

## Nutrition and Disease

# A Mediterranean Diet Is Cost-Effective in Patients with Previous Myocardial Infarction<sup>1-3</sup>

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**ABSTRACT** This evaluation aimed to assess the economic performance of the Mediterranean diet for patients after a first acute myocardial infarction (AMI). A cost utility analysis using a Markov model was used to compare the Mediterranean diet to a prudent Western diet over a time frame of 10 years. After a systematic review of the literature, program effectiveness was based on the Lyon Diet Heart Study (605 patients, mean age 54 y, randomized to the Mediterranean diet delivered by a dietician and cardiologist, or a prudent Western diet). Costs were estimated in AU\$ [and converted to US\$ and Euros (€)] based on the resource use to which published unit costs were applied. Cost and benefits were discounted at 5% per annum. The main outcome measure was cost per quality-adjusted life year (QALY) gained. Extensive 1-way sensitivity analyses were performed. The Mediterranean diet compared with a prudent Western diet was estimated to cost AU\$1013 (US\$703, €579) per QALY gained per person. There was a mean gain in life years of 0.31/person and a gain in quality-adjusted life years of 0.40/person. Based on the published results from the Lyon Diet Heart Study and conservative assumptions, the Mediterranean diet is highly cost-effective for persons after a first AMI and represents an exceptional return on investment. Policy makers should strongly consider the generalizability of results to their own setting. *J. Nutr.* 136: 1879–1885, 2006.

**KEY WORDS:** • myocardial infarction • nutrition • Mediterranean diet • economic analysis • cost-effectiveness

Heart disease comprised around one third of global deaths in 2001 (1); ~80% of cardiovascular deaths took place in low-to-middle income countries, and it is anticipated that heart disease will be the leading cause of death in developing countries by 2010 (1). It was estimated that more than half of the deaths and disability from heart disease and stroke could be prevented by modifications to lifestyle such as diet, activity, and smoking (1). At least 20 million people world wide survive heart attacks and strokes each year with a significant portion requiring costly ongoing clinical care (1). In 2005, the cost of heart disease and stroke in the United States is projected to exceed \$394 billion (2).

Lifestyle changes related to diet have the potential to modify disease outcomes and costs of management. Lifestyle interventions were successfully tried in several populations (3–6), including in patients surviving an initial heart attack. The

Mediterranean diet is one such lifestyle option found to be protective (3). Key elements of the Mediterranean diet are more whole-grain bread, more fruit and green vegetables, more fish, less red meat, no butter or cream, and oils/spreads restricted to olive oil. Moderate alcohol consumption (wine) is usually permitted.

Advice to adopt a Mediterranean diet was shown to induce behavior change in patients after a first myocardial infarction (7) confirmed by a change in nutrient intake (3) consistent with the dietary recommendations. The diet was also shown to be effective in preventing further cardiac events (3) and reducing mortality. The assessment of the economic performance of the Mediterranean diet is timely given the interest of policy makers in cost-effectiveness, the dearth of published literature on lifestyle interventions, and the continuing burden of heart disease.

The aim of our study was to assess the economic performance of the Mediterranean diet after myocardial infarction, in terms of cost per quality-adjusted life year (QALY).<sup>5</sup> By expressing performance as cost per QALY, it is possible to compare this nutrition intervention with other approaches to the prevention and management of disease. Cost-effectiveness analyses are a critical input to ensuring the best use of scarce

<sup>1</sup> Supported by a publication grant from the Faculty of Business and Economics, Monash University and by the Australian Government Department of Health and Ageing, Population Health Division.

<sup>2</sup> Supplemental Table 1 shows the full costing of the Mediterranean and Western diets and is available with the online posting of this paper at [www.nutrition.org](http://www.nutrition.org).

<sup>3</sup> We note the expression of concern recently published by the Lancet regarding the validity of this study (Horton R. Expression of concern: Indo-Mediterranean Diet Heart Study. *Lancet* 2005; 366: 354-6).

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<sup>5</sup> Abbreviations used: AMI, acute myocardial infarction; QALY, quality-adjusted life year; RCT, randomized controlled trial; RR, relative risk.

health care resources and are increasingly relied on by policy makers, health care managers, and clinicians.

## MATERIALS AND METHODS

**Perspective.** The economic evaluation took a societal perspective with the core analysis focused on patient outcomes and the health system. The comparator was a "prudent" Western diet control group who were advised to follow recommendations of the AHA as per "usual care."

**The intervention.** A search was conducted for high-quality studies [randomized controlled trials (RCTs) or meta-analyses] evaluating the effect of a Mediterranean diet in those with a previous acute myocardial infarction (AMI) on clinical outcomes compared with a typically recommended diet. Medline (OVID 1966 to current) and the Cochrane Database of Systematic Reviews (including American College of Physicians' Journal Club, Database of Abstracts of Reviews of Effectiveness, and Cochrane Controlled Trials Register) were searched in August 2005 using key words and subject headings for "myocardial infarction" and key words for "Mediterranean diet." A total of 43 studies were identified, 3 of which were RCTs assessing effectiveness of the Mediterranean diet in patients with previous heart disease (3,8,9).<sup>5</sup> The Lyon Diet Heart Study (3) was chosen as the key source of effectiveness data for this economic evaluation due primarily to the longer follow-up period.

The Lyon Diet Heart Study was conducted in 6 health services within Lyon, France between March 1988 and March 1992. The trial design and outcomes were described in detail in a number of key papers along with a detailed assessment of potentials for bias (3,7,10,11). A total of 605 patients aged <70 y were recruited into the study. Participants all had survived a myocardial infarction within 6 mo of enrolment. Recruitment took place in the hospital and patients were randomized at an outpatient clinic 2 wk after discharge to the Mediterranean diet ( $n = 303$ ) or Western diet ( $n = 302$ ) group. Participants' mean age was 54 y (SD 10 y) and 91% were men (549/56). The baseline characteristics of the 2 study groups were similar.

The intervention group received dietary advice during a 1-h consult with the research cardiologist and dietitian "to adopt a Mediterranean-type diet" as described in the introduction [for full diet composition refer to (7)]. In addition, intervention participants were supplied with rapeseed margarine (7). Intervention patients were seen at 8 wk, then annually for up to 4 y for further counseling by the research dietitian and completion of a dietary survey, and for data collection and counseling by the research cardiologist.

Control group participants received the usual advice for cardiac patients from the hospital dietitian or attending physician [for full diet composition refer to (7)]. They also saw the cardiologist for data collection at 8 wk, then annually for up to 4 y.

**Effectiveness.** Results were analyzed on an intention to treat basis aside from 21 randomized patients who refused follow-up shortly after the start of the study (3). The majority (92.4 and 93.4%) of the original 302 intervention group and 303 control group participants randomized, who were still alive and not censored, attended the final study visit. Of the 15 control and 19 intervention patients who did not attend the final visit, vital status was known for all except 4.

At the 4-y follow-up, the Mediterranean diet group had 6 cardiac deaths compared with 19 in the control group [relative risk (RR) 0.35, 95% CI 0.15–0.83,  $P = 0.01$ ] and there were 14 combined cardiac deaths or nonfatal AMIs in the Mediterranean diet group compared with 44 in the control group (RR 0.28, 95% CI 0.15–0.53,  $P = 0.0001$ ). There were 14 deaths from all causes in the Mediterranean diet group compared with 24 in the control group (RR 0.44, 95% CI 0.21–0.94,  $P = 0.03$ ). There were 68 minor events (e.g., stable angina, revascularization, or restenosis) in the Mediterranean diet group compared with 90 in the control, 13 major events excluding stroke (e.g., unstable angina, heart failure, or pulmonary embolism) in the Mediterranean diet group compared with 42 in the control group, and 4 strokes in the control group with none in the Mediterranean diet group. Results were used to inform the economic model and are reported in full in (3).

**Measurement of economic performance.** The primary measure of economic performance was the cost per QALY (quality-adjusted life year) gained, a measure combining the effect on quality of life and mortality. The QALY is a commonly adopted health outcome measure and is derived by combining length of time in a health state with the "utility" of that health state. Utility is measured on a scale from 0 to 1 [using specified techniques (12,13)] in which 0 corresponds to a health state equivalent to death and 1 represents full health. Thus, for example, an extra year spent in full health would contribute +1 QALY, as would 4 y in better health involving a change in "utility score" from 0.45 to 0.7.

Utilities applied to the 5 distinct health states were obtained from the published literature: 0.93 for event free (14), 0.89 for minor events (14), 0.88 for AMI (15), 0.78 for major events (14), and 0.54 for stroke (16). The cost per additional cardiac death or AMI averted (the major primary endpoint for the trial), was also calculated for the Mediterranean diet compared with the Western diet.

**Costing.** The cost of the intervention was based on the incremental resource use for the Mediterranean diet group compared with the Western diet group described in the reports of the clinical trial (7), to which Australian published unit costs (2003) were applied and converted into US\$ and Euros (€) using published exchange rates (June 2004). The additional costs were composed of an initial consult with a cardiologist and a dietitian, a follow-up visit with a dietitian at 8 wk, and again annually for y 2 to 4 (Table 1), with unit costs derived from the Australian Medicare Benefits Schedule (17), plus differential food costs (see below).

In the Lyon Diet Heart Study, both the control and intervention groups received follow-up visits with the cardiologist with no observed increase in physician time. Thus no additional costs were allocated to the intervention group for this activity. The additional food costs incurred by patients adhering to the Mediterranean diet were estimated by applying food unit costs obtained from a major Australian retailer [Coles Myer, (19)] to the mean differences in grams per day for each major food group reported in the Lyon Heart Study (7). The food basket was chosen to provide an upper limit on the possible cost difference, (see Supplemental Table 1). The total cost of the intervention was estimated at AU\$406 (US\$282, €232) for y 1 plus an additional AU\$224 (US\$155, €128) per year for y 2 to 4, or AU\$1076 (US\$747, €615) in total (Table 1).

The costs of management were captured in transition costs, which were incurred each time a person experienced an event regardless of

TABLE 1

Incremental cost of Mediterranean diet intervention based on described resource inputs (7)

Item	Mean incremental increase in cost per person AU\$	Reference for unit cost
y 1		
Initial consult with cardiologist	128.05	(17) <sup>1</sup>
Initial consult with dietitian	52.85	(17) <sup>2</sup>
Follow-up visit at 8 weeks with dietitian	52.85	(17) <sup>2</sup>
Written instructions	1.27	(18)
Food costs <sup>1</sup>	170.67	(19)
Total y 1	406 (US\$282, €232)	
y 2–4		
Follow-up visit with dietitian	52.85	(17)
Food costs <sup>3</sup>	170.67	(19)
Total y 2–4 (annual cost)	223.52	
Total cost over 4 y	1076 (US\$747, €615)	

<sup>1</sup> Item number 110.

<sup>2</sup> Item number 10954.

<sup>3</sup> See Supplemental Table 1.

TABLE 2

Event costs applied to the cohort as it transitions between health states

Event <sup>1</sup>	Cost per person AU\$	Reference
Minor event (e.g., stable angina, revascularisation, or restenosis)	1304 (US\$905, €745)	(20) <sup>2</sup>
Nonfatal AMI	4851 (US\$3367, €2772)	(20) <sup>3</sup>
Major event (e.g., unstable angina, heart failure or pulmonary embolism)	2981 (US\$2069, €1703)	(20) <sup>4</sup>
Stroke: new event	18,956 (US\$13,159 €10,832)	(21) <sup>5</sup>
Stroke: ongoing management	1777 (US\$1234, €1,015)	(21)

<sup>1</sup> Events are all subsequent to a first AMI (the primary entry criteria for entry into the trial).

<sup>2</sup> Australian refined diagnosis related groups (see Table S11.19) AR-DRG F74Z.

<sup>3</sup> Weighted mean for AR-DRG 41A, F41B, F60A, F60B.

<sup>4</sup> Weighted mean for AR-DRG F62A, F62B, F72A, F72B.

<sup>5</sup> Communication with author C. Mihalopoulos was required to interpret published costs.

study group—see modeling section below. Mean per patient costs of management associated with each event category and data sources were also incorporated (Table 2). These included hospital costs only and thus provided a lower bound estimate, except for stroke, which also included community-based costs for y 1 after the event. In addition, in the sensitivity analysis, costs for stroke were also assigned to each patient each cycle to reflect the on-going cost of management.

**Modeling.** A state transition model (Markov) was developed in TreeAge Pro (2004) to estimate the effects on disease, mortality, and quality of life for each group during the 4 y of the trial and beyond. In accordance with the trial data, the economic model assumed that the cohort was 91% male (549/56) with a mean age of 54 y.

Individuals were allocated into one of 5 discrete health states: alive free of further events, alive following minor events (e.g., stable angina, revascularization, or restenosis), alive following AMI, alive following major event (e.g., unstable angina, heart failure or pulmonary embolism), alive following stroke, and death (Fig. 1). The cohort progressed annually (cycle length 1 y) between these health states according to transition probabilities derived from the trial and from the published literature (Table 3). Each year, the cohort for each intervention group accumulated costs and quality-adjusted length of life. Results were summed over the period of the model and total costs and total QALYs compared for the control and intervention groups. Rates were transformed into transition probabilities using the generally accepted approach (22). The model commenced with all people in “alive free of events.” The model presumed a 1-way progression in health state (from least severe to most severe). The model assumed that no transitions other than from “alive free of events” were permitted in y 1 to 4 (the original trial period). The model also assumed that the intervention group transitions from “alive free of events” reverted to the control probabilities after y 4.

**Analysis.** The base case model was applied over 10 y, that is, 6 y beyond trial end point. Estimated costs, utilities, and life years for the intervention and control cohort were summed over the model period and compared. A half-cycle correction was applied to costs and benefits. Costs and benefits were discounted at 5%/annum according to current Australian guidelines (28). Extensive univariate sensitivity analyses were performed and involved varying estimates of effect size, cost, utility, time horizon, and discount rate.

## RESULTS

The cost-effectiveness results of the Mediterranean diet compared with a prudent Western diet, based purely on the trial results, led to a cost per cardiac death or AMI averted

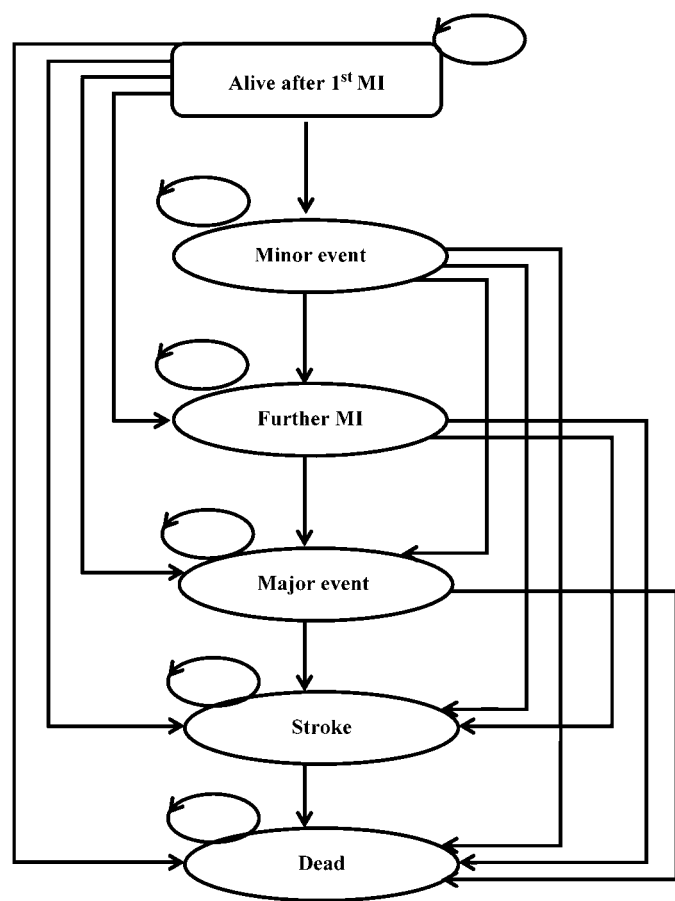


FIGURE 1 Markov model diagram showing health states and permitted transitions.

ranging from AU\$10,879 (US\$7552, €6217) when program and food costs were included to AU\$1778 (US\$1234, €1016) when the costs of cardiac events were also incorporated (Table 4). When modeled over 10 y, the Mediterranean diet resulted in an incremental cost per QALY gained of AU\$1013 (US\$703, €579) per person. It also led to mean gains of 0.31 life years per person or 0.40 quality adjusted life years per person.

**Sensitivity analyses.** One-way sensitivity analyses showed that the Mediterranean diet remained highly cost-effective under all scenarios (Table 5). The model was most sensitive to the cardiac event rates, the costs of the intervention, and the time horizon of the model. The Mediterranean diet dominated (cheaper and more effective) the Western diet under 1 scenario, i.e., when food costs were excluded from the analysis. The estimated cost per QALY gained ranged from AU\$417 (US\$289, €238) when the number of consultations was halved to AU\$7149 (US\$4963, €4085) when the lower limit for the intervention effect (more cardiac events) was used.

## DISCUSSION

Economic evaluation of the Mediterranean diet in those with a previous AMI resulted in an estimated cost per QALY gained of AU\$1013 (US\$703, €579) per person, with estimates remaining highly cost-effective under all scenarios considered in sensitivity analyses. This economic evaluation was based on effectiveness from a high-quality randomized

**TABLE 3**  
*Transition probabilities after first AMI*

Time <i>t</i>	Time <i>t</i> +1					
	Event-free	Minor event	Nonfatal AMI	Major cardiac event	Nonfatal stroke	Dead
Event-free	# <sup>1</sup>	0.063	0.007	0.011	0.000	0.012
Intervention group (3)	#	[0.048–0.086] <sup>2</sup>	[0.003–0.016] <sup>2</sup>	[0.006–0.021] <sup>2</sup>	0.004	[0.006–0.024] <sup>2</sup>
Control group (3)	—	0.090	0.023	0.039	—	0.022
Minor event	—	#	0.014 (23)	0.030 <sup>3</sup>	0.011 <sup>4</sup> (24)	0.033 <sup>5</sup>
Nonfatal AMI	—	—	#	0.183 (23)	0.055 (23)	0.159 (25)
Other major cardiac event	—	—	—	#	0.015 (23)	0.170 (26)
Nonfatal stroke	—	—	—	—	#	0.225

<sup>1</sup> Residual value (1 – the rest of the probabilities in the row) because the sum of each row must be one.

<sup>2</sup> Ranges represent upper and lower limits derived from the 95% CIs of the RRs calculated from the original study report (3) Table 1, p. 780. All differential variation is attributed to the intervention arm. Unable to calculate a risk ratio for stroke with zero events.

<sup>3</sup> Researcher judgement.

<sup>4</sup> The 5-y probability of survival following stroke was multiplied by the RR of already having congestive heart failure [2.28, (27)] adjusted for the prevalence of congestive heart failure in the original population (16.74%).

<sup>5</sup> This transition is assumed to be the same as alive free of events to dead.

control trial involving a follow-up period sufficient to observe the effect not just on behaviors but also on health. Results were confirmed by more recent epidemiological observations (29,30). Economic estimates are certain and robust as confirmed by the sensitivity analysis, which shows that under a range of plausible assumptions, provision of advice to adopt a Mediterranean-style diet in persons after AMI is cost-effective. The results of this economic evaluation support the adoption of this intervention in similar patient cohorts.

**Strengths and limitations.** The main area of uncertainty is the generalizability of effectiveness results, although the original Lyon Diet Heart study was conducted in French patients not usually consuming a Mediterranean-type diet. The analysis was based on a single high-quality study rather than a meta-analysis, although we note that the results of the other 2 identified trials of the use of a Mediterranean diet reported similar outcomes. Issues that might affect the generalizability include the following: first, the baseline prevalence of first and

**TABLE 4**  
*Cost-effectiveness and cost utility*

	Mediterranean diet	Western diet	Difference
Cost effectiveness <sup>1</sup> over 4 y AU\$			
Costs/person			
Program costs <sup>2</sup>	394	0	394
Food costs <sup>2</sup>	1375	692	683
Cardiac event costs <sup>3</sup>	550	1451	–901
Outcomes			
Cardiac death and nonfatal AMI events <sup>4</sup>	14/302 (4.6%)	44/303 (14.5%)	9.9%
Cost/cardiac death or AMI averted			
Includes program costs only			3980 (US\$2763, €6217)
Includes program and food costs			10879 (US\$7552, €6217)
Includes program, food and event costs			1778 (US\$1234, €1016)
Cost utility <sup>5</sup> modeled over 10 y AU\$			
Total costs/person	3649 (US\$2533, €2085)	3244 (US\$2252, €1854)	405 (US\$281, €231)
Mean life years/person	7.29	6.98	0.31
Mean QALYs/person <sup>6</sup>	6.62	6.22	0.40
Discounted cost per QALY gained/person			1013 (US\$703, €579)

<sup>1</sup> Derived from the events reported by the trial and described resource use.

<sup>2</sup> See Table 1.

<sup>3</sup> Costs from Table 2 and event rates from (3) Table 1, p. 780.

<sup>4</sup> This is the major primary endpoint (composite outcome 1) from the clinical trial (3), assuming each AMI and death within the 4 years affects a separate person.

<sup>5</sup> Modeled using assumptions and parameters outlined in Table 3 and methods section.

<sup>6</sup> Mean QALYs are less than mean life years because this incorporates the negative effect on quality of life of the cardiovascular events.

TABLE 5

*Sensitivity analysis assumptions and results*

Scenario	Incremental cost (Mediterranean diet compared with Western diet) per person AU\$	Incremental QALYs (Mediterranean diet compared with Western diet) per person	Cost/QALY AU\$
Base case	405 (US\$281, €231)	0.40	1013 (US\$703, €579)
Upper estimate of intervention effect (fewer cardiac events) <sup>1</sup>	258 (US\$179, €147)	0.58	445 (US\$309, €254)
Lower estimate of intervention effect (more cardiac events) <sup>1</sup>	656 (US\$455, €375)	0.09	7149 (US\$4963, €4085)
Utilities all decreased by 0.05	405 (US\$281, €231)	0.39	1054 (US\$732, €602)
Utilities all increased by 0.05	405 (US\$281, €231)	0.42	975 (US\$677, €557)
Discount rate 3%	447 (US\$310, €255)	0.45	991 (US\$688, €566)
Discount rate 0%	515 (US\$358, €294)	0.54	948 (US\$658, €542)
Time horizon 15 y	626 (US\$435, €358)	0.63	992 (US\$689, €567)
Time horizon 5 y	310 (US\$215, €177)	0.13	2332 (US\$1619, €1333)
Number of consultations doubled	882 (US\$612, €504)	0.40	2204 (US\$1530, €1259)
Number of consultations halved	167 (US\$116, €95)	0.40	417 (US\$289, €238)
Addition of state costs for stroke of AU\$1777 <sup>2</sup>	228 (US\$158, €130)	0.40	569 (US\$395, €325)
Food costs doubled	1096 (US\$761, €626)	0.40	2738 (US\$1901, €1565)
No additional food costs	-285 (-US\$198, -€163) <sup>3</sup>	0.40	Intervention dominates

<sup>1</sup> Calculated using the range presented in Table 3.

<sup>2</sup> State costs are assigned to each patient for each cycle they spend in the stroke health state, they reflect the ongoing costs associated with living in this condition.

<sup>3</sup> A negative value indicates that the Mediterranean diet is cost saving.

subsequent AMIs in the community because any substantial departure from the study experience will affect absolute risks even if relative risks are unchanged; second, the typical current management of heart disease; and third, the cultural acceptance of the intervention, usual dietary patterns in the community, and usual dietary advice in this cohort.

There is an argument that more than a decade after the original trial, the prevalence and management of heart disease and AMI have changed such that there is now less scope for potential benefit. It should be noted, however, that France (the setting of the original study) had and still has very low rates of heart disease compared with most other countries. There were 10.46 AMI female deaths/100,000 population in France in 1997 compared with 33.89 in Australia, and 28.45 in the United States. Similarly, there were 29.35/100,000 population male AMI deaths in France in 1997 compared with 64.45 in Australia, and 56.40 in the United States [age standardized to world population, (31)]. Thus, although countries like Australia have seen a decreasing rate of fatal AMIs over the last 2 decades, down from 203.9/100,000 population in 1980, 145.8 in 1990, to 78.2 in 2000 [age standardized to Australian population, (32)], current rates are still higher than those in France in the early 1990s when the Lyon Diet Heart Study was being conducted. Given that the Lyon Diet Heart Study found a large effect in a population with low rates of heart disease, the potential benefit could well be greater in a population with higher rates of heart disease.

In relation to estimated costs, generalizability is more problematic because management patterns and cost of hospitalization vary across health systems. However, the transparency of the evaluation process will aid comparisons. Ideally, costs would have been estimated on the basis of resource use in America and Europe, rather than the currency conversion provided. However, lower inpatient costs in Australia for events avoided mean that the intervention is likely to be associated with an even greater cost savings in other countries, and reported estimates should therefore be conservative. Food costs may also vary across countries depending on local

availability of products and local cost of living. Our evaluation provided costing based on Australian data for a subset of foods that make up each typical diet. Although this is a simplistic approach, the selected food basket was chosen to provide a high estimate of the differential cost of the Mediterranean diet. Furthermore, sensitivity analysis shows that even if food costs were doubled for each diet, the intervention would still be cost effective at \$2738 per QALY gained. We also note that estimated cost effectiveness is likely to be conservative for the following reasons: we included only transition or event costs in our analysis and not on-going differentials in costs of management, which would lead to an increase in the cost differential between the Mediterranean diet and Western diet groups; the analysis used an intention to treat approach that will bias results toward the null; and the Mediterranean diet may also significantly reduce other disease such as cancer even in the short term [(33) such probable benefits are included only to the extent that they are captured in all-cause mortality]. Thus, it is likely that the Mediterranean diet would prove cost saving under a range of highly plausible scenarios.

The preparedness and capacity of other groups to adopt a Mediterranean-style diet are also important. According to recent studies, the uptake of a Mediterranean diet is theoretically possible in other countries such as Germany based on the availability of food (34). However, nutrition is not just about food availability; it is also about lifestyle, culture, and social structure. It would seem that the Mediterranean diet, or the key protective elements of the diet are transferable to people not living in the region as evidenced by the fact that the original population in the Lyon Diet Heart Study did not normally consume the traditional Mediterranean diet (35). It may be that some people prefer a Western diet as evidenced by its large uptake, although there are other possible explanations such as habit, lack of exposure, necessary food/cooking skills, and the availability of information to make informed decisions. It seems that although the diet is theoretically transferable, this would not be automatic. Further research into implementation

of the Mediterranean diet in other regions of the world is warranted. The adoption of the diet is aided in that it is attractive for its famous palatability (36).

Important changes in the management of heart disease may affect generalizability, but this is uncertain. At the time of the Lyon Diet Heart Study, acetylsalicylic acid therapy, angiotensin-converting enzyme inhibitors, and  $\beta$ -blockers were used similarly to current management, but the use of statins has increased substantially. However, a recent trial in which patients were randomized to the Mediterranean diet plus statin treatment or statin treatment alone found that the addition of the diet substantially and significantly improved clinical outcomes (8). There is an inherent contradiction in study design, with a lengthy follow-up period desirable for assessment of longer term effects, but with the increased likelihood that management will have changed since study commencement.

Although utility data would be based ideally on directly collected utility/quality of life scores for the original patient cohort, quality of life was not measured in the Lyon Diet Heart Study. We thus relied on published utilities chosen to closely match the reported health states (generated using the preferred time trade-off technique) (12,13). Any potential error is small because the vast majority of QALY gain is driven by a reduction in events observed directly from the trial rather than the assigned utilities.

**Relation to previous research.** To our knowledge, this is the first cost-effectiveness study of the Mediterranean diet for any patient group; we were able to locate only one other cost utility study of any nutrition intervention in cardiology (37). The results can be compared with other interventions for persons with established heart disease. For example, another study (38) reported a cost per life year saved of US\$3,600 for  $\beta$ -blocker therapy, US\$20,200–US\$2,024,800 for lovastatin, US\$9200–US\$1,142,00 for coronary artery by-pass grafting, US\$1300–US\$3900 for physician counseling to stop smoking, and US\$124,400 for exercise electrocardiogram. The WHO defines very cost-effective interventions as costing less than mean gross domestic product per head which equates to ~\$24,000 for Europe, \$31,000 for the United States, and \$28,000 for Australia in 2000 international dollars (39). The Mediterranean diet compares most favorably and is well below WHO cost-effectiveness thresholds, reflecting the large reduction in cardiac event rates achieved, through a relatively low cost intervention.

In conclusion, based on the published results from the Lyon Diet Heart Study, and conservative assumptions, the Mediterranean diet was highly cost-effective for persons after a first AMI. Replicating the Mediterranean diet intervention in other countries and health settings could substantially improve health outcomes and reduce the use of health care resources. With risk factors related to coronary heart disease continuing to rise across the world, this represents an important opportunity for cost-effective preventive care.

## ACKNOWLEDGMENTS

The authors acknowledge Susan Day (research fellow) and Rachelle Katz (research assistant), who assisted with the identification of model parameters including costs and Duncan Mortimer (senior research fellow), who provided advice regarding the economic modeling.

## LITERATURE CITED

1. World Health Organisation (WHO). Cardiovascular disease (CVD): facts. global strategy on diet, physical activity and health. [Online] [cited March, 2005]. Available from: [www.who.int](http://www.who.int).

2. National Center for Chronic Disease Prevention and Health Promotion (CDC). Preventing heart disease and stroke. [Online] [cited March, 2006]. Available from: [www.cdc.gov/nccdphp/bb\\_heartdisease](http://www.cdc.gov/nccdphp/bb_heartdisease).

3. de Lorgeril M, Salen P, Martin JL, Monhaud I, Delaye J, Mamelle N. Mediterranean diet, traditional risk factors, and the rate of cardiovascular complications after myocardial infarction: final report of the Lyon Diet Heart Study. *Circulation*. 1999;99:779–85.

4. Elley CR, Kerse N, Arroll B, Robinson E. Effectiveness of counselling patients on physical activity in general practice: cluster randomised controlled trial. *BMJ*. 2003;326:793–8.

5. Steptoe A, Perkins-Porras L, McKay C, Rink E, Hilton S, Cappuccio FP. Behavioural counselling to increase consumption of fruit and vegetables in low income adults: randomised trial. *BMJ*. 2003;326:855–61.

6. Eriksson J, Lindström J, Valle T, Aunola S, Hämäläinen H, Ilanne-Parikka P, Keinänen-Kiukaanniemi S, Laakso M, Lauhkonen M, et al. on behalf of the Finnish Diabetes Prevention Study Group. Prevention of type II diabetes in subjects with impaired glucose tolerance: the Diabetes Prevention Study (DPS) in Finland. *Diabetologica*. 1999;42:793–801.

7. de Lorgeril M, Renaud S, Mamelle N, Salen P, Martin JL, Monjaud I, Guidollet J, Touboul P, Delaye J. Mediterranean alpha-linolenic acid-rich diet in secondary prevention of coronary heart disease. *Lancet*. 1994;343:1454–9.

8. Sondergaard E, Møller JE, Egstrup K. Effect of dietary intervention and lipid-lowering treatment on brachial vasoreactivity in patients with ischemic heart disease and hypercholesterolemia. *Am Heart J*. 2003;145:E19.

9. Singh RB, Dubnov G, Niaz MA, Ghosh S, Singh R, Rastogi SS, Manor O, Pella D, Berry EM. Effect of an Indo-Mediterranean diet on progression of coronary artery disease in high risk patients (Indo-Mediterranean Diet Heart Study): a randomised single-blind trial. *Lancet*. 2002;360:1455–61.

10. de Lorgeril M, Salen P, Martin J-L, Mamelle N, Monjaud I, Touboul P, Delaye J. Effect of a Mediterranean type of diet on the rate of cardiovascular complications in patients with coronary artery disease. Insights into the cardioprotective effect of certain nutrients. *J Am Coll Cardiol*. 1996;28:1103–8.

11. de Lorgeril M, Salen P, Caillat-Vallet E, Hanauer MT, Barthelemy JC, Mamelle N. Control of bias in dietary trial to prevent coronary recurrences: the Lyon diet heart study. *Eur J Clin Nutr*. 1997;51:116–22.

12. Richardson J. Cost utility analysis: what should be measured? *Soc Sci Med*. 1994;39:7–21.

13. Pope R. Biases from omitted risk effects in standard gamble utilities. *J Health Econ*. 2004;23:695–735.

14. Kuntz KM, Tsevat J, Goldman L, Weinstein MC. Cost-effectiveness of routine coronary angiography after acute myocardial infarction. *Circulation*. 1996;94:957–65.

15. Lee TT, Solomon NA, Heidenreich PA, Oehlert J, Garber AM. Cost-effectiveness of screening for carotid stenosis in asymptomatic persons. *Ann Intern Med*. 1997;126:337–46.

16. Derdeyn CP, Powers WJ. Cost effectiveness of screening for asymptomatic carotid atherosclerotic disease. *Stroke*. 1996;27:1944–50.

17. Australian Government Department of Health and Ageing. Medicare Benefits Schedule Book, Nov 2004. Commonwealth of Australia, Canberra.

18. Melbourne University Design and Print Centre (2003) Quote based on eight A4 pages.

19. Coles Myer. Coles Online. [www.colesonline.com.au](http://www.colesonline.com.au) (accessed April, 2005)

20. Australian Institute of Health and Welfare (AIHW) 2005 Australian Hospital Statistics, 2002–3 for public hospitals.

21. Dewey HM, Thrift AG, Mihalopoulos C, Carter R, Macdonell RAL, McNeil JJ, Donnan G. Lifetime cost of stroke subtypes in Australia: findings from the North East Melbourne Stroke Incidence Study (NEMESIS). *Stroke*. 2003;34:2502–7.

22. Miller DK, Homan SM. Determining transition probabilities: confusion and suggestions. *Med Decis Making*. 1994;14:52–8.

23. Antiplatelet Trialists' Collaboration. Collaborative overview of randomised trials of antiplatelet therapy. *BMJ*. 1994;308:81–106.

24. Tanne D, Shotan A, Goldbourt U, Haim M, Boyko V, Adler Y, Mandelzweig L, Behar S, for the Bezafibrate Infarction Prevention Study Group. Severity of angina pectoris and risk of ischemic stroke. *Stroke*. 2002;33:245–50.

25. Peltonen M, Lundberg V, Huhtasaari F, Asplund K. Marked improvement in survival after acute myocardial infarction in middle-aged men but not women. The Northern Sweden MONICA study 1985–94. *J Intern Med*. 2000;247:579–87.

26. Heit JA, Silverstein MD, Mohr DN, Petterson TM, O'Fallon WM, Melton LJ. Predictors of survival after deep vein thrombosis and pulmonary embolism: a population-based cohort study. *Arch Intern Med*. 1990;150:445–53.

27. Petty GW, Brown RD, Whisnant JP, Sicks JD, O'Fallon WM, Wiebers DO. Survival and recurrence after first cerebral infarction: a population based study in Rochester, Minnesota, 1975 through 1989. *Neurology*. 1998;50:208–16.

28. Commonwealth Department of Health and Ageing. Guidelines for the pharmaceutical industry on preparation of submissions to the pharmaceutical benefits advisory committee. Sept 2002. Commonwealth of Australia.

29. Trichopoulos A, Costacou T, Barnia C, Trichopoulos D. Adherence to a Mediterranean diet and survival in a Greek population. *N Engl J Med*. 2003;348:2599–608.

30. Knuops KT, de Groot LC, Kromhout D, Perrin AE, Moreiras-Varela O, Menotti A, van Staveren WA. Mediterranean diet, lifestyle factors, and 10-year mortality in elderly European men and women: The Hale Project. *JAMA*. 2004;292:1433–39.

31. Collaborating WHO. Centre on Surveillance of Cardiovascular Diseases. Global Cardiovascular infobase: country comparisons [online] [accessed March 2005]. Available from: <http://www.cvdinfobase.ca/data.htm>.

32. Australian Institute of Health and Welfare (AIHW) National Cardiovascular disease and diabetes database. Deaths from acute myocardial infarction in

Australia. 2001 [online] [accessed March 2005] .Available from: [http://www.aihw.gov.au/pls/cvd/cvd\\_death.show\\_form](http://www.aihw.gov.au/pls/cvd/cvd_death.show_form).

33. de Lorgeril M, Salen P, Martin JL, Monjaud I, Boucher P, Mamell N. Mediterranean dietary pattern in a randomized trial: prolonged survival and possible reduced cancer. *Arch Intern Med.* 1998;158:1181–7.

34. Leonhauser IU, Dorandt S, Willmund E, Honsel J. The benefit of the Mediterranean diet—considerations to modify German food patterns. *Eur J Nutr.* 2004;43: Suppl 1:31–8.

35. de Lorgeril M, Salen P, Paillard F, Laporte F, Boucher P, de Leiris J. Mediterranean diet and the French paradox: two distinct biogeographic concepts for one consolidated scientific theory on the role of nutrition in coronary heart disease. *Cardiovasc Res.* 2002;54:503–15.

36. Willett WC, Sacks F, Trichopoulou A, Drescher G, Ferro-Luzzi A, Helsing E, Trichopoulos D. Mediterranean diet pyramid: a cultural model for healthy eating. *Am J Clin Nutr.* 1995; 61(6, Suppl 1):1402S–6.

37. Prosser LA, Stinnett AA, Goldman PA, Williams LW, Hunink MG, Goldman L, Weinstein MC. Cost-effectiveness of cholesterol-lowering therapies according to selected patient characteristics. *Ann Intern Med.* 2000;132: 769–79.

38. Probstfield JL. How cost-effective are new preventive strategies for cardiovascular disease. *Am J Cardiol.* 2003;91:22G–7.

39. World Health Organisation. Choosing interventions that are cost effective (WHO-CHOICE) [online] [cited March, 2006]. Available from: [http://www.who.int/choice/costs/CER\\_levels/en/index.html](http://www.who.int/choice/costs/CER_levels/en/index.html).