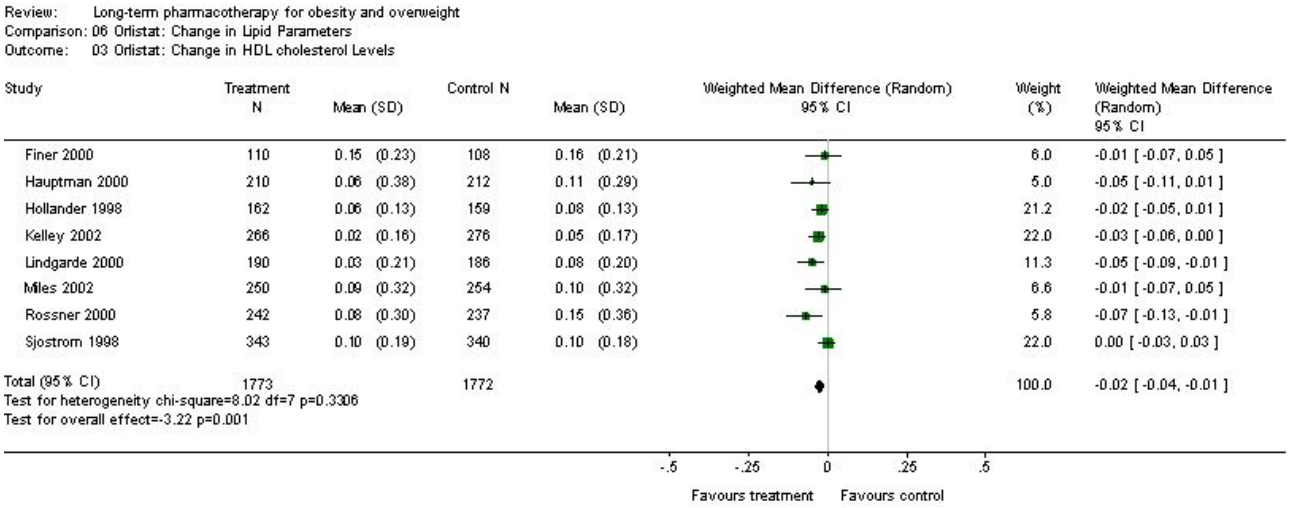
Figure 4.4 Meta-analysis (random effects)- weighted mean difference between orlistat and placebo for change in low density lipoprotein cholesterol levels



(Source: Padwal et al, 2003)

In 8 RCTs the orlistat/diet group showed a reduction in high density lipoprotein cholesterol levels of 0.02 mmol/L (95%cCI 0.01 to 0.04) compared to placebo/diet when data were pooled (Figure 4.5).

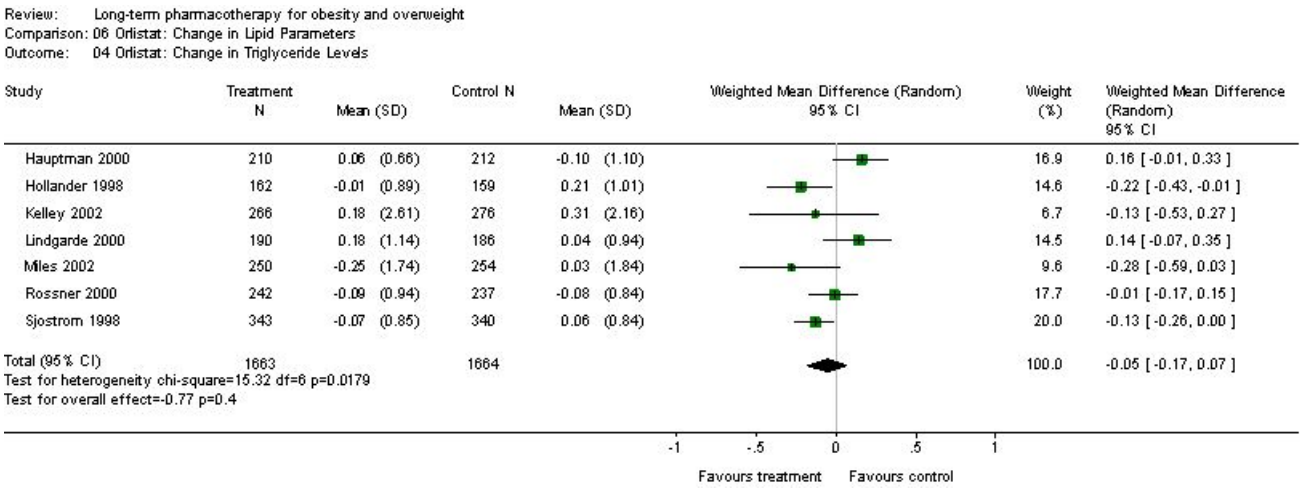
Figure 4.5 Meta-analysis (random effects)- weighted mean difference between orlistat and placebo for change in high density lipoprotein cholesterol levels



(Source: Padwal et al, 2003)

Triglyceride levels reported by 7 RCTs were not statistically significantly different in the orlistat/diet group compared to the placebo/diet group when results were pooled (Figure 4.6).

Figure 4.6 Meta-analysis (random effects)- weighted mean difference between orlistat and placebo for change in triglyceride levels

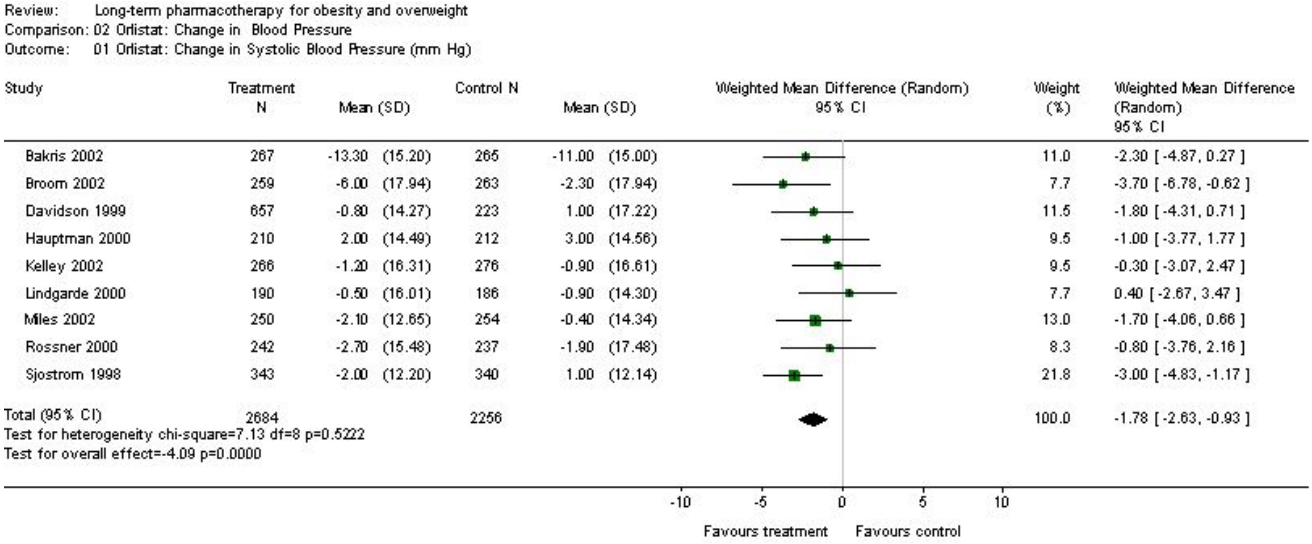


(Source: Padwal et al, 2003)

Blood pressure control:

Systolic blood pressure was statistically significantly decreased in the orlistat/diet groups compared to placebo/diet in 9 RCTs (pooled mean reduction of 1.8mmHg, 95%CI 0.9 to 2.6) as shown in Figure 4.7.

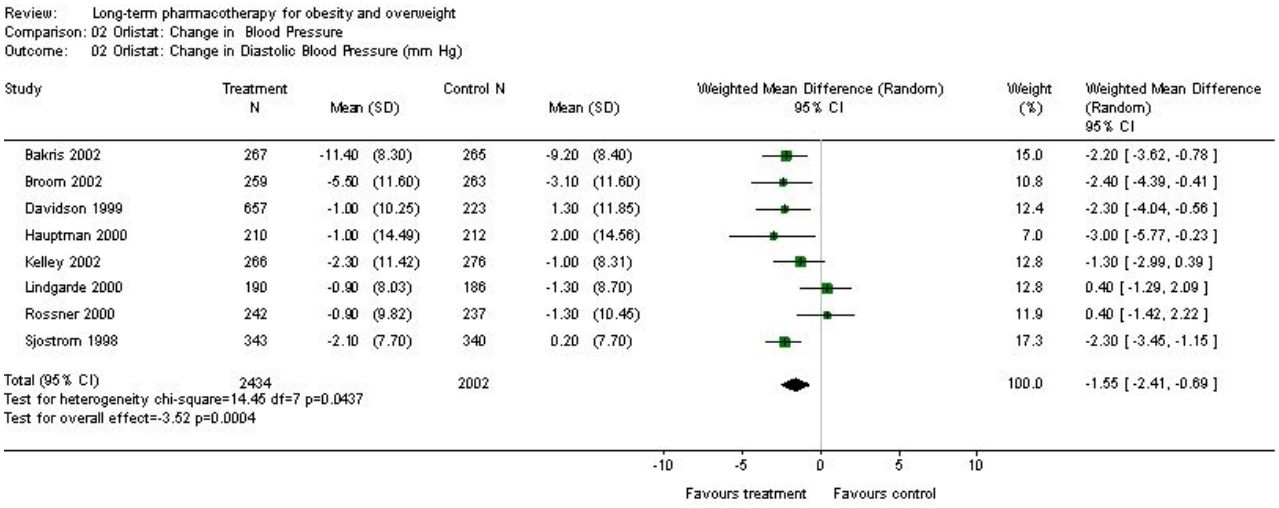
Figure 4.7 Meta-analysis (random effects)- weighted mean difference between orlistat and placebo for change in systolic blood pressure



(Source: Padwal et al, 2003)

Diastolic blood pressure also showed an overall decrease of 1.6 mmHg (95%CI 0.7 to 2.4) when data were pooled from 8 RCTS in the orlistat/diet group compared to placebo/diet (Figure 4.8)

Figure 4.8 Meta-analysis (random effects)- weighted mean difference between orlistat and placebo for change in diastolic blood pressure



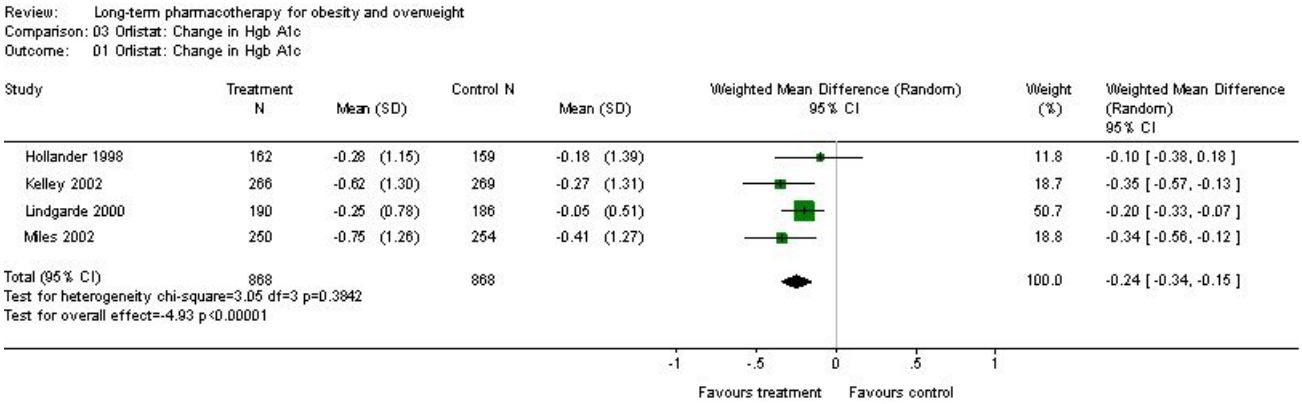
(Source: Padwal et al, 2003)

Metabolic parameters:

Fasting plasma glucose levels were reported for 9 RCTs and there was a greater reduction in the orlistat/diet group compared to placebo/diet which varied from 0.1 to 1.3mmol/L and the reduction was statistically significant in 5 RCTs.

Changes in HbA1c were reported by 4 RCTs that enrolled high risk patients and when results were pooled there was a 0.2% (95%CI 0.2% to 0.3%) greater reduction in the orlistat/diet group compared to placebo/diet (Figure 4.9)

Figure 4.9 Meta-analysis (random effects)- weighted mean difference between orlistat and placebo for change in HgbA1c levels



(Source: Padwal et al, 2003)

Weight maintenance:

Four of the included RCTs also followed patients for a weight maintenance period. In all studies the orlistat/diet group regained less weight than the placebo/diet group (ranging from 0.5% less to 0.5% more with weight loss measured as % of initial body weight). The orlistat/diet group regained 7% to 22% less weight than those in the placebo/diet group (with weight loss expressed as percentage of weight lost during year 1).

Service utilisation

Not reported.

Mortality

Not reported.

Morbidity

Adverse effects were reported by a number of the included studies. Gastrointestinal events were reported by 9 RCTs and ranged from 16% to 40% higher in the orlistat/diet group compared to placebo/diet. Approximately 2% (95%CI 1% to 4%) more orlistat/diet patients discontinued treatment due to gastrointestinal events than those in the placebo/diet group.

Faecal incontinence was 6% (95%CI 5% to 8%) higher for orlistat/diet compared to placebo/diet in the 3 RCTs that reported this outcome separately. Levels of fat-soluble vitamins (A,D and E) and beta-carotene were lower in the orlistat/diet group compared to placebo/diet in the 4 RCTS reporting these outcomes.

4.4 Program costs

As reported by trial

The systematic review by Padwal et al (2003) does not report the costs of orlistat treatment. The costs of orlistat treatment are reported in the review by Foxcroft and Milne (2000) and are summarised in Table 4.3. All costs presented in the 2000 publication have been exchanged into Australian dollars and inflated to 2003 figures and are shown in brackets.

Table 4.3 Costs of orlistat treatment (Foxcroft and Milne, 2000)

Description	Amount
Patient consultation (initial and follow up including lab tests)	£118 ($397)
Monthly treatment with orlistat (120mg)	£45 ($151)
GP consultation	£16 ($54)

Additional assumptions included that an average of 4 outpatients appointments are received per patient per year and that drop outs are treated for 3 months.

This gives an average cost for 100 patients treated for 2 years of £73,436 ($246,851). This translates into a cost of £734.36 ($2469) per person for 2 years.

Foxcroft and Milne (2000) also report the cost utility of treatment with orlistat compared to placebo. They calculated the utility benefit for 100 patients treated with orlistat for 1 year of 1.601 (or 0.016 per person). 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.

Based on resource use

Costs have also been estimated from the description of resource use in 2003 Australian dollars, according to the likely costs incurred in the Australian setting.

Intervention group:

Based on resource use arising from the systematic review in general, the costs can be broken down into consultation, monitoring and drug costs (Table 4.4 and Table 4.5). Costs are estimated based on 1000 people in each of the intervention and control groups.

Table 4.4 Consultation costs

	Number per person	Length of consult	Cost per hour	Cost for group	Average cost per person
Initial consultation with GP	1	10	$122.15	$20,358.33	$20.36
Follow up consultation	1	10	$122.15	$20,358.33	$20.36
Regular GP consults	4	10	$122.15	$81,433.33	$81.43

The following assumptions were made in estimating consultation costs:

- Each person is assumed to receive one initial consultation with a GP, another follow up visit and 4 routine consults per year. All consults are assumed to last an average of 10 minutes.
- The cost of a GP is $120 per hour (REF)

Table 4.5 summarises the monitoring costs associated with orlistat treatment.

Table 4.5 Monitoring costs

	Number required per person	Cost per item	Cost for group	Average cost per person
Total cholesterol and triglyceride test	1	$11.40	$11,400	$11.40
Glucose tolerance test	1	$18.70	$18,700	$18.70

The following assumptions were made in estimating consultation costs:

- The total cholesterol and triglyceride tests cost $11.40 each (MBS item number 66503, Nov 2002)
- The glucose tolerance test costs $18.70 (MBS item number 66542, Nov 2002)

It is estimated that treatment with orlistat will cost $140 per person per month (www.medicine.net.au). In addition it is assumed that 27% of patients will drop out of therapy within the first year and 23% in the second year (Foxcroft and Milne, 2000). Patients who drop out are assumed to drop out after three months of treatment. It is assumed that there are no drug costs associated with placebo treatment.

Placebo/ diet group:

The placebo diet group are assumed to incur the same consultation and monitoring costs as the orlistat/diet group.

Total costs:

Table 4.6 summarises the total cost per person for year 1 of treatment with orlistat or placebo.

Table 4.6 Total cost per person for orlistat and placebo

	ORLISTAT/DIET		PLACEBO/DIET	
Year 1	**Cost for group**	**Average cost per person**	**Cost for group**	**Average cost per person**
Consultation costs	$122,150.00	$122.15	$122,150.00	$122.15
Monitoring costs	$30,100.00	$30.10	$30,100.00	$30.10
Drug costs	$1,339,800.00	$1,339.80	$0.00	$0.00
Total costs	$1,492,050.00	$1,492.05	$152,250.00	$152.25

The costs of adverse events have not been incorporated. The most common adverse event is gastrointestinal (16% to 40%) but the majority of these resolve spontaneously without further investigation or treatment. The cost of the adjunctive diet in both groups is assumed to be equal and is therefore not incorporated.

4.5 Performance

Cost effectiveness

Weight loss:

Figure 3.1 showed a pooled weighted mean difference of 2.7kg greater loss in the orlistat/diet group compared to placebo/diet.

The incremental cost per additional kilogram lost for treatment with orlistat/diet compared to placebo/diet is therefore:
ICER= ($1492.05-$152.25)/2.7
=$1,339.80/2.7
=$496.22 per additional kilogram lost per person

Orlistat/ diet group versus no control:

It is possible that the placebo/diet group received more treatment than would occur in the clinical setting through involvement in the trial. For this reason we also compare the orlistat/diet group to a "no control" group which is assigned baseline values and no costs. This is also not ideal as all patients may change over time and we are unable to account for the possible effects of other confounders.

The weighted (by sample size) mean absolute weight loss for the orlistat/diet group compared to baseline is derived from Figure 18.1 and is 7.04kg.

The incremental cost per additional kilogram lost for treatment with orlistat/diet compared to no control (baseline) is therefore:
ICER= ($1492.05-$0)/7.04
=$211.94 per additional kilogram lost per person

Cost utility

The utility gain is estimated in the review by Foxcroft and Milne (2000) as 1.601 per 100 patients receiving 1 year of treatment. This equates to a utility gain of 0.01601 per person.

The incremental cost utility of treatment with orlistat/diet compared to placebo/diet is therefore:
ICER= ($1492.05-$152.25)/0.01601
=$1339.80/0.01601
=$83,685.20 per additional QALY gained per person

This however, excludes possible benefits beyond the trial, or any mortality gain.

4.6 Modelling

We have not performed detailed modelling for this intervention. We have applied the utility gain reported by Foxcroft and Milne (2000) to our own estimates of cost in a preliminary analysis (Section 4.5). We also refer in Section 4.4 to results presented of the Health Technology Assessment prepared for the NHS in the UK, which we include for comparison purposes. These estimates will provide a broad upper estimate of the cost utility of the orlistat intervention. We determined that detailed modelling of this intervention was unnecessary as it was unlikely to greatly alter general broad conclusions and comparisons.

5. Lifestyle changes to prevent type 2 diabetes in those with impaired glucose tolerance

5.1 Description

Intervention type

This is a lifestyle intervention consisting of both nutritional counselling and assistance to increase physical activity for those with impaired glucose tolerance.

Reference

Evidence for this intervention comes from the Finnish Diabetes Prevention Study conducted from 1993 to 1998 in five centres in Finland. A number of publications summarise aspects of this study and results (Table 5.1).

Table 5.1 Summary of publications from the Finnish Diabetes Prevention Study

Study authors	Year of publication	Number of patients enrolled	Number of patients with results presented	Length of follow up
Eriksson et al	1999	523	212	1 year
Uusitupa et al	2000	523	295	1-2 years
Tuomilehto et al	2001	523	522	Mean 3.2 years
Lindstrom et al	2003	523	522	Mean 3.2 years

The study targeted overweight subjects aged 40 to 64 with impaired glucose tolerance.

The main aim of the study was to determine the feasibility and effects of a lifestyle intervention program on type 2 diabetes onset in subjects with impaired glucose tolerance.

Recruitment: target population and participants

Participants were recruited from five participating centres in Finland. The study participants were recruited through a number of different methods including:

- Identification of those potentially eligible from previous epidemiological surveys
- Opportunistic population screening with emphasis on high risk groups such as those who were obese or had first degree relatives with type 2 diabetes
- Advertising in local newspapers

Overweight subjects with a BMI of >25 kg/m2, aged 40 to 64 years with impaired glucose tolerance (IGT) were eligible for inclusion in the study. The definition of IGT was based on the WHO 1985 criteria: fasting plasma glucose<7.8 mmol/l (<140mg/dl) and plasma glucose 7.8 to 11.0 mmol/l (140 to 200mg.dl) two hours after the administration of 75g of glucose. In 90% of subjects two oral glucose tolerance tests (OGTT) were taken and the mean value of the plasma glucose concentration was used to determine eligibility for study inclusion, in the other 10% of subjects only one OGTT was used.

Subjects were excluded from the study if they had a previous diagnoses of diabetes mellitus (other than gestational), were regularly involved in a vigorous exercise program, were receiving treatment to lower blood glucose, had a chronic disease with unlikely 6-year survival, had other medical characteristics that could interfere with glucose metabolism or had other characteristics (psychological or physical) that could interfere with study participation.

A total of 523 subjects were randomised to intervention or control groups. One participant was excluded 2 years after study commencement by the end-points committee as she had diabetes at baseline, with the diagnosis confirmed at her 2 year visit. This left 522 study subjects.

Of those randomised, results at 1 and 2 years are reported for 506 (97%) participants.

The demographic data for the intervention and control groups are shown in Table 5.2. The baseline characteristics of the two groups were similar.

Table 5.2 Baseline characteristics of the intervention and control groups (values are means and SDs unless otherwise stated)

Variable	Intervention group (n=265) ±SD	Control group (n=257) ±SD
Age (years)	55 ±7	55 ±7
Sex (M:F)	91:174	81:176
Body mass index (kg/m^2)	31.3 ±4.6	31.0 ±4.5
Waist circumference (cm)	102.0 ±11.0	100.5 ±10.9
Hip circumference (cm)	110.4 ±10.5	109.4 ±9.7
Fasting plasma glucose (mg/dl)	109 ±14	110 ±13
2-h plasma glucose (mg/dl)	159 ±27	159 ±26
Fasting serum insulin (µU/ml)	15 ±7	15 ±8
2-h serum insulin (µU/ml)	98 ±74	93 ±54
Serum total cholesterol (mg/dl)	215 ±37	215 ±35
Serum high density lipoprotein cholesterol (mg/dl)	46 ±12	47 ±11
Serum triglycerides (mg/dl)	154 ±72	158 ±69
Systolic blood pressure (mmHg)	140 ±18	136 ±17
Diastolic blood pressure (mmHg)	86 ±9	86 ±10

Source (Lindstrom et al 2003, pg S109 & Tuomilehto et al 2001, pg 1345)

Intervention

At the start of the study a physician and nutritionist gave general advice about risk factors for diabetes (eg obesity, sedentary life-style, genetics). A weight goal was established, with the general goal being a BMI<25kg/m^2, but in practice the goal was often to lose 5-10kg.

The study tailored dietary advice to each individual and the person responsible for meal preparation in the family was also invited to join nutrition sessions. A 3-day food record was completed at baseline and was the basis for dietary advice. The following diet recommendations were made:

- more than 50% of daily calories from carbohydrates
- less than 10% of daily calories from saturated fat (by use of low-fat milk and milk products, low-fat meat and meat products, soft margarines and vegetable oil rich in monounsaturated fatty acids)
- less than 20% of daily calories from mono and poly unsaturated fat, or up to 25% if the surplus is from monounsaturated fat if weight goal was achieved
- Cholesterol less than 300mg/day
- Approximately 1g protein per kilogram ideal body weight per day
- Increase in intake of dietary fibre to 15g per 1000 kcal or more is encouraged (by eating foods rich in natural fibre such as wholemeal products, vegetables, berries and fruit)

Study visits took place 1-2 weeks, 5-6 weeks, 3, 4 and 6 months from the beginning of the study and thereafter every 3 months (a total of 7 dietary advice sessions in the first year). A 3-day food diary was completed every 3 months (4 times per year). At each visit weight was measured, lifestyle

changes were discussed and diet re-evaluated if necessary. If weight loss did not occur after 6 months and BMI remained over 30kg/m^2 subjects were assigned to a very low calorie diet and attended regular group meetings every 1-2 weeks for 6-12 weeks.

In addition subjects received advice and assistance to increase their physical activity (through both aerobic exercise and resistance training). Endurance exercise was recommended and supervised, individually tailored circuit-type resistance training sessions were organised twice a week where possible. Subjects were instructed to perform a moderate to high number of repetitions and to take a break of 15 to 60 seconds between stations on the circuit. Exercise programs varied between study centres. A 2km walking test was organised for both groups annually.

5.2 Quality of evidence

Recruitment

There were five participating centres in Finland and each recruited over 100 subjects. The study reports do not describe how many people were screened to identify the 523 randomised subjects. The study reports do not state how many people refused to participate in the study. It is difficult to determine if there was any selection bias and if the study population is representative of the general population of overweight people with impaired glucose tolerance.

A sample size calculation was performed to detect a 35% reduction in diabetes incidence in the intervention group (ά=0.05, power=80%). A sample of 3,252 person years was required or 650 subjects followed for 5 years or 542 subjects followed for 6 years. It is therefore possible that the study which has currently followed patients for a mean of 3.2 years has not followed patients for sufficiently long to detect a difference between groups.

Participants were randomly assigned to intervention or control groups by the study physician with the use of a randomisation list. Randomisation was stratified by centre, sex, and the mean 2-h plasma glucose concentration (7.8-9.4mmol/l or 9.5-11.0mmol/l). The baseline characteristics of the two groups were similar.

Of those patients enrolled a total of 506 (97%) have 1 and 2 year results reported so attrition bias is unlikely.

Control group

Subjects randomised to the control group received dietary advice from a nutritionist at the start of the trial advising them to adjust total energy intake in order to reduce BMI below 25kg/m2 and to keep a diet with less than 30% fat. They were also advised to reduce alcohol intake and to stop smoking. Advice was provided by verbal and written means (a 2 page pamphlet). Additional routine advice was given to participants at their annual follow up visits. Some verbal information about the benefits of exercise was provided but no specific propositions or programs. In general advice was not tailored to individuals. At baseline and annual follow up they completed a 3-day food diary which used a booklet illustrating food portions.

Randomisation was stratified by centre which lessens the possibility of bias due to contamination across study groups.

Evaluation method

Differences within groups over time and differences between groups at certain time points were analysed using t tests. Survival curves were calculated to estimate the cumulative incidence of diabetes and the log rank test used to compare the curves for each group. Study reports state that all analyses of endpoints were based on the intention to treat principle.

In order to assess the dependence of the incidence of diabetes on lifestyle changes, subjects were given a grade for each goal of the intervention at 1 year follow up (0= goal not achieved, 1=goal achieved). An overall success score was the sum of the grades. For each sub-group defined according to success a proportion of subjects developing diabetes was calculated. Logistic regression (linear function) was used to assess the association between success and diabetes.

The initial study sample size calculation was based on 160 cases of type 2 diabetes by 6 year follow up. At the study midpoint 80 cases had been reported and based on an independent statistician's analysis the Endpoint Committee recommended that the trial end.

Outcome measures

Outcomes were measured at baseline and then annually and are summarised below:

Primary outcome:

- Development of diabetes

Secondary outcomes:

- Glucose tolerance
- Insulin values
- Cardiovascular risk factors (eg blood pressure, serum lipids, uric acid)
- Cardiovascular risk score
- Cardiovascular morbidity and mortality
- Quality of life

Most outcomes were objective which lessens the possibility of measurement bias. The study report states that laboratory staff were not aware of the subjects' group allocation.

Diet and exercise were measured using a 3-day food record and a 24 hour exercise history completed every 3 months for the intervention group. There is a possibility of responder bias as keeping a record diary may have prompted more favourable behaviour than was usually the case. This is especially relevant when considering success in achieving the study goals, as the intervention participants were aware of the goals and so were in a position to be able to respond positively in self-reports whereas the control group were unaware of the study goals.

Bias, confounders, efficacy

The trial has taken a number of measures to lessen the possibility of bias. Practises were randomised into the two groups, randomisation was stratified by centre to reduce contamination, the baseline characteristics of the two groups were similar, outcome assessors were blinded to group allocation, loss to follow up was minimal, analyses were performed on an intention to treat basis.

The main sources of potential bias include the lack of blinding of study investigators and patients to group allocation and the lack of information provided as to those who declined participation in screening or enrolment. It is possible that selection bias was present and this may potentially affect the generalisabilty of the results.

5.3 Outcomes – as reported

All analyses compare outcomes between the intervention and control groups and Table 5.3 shows the main analyses reported in the study.

Table 5.3 Outcome measures, data sources and analyses reported in the trial

Outcome measures	Data sources	Analyses
BEHAVIOUR CHANGE		
▪ 24 hour exercise diary ▪ 3-day food record ▪ Success score	A 24 hour exercise diary was kept every 3 months and a 12 month leisure physical activity history was completed on annual visits. 3-day food records were kept annually for controls and every 3 months for intervention groups. Portion sizes were estimated using a validated picture booklet. Nutrients were completed based on annual food records using a computer program. Success score was composed of 1 point for each goal achieved (maximum 5) at the one year visit	Comparisons between baseline, 1 year and 2 years and between groups. Proportion in each group achieving goals. Proportion in each group changing specific dietary and exercise habits.
CLINICAL PARAMETERS		
Weight (kg)	Measured at baseline and annually	Change from baseline to 1 and 2 years, comparison between groups.
Waist circumference (cm)	Was measured midway between the lowest rib and iliac crest	Change from baseline to 1 and 2 years, comparison between groups.
Hip circumference	Was measured over the great trochanters, with 0.5cm precision with the subject standing	Change from baseline to 1 and 2 years, comparison between groups.
Fasting plasma glucose 2-h plasma glucose	Determined locally according to local guidelines. Samples were taken at baseline, 30min, 60min and 120 min.	Change from baseline to 1 and 2 years, comparison between groups.
Fasting serum insulin 2-h serum insulin	Determined with a radioimmunoassay- intra-assay CV 5.3% and interassay CV 7.6%. Samples were taken at baseline, 30min, 60min and 120 min.	Change from baseline to 1 and 2 years, comparison between groups.
Serum total cholesterol Serum HDL cholesterol Serum triglycerides	Laboratory assessments were made using the intra-assay CV 1.0, 1.3 and 1.1% respectively and the interassay CV 1.2, 2.2 and 1.5% respectively.	Change from baseline to 1 and 2 years, comparison between groups.
Systolic blood pressure Diastolic blood pressure	Blood pressure was measured annually on the right arm, with the subject sitting and measured again after a 10 minute rest using a sphygmomanometer.	Change from baseline to 1 and 2 years, comparison between groups.
SERVICE UTILISATION		
Not reported		
MORTALITY		
Death	Only 1 patient died throughout the duration of the study	Numbers of deaths
MORBIDITY		
Diabetes	An OGTT was given annually. Diabetes was defined as the WHO criteria: fasting plasma glucose >140mg/dl or 2-h plasma glucose≥200mg/dl. The diagnosis was confirmed by another OGTT at least a week later	Number of cases of diabetes in each group. Cumulative incidence of diabetes in both groups. Association between success and risk of diabetes.

Behaviour change

Table 5.4 shows self-reported change in dietary and exercise habits for each study group during the first year of the study. Three patients from each group who remained in the study at 12 months had missing data and are excluded from the table. Increased activity was defined as shifting to a higher frequency category where the categories were defined as follows: 1)"I read, watch television, and work in the household at tasks that don't strain me physically" 2)"I walk cycle, or exercise lightly in other ways at least 4 hours per week" 3)I exercise to maintain my physical condition by running, jogging, skiing, doing gymnastics, swimming, playing ball games, et for at least 3 hours per week" 4)"I exercise competitively several times a week by running, orienteering, skiing, playing ball games, or engaging in other sports involving heavy exertion".

The intervention group changed significantly more than the control group for all variables except alcohol consumption.

Table 5.4 Self-reported change in diet and exercise for the intervention and control groups at 12 months

	Intervention group (n=253) %	Control group (n=247) %	P value
Decreased consumption of fat	87	70	0.001
Changed the quality of fat	70	39	0.001
Increased consumption of vegetables	72	62	0.01
Decreased consumption of sugar	55	40	0.001
Decreased consumption of salt	59	50	0.03
Decreased consumption of alcohol	26	23	0.43
Increased exercise (shift to a higher category)	36	16	0.001

Source (Tuomilehto et al 2001, pg 1346)

Success in achieving study goals at 12 months for each group is reported in Table 5.5. Nutrient intake was calculated from subject's 3 day food records, and exercise frequency corresponds to a frequency of category 2 or higher (as described above). The intervention group performed significantly better than the control group at achieving each of the 5 study goals.

Table 5.5 Success in achieving study goals for each group at 12 months

Goal	Intervention group %	Control group %	P value
1. Weight reduction >5%	43	13	0.001
2. Fat intake <30% of energy intake	47	26	0.001
3. Saturated fat intake <10% of energy intake	26	11	0.001
4. Fibre intake ≥15g/1000 kcal	25	12	0.001
5. Exercise >4 hours/week	86	71	0.001

Source (Tuomilehto et al 2001, pg 1347 &Lindstrom et al 2003, pg S111)

Clinical parameters

Clinical parameter results are presented in Table 5.6, for weight and measurements, glucose, insulin, serum lipids and blood pressure at 1 and 2 years.

During the first year of the study the mean body weight decreased by significantly more in the intervention group compared to the control group. Waist circumference, fasting plasma glucose, 2-h plasma glucose, and serum insulin concentrations also decreased significantly more in the intervention group than the control group.

During the second year of the study weight reduction remained significantly greater in the intervention group compared to the control group. Reductions in 2-h serum insulin, serum triglyceride, and blood pressure were also significantly greater in the intervention group.

Table 5.6 Trial results at 1 and 2 years: mean changes ±SD (95%CI) in clinical parameters

	Intervention group (n=256)		Control group (n=250)		P value
	Mean ±SD	95%CI	Mean ±SD	95%CI	
Change from baseline to year 1					
Weight (kg)	-4.2 ±5.1	-4.8 to -3.6	-0.8 ±3.7	-1.3 to -0.3	0.0001
Waist circumference (cm)	-4.4 ±5.2	-5.1 to -3.9	-1.3 ±4.8	-1.9 to -0.7	0.0000
Fasting plasma glucose (mg/dl)	-4 ±12	-6 to -3.9	1 ±12	0 to 2	0.0000
2-h plasma glucose (mg/dl)	-15 ±34	-19 to -11	-5 ±40	-8 to -2	0.0026
Fasting serum insulin (µU/ml)	-2 ±9	-3 to -1	-1 ±7	-2 to 0	0.1369
2-h serum insulin (µU/ml)	-29 ±64	-37 to -21	-11 ±51	-18 to -4	0.0013
Serum total cholesterol (mg/dl)	-5 ±28	-8 to -2	-4 ±28	-7 to -1	0.6232
Serum HDL- cholesterol (mg/dl)	2 ±7	1 to 3	1 ±6	0 to 2	0.0604
Serum triglycerides (mg/dl)	-18 ±51	-24 to -12	-1 ±60	-8 to 6	0.0010
Systolic blood pressure (mmHg)	-5 ±14	-7 to -3	-1 ±15	-3 to 1	0.0066
Diastolic blood pressure (mmHg)	-5 ±9	-6 to -4	-3 ±9	-4 to -2	0.0163
Change from baseline to year 2					
Weight (kg)	-3.5 ±5.5	-4.2 to -2.8	-0.8 ±4.4	-1.4 to -0.2	0.0001
Waist circumference (cm)	-4.2 ±5.2	-4.9 to -3.5	-1.3 ±5.4	-2.0 to -0.6	0.0000
Fasting plasma glucose (mg/dl)	-2 ±13	-4 to 0	4 ±14	2 to 5	0.0001
2-h plasma glucose (mg/dl)	-14 ±38	-20 to -9	0 ±45	-5 to 5	0.0002
Fasting serum insulin (µU/ml)	-2 ±6	-3 to -1	-1 ±6	-2 to 5	0.0699
2-h serum insulin (µU/ml)	-29 ±69	-39 to -19	-12 ±44	-18 to -6	0.0037
Serum total cholesterol (mg/dl)	-4 ±31	-8 to 0	0 ±27	-4 to 4	0.1834
Serum HDL- cholesterol (mg/dl)	4 ±7	3 to 5	3 ±7	2 to 3	0.2003
Serum triglycerides (mg/dl)	-18 ±53	-25 to -12	0 ±75	-9 to 9	0.0026
Systolic blood pressure (mmHg)	-5 ±14	-7 to -3	0 ±15	-2 to 2	0.0005
Diastolic blood pressure (mmHg)	-5 ±9	-6 to -4	-3 ±9	-4 to -2	0.0125

Source (Lindstrom et al 2003, pg S110 & Tuomilehto et al 2001, pg 1346)

Service utilisation

Not reported.

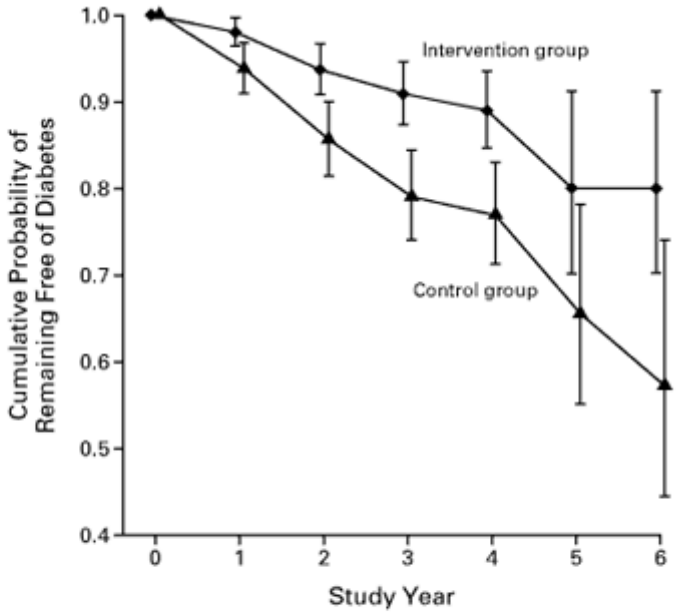
Mortality

During the first 12 month period of the study 1 patient (0.19%) from the 523 who were randomised died. The study was not powered to detect significant differences between the groups in mortality.

Morbidity

Diabetes was diagnosed in 27 people in the intervention group and 59 in the control group. An average of 3% per year with IGT progressed to diabetes in the intervention group compared to 6% per year in the control group. The relative risk of diabetes was 0.4 ($p<0.001$) for the intervention group compared to the control group.

Figure 5.1 Cumulative probability of remaining free of diabetes for the intervention and control groups



Subjects at Risk						
Total no.	507	471	374	167	53	27
Cumulative no. with diabetes:						
Intervention group	5	15	22	24	27	27
Control group	16	37	51	53	57	59

Source (Tuomilehto et al 2001, pg 1347)
The vertical bars indicate 95%CIs.

The cumulative incidence of diabetes during the study for the intervention and control groups is shown in Table 5.7. The cumulative incidence of diabetes was lower in the intervention group compared to the control group, and the difference became statistically significant after 2 years.

Table 5.7 Cumulative incidence of diabetes in the intervention and control groups

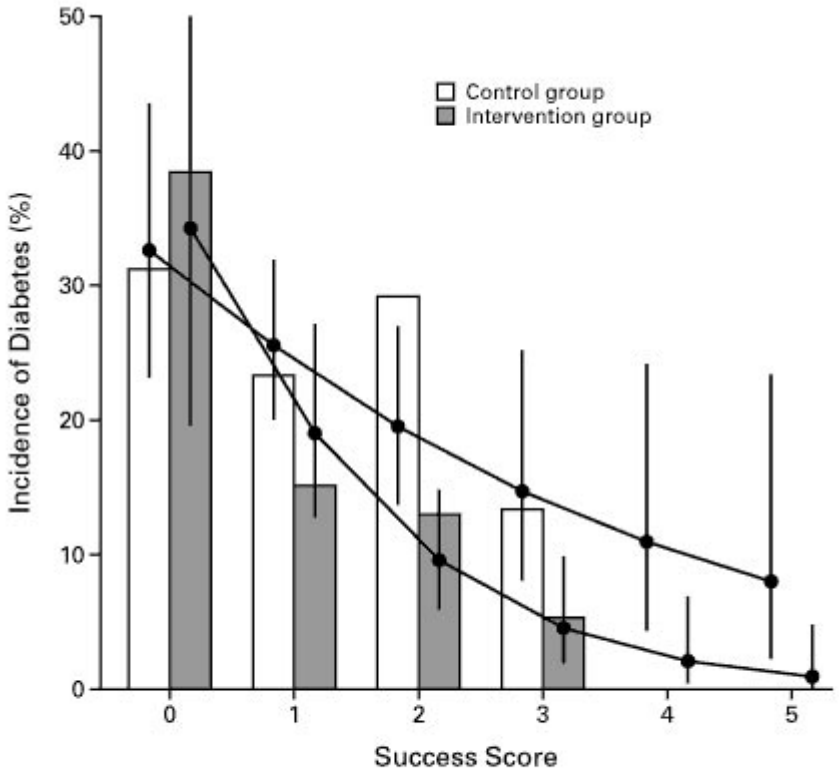
Year	Intervention group		Control group	
	Cumulative incidence	95% CI	Cumulative incidence	95% CI
1	1.9	0.2 to 3.6	6.1	3.2 to 9.0
2	6.3	3.2 to 9.2	14.4	9.9 to 18.6
3	9.1	5.4 to 12.6	20.9	15.5 to 25.9
4	10.9	6.4 to 15.2	23.0	16.9 to 28.6
5	20.0	8.8 to 29.8	34.4	21.9 to 44.9
6	20.0	8.8 to 29.8	42.6	26.0 to 55.5

Source (Lindstrom et al 2003, pg S111)

According to a Cox regression analysis of all person-years accumulated. The cumulative incidence of diabetes was 58% lower in the intervention group compared to the control group (hazard ratio=0.4, 95%CI 0.3 to 0.7, p<0.001).

Subjects were assigned a success score of between 0 and 5 according to how many study goals they had achieved, with a higher score indicating more success. The relationship between incidence of diabetes and success score is shown in Figure 5.2. There was a strong inverse relationship between success score and incidence of diabetes.

Figure 5.2 Incidence of diabetes according to lifestyle change success score during the trial for the intervention and control groups



No. with Diabetes/Total No.						
Intervention group	5/13	10/66	9/69	2/38	0/25	0/24
Control group	15/48	25/107	14/48	2/15	0/11	0/4

Source (Tuomilehto et al 2001, pg 1348)
The vertical bars indicate 95% CIs

Univariate analyses were used to calculate odds ratios for diabetes according to achievement of certain study goals compared to not achieving those goals. Separate odds ratios are presented for intervention and control groups (Table 5.8). For a description of goal numbers refer to Table 5.9.

Table 5.8 Odds ratio for diabetes according to success with goals versus non success

Goal	Group	Odds ratio	95%CI
1	Intervention Control	0.3 0.4	0.1 to 0.7 0.1 to 1.2
Not 1 but 5	Intervention Control	0.2 0.6	0.1 to 0.6 0.3 to 1.1
1 adjusted for BMI	Intervention	0.3	0.1 to 0.7

Source (Tuomilehto et al 2001, pg 1347-8)

The predicted rates of incidence were also calculated using logistic regression treating success score as a continuous variable (Table 5.9)

Table 5.9 Predicted rates of diabetes incidence by success score for intervention and control groups

Success score	Intervention group		Control group	
	Predicted rate of incidence	95%CI	Predicted rate of incidence	95%CI
0	0.34	0.20 to 0.52	0.33	0.23 to 0.43
1	0.19	0.13 to 0.27	0.26	0.20 to 0.32
2	0.10	0.06 to 0.15	0.20	0.14 to 0.27
3	0.05	0.02 to 0.10	0.15	0.08 to 0.25
4	0.02	0.01 to 0.07	0.11	0.05 to 0.24
5	0.01	0.00 to 0.05	0.08	0.02 to 0.23

Source (Lindstrom et al 2003, pg S111)

5.4 Program costs

As reported by the trial

The trial reported by Eriksson et al (1999), Uusitupa et al (2000), Tuomilehto et al (2001) and Lindstrom et al (2003) does not report any costs associated with the lifestyle intervention.

Based on resource use

Costs have therefore been estimated in Australian dollars (2003) based on the description of resource use from the study reports.

Intervention group:

The trial involved comparison of a lifestyle intervention (n=265) with usual care (n=257) for people with IGT.

Follow up:

In general, the intervention costs can be broken down into consultation, program and intensive very low calorie diet (VLCD) costs (Table 5.10, Table 5.11 and Table 5.12).

Table 5.10 Summary of consultation costs for the intervention group

	Number per person	Length of consult	Cost per hour	Cost for group	Average cost per person
Initial consult GP	1	15	$120.00	$30,000.00	$30.54
Initial consult dietician	1	60	$63.85	$63,850.00	$63.85
Follow up consult dietician	7	60	$63.85	$446,950.00	$446.95

The following assumptions were made when calculating the consultation costs:

- Participants receive one initial visit with a GP and a dietician and a further 7 follow up visits in the first year with a dietician

Table 5.11 Program costs

	Number required	Cost per item	Items per year	Cost for group	Average cost per person
Food diaries	1	$4.95		$1,311.75	$4.95
Portion size booklet	1	$4.95		$1,311.75	$4.95
Initial exercise program	1	$34.05		$9,023.25	$34.05
Exercise sessions	10 people per class	$34.05	2 sessions per week for 1 year	$98,841.80	$354.12

The following assumptions are made when calculating program costs

- Each person receives one food diary and portion size booklet
- All patients receive an initial exercise program which takes 1 hour with a physiotherapist
- All patients attend 2 exercise sessions per week lasting 1 hour with 10 participants per class

Table 5.12 Intensive very low calorie diet (VLCD) costs

	Number of people	Number sessions	Cost per meeting	Cost for group	Average cost per person
Group meeting	66.25	10 people in 12 sessions	$34.05	$2,706.98	$10.22

The following assumptions are made when calculating VLCD costs:

- 25% of all patients will require the intensive VLCD due to failing to lose weight within 6 months and BMI remaining over 30kg/m^2
- the intensive VLCD consists of regular group meetings every week for 12 weeks
- A dietician will conduct each group session for 1 hour
- 10 participants will attend each group session

Control group:

The control group receive an initial consult with dietician and one follow up visit with dietician per year. The control group are assumed to receive a food diary, portion size booklet and a dietary advice pamphlet each which is estimated to cost $4.95.

Total costs:

The total cost per person for the intervention and control groups is summarised in Table 5.13 along with the average cost per person.

Table 5.13 Total cost and average cost per person for the control and intervention groups

Costs	INTERVENTION GROUP		CONTROL GROUP	
	Cost for group	Average cost per person	Cost for group	Average cost per person
Consultation	$143,454.44	$541.34	$33,840.50	$127.70
Program	$105,488.55	$398.07	$3,935.25	$14.85
VLCD	$2,706.98	$10.22	$0.00	$0.00
Total	$251,649.96	$949.62	$37,775.75	$142.55

5.5 Performance

Cost effectiveness

The trial followed the lifestyle intervention and usual care groups for a total of 6 years. The cumulative incidence of diabetes is summarised in Table 5.7 and was 20.0 for the intervention group compared to 42.6 for the control group over 6 years. This leads to the following incremental cost effectiveness ratio:

ICER= (cost intervention/ cost control)/ (outcome intervention/ outcome control)

= ($251,649.96-$37,775.75)/ (42.6-20.0)

=$213,874.21/ 22.6

=$9463.46 per incident case of diabetes prevented in the intervention group compared to the control group over the 6 year study period.

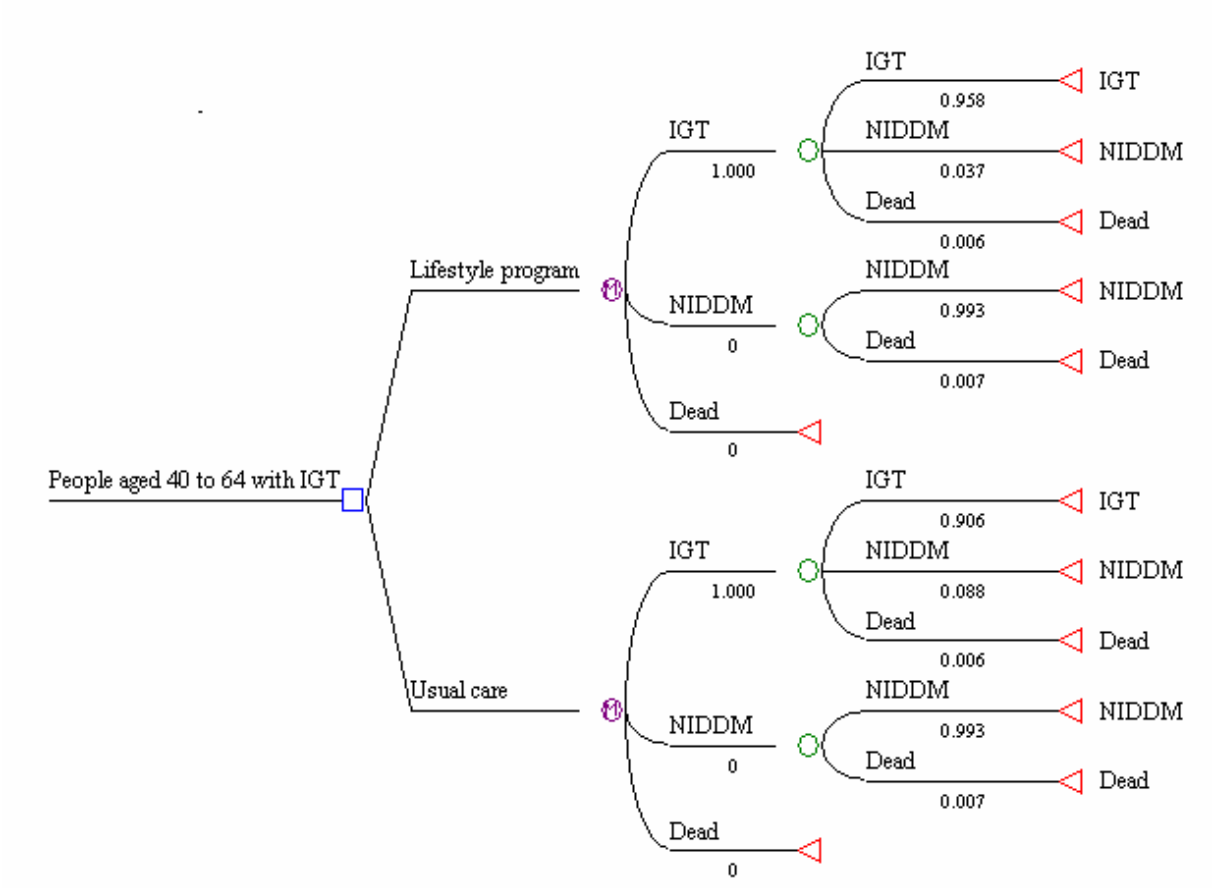
This however, excludes possible benefits beyond the trial, such as quality of life or mortality gains. These more complete estimates are modelled below.

5.6 Modelling

Methods

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 myelitis (NIDDM) and death. The transitions that are permitted are illustrated in Figure 5.3.

Figure 5.3 Representation of states and permitted transitions in Markov model (transitions shown are for first cycle)



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 (350/522) with an average age of 55 years.

The cohort progressed annually between health states over a 20-year time horizon according to transition probabilities derived from the study by Lindstrom et al (2003) for progression from IGT to NIDDM (Table 5.14). The model commences with all people in the IGT health state as was the case in the trial by Eriksson et al (1999).

Table 5.14 Transition matrix for each study group

Lifestyle intervention

	NIDDM	IGT	Dead
NIDDM	#	-	Death table
IGT	0.037	#	Death table
Dead	-	-	1

Usual care

	NIDDM	IGT	Dead
NIDDM	#	-	Death table
IGT	0.088	#	Death table
Dead	-	-	1

residual value, - no transition permitted

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. An overall weighted mortality rate for each age year was obtained assuming 67% of our cohort are female (Eriksson et al, 1999). These figures were adjusted using a relative risk of mortality for those with IGT or NIDDM. Balkau et al. (1993) reported that, compared with NGT, the relative risk of premature mortality was 2.1 for people with NIDDM and 1.6 for people with IGT, these figures have been adjusted for the prevalence of NIDDM and IGT in the population to give relative risks of 1.9 and 1.5. The resulting mortality rates are shown in Table 5.15.

Table 5.15 Mortality rates (weighted for gender and adjusted for NIDDM and IGT status)

Age	NIDDM	IGT
55	0.0072	0.0057
56	0.0080	0.0063
57	0.0088	0.0070
58	0.0097	0.0077
59	0.0106	0.0084
60	0.0117	0.0092
61	0.0128	0.0101
62	0.0140	0.0111
63	0.0154	0.0122
64	0.0170	0.0134
65	0.0188	0.0148
66	0.0208	0.0164
67	0.0230	0.0182
68	0.0256	0.0202
69	0.0284	0.0224
70	0.0316	0.0249
71	0.0352	0.0278
72	0.0392	0.0309
73	0.0436	0.0344
74	0.0485	0.0383
75	0.0540	0.0426

The costs for each of the study groups for year 1 were taken from Table 5.13. 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. The down stream costs associated with diabetes are excluded in the base case analysis (although an annual cost of $5540 is included in sensitivity analysis).

Costs and benefits are discounted at 5% per annum. Extensive univariate sensitivity analyses were performed for the assumptions and values described in Table 5.16.

Table 5.16 Sensitivity analysis: attributes, base case and alternative assumed values

Assumptions	Base case	Alternative Values	Source
Incidence of diabetes	I=20 C=42.6	Lower CI: I=8.8, C=29.8 Upper CI: I=26.0, C=55.5	95%CIs Lindstrom et al 2003
Annual cost of managing NIDDM	$0	$5540	Health Costs; DiabCost Study; (Colagiuri et al., 2003
Time horizon	20	5, 10, 15	Researcher judgement
Utility of diabetes	0.7	0.80	Utility of a person with diabetes and no complications Health Costs; DiabCost Study; (Colagiuri et al., 2003
Length of intervention benefit	20 years	6 years	Probability of developing NIDDM reverts to control group figure after year 6 (Lindstrom et al, 2003)
Discount rate	5%	0%, 3%	Researcher judgement

Results

Table 5.17 presents the economic performance of the lifestyle program, at an incremental cost utility ratio of $1,879 per QALY gained (for base case assumptions, see table 5.16).

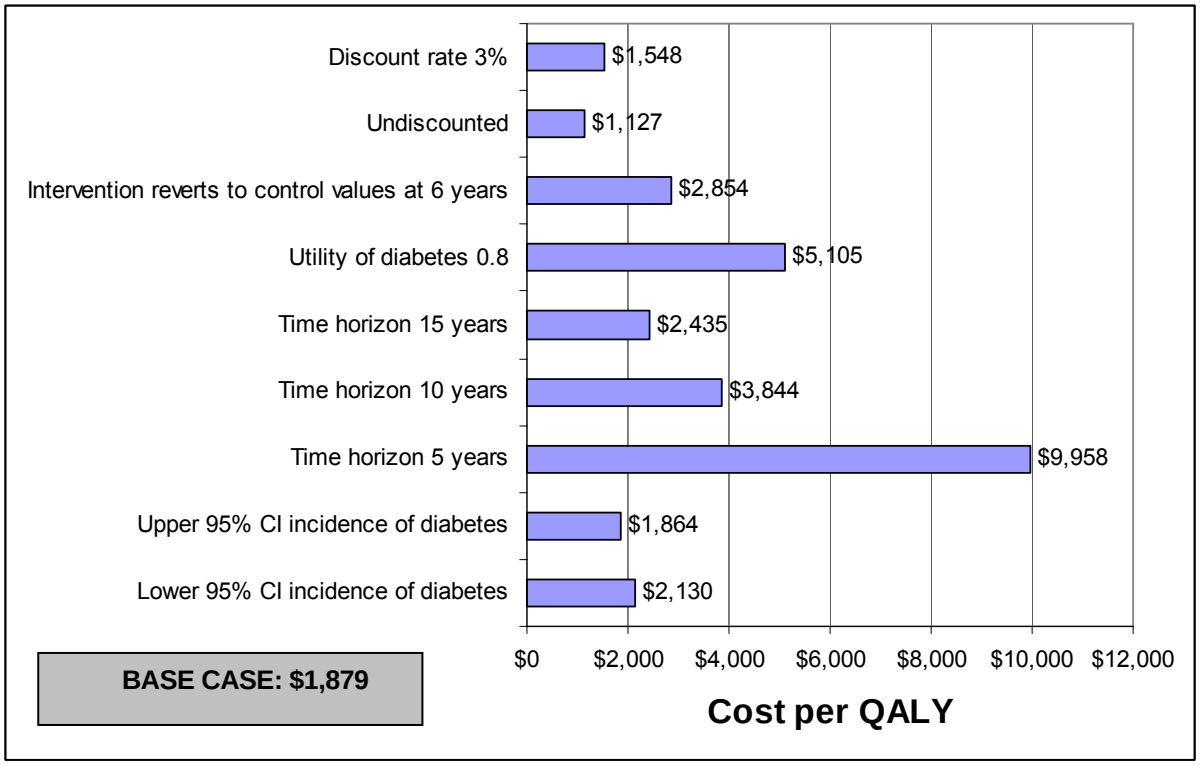
Table 5.17 Modelled cost utility base case results

	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

Sensitivity analyses

One way sensitivity analyses gave results ranging form $1,127 to $9,958, with the model being most sensitive to the time horizon and the utility assigned to diabetes (Figure 5.4).

Figure 5.4 Results of one way sensitivity analyses



Inclusion of downstream costs:

When a downstream cost associated with NIDDM is included of $5,540 the Intervention group dominates the control group as seen in Table 5.18.

Table 5.18 Modelled cost utility base case results

	Lifestyle program	'Usual care' group	Difference
Total costs	$29,971	$53,610	-$23,639
Total life years	13.43	13.36	0.07
Total QALYs	10.78	10.27	0.51
Discounted $/LY gained			Intervention dominates
Discounted $/QALY gained			Intervention dominates

The results of a threshold analysis show that the intervention lifestyle program will dominate the usual care control group when the downstream costs associated with diabetes are greater than $175 per person per year.

6. Interactive, computer-based telecommunications system to improve diet quality

6.1 Description

Intervention type

A computer based telecommunications system in general terms is an automated, interactive system that works via the telephone. A computerised system (and digitalised voice) interacts with people in order to monitor, educate or counsel them. The system can potentially be used to modify any health related behaviour providing software is available. In this case the focus is nutrition.

References/ sources of evidence

The analysis of the interactive computer-based system called Telephone-Linked Communications (TLC) is based on the study by Delichatsios et al (2001) conducted in Massachusetts USA. The intervention targeted those over 25 years of age who were sedentary and had a suboptimal diet.

The objective of this study was to evaluate the effectiveness of the TLC system at improving the quality of diet in adults over a 6-months period. Specifically the intervention aimed to increase consumption of fruit, vegetables and wholegrain goods and decrease consumption of red meats and processed foods and whole fat dairy products.

Recruitment: target population and participants

Participants were identified from the membership of the Harvard Vanguard Medical Association (HVMA), a large multisite, multispeciality group practice in eastern Massachusetts. From a random sample 4,364 participants were identified of whom 2,884 were contacted to participate in a screening interview. A total of 298 (10%) participants were eligible for inclusion and agreed to participate in the study (Figure 6.1).

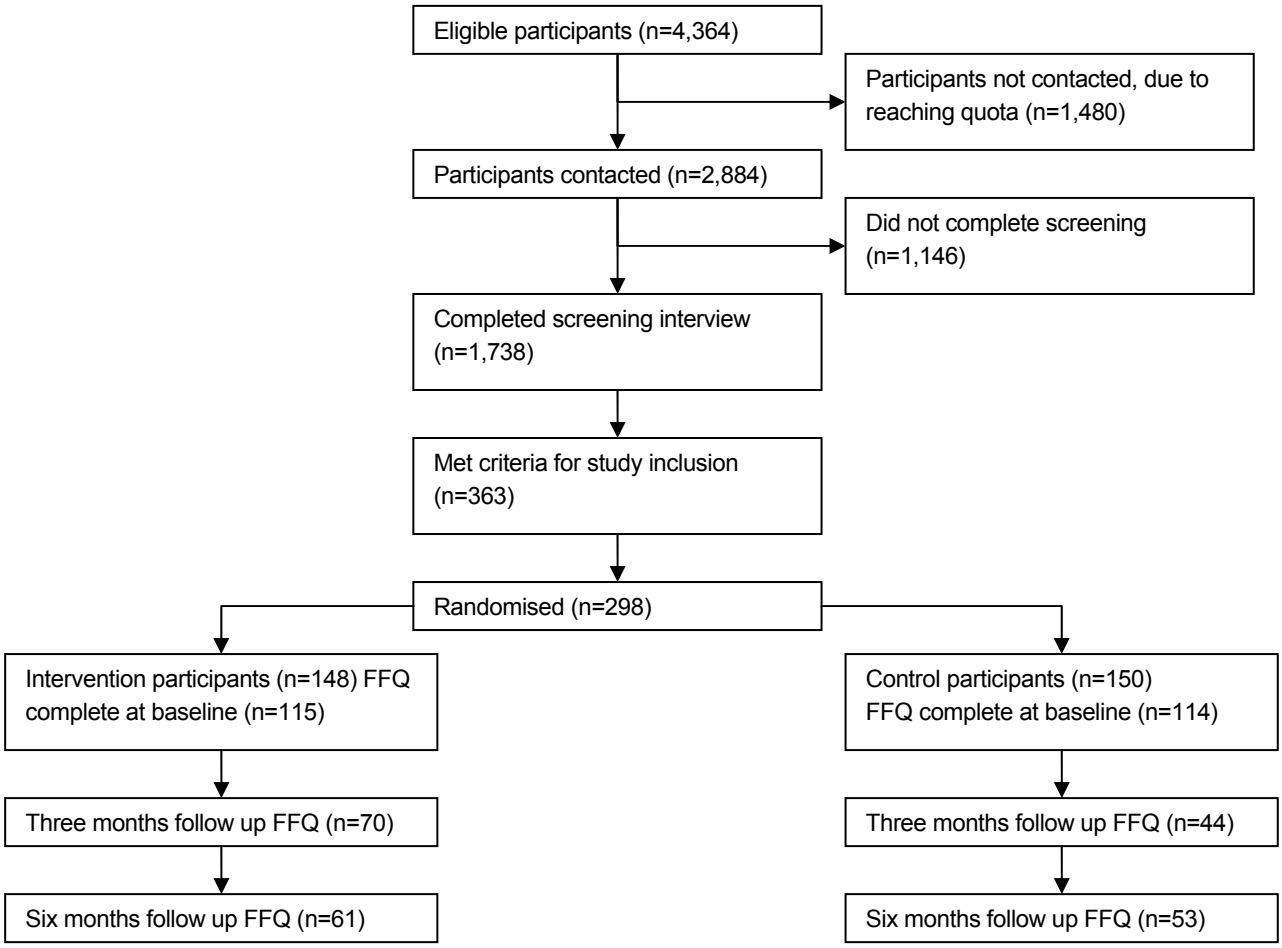
Patients were excluded if they were less than 25 years old and had conditions that would limit their ability to participate in the study (eg dementia, severe psychiatric disorders). To be eligible participants had to be classified as sedentary and have a suboptimal diet.

Participants were defined as active if:

- They regularly engaged in moderate activity (30 minutes or more per day for 5 or more days per week)
- They regularly engaged in vigorous activity (more than 3 days per week for 20 minutes or more per day)

A suboptimal diet was assessed based on initial testing with the 18-item food frequency questionnaire- PrimeScreen. For assessment of suboptimal diet the focus was on the food groups: fruits, vegetables, red and processed meats, whole fat dairy products and whole grain foods. A priori cut-off points for frequency of consumption for each of the 5 food groups were set. A participant was considered to have a suboptimal diet if they were scored worse than the cut-off for at least one of the food groups.

Figure 6.1 Process of recruitment of general practitioners



Source (Delichatsios et al 2001, pg 216)

The demographic data for the intervention and control groups is shown in Table 6.1.

Table 6.1 Characteristics of study participants at baseline

Variable	Intervention group (n=148)	Control group (n=150)
Age in years (mean [SD])	46.2 (12.2)	45.7 (12.5)
Gender, percent female	72.3	72.0
Race Percent white Percent African-American	 46.6 43.2	 43.3 46.0
Income, percent >$2000/month	57.4	58.2
Education Percent 13-16 years Percent 17 plus years	 48.3 24.5	 46.0 24.0
Percent married/living with partner	63.5	54.0
Percent employed	83.1	87.3
Percent excellent/ very good health	51.4	42.7
Body mass index in kg/m^2 (mean [SD])	28.7 (7.4)	28.7 (6.5)

Source (Delichatsios et al 2001, pg 219)

Baseline characteristics appear similar for the two groups although there were higher proportions with excellent or very good health in the intervention group. There were no statistically significant differences in characteristics between those who completed the Food Frequency Questionnaire (FFQ) at baseline and those who did not, except for race which was 51% white for completers compared to 26% white for non-completers.

Intervention

Participants in both groups used an interactive, computer-based system called Telephone Linked communications (TLC). The difference between the groups was that for the intervention group the TLC was programmed with the TLC-Eat programme which is specific to nutrition whereas the control group TLC was programmed with an intervention focussed on increasing physical activity.

TLC functions as an "at-home" means of monitoring, educating and counselling individuals on health related behaviours. The TLC works over the telephone and uses computer mediated digitalised human speech. It asks questions to monitor patient behaviour and health conditions and provides education and behavioural reinforcement. Participants respond to TLC questions by pressing their telephone key pads.

For the intervention group the TLC-Eat program was used which is based on nutrition. It focuses on fruit, vegetables, red and processed meat, whole fat dairy products and whole grain foods. The conversations are based on social cognitive theory as a guide to behaviour change and include food consumption, food knowledge, food purchasing, food preparation and cooking, food serving and garnishing and restaurant food selection. The intervention focuses on interpersonal factors by linking the behaviour of eating to personally valued outcomes. The TLC-Eat program will also negotiate future goals for the participant using shared decision making.

Each study participant received a home visit at the start of the study to train them to use the TLC system. Participants were instructed to call the system once a week for 6 months. If they were late in calling by two weeks they received a reminder call from the TLC system. Participant's answers were stored in a database. Each TLC phone conversation lasted 5 to 7 minutes and focussed on a specific food group.

The patient's doctors received reports so they could be aware of their patient's progress and incorporate follow up into their visits if desired.

6.2 Quality of evidence

Recruitment

The study enrolled a total of 298 patients (82% of those screened and eligible). It should be noted that of those contacted to participate in screening only 1738 (60%) participated in screening and that of those screened only 363 were eligible for study inclusion (21%). It is possible that those who declined participation were different from those who agreed to participate.

The study does not report any sample size calculations. It is possible that the study did not have sufficient power to detect clinically meaningful differences between the groups.

Patients screened and eligible were randomised to the nutrition intervention or to the control group. Details of the randomisation method and process are not described. The randomisation process was not stratified, although the original selection of the sample to be contacted for participation was stratified by race.

Of those patients enrolled a total of 61 (41%) in the intervention group and 53 (35%) in the control group completed 6 months follow up. Those who did not complete the study were not statistically

significantly different in baseline characteristics than those who did (except for race). There is a possibility of bias due to the large proportion of participants not completing follow up. This may be potentially related to the race of participants.

Control group

Patients were randomised to intervention or control groups. The term “control” group is potentially misleading as this group also received an intervention- physical activity. In all respects other than the content of their intervention program the two groups appear to have been treated equally. It is more appropriate to refer to the groups as the nutrition group and the physical activity group as the study really assesses which of these is more effective at improving diet quality. For these reasons the effects of the nutrition group are compared to baseline for a reflection of how much the group improved over time (similar to a before after study).

Evaluation method

The study states that outcome analyses were performed on an intention to treat basis and that missing data were handled using a last-observation-carried –forward approach (Delichatsios et al 2001, pg 218). In reality many analyses are actually reported for a subgroup of patients who completed questionnaires etc and are not reported on intention to treat.

The two study groups were compared for changes in food consumption, change in the FFQ global diet quality score, and changes in intakes of nutrients using analysis of covariance (ANCOVA) controlling for age, gender, race and baseline intake. Positive movement in stage of change was also compared for the two groups.

Analyses are presented separately for 3 and 6 months. At each time period baseline data are only included for those patients who completed the follow-up.

Outcome measures

Outcomes were measured at baseline, 3 months and 6 months. Diet was assessed with two instruments- FFQ and PrimeScreen.

Food frequency questionnaire (FFQ): This is a 131 item, validated, semiquantitative questionnaire which asks multiple questions about average vitamin, dairy, fruit, vegetable, meat, starch, sweets and beverage intake as well as questions about food preparation. The questionnaire offers 9 response categories.

PrimeScreen questionnaire: This is an 18-item, validated instrument asking questions about intake of fruit, vegetables, dairy products, whole grains and meats. Five response categories are available.

For each participant usual intake of the five food groups was calculated and using the FFQ a global diet quality score was obtained. The scoring of this measure was based on published guidelines, expert opinion, and the frequency of distributions in the study (Table 6.2). The composite score was the unweighted average of each of the five groups.

Table 6.2 Summary of scoring system for the global diet quality score

Food group	0 points (worst)	100 points (best)
Fruits	0 servings per day	≥4 servings per day
Vegetables	0 servings per day	≥5 servings per day
Whole grain foods	0 servings per day	≥2 servings per day
Red and processed meat	≥2 servings per day	<2 servings per week
Whole fat dairy products	≥2 servings per day	<2 servings per week

The validity of the global diet quality score is questionable and the chosen cut-offs are not sourced or validated.

Consumption of selected nutrients was also assessed including: folate, calcium, iron, vitamin A, vitamin C, fiber, beta-carotene and saturated fat. These were determined by multiplying the weighted frequency of use by the known vitamin composition of each food or food group (from the Harvard nutrient database program). The nutrients were then summed across all food groups to give a total daily intake for each individual.

Readiness to change dietary behaviour was assessed at baseline and follow up for each of the food groups (from PrimeScreen) using an algorithm described by Kristal et al, 1999.

All outcomes are patient reported (and therefore subjective). It is possible that bias is present with participants giving the answers they see as desirable. The study report does not state if patients and investigators were blinded to their group allocation which is another potential source of bias.

Bias, confounders, efficacy

The trial has taken a number of measures to lessen the possibility of bias. Patients were randomised into the two groups, the baseline characteristics of the two groups were similar, the intervention was identical for each group apart from the content and some analyses were performed on an intention to treat basis.

The main sources of potential bias include the high rates of loss to follow up between baseline and 6 months, the lack of blinding, and the lack of objective outcome measurement.

There were a number of patients who declined participation in screening or enrolment and the number of patients eligible for the trial was a small subset of those screened. The results may not be generalisable to the general population but are more likely applicable to a select group who are sedentary with poor diet.

6.3 Outcomes – as reported

All analyses compare outcomes between the nutrition intervention and physical activity groups at baseline, 3 months and 6 months. Table 6.3 shows the main analyses reported in the study.

Table 6.3 Outcome measures, data sources and analyses reported in the trial

Outcome measures	Data sources	Analyses
BEHAVIOUR CHANGE		
• Mean intake of selected food groups (FFQ) • Mean intake of selected food groups (PrimeScreen) • Global diet quality score • Mean intake of selected nutrients (FFQ) • Mean intake of selected nutrients (PrimeScreen) • Stage of change • Use of the TLC system	Self reported intake of food. Dietary score and intake of nutrients are calculated as described in section 5.2.4. Stage of change assesses whether subjects had positive movement in stage for each food group. Positive movement is any movement to a later stage (ie precontemplation, contemplation, preparation, action or maintenance). Use of the TLC system measured by number of times the system was accessed.	Change from baseline to 3 and 6 months, comparison between groups.
CLINICAL PARAMETERS		
Not reported		
SERVICE UTILISATION		
Not reported		
MORTALITY		
Not reported		
MORBIDITY		
Not reported		

Behaviour change

Food group intake: Results obtained using the two food questionnaires are reported separately. Results were adjusted by controlling for age, gender, race and baseline intake. Table 6.4 shows the mean results for the nutrition intervention and physical activity intervention groups for the FFQ and Table 6.5 shows the same results for the PrimeScreen questionnaire.

Table 6.4 Mean change in intake of food groups on the FFQ

Food groups	Group	Baseline (n=70 nutrition, 44 activity)	3 months	Adj difference baseline to 3 months (95%CI)	Baseline (n=61 nutrition, 53 activity)	6 months	Adj diff baseline to 6 months (95%CI)
Fruit	Nutrition Activity	2.9 2.7	2.9 2.4	0.5 (-0.1 to 1.1)	2.8 2.4	3.2 2.0	1.1 (0.4 to 1.7)*
Vegetables	Nutrition Activity	4.1 3.8	4.2 3.8	0.2 (-0.7 to 1.0)	3.8 3.5	4.5 3.6	0.8 (-0.3 to 1.8)
Red/ processed meats	Nutrition Activity	0.7 0.7	0.6 0.7	-0.1 (-0.3 to 0.2)	0.7 0.7	0.5 0.6	-0.1 (-0.3 to 0.1)
Whole fat dairy products	Nutrition Activity	1.6 1.0	0.8 0.9	-0.3 (-0.5 to 0.0)	1.6 1.4	1.0 1.1	-0.2 (-0.5 to 0.2)
Whole grain foods	Nutrition Activity	0.7 0.6	0.6 0.6	0.0 (-0.3 to 0.3)	0.7 0.6	0.7 0.7	0.0 (-0.3 to 0.4)
Global dietary quality score	Nutrition Activity	55.1 57.3	62.1 58.0	5.2 (0.4 to 10.1)*	54.7 55.0	64.0 55.4	8.9 (4.4 to 13.4)*

* statistically significant p<0.05

Source (Delichatsios et al 2001, pg 220)

Table 6.5 Mean change in intake of food groups on the PrimeScreen

Food groups	Group	Baseline (n=148 nutrition, 150 activity)	3 months	6 months	Adj difference baseline to 3 months (95%CI)	Adj diff baseline to 6 months (95%CI)
Fruit	Nutrition Activity	1.1 1.2	1.5 1.2	1.5 1.2	0.3 (0.2 to 0.5)	0.4 (0.2 to 0.6)*
Vegetables	Nutrition Activity	1.3 1.2	1.5 1.3	1.5 1.4	0.2 (0.0 to 0.4)	0.1 (-0.1 to 0.3)
Red/ processed meats	Nutrition Activity	0.4 0.4	0.4 0.3	0.4 0.4	0.0 (0.0 to 0.1)	0.0 (-0.1 to 0.1)
Whole fat dairy products	Nutrition Activity	0.6 0.5	0.4 0.5	0.4 0.4	-0.1 (-0.2 to 0.0)	0.0 (-0.1 to 0.1)
Whole grain foods	Nutrition Activity	0.4 0.4	0.5 0.4	0.5 0.4	0.0 (-0.1 to 0.1)	0.1 (-0.1 to 0.2)

* statistically significant p<0.05

Source (Delichatsios et al 2001, pg 221)

For the FFQ results it is important to note that only 70 (47%) nutrition participants and 44 (29%) activity participants were included in the 3 months analysis and that only 61 (41%) nutrition participants and 53 (35%) activity participants were included in the 6 months analysis.

The results from the FFQ questionnaire indicate that from baseline to 6 months the nutrition intervention group compared to the physical activity group increased their average intake of fruit by 1.1 (95%CI 0.4 to 1.7) servings per day (Delichatsios et al 2001, pg 219). There were no statistically significant differences for the other food groups. At 6 months the nutrition group had an 8.9 point greater increase in the diet quality score than the physical activity group (95%CI 4.4 to 13.4). This difference is reported to translate into approximately 0.4 servings of fruit or 0.5 servings of vegetables per day (Delichatsios et al 2001 pg 219).

For the PrimeScreen questionnaire results were analysed on an intention to treat basis with all 148 nutrition participants and 150 activity participants included. There were no statistically significant effects except for fruit intake at 6 months which increased by 0.4 pieces per day (95%CI 0.2 to 0.6) in the nutrition group compared to the activity group.

Nutrient intake: The study also estimated the effects for each study group on intake of nutrients (see section 12.2.4 for a description of outcome composition and scoring). Table 6.6 and Table 6.7 show results for the two study groups using the FFQ and PrimeScreen questionnaires respectively.

Table 6.6 Mean change in intake of nutrients on the FFQ

Nutrient	Group	Baseline (n=70 nutrition, 44 activity)	3 months	Adj diff baseline to 3 months (95%CI)	Baseline (n=61 nutrition, 53 activity)	6 months	Adj diff baseline to 6 months (95%CI)
Dietary fiber (g)	Nutrition Activity	22 21	21 20	1.5 (-2.1 to 5.1)	21 20	22 18	4.0 (0.1 to 7.8)*
Saturated fat (% energy)	Nutrition Activity	10.2 10.0	9.4 10.5	-1.4 (-3.0 to 0.3)	10.1 10.3	8.8 10.5	-1.7 (-2.7 to -0.7)*
Folate (µg)	Nutrition Activity	357 341	335 320	8.7 (-41.1 to 58.5)	339 316	340 290	39.8 (-11.0 to 90.7)
Calcium (mg)	Nutrition Activity	836 799	680 724	-57 (-161 to 47)	806 795	648 680	-31 (-147 to 84)
Iron (mg)	Nutrition Activity	15.0 13.4	14.4 13.9	-0.6 (-2.8 to 1.7)	14.4 13.5	13.6 12.1	1.1 (-1.0 to 3.2)
Vitamin A (retinol equivalents)	Nutrition Activity	1856 1659	1747 1737	-165 (-619 to 289)	1917 2020	1811 1619	198 (-354 to 749)
Vitamin C (mg)	Nutrition Activity	187 175	182 154	21 (10 to 52)	183 156	183 142	30 (-6 to 66)
Beta-carotene (µg)	Nutrition Activity	13,200 12,031	14,521 13,634	-441 (-3699 to 2816)	12,678 10,094	14,561 11,692	1052 (-2598 to 4703)

* statistically significant p<0.05

Source (Delichatsios et al 2001, pg 220)

Table 6.7 Mean change in intake of nutrients on PrimeScreen

Nutrient	Group	Baseline (n=148 nutrition, 150 activity)	3 months	6 months	Adj difference baseline to 3 months (95%CI)	Adj diff baseline to 6 months (95%CI)
Dietary fibre (g)	Nutrition Activity	6.2 6.0	7.2 6.1	7.3 6.2	1.0 (0.4 to 1.6)*	1.0 (0.4 to 1.6)*
Saturated fat (% energy)	Nutrition Activity	12.6 12.2	10.9 11.8	10.7 11.5	-1.2 (-2.1 to -0.4)*	-1.0 (-1.9 to -0.2)*
Folate (µg)	Nutrition Activity	125 123	147 127	144 124	18 (5 to 31)*	18 (6 to 31)*
Calcium (mg)	Nutrition Activity	295 315	320 336	318 304	-7.0 (-44 to 30)	23 (-15 to 60)
Iron (mg)	Nutrition Activity	4.2 3.8	4.2 3.8	4.2 3.8	0.3 (-0.002 to 0.7)	0.3 (-0.1 to 0.7)
Vitamin A (retinol equiv.)	Nutrition Activity	621 644	749 648	776 660	112 (11 to 212)*	126 (13 to 238)*
Vitamin C (mg)	Nutrition Activity	74 78	91 77	92 75	16 (6 to 26)*	19 (9 to 29)*
Beta-carotene (µg)	Nutrition Activity	2432 2382	3039 2451	3077 2551	554 (149 to 960)*	484 (62 to 905)*

* statistically significant p<0.05

Source (Delichatsios et al 2001, pg 221)

It was estimated that the nutrition group increased dietary fibre intake by 4.0 g/day (95%CI 0.1 to 7.8) compared to the activity group on the FFQ. The nutrition group also decreased estimated saturated fat as a proportion of energy intake by 1.7% (95%CI -2.7 to -0.7) compared to the activity group. There was no statistically significant estimated change in the intake of other nutrients at 3 or 6 months using the FFQ (Delichatsios et al 2001, pg 219).

The Prime screen results showed an increase in estimated dietary fibre of 1.0 g/day (95%CI 0.4 to 1.6) for the nutrition group compared to the activity group at 6 months, as well as an estimated increase in folate of 18µg/day (95%CI 6 to 31), an increase in vitamin A of 126 retinol equivalents per day (95%CI 13 to 238), an increase in vitamin C of 19mg/day (95%CI 9 to 29) and an increase of beta-carotene of 484µg/day (95%CI 62 to 905). At 6 months, there was also a significant decrease in estimated saturated fat in the nutrition group compared to the activity group of 1% of energy intake (95%CI -1.9 to -0.2).

Use of TLC: The median number of calls made to the TLC system during the 6 month study period was 6.5 (range 0 to 28) by the nutrition group (Table 6.8). A quarter of the nutrition group did not access the system during the study. Access figures are not provided for the physical activity group.

Table 6.8 Access to the TLC system by the nutrition group during the 6 mth intervention period

Accessed the TLC system	Number of subjects (%) n=148
Never	36 (24)
1-10 (low)	53 (36)
11-20 (medium)	34 (23)
>21 (high)	27 (18)
Median in 6 months	6.5 (range 0 to 28)

Stage of change: The stage of change results indicate that the greatest differences between the two groups were for fruit and whole grain foods (Table 6.9). Data to inform this analysis were available for 131/148 (89%) for the nutrition group and for 115/150 (77%) of the activity group. Results are presented on an intention to treat basis.

Table 6.9 Number of participants in each good having positive movement in stage of readiness to change between baseline and 6 months for each food group

Food group	Nutrition group n=148* (%)	Activity group n=150* (%)
Fruits	72 (49)	42 (28)
Whole grain foods	52 (35)	30 (20)
Vegetables	50 (34)	35 (23)
Red and processed meats	74 (50)	58 (39)
Whole fat dairy goods	75 (51)	61 (41)

Source (Delichatsios et al 2001, pg 220-221)

*Results have been recalculated to reflect an intention to treat analysis

Clinical parameters

Not reported.

Service utilisation

Not reported.

Mortality

Not reported.

Morbidity

Not reported.

6.4 Program costs

As reported by trial

The trial by Delichatsios et al (2001) does not report any costs associated with the nutrition or physical activity interventions.

Based on resource use

The resource use for the two groups compared in the Delichatsios et al (2001) study would be exactly the same. The nutrition intervention is therefore compared with a control group who are assumed to incur only the costs of screening. Costs are estimated based on described resource use.

Nutrition intervention group: The costs would include personnel costs and technical costs. These are summarised in Table 6.10 and Table 6.11.

Table 6.10 Summary of personnel costs

	Number	Length of consult	Cost per hour	Cost for study	Average cost per person
Screening interview	1738	10	$122.15	$35,382.78	$118.73
Training and education session	148	60	$122.15	$18,078.20	$122.15
IT support for system				$50,000.00	$337.84

The following assumptions are made when estimating the personnel costs:

- A GP costs $122.15 per hour (AMA, 2003)
- Training and education are assumed to take 1 hour and to be undertaken by a GP
- IT support for the system is assumed to cost a lump sum of $50,000 for 1 year to service 1000 people

Table 6.11 Summary of technical costs

	Number per person	Number	Cost per item	Cost for group	Average cost per person
Cost of TLC system				$200,000.00	$1,351.35
Cost of nutrition program				$20,000.00	$135.14
Telephone calls	6	148	$0.40	$355.20	$2.40

The following assumptions were made when estimating the technical costs

- The cost of developing a TLC system is estimated as a lump sum of $200,000
- The cost of developing the nutrition program is estimated as a lump sum of $20,000
- 6 telephone calls would be required per person per year to access the system at a cost of 40 cents each (Telstra, 2003)

No diet group: The no diet group is assumed to incur no costs.

Total cost: The total cost and the average cost per person for each of the groups is shown in Table 6.12.

Table 6.12 Total costs and average cost per person for the intervention and control groups

	NUTRITION GROUP		NO DIET GROUP	
Year 1	Cost for group	Average cost per person	Cost for group	Average cost per person
Personnel costs	$85,769.59	$578.72	$0.00	$0.00
Technical costs	$220,355.20	$1,488.89	$0.00	$0.00
Total costs	$306,124.79	$2,067.61	$0.00	$0.00

It should be noted that researcher estimates are used for the costs of the computer technology as actual costs were unavailable. These estimates should be interpreted with care due to the uncertainty.

6.5 Performance

Cost effectiveness

The trial compared a nutrition intervention to a physical activity intervention. The costs of the two are identical and the nutrition intervention proved more effective at changing people's diet. The nutrition intervention therefore dominates the physical activity intervention (more benefit for same cost) and the physical activity intervention is not further considered in the economic section of this report.

The economic section of this report concentrates on comparing the nutrition intervention to a 'do nothing' alternative or a true control group. The outcomes for the control group are assumed to be the baseline values for the nutrition intervention group and the cost of this control group is assumed to be zero. This poses some methodological problems such as the effects of the intervention cannot be distinguished from the natural course of the disease, regression to the mean, and the effects of other factors.

At baseline those in the nutrition group were consuming a mean of 2.8 serves of fruit per day compared to 3.2 at 6 months. At baseline those in the nutrition group were consuming a mean of 3.8 serves of vegetables per day compared to 4.5 at 6 months. At baseline the mean global diet quality score was 54.7 in the nutrition group rising to 64.0 at 6 months.

The cost per person of the nutrition intervention is estimated as $487.94 compared to no cost for a control group (assumed to have baseline outcomes).

The ICERs for the nutrition intervention compared to a control group are as follows:

For an increase of one serve of fruit or vegetables per day on average
ICER= ($2,067.61-$0.00)/(7.7-6.6)
=$1,879.65 per additional serve of fruit or vegetables per day

For an increase of one point on the global diet quality score
ICER= ($2,067.61-$0.00)/(64-54.7)
=$2,067.61/9.3
=$222.32 per point increase on the global score

6.6 Modelling

This intervention has not been modelled for several reasons. Firstly the estimates of cost based on resource use are arbitrary due to our inability to obtain exact estimates for the very specific computer technology. Cost is likely to be a key input to any economic model. Secondly the results of this analysis are not presented in a form that is compatible with the fruit and vegetable model developed. In order for this intervention to be modelled we would require the proportion of people consuming more than 5 serves of vegetables at baseline and final follow up. For these reasons the preliminary estimates of cost effectiveness are the best estimates given the uncertainty.

7. General practice based brief counselling by nurses for low-income groups

7.1 Description

Intervention type – broad description

This chapter was concerned with general practice based dietary interventions. The exemplar used was a UK intervention designed to measure the effect of brief behavioural counselling by nurses based in general practices on the consumption of fruit and vegetables by adults from a low income population. Participants were recruited between 25th June 1999 and 3rd November 2001.

References/sources of evidence

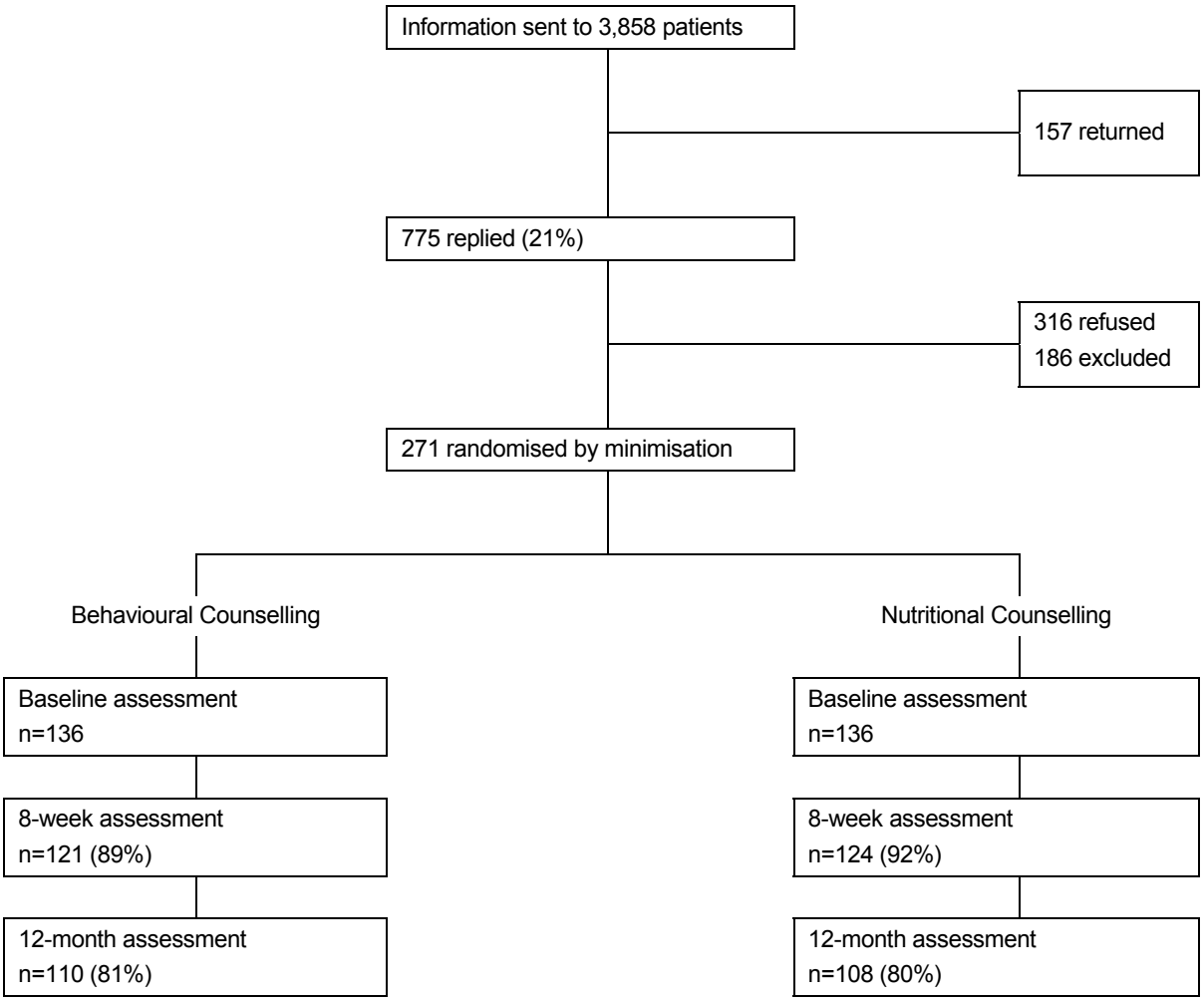
This intervention is reported in:
"Behavioural counselling to increase consumption of fruit and vegetables in low income adults: randomized trial" (Steptoe et al., 2003).

Recruitment and target population

Over three and a half thousand patients aged 18-70 years who were registered at one primary health centre in a deprived inner city area (Jarman[1] score of 40.3) were sent an invitation to participate. Seven hundred and seventy-five participants replied. From among those who replied, people with a serious illness, pregnant women or women who planned to become pregnant within the next 12 months, were excluded and only one person per household was eligible. People taking vitamin supplements were not excluded but participants who were doing so were asked to maintain a constant dose throughout the trial. In total, 271 people were randomized to either the behavioural counselling (136) or nutritional counselling (135) group. One hundred and ten people in the behavioural counselling and 108 people in the nutrition counselling groups completed the 12-month follow-up. (Figure 7.1)

[1] 'The Jarman underprivileged area score … was introduced in 1983 and is a composite measure of eight factors derived from census data. Although the Jarman score is often described and used as if it were a measure of social deprivation, it is, in fact, related to general practitioners' perceptions of the census factors that most affect their workload.' Jarman, B. 1983. Identification of underprivileged areas. *Br Med J (Clin Res Ed),* **286,** 1705-9. The Department of Health currently sets three bands of deprivation payment corresponding to Jarman scores of 30, 40 and 50.' A higher score attracts a higher level of deprivation payment. Crayford, T., Shanks, J., Bajekal, M. and Langford, S. 1995. Analysis from inner London of deprivation payments based on enumeration districts rather than wards. *Bmj,* **311,** 787-8.

Figure 7.1 Recruitment and retention of participants



Source: (Steptoe et al., 2003)

After several months of recruitment, the recruitment invitations were modified to discourage people with a weekly income of more than £400 (AU$996)[2] from volunteering, because it was found that many participants had relatively high incomes, suggesting that the study was attracting more affluent residents. Approximately two-thirds of participants were in the low income category (defined as (<£400/week). The average age of the participants was 43 years and approximately 60% were female. (Table 7.1)

[2] Exchange rate UK£1 = AU$2.49064123.0

Table 7.1 Baseline characteristics of the behavioural and nutritional counselling groups

	Behavioural Counselling (n=136)	Nutritional Counselling (n=135)	Chisq p values*
Women	82 (60%)	84 (62%)	0.745
Weekly household income			0.567†
<£400	91 (67%)	86 (64%)	
>£400	40 (29%)	44 (33%)	
Missing	5 (4%)	5 (4%)	
Mean (SD) age	43.3 (13.8)	43.2 (14.0)	
Ethnicity			0.714‡
White	94 (69%)	96 (71%)	
Black	37 (27%)	32 (24%)	
Asian	3 (2%)	5 (4%)	
Missing	2 (1%)	2 (1%)	
Home ownership	69 (51%)	59 (44%)	0.246
In receipt of benefits	50 (37%)	43 (32%)	0.394
Mean (SD) body weight (kg)	71.2 (15.5)	73.0 (16.6)	NA
Mean (SD) BMI (kg/m^2)	25.5 (4.9)	26.3 (5.8)	NA
Current smokers	47 (35%)	44 (33%)	0.732
Mean (SD) plasma chol (mmol/l)	4.90 (0.97)	5.03 (1.0)	NA
Mean (SD) blood pressure			NA
Systolic (mm Hg)	123.0 (17.8)	123.0 (17.6)	
Diastolic (mm Hg)	78.8 (10.7)	77.8 (10.4)	
Taking vitamin supplements	40 (29%)	38 (28%)	0.818
Stage of readiness for change			0.598
Precontemplation	38 (28%)	31 (23%)	
Contemplation	25 (18%)	29 (21%)	
Preparation	73 (54%)	75 (56%)	

Notes:

* No significance test included in (Steptoe et al., 2003). Chisq tests undertaken at HEU during the preparation of this report.

† Missing data excluded from the chisq test

‡ Missing data excluded and, because of the small number of expected counts in some of the cells, the categories were recoded into two groups 'white' and 'others' for the chisq test.

NA = chisq test not appropriate for these data

Intervention

Each intervention consisted of two 15 minute individual consultations; one was carried out immediately after the baseline assessment and the second two weeks later. Written information was prepared to support the consultations. Two research nurses undertook both the nutritional and behavioural counselling. Sessions were audio taped to monitor the quality of interventions and to ensure that the two types of counselling remained distinct.

Nutrition counselling (n= 135): Members in the nutritional counselling group received education about the importance of increasing consumption of fruit and vegetables, emphasising beneficial nutritional constituents and the way these act biologically to maintain health. The bioactive constituents of fruit and vegetables were described in lay terms, together with the range of effects that they have on bodily processes. The nurses emphasised the 'five a day' message which indicated that participants should aim to eat at least five portions of a variety of fruit and vegetables

each day and included examples of what constitutes one portion of fruit and one portion of vegetables. Three participants did not attend the second counselling session.

Behavioural counselling (n=136): Behavioural counselling was founded on social learning theory and the stage of change model which posits that the most appropriate methods of encouraging behaviour change vary with the motivational readiness of the individual. Interventions were tailored to the individual, with personalised specific advice, and setting of short and long term goals.

7.2 Quality of the trial

Recruitment

Participants were recruited progressively but it is not clear over what period of time. Enrolled patients were sent invitations in the mail, but the steps involved in the progression from invitation to acceptance into the trial are not specified. Response to the invitation was low (775), and of those who responded, 316 were refusals. This meant that 459 out of 3701 (12%) indicated that they wished to participate. Reasons for not replying to the invitation are not known and could include ineligibility because of the income criteria. No information was available about the eating habits or income of those who did not respond and those who refused to participate so it is unclear how representative the participants were of the study population – low income earners enrolled in the practice. Based on information available from other sources, the authors indicated that those who participated did not seem 'remarkable' with respect to their fruit and vegetable intake at the start of the study.

Control group

Only one person from each family was eligible to participate and those who participated were randomized to either the control and intervention group on an individual basis. The control group received nutritional counselling which had 'substantive' effects on behaviour. Randomization was undertaken by a member of the research team who had no contact with the participants. The 'minimization' method of randomization was used. In this method, group allocation is designed to reduce differences between the groups in the distribution of factors which are known (or suspected) to determine outcome. When a patient is about to enter a trial, the factors are listed and allocation to either group is made by determining in which group inclusion would minimise any differences in these factors between the groups. For example if the intervention group has a higher average age and a disproportionate number of smokers, other things being equal, the next elderly smoker is likely to be allocated to the control group.

Evaluation method

The evaluation method used a comparison of the pre-post differences for the control and intervention groups on a range of outcome measures. A sub-group analysis was undertaken for those designated as low-income. All analyses were performed on an intention-to-treat basis.

Bias, confounders, effectiveness and efficacy

The control group received nutritional counselling which had an effect on the dietary behaviour of participants. Comparison of the pre-post difference in the behavioural counselling group with the pre-post difference in the nutritional counselling group may not give a true indication of the impact of the intervention.

The average baseline ascorbic acid level for the behavioural counselling group was 75.6 µmol/l (SD 33.3) and for the nutritional group it was 78.0 µmol/l (SD 33.0). For the low income group the levels were very similar; 71.2 µmol/l (SD 34.7) for the behavioural group and 75.8 µmol/l (SD 33.0) for the nutritional group. Compared to the EPIC-Norfolk study the average levels fall within the highest

quintile range for plasma ascorbic acid concentration, but the spread of the scores means that the study will have attracted some participants with much lower levels. (Table 7.2) To the extent that the study attracted participants with relatively high levels of ascorbic acid levels this may have limited the effectiveness of the intervention when measured in terms of the biochemical markers.

Table 7.2 Plasma ascorbic acid concentrations for men and women in the EPIC-Norfolk study

	Ascorbic acid quintile:				
	1	2	3	4	5
Women					
Mean conc. (SD)	30.3 (10.1)	49.5 (3.1)	59.1 (2.6)	67.8 (2.6)	85.1 (13.7)
Mean age (SD)	59.8 (9.1)	58.8 (9.0)	58.0 (8.6)	58.6 (8.6)	58.6 (8.5)
Men					
Mean conc. (SD)	20.8 (7.1)	38.1 (3.5)	48.1 (2.6)	56.8 (2.6)	72.6 (11.5)
Mean age (SD)	60.1 (9.0)	59.4 (8.9)	58.9 (8.6)	58.6 (8.7)	58.8 (8.7)

7.3 Outcomes – as reported

The trial was analysed on an intention-to-treat basis. Baseline values were brought forward for participants with data missing at 12 months. Outcome measures included change in dietary behaviour and clinical indicators including potential biological mediators. (Table 7.3)

Table 7.3 Outcome measures, data sources and analyses reported in the study

Outcome measures	Data sources	Analyses
1. BEHAVIOUR CHANGE		
Consumption of fruit and vegetables	A two-item frequency questionnaire which asked participants how may pieces of fruit and how many portions of vegetables they ate on a typical day. (Participants were given detailed information about portion sizes.)	Comparison of change between baseline and 12-month follow-up in behavioural and nutritional counselling groups: - average number of portions of fruit and vegetables eaten per day - proportion of participants in each group who ate five portions per day.
Diet	Dietary instrument for nutrition education (DINE) that accounts for most fat and fibre in the typical UK diet	Comparison of change between baseline and 12-month follow-up in behavioural and nutritional counselling groups in:: - DINE scores for fat consumption - DINE scores for fibre consumption.
2. SERVICE USE – no reported measures		
3. MORTALITY – no reported measures		
4. CLINICAL INDICATORS		
Blood pressure	Measured after the participants had been sitting for 10 minutes using the average of three consecutive readings with a digital sphygmomanometer (Omron HEM705CP).	Comparison of changes between baseline and 12-month follow-up for behavioural and nutritional counselling groups.
Weight/BMI	Not stated	As above

Outcome measures	Data sources	Analyses
Cholesterol concentration	Not stated	As above
Potential biological mediators	Non-fasting blood samples stored at –70°C until the end of the trial and then analysed	Blood samples analysed for plasma ascorbic acid (Vitamin C), α tocopherol (Vitamin E) and β carotene*
	24-hour urine samples collected by participants	Measurement of potassium excretion

Notes:

* Ascorbic acid assays were carried out at the University of Cambridge with a fluorimetric assay and analyses of, α tocopherol and β carotene were conducted with normal phase high performance liquid chromotography (AASC, Hampshire).

Behaviour change

Both groups increased the number of portions of fruit and vegetables consumed per day. After adjustment for covariates, the increase was greater in the behavioural counselling group than in the nutrition counselling group and this was statistically significant ($p = 0.021$). The number increase in those eating five or more portions a day was also greater in the behavioural group compared to the nutritional group ($p = 0.019$). DINE scores for fat consumption fell for both groups, while fibre intake scores increased in the behavioural group only. The differences between the groups were not statistically significant. (Table 7.4)

In the low income group only, the increase in the number of portions was twice as great in the behavioural than in the nutrition group (1.67 vs 0.87, $p = 0.007$) but the difference between the groups in the proportion of participants reporting that they ate at least five portions of fruit and vegetables per day was not statistically significant (41% vs 28%, $p = 0.12$).

Clinical parameters

Plasma β carotene and α tocopherol concentrations increased in both groups, with no changes in plasma ascorbic concentration or potassium excretion. The difference between the groups in terms of the β carotene concentration approached statistical significance at $p < 0.05$. (Table 7.5)

In the low income group, the behavioural group showed significantly larger increases in plasma β carotene concentration ($p=0.023$) and potassium:creatinine ratio ($p=0.046$) compared to the nutritional group.

Table 7.4 Comparison of changes in behaviour between baseline and follow-up at 12 months

Outcome measure	Behavioural Counselling			Nutritional Counselling			Adjusted difference in change at 12 months		P value for adjusted difference
	Baseline	Mean Change at 12 Months (95% CI)		Baseline	Mean Change at 12 Months (95% CI)				
	Mean (SD)	Unadjusted	Adjusted*	Mean (SD)	Unadjusted	Adjusted*	Mean	95% CI	
Complete Sample									
Portions of fruit and veg/ day	3.60 (1.81)	1.44 (1.09 , 1.80)	1.49 (1.2 , 1.86)	3.67 (2.00)	0.99 (0.63 , 1.34)	0.87 (0.50 , 1.25)	0.62	(0.09 , 1.13)	0.021
Participants eating ≥5 portions/day (%)	21.3%	40.2% (31.3 , 49.0)	42.2% (33.1 , 51.2)	26.7%	28.7% (19.9 , 37.6)	26.8% (17.6 , 36.0)	15.4%	(2.52 , 28.3)	0.019
DINE Scores									
-Fibre intake	15.0 (6.8)	0.08 (0.01 , 0.16)	0.11 (0.03 , 0.19)	13.8 (6.0)	0.08 (0.1 , 0.15)	0.07 (-0.01 , 0.15)	0.04	(-0.08 , 0.15)	0.55
-Fat intake	28.5 (13.4)	-4.06 (-5.71, -2.40)	-4.10 (-5.93, -2.28)	27.1 (13.9)	-2.92 (-4.59,-1.26)	-2.09 (-3.91, -0.24)	-2.01	(-4.60 , 0.58)	0.13
Low Income Sample									
Portions of fruit and veg / day	3.34 (1.67)	1.64 (1.20 , 2.08)	1.67 (1.22 , 2.11)	3.76 (2.11)	0.87 (0.41 , 1.23)	0.78 (0.31 , 1.24)	0.89	(025 , 1.54)	0.007
Participants eating ≥5 portions/day (%)	16.5%	40.5% (29.4 , 51.7)	41.0% (29.7 , 52.4)	27.9%	29.9% (18.3 , 41.5)	28.0% (16.2 , 39.9)	13.0%	(-3.41 , 29.4)	0.12

Self report data

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

Table 7.5 Change in clinical indicators between baseline and follow-up at 12 months (complete sample)

Outcome measure	Behavioural Counselling			Nutritional Counselling			Adjusted difference in change		P value for adjusted difference
	Baseline	Mean Change (95% CI)		Baseline	Mean Change (95% CI)				
	Mean (SD)	Unadjusted	Adjusted*	Mean (SD)	Unadjusted	Adjusted	Mean	95% CI	
BMI (kg/m^2)	25.5 (4.9)	-0.03 (-0.23 , 0.17)	0.01* (-0.20 , 0.21)	26.2 (5.8)	-0.03 (-0.20 , 0.20)	-0.04 (-0.24 , 0.17)	0.04	(-0.25 , 0.33)	0.77
Systolic BP (m Hg)	123.0 (17.8)	-0.86 (-3.06 , 1.34)	-0.80 (-3.08 , 1.48)	123.0 (17.6)	-0.54 (-2.76 , 1.68)	-0.56 (-2.88 , 1.76)	-0.24	(-3.50 , 3.02)	0.88
Diastolic BP (m Hg)	78.6 (10.7)	-0.07 (-1.54 , 1.41)	-0.13 (-1.68 , 1.42)	77.8 (10.4)	0.05 (-1.43 , 1.54)	0.03 (-1.54 , 1.59)	-0.16	(-2.36 , 2.05)	0.89
Cholesterol (mol/l)	4.90 (1.0)	-0.08 (-0.18 , 0.02)	-0.09 (-0.19 , 0.01)	5.03 (1.0)	-0.07 (-0.17 , 0.03)	-0.07 (-0.17 , 0.04)	-0.02	(-0.17 , 0.12)	0.77
β Carotene (μmol/l)*	0.90 (0.62)	1.22 (1.08 , 1.39)	1.20 (1.08 , 1.33)	0.92 (0.68)	1.06 (0.94 , 1.21)	1.04 (0.94 , 1.15)	0.16	(0.001 , 1.34)	0.05
α Tocopherol (μmol/l)†	25.6 (11.3)	8.87 (6.85 , 10.9)	8.81 (7.12 , 10.5)	27.4 (10.9)	7.28 (5.25 , 9.31)	7.30 (5.58 , 9.02)	1.52	(-0.91 , 3.95)	0.22
Ascorbic acid (μmol/l)‡	75.6 (33.3)	-2.80 (-7.76 , 2.17)	-4.06 (-8.52 , 0.41)	78.0 (33.0)	0.12 (-4.89 , 5.12)	0.51 (-4.00 , 5.01)	-4.57	(-10.9 , 1.80)	0.16
Potassium excretion (mmol/24 hr)	73.0 (26.0)	0.19 (-3.33 , 3.70)	0.19 (-3.14 , 3.52)	75.0 (27.6)	-0.63 (-4.04 , 2.77)	-0.27 (-3.52 , 2.98)	0.46	(-4.22 , 5.13)	0.85
Potassium/creatinine ratio	6.34 (2.26)	-0.05 (-0.34 , 0.24)	-0.07 (-0.35 , 0.21)	6.69 (2.32)	-0.24 (-0.53 , 0.03)	-0.20 (-0.48 , 0.07)	0.13	(-0.27 , 0.53)	0.52

* Adjusted for sex, age, ethnicity, income, smoking and body mass index

7.4 Program costs

As reported

There were no reported costs for the intervention.

Based on resource use

The estimated cost of implementing both arms of the trial was$262,162. The cost per enrolled participant was $964 and the cost per completer.

Table 7.6 Estimated costs of implementing the 12 trial in 2003 AUS$ based on resource use

Cost item	Number	EFT	Duration	Rate	AUS$ 2003
Staff					
Nurses*	2	0.50	2 yrs	$52,136	$143,985
Pgm Management†	1	0.10	2 yrs	$77,496	$19,374
Overheads					
Nurses' rooms‡	1		2	$6,500	$13,000
Fixtures and fittings§					$4,527
Consumables¶					$3,491
Counselling information**					$2,461
Clinical assessment					
Pathology tests††					$73,000
Devices‡‡					$1,227
Estimated total costs					$262,162
Cost per enrolled participant			(n = 272)		$964
Cost per participant completing the 12 month assessment			(n = 218)		$1,203

Notes:

* Nurses (Department of Human Services) Agreement 2001, includes 25% on-costs, and health CPI used to inflate 2001 rates to 2003: 2002=3.41%, 2003 = 6.83%. (Data Source: ABS, 2004)

† Monash University Academic Staff Salary Structure – Senior Research Fellow Level C Step 1, available at http://www.adm.monash.edu.aus/ss/handbook

‡ Based on a commercial quotation mid-range

§ Includes one desk, one staff chair, one computer chair, two client chairs, computer and printer, prices based on commercial quotations

¶ Includes all stationery and telephone calls for recruitment and follow-up and questionnaires

** Commercial quotation from Melbourne University Printing service 1,000 x two types of printed material

†† Commercial quotation for 734 ascorbic acid (plasma), vitamin E (plasma), vitamin D (plasma) and potassium (24 hour urine) from Dorevitch Pathology

‡‡ One set of scales, digital sphygmomanometer and height measures based on prices quoted by Mentone Educational Centre available at http://www.mentone-educational.com.au accessed 27/08/2003

7.5 Performance

Cost effectiveness

The aim of the program was to examine the impact of behavioural counselling by nurses on the consumption of fruit and vegetables by adults from a low income population. As shown in Table 7.7, the cost per person changing to the recommended diet in the behavioural counselling group was 2003 $5,754.

Table 7.7 Cost per changer in the behaviour group

	Baseline	Follow-up
Number of completers	110	110
% eating>=5 portion of fruit and veg per day*	21.30%	42.20%
Number eating >= 5 portions of fruit and veg per day	23	46
Increase in number eating required amounts of fruit and veg per day	23	
Cost per completer	$1,203	
Total costs for completers in behavioural counselling	$132,283	
Cost per changer†	$5,754	

* Assumes that the percentage of completers eating ≥5 portions of fruit and vegetables per day is the same in the completers as in the non-completers.

† Assumes that the only change is an increase in the number of completers eating the required amount.

Cost utility

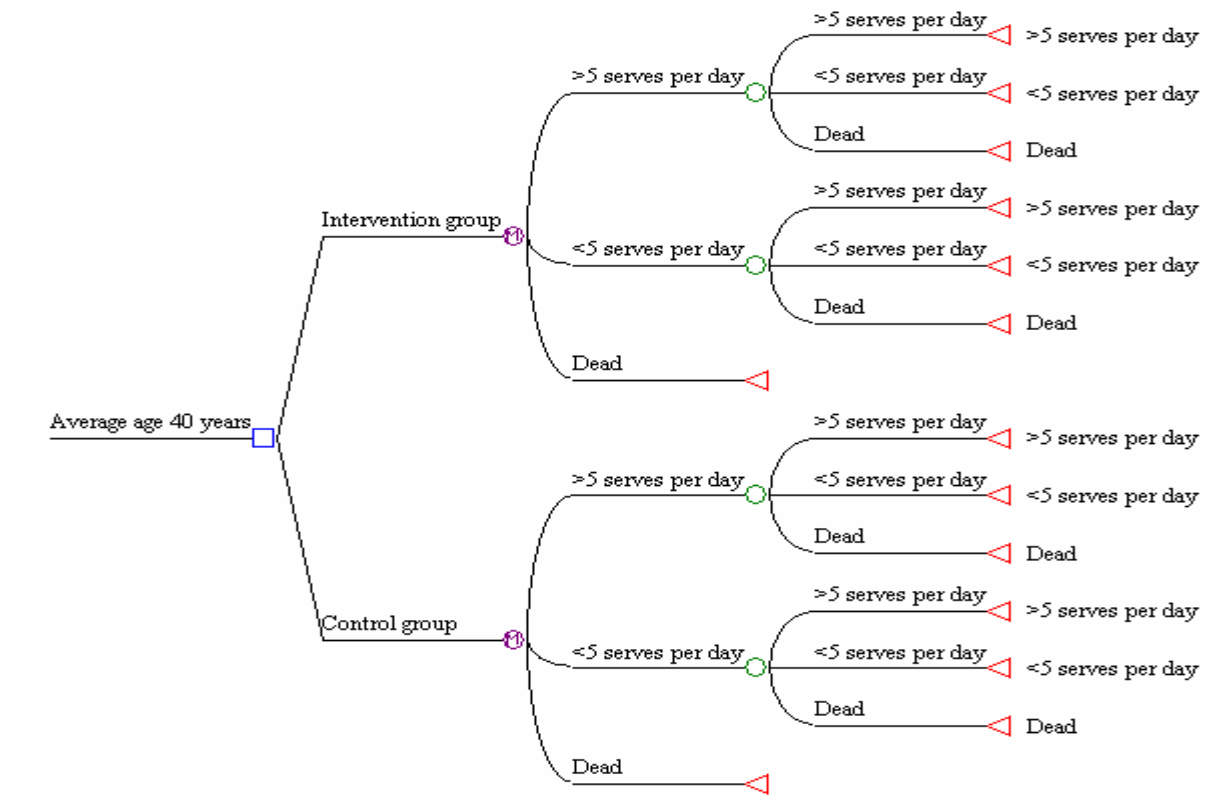
It was estimated the utility score of a person from a low income population eating less than five pieces of fruit and vegetables was 0.7573 and the utility score of such a person eating the required amount would be 0.7770 (based on a Brazier transformation, Brazier, 2002 of the SF-36 scores for people in the first five income deciles in the National Nutrition Survey, 1995). If this increase occurred over twelve months then the increase in utility over the course of a year would be 0.0099 ([0.0.7770-0.7573] x 0.5) and the cost per unit increase in utility would be $584,185 ($5754/0.0099).

7.6 Modelling

Methods

A modelling approach was used to enable the surrogate or intermediate outcome measure of fruit and vegetable consumption (reported by Steptoe et al, 2003) 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: 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) and death. The transitions that are permitted are illustrated in Figure 7.2.

Figure 7.2 Representation of states and permitted transitions in Markov model



We determined the progression, costs and utilities of a cohort of 1000 people receiving the 2 fruit and 5 vegetable campaign compared with a control group who were assumed to receive no program (and who are assigned baseline values with no change from the Steptoe et al, 2003 study). The economic model assumes the cohort is 50% female with an average age of 40 years.

The cohort progressed annually between health states over a 20-year time horizon. 20.9% of people in the intervention group progress from failure to success in the first year of the model according to results from the study by Steptoe et al (2003). It is assumed that all success is maintained and that there is no success in the control group. The model commences with 21.3% of each group in the success state as was the case in the study by Steptoe et al (2003).

Table 7.8 Transition matrix (for cycle 1)

Steptoe intervention

	Success	Failure	Dead
Success	#	-	Mortality rate table
Failure	0.209	#	Mortality rate table
Dead	-	-	1

residual value, - no transition permitted

Transition probabilities vary by cycle for all-cause mortality which was estimated using life tables for the Australian population (ABS, 2002) for adults aged 40 to 60 years. An overall weighted mortality rate for each age year was obtained assuming 50% of our cohort are female. Whiteman et al. (1999) reported that those consuming greater than 5 serves of vegetables per day had a relative risk of premature morality of 0.68, this figure has been adjusted for the prevalence of people in the Australian population consuming more than 5 serves of vegetables (10%, Department of Health, WA, 2003). This adjustment gives relative risk of 0.94 for those consuming more than 5 serves and 1.38 for less than 5 serves. The resulting mortality rates are shown in Table 7.9.

Table 7.9 Mortality rates (weighted for gender and adjusted for % eating more than 5 serves per day)

Age	<5 serves	>5 serves
40	0.0017	0.0012
41	0.0019	0.0013
42	0.0020	0.0014
43	0.0022	0.0015
44	0.0023	0.0016
45	0.0025	0.0017
46	0.0026	0.0018
47	0.0028	0.0019
48	0.0030	0.0020
49	0.0033	0.0022
50	0.0035	0.0024
51	0.0039	0.0026
52	0.0043	0.0029
53	0.0047	0.0032
54	0.0053	0.0036
55	0.0058	0.0040
56	0.0064	0.0044
57	0.0071	0.0048
58	0.0079	0.0053
59	0.0087	0.0059
60	0.0095	0.0065

A utility weight 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. These values were obtained by performing a Brazier transformation on data from the National Nutrition survey (1995).

The costs for the intervention group were obtained from Table 7.6 giving an estimate of $964 per person for the first year of the model. The control group are not assumed to incur any costs. The downstream costs associated with consuming less than 5 serves are not considered in the base case analysis (although a threshold analysis is presented in sensitivity analysis).

Costs and benefits are discounted at 5% per annum. Extensive univariate sensitivity analyses were performed for the assumptions and values described in Table 7.10.

Table 7.10 Sensitivity analysis: attributes, base case and alternative assumed values

Assumptions	Base case	Alternative Values	Source
Cost of intervention per person	$964	$1203	Table 21.6 Cost per person completing 12 month assessment
Time horizon	20	5, 10, 15	Researcher judgment
RR of mortality	1.38 <5 serves 0.94 >5 serves	Upper: 1.65 (<5 serves) 0.89 (>5 serves) Lower: 1.15 (<5 serves) 0.98 (>5 serves)	95% confidence intervals from Whiteman et al 1999
Discount rate	5%	0%, 3%	Researcher judgment

Results

Table 7.11 presents the economic performance of the Steptoe intervention, at an incremental cost utility ratio of $10,555 per QALY gained (for base case assumptions, see Table 7.10)

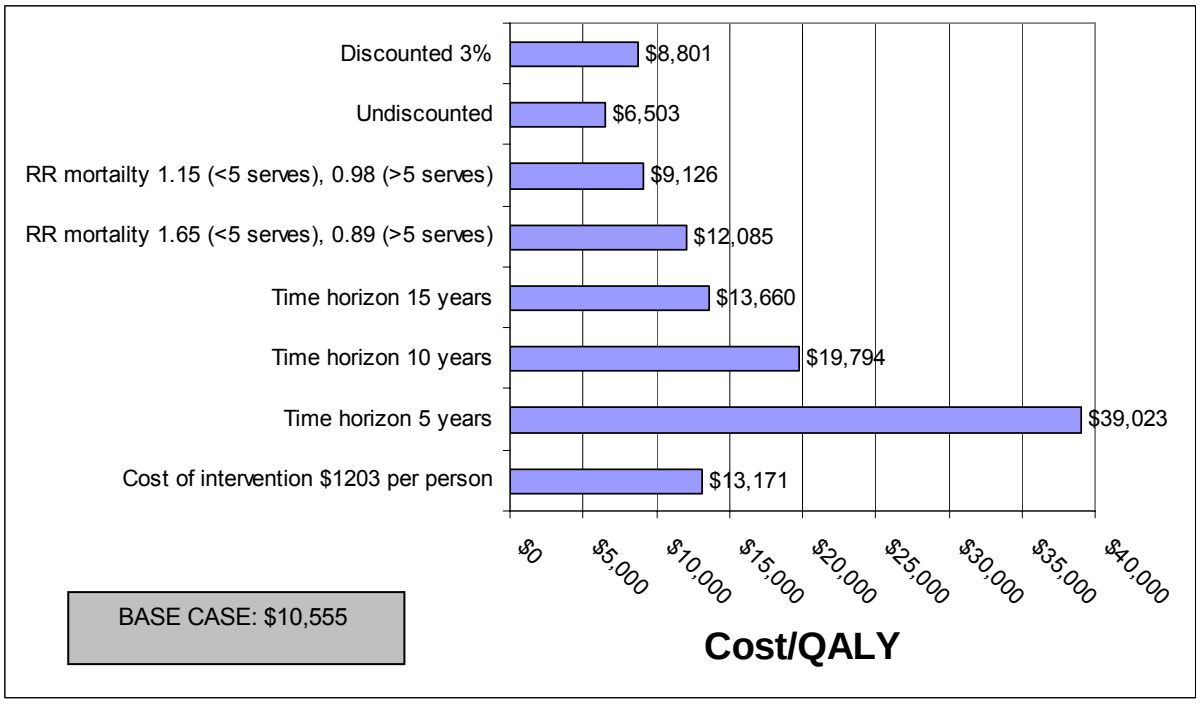
Table 7.11 Modelled cost utility base case results

	Steptoe intervention	Control group	Difference
Total costs	$916.60	$0	$916.60
Total life years	12.217	12.193	0.024
Total QALYs	9.372	9.285	0.087
Discounted $/LY gained			$38,441
Discounted $/QALY gained			$10,555

Sensitivity analyses

The results of univariate sensitivity analyses are presented in Figure 7.3. Results ranges from $6,503 to $39,023 per QALY gained with results being most sensitive to the time horizon of the model.

Figure 7.3 Results of univariate sensitivity analyses



Inclusion of downstream costs: If the downstream costs associated with failing to consume 5 serves of fruit and vegetables per day are 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).

8. Multi media nutrition campaign – 2 fruit 'n' 5 veg every day

8.1 Description

Intervention type – broad description

The broad type of interventions being considered in this chapter are multi-media campaigns aimed at changing people's dietary knowledge and behaviour. Three Australian campaigns were considered:

1. *Go for 2&5* – This was a statewide multi-media campaign aimed at adults resident in Western Australia. The campaign was launched on 21st April 2002 and Phase 1 activities were scheduled to run throughout the year. The campaign was to be evaluated by pre and post telephone surveys. Stated outcome measures were 'awareness of, reaction to and message take-out of the campaign' and 'television advertising effects on adults' beliefs and attitudes' (Department of Health, 2002) At the time of making the decision on which study to include in the report no published data were available in relation to this study. Media statements by the Department of Health, Government of Western Australia in July and November 2003 and conference abstracts[3] indicated that data had been collected and analysed, but there do not appear to be any published literature relating to the results of the campaign and cost data were not available. We were not able to obtain results even by directly petitioning authors.
2. *2 Fruit 'n' 5 Veg Every Day* – This was a statewide, multi-media campaign in Victoria which was launched in 1992 and ran until the end of 1995. The broad objective of the campaign was to increase consumption of fruit and vegetables to recommended levels across all population groups but the 'media buy' in each phase was designed to have maximal impact on subgroups of the population. Results relating to the impact of the campaign were published in 1998 (Dixon, 1998) and some cost data were available. This campaign was based on the campaign strategy for the WA Fruit and Veg Campaign which had been running for three years.
3. *WA Fruit and Veg Campaign* – This was a multi-media campaign in Western Australia aimed primarily at resident adults in the 20-50 year age group. The campaign was implemented in five phases from February 1990 to September 1994. Results of this campaign have been quoted in *An Intervention Portfolio To Promote Fruit and Vegetable Consumption* (National Public Health Partnership, 2000) based on a paper delivered by Miller et al at the Multidisciplinary Approaches to Food Choice conference in Adelaide in 1996. (Miller, 1996)

Clearly if outcome data and cost data were available for the most recent campaign in Western Australia, this would have been included in the risk factor study. But, the most recent campaign for which data were publicly available was the Victorian campaign and therefore this was included in the study.

References/sources of evidence

The description and analysis of the effectiveness of the campaign have been based on reports contained in *Public reaction to Victoria's "2 Fruit 'n' 5 Veg Every Day" campaign and reported consumption of fruit and vegetables* (Dixon et al., 1998) which investigated the campaign's impact on diet-related attitudes, beliefs and behaviours of individual Victorians.

[3] Available on http://www.gofor2and5.com.au, accessed 23rd March 2004 and Daly A. & Pollard C. Health promotion and surveillance: does it take two to tango? XVIII World Conference on Health Promotion and Health Education 2004

Intervention description

Recruitment and target population: This intervention did not require recruitment of the target population. However, the campaign was targeted at different sociodemographic groups in each phase of the campaign. Phase 1 targeted women with children. Phase 2 included men to generalize the message and 'because of the influence men have over food selection and meal preparation in the home', and Phase 3 specifically targeted young men. (Table 8.1)

Intervention: The intervention consisted of a range of promotional strategies between October 1992 and November 1995. The 'central feature' of the campaign was an intensive burst of television advertising conducted over a three-week period in Phases 1 and 2 and for one week in Phase 3. The television commercials were screened at approximately the same time of the year in each phase and coincided with a campaign launch to which health and education professionals, food industry representatives, journalists and politicians were invited. There was a relatively high level of media activity in Phases 1 and 2, but resource constraints meant there were less activity in Phase 3 and none in Phase 4. There were other purchased promotional activities (eg print advertising, transit advertising, sport/arts sponsorships and point of sale promotions), especially in Phase 1 and Phase 2. (Table 8.1)

Table 8.1 Target audience and reported costs of activities in 2 fruit 'n' 5 veg every day campaign

	1992	**1993**	**1994**	**1994**
Purchased promotional activities				
Television advertising	✓ (3 weeks)	✓ (3 weeks)	✓ (1 week)	
Radio advertising		✓		
Print advertising	✓	✓		
Transit advertising	✓			
Sport/arts sponsorships	✓	✓		
Point of sale promotions	✓	✓	✓	
Unpurchased – other*	✓	✓	✓	✓
Target audience for Television advertising	Women with Children	Adults aged 16-54 years	Men aged 18-34 years	No television advertising
Date of television campaign	1-19 Sept	3-23 Oct	9-16 Oct	-

Source: (Dixon et al., 1998) pp. 574-575

Notes:

* 'Other' was not defined but included public relations activities.

8.2 Quality of evidence

Evaluation description

Design: A pre-post design was used to evaluate the trial. However, there were no baseline measures for the outcome variables. The first measurement was performed after Phase 1 of the TV campaign.

Methodology: Four telephone surveys were conducted using identical sampling frames and a set of common questions to examine public awareness of, and reactions to, the campaign, belief about desirable fruit and vegetable eating habits, and self-reported consumption of fruit and vegetables. Surveying was conducted at approximately the same time each year, at 2-3 weeks after the bulk of campaign activity had been conducted in each phase to control for seasonal variability in the consumption of fruit and vegetables. A commercial research company conducted the surveys using a computer-assisted telephone interviewing (CATI) system. Methods of recruitment were identical for all surveys. The respondent for each telephone contact was either the youngest man aged 20 years

or over or, if there was no suitable man, the youngest woman in the age group. Participation rates were highest in the first survey (64%) and lowest in the fourth (44%). (Table 8.2) Half the sample in each survey was female and approximately 55% of each sample was aged 25-49 years. (Table 8.3)

Table 8.2 Participation rates for each survey

	1992	1993	1994	1995
Date of survey	2-5 Oct	3-23 Oct	9-16 Oct	3-5 Nov
Approached	801	1,048	985	1,145
Refused	286	539	474	636
Sample (Participation rate*)	515 (64%)	509 (49%)	511 (52%)	509 (44%)

Source: (Dixon et al., 1998) p. 575

Notes:

* As a percentage of those approached

Table 8.3 Date of the surveys and sociodemographics of the respondents

	1992	1993	1994	1994
Date of survey	2-5 Oct	3-23 Oct	9-16 Oct	3-5 Nov
Total sample	515	509	511	509
Females	260 (50%)	252 (50%)	257 (50%)	254 (50%)
Age				
20 – 24 years	82 (16%)	76 (15%)	69 (13%)	57 (11%)
25 – 34 years	144 (28%)	132 (26%)	92 (18%)	129 (26%)
35 – 49 years	134 (26%)	158 (31%)	183 (36%)	148 (29%)
50+ years	155 (30%)	143 (28%)	167 (33%)	173 (34%)

Source: (Dixon et al., 1998) p. 575

Outcome measures: The outcome measures were survey self-report data relating to awareness of the campaign, beliefs about the appropriate levels of fruit and vegetable consumption and actual levels of fruit and vegetable consumption.

Analysis: The individual was the unit of analysis and comparisons were made between each survey.

Assessment

Sources of bias: The potential sources of bias in the evaluation of the trial were selection bias and measurement bias.

Selection bias: The authors note a number of methodological issues relating to the data. The number of refusals to complete the survey increased markedly in the Phase 2 survey. (See Table 8.2) This may have resulted in a non-response bias if those who refused differed systematically from those who responded.

Measurement bias: There were no baseline measures undertaken before the campaign began and all measures were self-report.

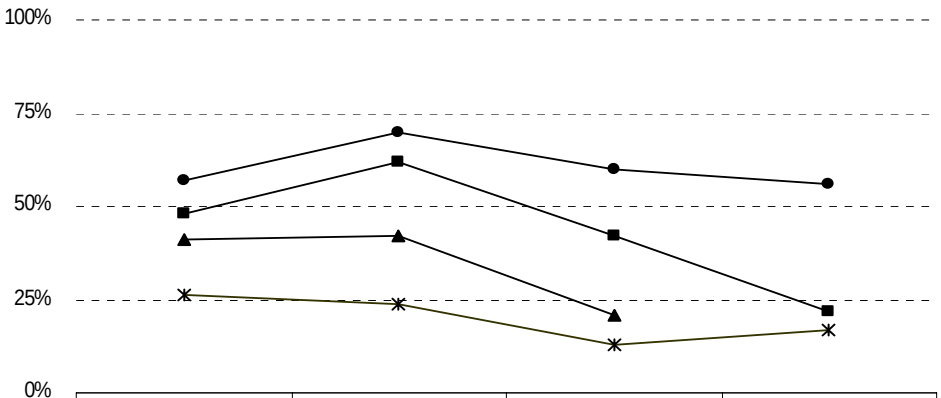
8.3 Outcomes – as reported

The main outcome measures reported were awareness of the campaign and dietary behaviour.

Awareness of the campaign

There were statistically significant differences between the respondents to each survey in terms of their awareness of the campaign. Awareness either increased or stayed the same between the Phase 1 and Phase 2 surveys and then deteriorated in Phases 3 and 4. (Figure 8.1)

Figure 8.1 Proportion of respondents in each survey indicating they were aware of the campaign and specific aspects of it



	1992	1993*	1994**	1995***
Slogan	57%	70%	60%	56%
Campaign	48%	62%	42%	22%
TV advertisements	41%	42%	21%	
Fruit/Veg ads	26%	24%	13%	17%

Source: (Dixon et al., 1998) p. 576

Notes:

* Slogan and Campaign 1993 significantly different from 1992 at $p<0.05$.

** All measures for 1994 significantly different from 1993 at $p<0.05$.

*** Campaign 1995 significantly different from 1994 at $p<0.05$. There were no TV advertisements in 1995.

Behaviour Change

To estimate the consumption of fruit and vegetables, respondents were asked 'On average, how many days per week do you usually eat fruit (vegetables)' and 'When you do eat fruit (vegetables), how many servings of fruit (vegetables) do you eat per day'. Respondents were given descriptions of a serving size for fruit (one medium sized piece of fruit) and vegetables and salad (one small potato or two rounded tablespoons of cooked vegetables or ¾ of a cup of salad). According to Dixon et al these serving sizes corresponded to 120g to 150g of fruit and 60g to 90g of vegetables. Analysis of the results indicated that between Phases 1 and 2 there were significant increases in the average intake of fruit ($p < 0.05$) and vegetables ($p < 0.001$) but no statistically significant changes between Phases 2-3 and 3-4. (Table 8.4)

Table 8.4 Daily consumption of fruit and vegetables and proportion of people eating the recommended levels of fruit and vegetables over the course of the campaign[#]

	Phase 1 Survey	Phase 2 Survey	Phase 3 Survey	Phase 4 Survey
Average daily serves (SD)				
Fruit	1.53 (1.08)	1.71 (1.26)*	1.69 (1.16)	1.67 (1.15)
Vegetables	2.65 (1.51)	3.10 (1.68)**	3.01 (1.65)	3.00 (1.57)
Fruit + Vegetables (Change)	4.18	4.81 (+0.63)	4.70 (-0.18)	4.67 (-0.03)
Proportion of respondents eating the recommended levels (change)				
Fruit ≥2 serves/day	44%	47% (+3%)	48% (+1%)	46% (-2%)
Vegetables ≥5 serves/day	10%	16% (+6%)	16% (+0%)	14% (-2%)

Source: (Dixon et al., 1998) p. 577

Notes:

Because of age and gender distribution in the sample were similar to estimates of the distributions within the Victorian population, it was considered that the results obtained in the survey would be similar to those achieved if the survey responses had been weighted, so the unweighted responses were reported.

* Phase 2 significantly different from Phase 1 at $p<0.05$.

** Phase 2 significantly different from Phase 1 at $p<0.001$.

8.4 Program costs

As reported

The cost of the TV buys for the campaign was $376,544. (Dixon et al., 1998) There was no report of total costs of the campaign.

Based on resource use

It was estimated that the cost of staff, television buys and evaluation of the campaign would have been $782,664. It was not possible to estimate the costs for the other elements of the campaign[4] so these have been estimated to add an additional 10% to the year 1 cost of the media component, 5% to the year 2 cost and 2.5% to year 3. This increased the cost of the media component to $569,760 and the total cost to $819,414. (Table 8.5)

Table 8.5 Estimated costs of the 2 fruit 'n' 5 veg campaign based on resource use

Component		Published costs	Estimated costs A$ June 2003§	
			Only television buys included	Plus other media activities¶
Television Buys*		1992 $163,480 1993 $163,064 1994 $ 50,000	$201,130 $198,632 $ 59,829	$245,385 $226,533 $ 64,107
Staff†	Program Management Research		$ 92,995 $112,250	$ 92,995 $112,250
Estimate excluding evaluation			$692,825	$741,272
Evaluation‡	Year 1 (n=801) Year 2 (n=1048) Year 3 (n=1085) Year 4 (n=1145)		$ 7,884 $ 10,213 $ 11,386 $ 11,621	$ 7,884 $ 10,213 $ 11,386 $ 11,621
Estimate including evaluation			$734,311	$782,757

[4] Including production of the TV commercials, the launch, radio, print and transit advertising, sports/arts sponsorships and point of sale promotions – see Table 8.1.

Notes:

* Actual costs reported in Dixon et al. (1998) p. 574. No television buys in 1995.

† Program management estimated based on a 0.2 EFT Monash University Senior Research Fellow Level C Step 1 $77,496 at 08/03/2003 and Research based 0.5 EFT Monash University Research Assistant Level A Step 4 $46,771 at 08/03/04 (Source: Monash University Staff Handbook available at http://www.adm.monash.edu.au). On-costs of 25% and overheads and administration costs of 25% added to the base rates.

‡ Source for number of households surveyed Dixon et al. (1998) p. 575, and cost per household of telephone survey estimated to be $8 in October 1992.

§ CPI used to convert current A$ to June A$ 2003. June: 1993 1.00%, 1994 1.80%, 1995 3.20%, 1996 4.20%, 1997 1.30%, 1998 0.00%, 1999 1.20%, 2000 2.40%, 2001 6.00%, 2002 2.90% 2003 3.10%. (Source: [ABS, 2004 #251])

¶ Premium estimated to be 15% of television buys in 1992, 7.5% in 1993 and 1% in 1994, based on level of activity outlined in Table 8.1.

8.5 Performance

Based on the level of promotional activities undertaken during each year of the campaign, the campaign has been assumed to run from 1992 to 1994 inclusive and the 1995 results have been treated as 12-months follow-up.

Cost effectiveness

The stated aim of the campaign was to increase consumption of fruit and vegetables to recommended levels across all groups in the population.

Table 8.6 Estimated cost effectiveness (1992-1994) of the 2 fruit 'n' 5 veg campaign (A$ Jun 2003)

Cost of Campaign 1992-1994* in 2003 A$	$689,961	
Victorian Population Aged 18+ in 1995†	3,385,521	
Target group (people aged18+ not eating 2 Fruit 'n' 5 Veg every day) ‡ 1992 1993 (+6%) 1994 (+0%) 1995 (- 2%)	 3,026,065 2,844,501 2,844,501 2,901,391	
Increase in the number of people eating 2 Fruit 'n' 5 Veg every day 1992 to 1994	Based on responders only: 181,564	Based on intention- to-treat: 1.9%§ of 1992 target group = 56,619
Estimated cost per changer	**$3.80**	**$12.19**

Notes:

* Included estimate for non-costed promotional activities 1992-1994 but excluded all evaluation costs.

† Persons aged 18+ in Victoria (Data Source: ABS Time Series File 320102.123, Table 2. Estimated Resident Population by Single Year of Age, Victoria. Available at http://www.abs.gov.au accessed 17th March 2004).
Assumption: Population stable between 1992 and 1995.

‡ Based on estimated 85.7% of1995 Victorian population aged 18+ not eating 2 fruit n 5 veg per day. (Data source: National Nutrition Survey (1995) CURF, Ref No 691); 1994, 1993 and 1992 estimated using changes in the proportion of people reporting they ate five serves of vegetables per day in the yearly surveys (Table 8.4).

¶ Assumptions: The 6% of people who changed their diet to include five serves of vegetables also had a diet which included two serves of fruit per day; and
The 4% of people who changed their diet to include two serves of fruit were among the 6% who changed their vegetable intake. (Table 8.4)

§ Assumptions: 1992: non-responders (286) + 90% of responders (464) did not eat 5 serves of vegetables = 93.6% of contacts/target group; and
1994: non-responders (474) + 84% of responders (429) did not eat 5 serves of vegetables = 91.7% of contacts/target group. (Table 8.2)
Therefore increase of 1.9% in proportion of people eating 5 serves of vegetables between 1992 and 1994.

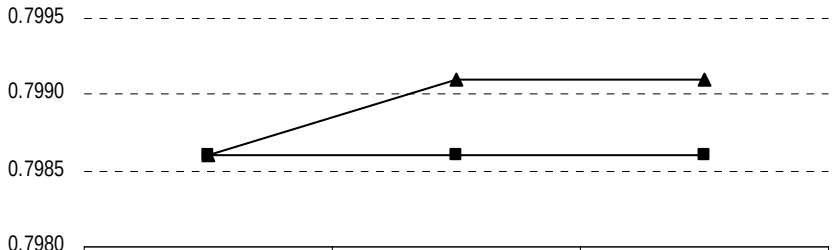
Cost utility

The preliminary performance estimates are based on a conservative scenario which assumes that:

- The 4% of people who changed to eating two serves of fruit per day are included in the 6% who changed to 5 serves of vegetables; and
- All the 6% who changed to five serves of vegetables per day also ate two serves of fruit per day.
- Therefore 6% of people changed to a diet of 2 Fruit 'n' 5 Veg.

Figure 8.2 shows preliminary estimates (non age adjusted) of the changes in utility that would occur for the people who increased their intake of fruit and vegetables to the recommended level compared to those who continued to eat less than the recommended levels. Based on the responders only analysis, the cost utility estimates for changers were $200/unit increase in undiscounted utility and $226 if the utility gains are discounted at 3.5%. Based on the intention to treat analysis, the corresponding estimates were $706 and $723. (Table 8.7)

Figure 8.2 Non age adjusted utility estimates (1992-1994) for changers and non-changers in the 2 fruit 'n' 5 veg campaign



	1992	1993	1994
Utility of changer	0.7986	0.7991	0.7991
Utility of non-changer	0.7986	0.7986	0.7986

Notes:
Utility scores based on a Brazier transformation [Brazier, 2002] of the SF-36 scores for people aged 18+ in the National Nutrition Survey (1995) CURF (Ref No 691).

Table 8.7 Cost per unit increase in utility (1992-1994) for changers in the 2 fruit 'n' 5 veg campaign

Year	Utility*		Increase in Utility	
	Changer	Non-changer	Undiscounted	Discount @ 3.5%
1992 Baseline Survey	0.7986	0.7986		
1993 Survey	0.7991	0.7986	0.00025	0.00025
1994 Survey	0.7991	0.7986	0.00050	0.0004825
Total increase in utility			0.00075	0.0007325
Responders only analysis	Cost per changer		$3.80	$3.80
	Cost per unit increase in utility		$5,067	$5,188
Intention to treat analys	Cost per change		$12.19	$12.19
	Cost per unit increase in utility		$16,248	$16,636

Notes:
* Utility scores based on a Brazier transformation [Brazier, 2002] of the SF-36 scores for people aged 18+ in the National Nutrition Survey (1995) CURF (Ref No 691).

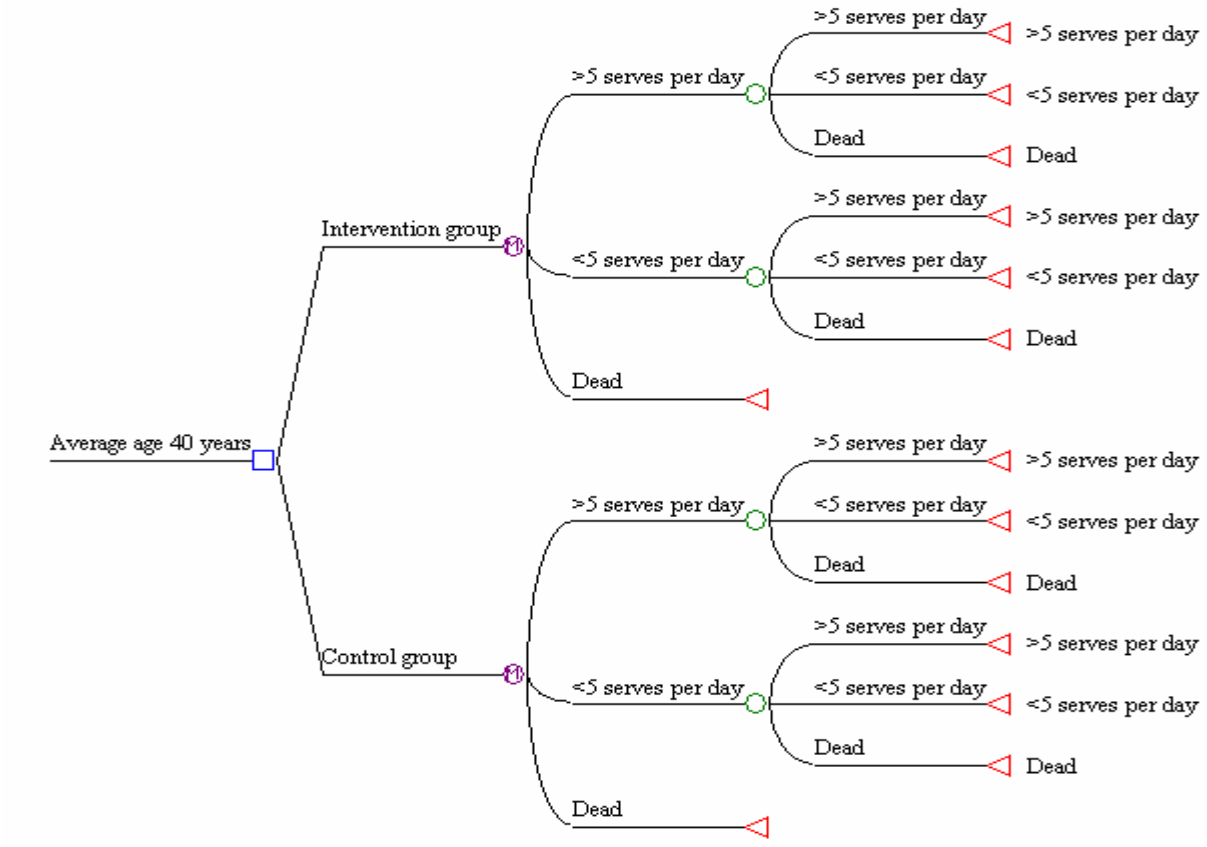
This estimate is based purely on the trial duration. In order to obtain longer term results economic modeling is required. This has been performed below.

8.6 Modelling

Methods

A modelling approach was used to enable the surrogate or intermediate outcome measure of fruit and vegetable consumption (reported by Dixon et al, 1998) 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 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) and death. The transitions that are permitted are illustrated in Figure 8.3.

Figure 8.3 Representation of states and permitted transitions in Markov model



We determined the progression, costs and utilities of a cohort of 1000 people receiving the 2 fruit and 5 vegetable campaign compared with a control group who were assumed to receive no program. The economic model assumes the cohort is 50% female and an average age of 40 years.

The cohort progressed annually between health states over a 20-year time horizon. Six percent of people in the intervention group progress from failure to success (an average of 3% for each of the first two years) according to results from the study by Dixon et al (1998). 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 was the case in the study by Dixon et al (1998).

Table 8.8 Transition matrix (for cycles 1 and 2)

2 fruit 5 veg intervention

	Success	Failure	Dead
Success	#	-	Death table
Failure	0.03	#	Death table
Dead	-	-	1

residual value, - no transition permitted

Transition probabilities vary by cycle for all-cause mortality which was estimated using life tables for the Australian population (ABS, 2002) for adults aged 40 to 60 years. An overall weighted mortality rate for each age year was obtained assuming 50% of our cohort is female. Whiteman et al. (1999) reported that those consuming greater than 5 serves of vegetables per day had a relative risk of premature morality of 0.68, this figure has been adjusted for the prevalence of people in the Australian population consuming more than 5 serves of vegetables (10%, Department of Health, WA, 2003). This adjustment gives relative risk of 0.94 for those consuming more than 5 serves and 1.38 for less than 5 serves. The resulting mortality rates are shown in Table 8.9.

Table 8.9 Mortality rates (weighted for gender and adjusted for % eating more than 5 serves per day)

Age	<5 serves	>5 serves
40	0.0017	0.0012
41	0.0019	0.0013
42	0.0020	0.0014
43	0.0022	0.0015
44	0.0023	0.0016
45	0.0025	0.0017
46	0.0026	0.0018
47	0.0028	0.0019
48	0.0030	0.0020
49	0.0033	0.0022
50	0.0035	0.0024
51	0.0039	0.0026
52	0.0043	0.0029
53	0.0047	0.0032
54	0.0053	0.0036
55	0.0058	0.0040
56	0.0064	0.0044
57	0.0071	0.0048
58	0.0079	0.0053
59	0.0087	0.0059
60	0.0095	0.0065

A utility of 0.7991 was assigned to those consuming the recommended amounts of fruit and vegetables per day with 0.7986 assigned to those not consuming recommended amounts. These values were obtained by performing a Brazier transformation on data from the National Nutrition survey (1995).

The costs for the intervention group were obtained by taking the total costs of the campaign from Table 8.6 and dividing by the number of people in Victoria who do not currently consume 2 serves of fruit and 5 of vegetables per day (n=3,026,065). This gives an estimate of $0.11 per person for each of the first two years of the model. The control group is assumed to not incur any costs. The down stream costs associated with consuming less than 5 serves are not considered in the base case analysis (although a threshold analysis is presented in sensitivity analysis).

Costs and benefits are discounted at 5% per annum. Extensive univariate sensitivity analyses were performed for the assumptions and values described in Table 8.10.

Table 8.10 Sensitivity analysis: attributes, base case and alternative assumed values

Assumptions	Base case	Alternative Values	Source
Cost of intervention per person	$0.11	$6.09	Table 22.6 Total cost divided by those people responding based on ITT (n=56,619)
Time horizon	20	5, 10, 15	Researcher judgment
RR of mortality	1.38 <5 serves 0.94 >5 serves	Upper: 1.65 (<5 serves) 0.89 (>5 serves) Lower: 1.15 (<5 serves) 0.98 (>5 serves)	95% confidence intervals from Whiteman et al 1999
Discount rate	5%	0%, 3%	Researcher judgment

Results

Table 8.11 presents the economic performance of the 2 fruit 5 vegetables intervention, at an incremental cost utility ratio of $46 per QALY gained (for base case assumptions, see Table 8.10)

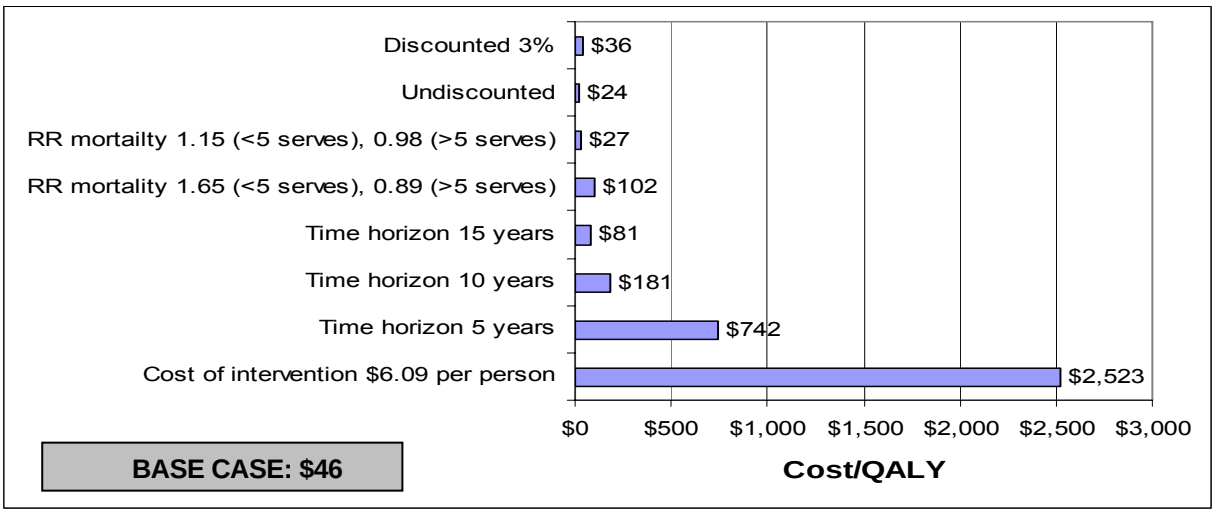
Table 8.11 Modelled cost utility base case results

	2 fruit 5 veg campaign	Control group	Difference
Total costs	$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

Sensitivity analyses

The results of univariate sensitivity analyses are presented in Figure 8.4. Results ranged from $24 to $2,523 per QALY gained and were most sensitive to the cost per person of the intervention.

Figure 8.4 Results of univariate sensitivity analyses



Inclusion of downstream costs: If the downstream costs associated with not consuming the recommended 2 serves of fruit and 5 of vegetables are greater than an average of $0.30 per person per year (over a 20 year time horizon) then the intervention will dominate the control group (greater benefits at lower cost).

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