

Effect Size Estimates of Lifestyle and Dietary Changes on All-Cause Mortality in Coronary Artery Disease Patients A Systematic Review

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Background—Guidelines for lifestyle and dietary modification in patients with coronary artery disease (CAD) are mainly supported by evidence from general population studies. CAD patients, however, differ from the general population in age (older) and treatment with preventive drugs. This review seeks to provide evidence for a prognostic benefit of lifestyle and dietary recommendations from studies in CAD patients.

Methods and Results—A literature search was performed on the effect of lifestyle and dietary changes on mortality in CAD patients. Prospective cohort studies and randomized controlled trials of patients with established CAD were included if they reported all-causes mortality and had at least 6 months of follow-up. The effect estimates of smoking cessation (relative risk [RR], 0.64; 95% CI, 0.58 to 0.71), increased physical activity (RR, 0.76; 95% CI, 0.59 to 0.98), and moderate alcohol use (RR, 0.80; 95% CI, 0.78 to 0.83) were studied most extensively. For the 6 dietary goals, data were too limited to provide reliable effect size estimates. Combinations of dietary changes were associated with reduced mortality (RR, 0.56; 95% CI, 0.42 to 0.74).

Conclusions—Available studies show convincingly the health benefits of lifestyle changes in CAD patients. Effect estimates of combined dietary changes look promising. Future studies should confirm these findings and assess the contribution of the individual dietary factors. (*Circulation*. 2005;112:924-934.)

Key Words: coronary disease ■ diet ■ lifestyle ■ mortality ■ patients

More than 40 years ago, Ancel Keys¹ was the first to explore the relationship between coronary artery disease (CAD) and environmental factors. Since then, several lifestyle and dietary factors have been found to be associated with the risk of cardiovascular morbidity and mortality.² This knowledge has been translated into recommendations for the general population (primary prevention) and clinical guidelines for those with manifest cardiovascular diseases (secondary prevention).

Patients with CAD, ie, myocardial infarction (MI) or angina pectoris (AP), are the largest of the secondary prevention groups. This group is characterized by older age (80% are older than 50 years) and a minority of women (30%).³ Although the prognosis of CAD patients has improved considerably during the last decades,⁴ they still carry a high absolute risk for future CAD events (10-year absolute risk from 20% to 80%).⁵ International guidelines⁶ defined this patient group as top priority for preventive strategies.

Guidelines for CAD prevention⁶⁻¹⁰ agree more or less on the 9 lifestyle and dietary recommendations shown in Table 1. These recommendations are supported largely by evidence from

population-based cohort studies and trials with surrogate end points. The effects on life expectancy in patients with CAD are unclear. These patients differ from the general population not only by their older age and compromised vasculature but also by the drugs they take to prevent secondary events. Patients contemplating behavioral changes, as well as professionals designing preventive strategies, want to be able to make choices and rationally prioritize one goal before another. Information on the magnitude of the effect that can be expected of each of the recommended lifestyle and dietary changes is therefore needed.

This study seeks to summarize the evidence that the individual lifestyle and dietary goals formulated in Table 1 can improve prognosis in CAD patients. Second, we want to provide estimates of the magnitude of the effects on survival for each individual lifestyle and dietary goal based on the available studies in CAD patients.

Methods

We conducted a systematic review of the literature on benefits of the recommended lifestyle and dietary changes in CAD patients applying the following selection criteria.

Received September 1, 2004; revision received February 10, 2005; accepted April 11, 2005.

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Circulation is available at <http://www.circulationaha.org>

DOI: 10.1161/CIRCULATIONAHA.104.503995

TABLE 1. Recommendations on Lifestyle and Dietary Factors to Improve Prognosis in CAD Patients

1.	Stop smoking
2.	Engage in moderate intensive physical activity (for ≥ 30 minutes on at least 5, but preferably all, days of the week)
3.	If you use alcohol: do so in moderation (maximum 2 alcoholic drinks per day for women and maximum 3 drinks per day for men)
4.	Maintain or attain a healthy body weight (BMI < 25 kg/m ²); obese patients (BMI > 30 kg/m ²) should try to lose 10–15% of their current body weight
5.	Limit your saturated fat intake (to a maximum of 10 energy%) and the intake of trans fatty acids (to maximal 1 energy%)
6.	Consume fish regularly (at least 1 and preferably 2 portions of oily fish per week)
7.	Consume sufficient amounts of fruits and vegetables (≥ 400 g/d)
8.	Use sufficient fiber containing grain products, legumes, and/or nuts (≥ 3 U/d)
9.	Reduce your salt intake (to maximal 2400 mg/d)

Study Population

Studies had to investigate a population of at least 50% patients diagnosed with CAD. CAD patients were defined as patients with a history of MI or AP or who underwent coronary artery bypass graft (CABG) or percutaneous transluminal coronary angioplasty (PTCA).

Determinants and Interventions

We excluded studies on nutrient supplements if the dosage of the nutrient they provide goes beyond the amount that can reasonably be achieved by changing food habits without the use of supplements. For each lifestyle and dietary recommendation (Table 1), we defined the following determinants or interventions to be accepted in our study.

Smoking Cessation

Studies reporting smoking cessation after the diagnosis of CAD were accepted.

Physical Activity

Time spent on moderate intensive activity is the best example of operationalization of the current recommendations.¹¹ Moderately intensive activities are those with an absolute intensity of 4 to 6 METs or a relative intensity of 40% to 60% of $\dot{V}O_{2max}$.¹² We also accepted studies on total energy expenditure, habitual daily activity scores, time spent in vigorous intensive physical activity, physical fitness, or participation in structured exercise programs.

Alcohol Consumption

Alcohol consumption had to be reported in the number of units or grams of alcohol per day. Studies reporting only alcohol intake as a percentage of total energy intake were excluded.

Energy Balance

The recommendation to maintain or attain a healthy body weight refers to both the actual as well as the previous history of the balance between energy intake and energy expenditure (physical activity). Accepted were studies on body weight maintenance after the first manifestation of CAD and studies on intentional body weight reduction in overweight or obese CAD patients in relation to survival. Studies on the association between body weight status (body mass index [BMI]) at time of event and survival were excluded because BMI at time of diagnosis does not reflect lifestyle and dietary habits after the first manifestation of CAD.

Saturated Fat and Trans-Fatty Acids

We accepted all studies investigating a reduced intake of saturated fat and/or trans-fatty acids without a substantial restriction of total fat intake. Interventions on total fat intake restrictions beyond 25 energy% were excluded because of supposed detrimental effects on HDL and triglyceride levels.¹³ Given the mean intake of saturated fat in most Western countries at ≈ 15 energy%, we defined a reduction of 5 energy% as a relevant difference.

Regular Fish (Oil) Consumption

The recommended 2 portions (400 g) of oily fish per week are equivalent to a daily dose of 500 to 1000 mg ω -3 fatty acids

(eicosapentaenoic acid [EPA] and docosahexaenoic acid [DHA]).¹⁴ We accepted all studies on fish consumption and on fish oil supplements to a maximum increase of 1000 mg ω -3 fatty acids per day. We excluded studies with higher doses because it is unlikely that these levels can be achieved by increasing fish consumption alone.

Fruits and Vegetables

We included studies that examined the effect of the daily intake of fruits and vegetables in all available forms (fresh, canned, frozen, dried, or as juice).

Whole Grains, Legumes, and Nuts

We included studies on the effect of the daily intake of whole grains, legumes, and nuts or that studied the effect of intake of fiber from these products.

Salt

We included all studies examining the effect of sodium restriction. Because the recommended maximal salt intake is 6 g/d¹⁵ (2400 mg or 100 mmol sodium) and current intake in Western societies is ≈ 9 g, a restriction was defined as a reduction of at least 30% or 50 mmol sodium.

Combined Lifestyle and Dietary Interventions or Combined Determinant Scores

We also included studies that examined a combination of ≥ 2 of the aforementioned individual factors.

Outcome Measures

We only included studies that reported an effect on all-causes mortality.

Study Design and Follow-Up Period

Studies had to have a prospective design, being either a cohort study or a randomized controlled trial, and the follow-up period had to be at least 6 months. If available, meta-analyses of prospective studies were preferred and replaced the individual studies that they described.

Search Strategy

Data for this review were identified by searches in PubMed (1966 to May 2004) with the Medical Subject Heading (MeSH) terms *coronary artery disease* and *patients* in combination with the MeSH terms or text words *lifestyle*, *smoking*, *physical activity*, *physical fitness*, *exercise*, *alcohol drinking*, *body weight*, *weight control*, *diet*, *saturated fat*, *trans-fatty acids*, *cholesterol*, *fish*, *fruit*, *vegetables*, *whole grains*, *cereals*, *legumes*, *nuts*, *fiber*, *salt*, *sodium*, *mortality*, *survival*, and *death*. There was a restriction on English language. Relevant articles not identified by this strategy, but referenced in the bibliographies of these selected articles, were also included.

Data Extraction and Standardization

Details of the included studies were systematically described as shown in Table 2. The relative risk (RR) was used as a measure of

strength of the relationship between exposure to the lifestyle or dietary factor and all-causes mortality or other end points. The RR should compare the risk in the group practicing the desired healthy behavior (exposed group) with the group not showing the healthy behavior (reference group). For studies that reported the RR from the unhealthy lifestyle or dietary factor (eg, BMI >30 kg/m²) compared with the healthy lifestyle or dietary factor (eg, BMI <25 kg/m²), the RR from the exposed group was calculated as 1 divided by the RR in the nonexposed group. If the RR or the 95% CI of the RR was not reported in the original studies, they were calculated from the study data with the use of the number of subjects (N) and the number of cases (A) in both the exposed (1) and the unexposed (0) groups: $RR = (A1/N1 \text{ divided by } A0/N0)$ and $95\% \text{ CI} = \text{EXP}[\ln RR \pm 1.96\sqrt{(1/A1 + 1/A0)}]$ if incidence is sufficiently rare.

Summary Effect Estimates

We decided that an effect estimate per lifestyle or dietary goal could only be provided if a meta-analysis was available or if at least 2 randomized controlled trials or 2 cohort studies were available meeting the following quality criteria: in case of cohort studies, the effect estimate should be based on findings that were adjusted for confounders, at least for age and gender; in case of randomized trials, information should be given that compliance with the intervention under study was checked and considered satisfactory; and the effect estimate of each study should be based on at least 20 mortality cases to guarantee that the power of the study allowed meaningful effect estimation.

Results for the lifestyle or dietary goals that fulfilled these criteria are shown in Table 3. Before we pooled the data, heterogeneity between the studies was tested with the χ^2 statistic. We used the random effects model for calculating a pooled estimate for the RR if the probability value for heterogeneity was ≤ 0.5 . In case the probability value for heterogeneity was > 0.5 , a fixed effects model was used.

Results

A total of 3 meta-analyses, 10 randomized controlled trials (studying 13 interventions), and 9 cohort studies fulfilled the inclusion criteria. Details of the available studies per lifestyle or dietary goal are shown in Table 2. For 5 goals (3 on lifestyle and 2 on dietary changes), the available studies fulfilled our additional criteria for calculating pooled effect size estimates (Table 3). For the combined interventions, only studies on combined dietary changes were available, and their pooled effect estimate is shown in Table 3.

Goals With Sufficient Studies to Calculate a Pooled Effect Estimate

Smoking Cessation

Two meta-analyses of cohort studies were found on smoking cessation. Duration of follow-up ranged from 2 to 20 years. All included studies consistently showed a protective effect of smoking cessation. Wilson et al¹⁶ performed a meta-analysis of 12 studies in patients with MI and found a pooled RR for all-causes mortality of 0.54 (95% CI, 0.46 to 0.62) for those who had quit smoking. Critchley and Capewell¹⁷ published a meta-analysis of 20 studies in patients with previous MI or AP and reported a pooled RR of 0.64 (95% CI, 0.58 to 0.71). Half of the studies were the same as in the first analysis. On the basis of these 2 meta-analyses, we conservatively estimate the effect size of smoking cessation in CAD patients as a 35% mortality risk reduction.

Habitual Physical Activity

We found no studies on the effect of increased physical activity on mortality in CAD patients. The effect of participation in a structured exercise program after a cardiac event (MI, AP, CABG, or PTCA) on morbidity and mortality has been evaluated in several meta-analyses.^{18–22} Reported effect size estimates of mortality reduction varied between 20% and 25%. Here we review the analysis by Brown et al,²¹ which is a 2003 update from earlier meta-analyses and which studied exercise-based rehabilitation programs separately from the comprehensive rehabilitation programs that also included educational and psychosocial interventions. In this study mortality data were available of 2585 patients in 12 randomized controlled trials. The interventions varied widely from gym-based aerobic exercise twice a week for 4 weeks to interventions lasting for 30 months with inpatient stays. Mean follow-up time was 24 months (range, 6 to 60 months). The study showed a significant beneficial effect of an exercise program. The effect on all-causes mortality was estimated as $\approx 25\%$ risk reduction (RR, 0.76; 95% CI, 0.59 to 0.98).

Moderate Alcohol Consumption

We found 5 cohort studies^{23–27} examining the effect of moderate drinking versus rare drinkers or nondrinkers in CAD patients. All studies, except for 1,²⁴ found a statistically significant reduction of all-causes mortality between 15% and 25% for moderate drinking. Duration of follow-up varied between 3 and 13 years. Effect estimates are shown in Table 3. The pooled effect estimate for the RR for all-causes mortality in the 5 studies was 0.80 (*P* for heterogeneity 0.53; 95% CI, 0.78 to 0.83), summarized in an effect estimate of 20% reduction of all-causes mortality.

Saturated Fat Reduction

Four^{28–31} randomized controlled trials and 1 cohort study³² met our criteria for fat modification. They all concerned saturated fat intake reduction. No studies were detected on the relation between trans-fatty acid intake and mortality in CAD patients. The randomized controlled trials were performed between 1960 and 1988 and intended to study a reduction of ≈ 5 energy% in saturated fat intake during 2 to 5 years of follow-up. The resulting reduction in serum cholesterol was $\approx 15\%$ in 2 studies^{28,29} and only 5% in the other 2,³¹ raising doubts on adherence to the regimen in the latter 2 studies.³⁰ Only in the 2 studies with the largest serum cholesterol reductions was total mortality reduced (12% and 25%), but the power of the studies was too limited to show statistically significant reductions. The probability value for heterogeneity was 0.18 for the 4 studies and 0.63 when the 2 studies with unsatisfying serum cholesterol reductions were excluded. The pooled effect estimates were not statistically significant for either the 4 or the 2 studies (Table 3). The cohort study³² in 400 Finnish CAD patients was supportive of a beneficial effect of a lower saturated fat intake. For every 4 energy% reduction in saturated fat, intake RR for all-causes mortality was 0.64 (95% CI, 0.46 to 0.88). However, this study on its own is not sufficient to be conclusive. Because the pooled effects are not statistically significant, we provide no summary effect estimate for saturated fat restriction.

TABLE 2. Studies on Lifestyle and Dietary Factors and All-Causes Mortality in CAD Patients

Study	Study Population	Enrollment/Follow-up	Determinant/Intervention	Reference/Controls	All-Causes Mortality, RR (95% CI)
Smoking cessation					
Critchley, 2003 Meta-analysis 20 cohort studies	CAD patients n=12 603; 2928 deaths Age: 20–95 y >70% men	Enrollment: 1960–1995 Mean follow-up: 5.5 y	Smoking cessation after CAD diagnosis	Continued smoking	0.64 (0.58–0.71)
Wilson, 2000 Meta-analysis 12 cohort studies	Post-MI patients n=5878; 915 deaths Age: not reported	Enrollment: 1949–1988 Follow-up: 2–10 y	Smoking cessation after MI diagnosis	Continued smoking	0.54 (0.46–0.62)
Physical activity					
Brown, 2003 Meta-analysis 12 RCTs	CAD patients n=2585; 212 deaths Age: 54 (50–70) y 95% men	Enrollment: 1970–2000 Mean follow-up: 2 y (range, 6 mo–5 y)	Rehabilitation program with exercise only	Usual care	0.76 (0.59–0.98)
Moderate alcohol consumption					
Cooper, 2000 Cohort study US	CAD patients with left ventricular dysfunction n=5331; 1200 deaths Mean age: 60 y 85% men	Enrollment: ≈1990 Follow-up: 33 ±14 mo Adjustments: demographics, risk factors, medication	1–4 alcoholic drinks per week	No alcohol drinkers	0.85 (0.75–0.97)
Shaper, 2000 Cohort study UK	CAD patients n=655; 294 deaths Age: 40–59 y at baseline 100% men	Enrollment: 1983–1985 Follow-up: 12.8 y Adjustments: demographics, risk factors	1–15 U/wk	Occasional drinking	1.05 (0.78–1.42)
Muntwyler, 1998 Cohort study US	Post-MI patients n=5358; 920 deaths Mean age: 63 (±9) y 100% men	Enrollment: 1982 Follow-up: 5 y Adjustments: demographics, risk factors	2–6 U/wk	Rare and non-drinkers	0.72 (0.58–0.89)
Thun, 1997 Cohort study US	Patients with vascular disease n=71 232; 8434 deaths Mean age: 57 y 55% men	Enrollment: 1982 Follow-up: 9 y Adjustments: demographics, risk factors, fat intake	2 drinks per day	Non-drinkers (ex-drinkers excluded)	0.8 (0.8–0.9)
Doll, 1994 Cohort study UK	Patients with vascular disease n=5402; 2396 deaths Age: 48–78 y 100% men	Enrollment: 1978 Follow-up: 13 y Adjustments: age, smoking	1–14 U/wk	Non-drinkers (including ex-drinkers)	0.79* (0.69–0.91)
Body weight control					
Singh, 1992 Cohort study India	CAD patients n=204; 21 deaths Age: 51 ±9 y 90% men	Enrollment: not reported Follow-up: 1 y Adjustments: none	Weight loss after MI >0.5 kg	Weight loss after MI <0.5 kg	0.46* (0.19–1.10)
Saturated fat					
Erkkila, 2003 Cohort study Finland	CAD patients n=415; 34 deaths Age: 61 (33–74) y 70% men	Enrollment: 1991–1994 Follow-up: 5 y Adjustments: demographic and diagnostic factors, risk factors, energy intake	9 energy% saturated fat (average, SD)	13 energy% saturated fat (average)	0.64 (0.46–0.88)
Burr, 1989 RCT UK	Post-MI patients n=2033; 224 deaths Mean age: 57 y 100% men	Enrollment: 1985–1987 Follow-up: 2 y Compliance: moderate; as shown by 5% decrease in serum cholesterol	11 energy% saturated fat	15 energy% saturated fat	1.0 (0.77–1.30)
Woodhill, 1978 RCT Australia	CAD patients n=458; 67 deaths Age: 30–59 y 100% men	Enrollment: 1966–1972 Follow-up: 5 y Compliance: moderate, as shown by 5% decrease in serum cholesterol	10 energy% saturated fat	13.5 energy% saturated fat	1.49* (0.92–2.43)
Morris, 1968 RCT UK	Post-MI patients n=395; 59 deaths Age: 60% 50–60 y 100% men	Enrollment: 1960–1965 Mean follow-up: 3.7 y Compliance: good, as shown by a 15% decrease in serum cholesterol	≈12 energy% saturated fat	≈17 energy% saturated fat (ordinary UK diet)	0.88* (0.53–1.47)
Leren, 1966 RCT Norway	Post-MI patients n=412; 96 deaths Age: 30–64 y 100% men	Enrollment: 1958–1959 Follow-up: 5 y Compliance: good, shown by a 15% decrease in serum cholesterol	9 energy% saturated fat	Not described	0.75* (0.50–1.12)
Regular fish (oil) consumption					
Barzi, 2003 Cohort study Italy	Post-MI patients n=11 246; 1660 deaths Age: 59 ±11 y 85% men	Enrollment: 1993–1995 Follow-up: 6.5 y Adjustments: demographic, risk factors, food variables	2 portions of fish per week	(Almost) never fish	0.81 (0.69–0.94)
Erkkila, 2003 Cohort study Finland	CAD patients n=400; 34 deaths Age 61 (33–74) y 70% men	Enrollment: 1991–1994 Follow-up: 5 y Adjustments: demographic, diagnostic, risk factors, energy intake	1–57 g fish per day >57 g fish per day	0 g fish per day 0 g fish per day	0.50 (0.20–1.28) 0.37 (0.14–1.00)

TABLE 2. Continued

Study	Study Population	Enrollment/Follow-up	Determinant/Intervention	Reference/Controls	All-Causes Mortality, RR (95% CI)
Burr, 2003 RCT UK	AP patients n=3114; 525 deaths Mean age: 61 y 100% men	Enrollment: 1990–1996 Follow-up: 3 to 9 y Compliance checked by food records in subset at 6 mo; no significant difference in serum EPA level between groups	Advice to eat at least 2 weekly portions of oily fish (200–400 g) or fish oil capsules	“Sensible eating” advice	1.15 (0.96–1.36)
GISSI, 1999/2002 RCT Italy	Post-MI patients n=11 323; 1017 deaths Mean age: 59±11 y 85% men	Enrollment: 1993–1995 Follow-up: 3.5 y Compliance confirmed 3-mo by biomarkers and refill check drug supplies	Supplement 900 mg EPA/DHA	Placebo	0.79 (0.66–0.93)
Burr, 1989 RCT UK	Post-MI patients n=2033; 224 deaths Mean age: 57 y 100% men	Enrollment: 1985–1987 Follow-up: 2 y Compliance confirmed at 6 mo and at 2 y by food records and biomarkers (serum EPA)	Advice: eat at least 2 weekly portions of oily fish (200–400 g) or fish oil capsules	“Sensible eating” advice	0.71 (0.54–0.93)
Fruit and vegetables					
Burr, 2003 RCT UK	AP patients n=3114; 525 deaths Mean age: 61 y 100% men	Enrollment: 1990–1996 Follow-up: 3–9 y Compliance: bad; no change in biomarkers (serum levels of folate and carotenoids)	Advice: 4–5 portions of fruit and vegetables plus 1 glass of orange juice	“Sensible eating” advice	1.12 (0.94–1.34)
Barzi, 2003 Cohort study Italy	Post-MI patients n=11 246; 1660 deaths Age: 59±11 y 85% men	Enrollment: 1993–1995 Follow-up: 6.5 y Intake measured 4 times in 3.5 y Adjustments: demographic. Risk factors, food variables	Fruit: >1 time per day Raw vegetables: 1 time per day Cooked vegetables: 1 time per day	(Almost) never fruit (Almost) never raw vegetables (Almost) never cooked vegetables	Fruit: 0.73 (0.54–0.98) Raw: 0.67 (0.56–0.79) Cooked: 0.84 (0.71–1.00)
Whole grains, legumes, and nuts					
Erkkila, 2003 Cohort study Finland	CAD patients n=400; 34 deaths Mean age: 61 y 70% men	Enrollment: 1991–1994 Follow-up: 5 y Adjustments: demographic and diagnostic factors, risk factors, energy intake	30 g fiber/d	22 g fiber/d	0.81 (0.55–1.19)
Burr, 1989 RCT UK	Post-MI patients n=2033; 224 deaths Mean age: 57 y 100% men	Enrollment: 1985–1987 Follow-up: 2 y Compliance confirmed by food records at 6 mo and 2 y, no biomarkers	30 g total fiber, of which 20 g cereal fiber	20 g total fiber, of which 10 g cereal fiber	1.27 (0.99–1.65)
Combined lifestyle factor studies					
Barzi, 2003 Cohort study Italy	Post-MI patients n=11 246; 1660 deaths age: 59±11 y 85% men	Enrollment: 1993–1995 Follow-up: 6.5 y Adjustments: demographic, risk factors, food variables	4th quartile of dietary score for intake of fish, fruit, vegetables, olive oil	Lowest quartile of dietary score	0.51 (0.44–0.59)
Singh, 2002 RCT India	High-risk patients (59% CAD) n=1000, 65 deaths Age: 49±10 y 90% men	Enrollment: not reported Follow-up: 2 y Compliance was confirmed by 3-mo food records	Advice: AHA step 1 diet plus extra fruits, vegetables, whole grains, legumes, nuts, and α -linolenic acid–rich oil	Advice: AHA step 1 diet: \leq 30 energy% fat, \leq 10 energy% saturated fat, \leq 300 mg cholesterol/d	0.63* (0.38–1.06)
De Lorgeril, 1994/1999 RCT France	Post first MI-patients n=605; 38 deaths Mean age: 53.5 y 90% men	Enrollment: 1988–1992 Follow-up: 3.8 y Compliance was checked at each visit by 24-h recall and food frequency questionnaire and confirmed by biomarkers (plasma fatty acids)	Advice: Mediterranean diet and supply with α -linolenic acid–enriched margarine	Advice: AHA step 1 diet: \leq 30 energy% fat, \leq 10 energy% saturated fat, \leq 300 mg cholesterol/d	0.44 (0.21–0.94)
Singh, 1992 RCT India	Post-MI patients n=406; 59 deaths Mean age: 51±10 y 90% men	Enrollment: <24 h after MI Follow-up: 1 y Compliance was confirmed by 3-mo food records	AHA step 1 diet plus extra fruits and vegetables (\leq 400 g/d), legumes, nuts, and fish	Advice: AHA step 1 diet: \leq 30 energy% fat, \leq 10 energy% saturated fat, \leq 300 mg cholesterol/d	0.55 (0.34–0.75)

RCT indicates randomized controlled trial; AHA, American Heart Association.
*RR not reported but calculated from study data (see Methods).

Regular Fish (Oil) Consumption

We found 3 randomized controlled trials^{31,33–35} and 2 cohort studies^{32,36} fulfilling our selection criteria. The trials tested either the effect of advice to increase fatty fish consumption up to 200 to 400 g/wk^{31,33} or the effect of a fish oil supplement containing \approx 900 mg EPA and DHA per day.^{34,35} Two of them^{31,34,35} showed a significant mortality reduction, but the trial in AP patients³³ found a nonsignificant mortality increase in the intervention group.

Both cohort studies were supportive of a protective effect of a higher fish intake. The study by Barzi et al³⁶ (n=11 246) was performed in the participants of the GISSI-Prevenzione trial studying the effects of fish oil (900 mg EPA and DHA) and/or vitamin E (300 mg) supplements. Irrespective of their assignment to the study intervention, most patients increased their fish consumption subsequent to the MI, as was advised by the hospital. Fish intake was assessed 4 times during the intervention period of 3.5 years, and duration of follow-up

TABLE 3. Mortality Reduction Estimates of Lifestyle and Dietary Changes Based on Available Studies in CAD Patients

Goals	Randomized Controlled Trials, RR (95% CI)	Prospective Cohort Studies, RR (95% CI)
Lifestyle factors		
Smoking cessation		Critchley,* 2003, 0.64 (0.58–0.71) Wilson,* 2000, 0.54 (0.46–0.62)
Physical activity	Brown,* 2003, 0.76 (0.59–0.98)	
Moderate alcohol consumption		Cooper, 2000, 0.85 (0.75–0.97) Shaper, 2000, 1.05 (0.78–1.42) Muntwyler, 1998, 0.72 (0.58–0.89) Thun, 1997, 0.8 (0.8–0.9) Doll, 1994, 0.79 (0.69–0.91) Pooled estimate: 0.80 (0.78–0.83)†
Dietary factors		
Saturated fat reduction	Burr, 1989, 1.0 (0.77–1.30) Woodhill, 1978, 1.49 (0.92–2.43) Morris, 1968, 0.88 (0.53–1.47) Leren, 1966, 0.75 (0.50–1.12) Pooled (4 studies): 0.98 (0.81–1.18)§ Pooled (2 studies)‡: 0.79 (0.58–1.09)†	Erkkila, 2003, 0.64 (0.46–0.88)
Regular fish (oil) consumption	Burr, 2003, 1.15 (0.96–1.36) GISSI, 1999, 0.79 (0.66–0.93) Burr, 1989, 0.71 (0.54–0.93) Pooled (3 studies): 0.88 (0.69–1.11)§ Pooled (2 studies) : 0.77 (0.66–0.89)†	Barzi, 2003, 0.81 (0.69–0.94) Erkkila, 2003, 0.50 (0.20–1.28) Pooled estimate: 0.80 (0.69–0.93)†
Combined factors		
Combined dietary factors	Singh, 2002, 0.63 (0.38–1.06) Lorgeril, 1999, 0.44 (0.21–0.94) Singh, 1992, 0.55 (0.34–0.75) Pooled estimate: 0.55 (0.41–0.74)†	Barzi, 2003, 0.51 (0.44–0.59)

*Meta-analysis.

†*P* for heterogeneity >0.5; fixed effects model used.

‡Studies by Burr, 1989 and Woodhill, 1978 excluded.

§*P* for heterogeneity ≤0.5; random effects model used.

||Study by Burr et al, 2003 excluded.

was 6.5 years. In the small cohort study by Erkkila et al,³² fish consumption was assessed at baseline only, and patients were followed up for 5 years. Both cohort studies fulfilled our quality criteria on adjustment for confounding and the number of cases. Table 3 shows the effect estimates of the presented studies. Before the data were pooled, heterogeneity tests were performed. Heterogeneity existed ($P=0.002$) for the 3 fish trials but disappeared when the AP patients' trial was excluded ($P=0.56$). Pooled effect estimates for both the 3 and the 2 trials as well as for the 2 cohort studies are shown in Table 3. Because of the unexplained heterogeneity in the results, no summary effect estimate is provided for regular fish (oil) consumption.

Remaining Goals

For the remaining dietary goals, the available studies (Table 2) were insufficient to provide a reliable effect estimate on

life expectancy in CAD patients. For body weight control, we found only 1 study³⁷ on the effect of weight reduction after MI, but this study was considered of low quality because the results were not adjusted for confounding, not even for age and gender. For fruits and vegetables, the available randomized controlled trial³³ was not a good test for the effect of increased fruit and vegetable consumption because compliance with the intervention was doubted as a result of a lack of any rise in serum concentrations of folate or carotenoids. The cohort study by Barzi et al³⁶ supported a beneficial effect of the recommendations on both fruit (RR, 0.73; 95% CI, 0.54 to 0.98) and vegetables (raw vegetables: RR, 0.67; 95% CI, 0.56 to 0.79; cooked vegetables: RR, 0.84; 95% CI, 0.71 to 1.00) but was insufficient on its own to be included in Table 3. For dietary fiber and whole grain products, available studies were not consistent. The only trial³¹ showed no effect (because compliance was not measured, it is unclear whether this is

TABLE 4. Approximate Mortality Reduction Potential of Lifestyle and Dietary Changes Estimated From Studies in CAD Patients and the General Population

Recommendation	Mortality Risk Reduction Estimated From Studies in CAD Patients	Mortality Risk Reduction Estimated From Cohort Studies in General Population
Smoking cessation	35%	50%
Physical activity	25%	20%–30%
Moderate alcohol	20%	15%
Combined dietary changes	45%	15%–40%

due to a lack of effect or a lack of compliance), and the cohort study³² on total fiber intake was too small ($n=400$; 34 mortality cases) to show a statistically significant difference (RR, 0.81; 95% CI, 0.55 to 1.19). No studies were found relating the intake of trans-fatty acids, legumes, nuts, or salt to mortality in CAD patients.

Combined Interventions

We found no studies on the mortality effects of combinations of both lifestyle and dietary changes. On combined dietary changes alone, 3 randomized controlled trials^{37–40} and 1 cohort study³⁶ met our inclusion criteria for the summary effect estimate. The interventions consisted of an increased intake of fiber-rich foods (fruits, vegetables, nuts, legumes) and fish and eventually an enhanced intake of unsaturated fatty acid intake through the use of oils or special margarines. Average duration of follow-up varied between 1 and 4 years. Mortality reduction was statistically significant in 2 of the 3 trials.^{37,39} Both the individual and the pooled effect estimates on mortality are shown in Table 3. The pooled RR for all-causes mortality was 0.56 (P for heterogeneity=0.73; 95% CI, 0.42 to 0.74). The effect estimate in the cohort study³⁶ was based on a combined score on the consumption of fish, fruit, cooked vegetables, raw vegetables, and olive oil. All-causes mortality was 49% lower in patients in the highest quartile of the dietary score compared with the lowest quartile. We estimate the mortality risk reduction potential for combinations of individual dietary goals (as formulated in Table 1) to be 45%.

Discussion

Although many of the commonly provided lifestyle and dietary recommendations (Table 1) are supported with evidence from surrogate end point studies and studies in the general population, there is only limited evidence from studies in CAD patients that these recommendations indeed improve their life expectancy. The available studies show significant effects for 3 lifestyle recommendations on prognosis of CAD patients. Effects for smoking cessation, increased physical activity, and moderate alcohol consumption vary from a 20% to 35% reduction in all-causes mortality. For individual dietary goals, evidence from studies in CAD patients was not available or was too limited to provide reliable effect estimates. A few studies on combinations of dietary changes show promising results, with mortality reductions of $\approx 45\%$.

In this review we included both experimental and observational studies. Randomized controlled trials are generally

rated as a higher level of evidence than prospective cohort studies because they exclude self-selection and confounding by indication as a source of bias. Randomized clinical trials, however, have their own drawbacks: their inclusion criteria often limit generalization to the average patient population in routine care, their costs often limit the duration of the study, in the case of lifestyle or dietary interventions double blinding is often impossible, or the intervention itself is unethical (eg, smoking or alcohol consumption). Prospective cohort studies, on the other hand, may be confounded by unknown prognostic factors associated with lifestyle or dietary habits, but they have the advantage of giving a better reflection of the “real-life” situation with long-term exposure and mostly a mixed patient population. The advantages and disadvantages of each design do not outweigh those of the other. In this review we reported effect sizes of both study designs (if available) separately and did not make an attempt to rank one above the other.

This review has several potential limitations. Most evidence was available for studies on lifestyle changes in CAD patients. Studies on dietary changes are scarce, and several are of poor methodological quality. Confounding due to clustering of lifestyle and dietary factors as well as bias because of unblinding or poor compliance with the intervention or changes in habits of the control group is more common in lifestyle and dietary studies than in drugs trials. Many of the studies included in this review were underpowered to assess effects on total mortality. This problem may be solved by pooling the results of individual studies, but, even if tests for heterogeneity are not significant, this operation may be problematic because of the heterogeneity of studies with respect to background habits, intervention characteristics, exposure (time and dose), and length of follow-up. Sometimes the point estimates are impressive, but the wide CIs indicate a high degree of uncertainty. Therefore, caution is needed in interpreting the results and particularly in translating the effect size estimates to the individual patient.

Nevertheless, most of the presented effect estimates are in accord with results from studies performed in the general population. Table 4 compares the effect estimates in CAD patients with results from cohort studies in the general population.

Smoking Cessation

Our effect estimate of $\approx 35\%$ risk reduction is similar to findings from population-based cohort studies indicating that quitters before age 50 have a 50% lower risk of dying than continuing smokers.^{41,42}

Physical Activity Level

An effect estimate of 25% mortality risk reduction for an increased level of physical activity was obtained from a meta-analysis on the effect of exercise-based revalidation. Although the best available, this is not a good estimate for adherence to the guideline¹¹ to increase habitual physical activity level to a daily amount of at least 30 minutes of moderately intensive activity. Participation in a program is not necessarily related to a higher physical activity level in the long run.^{43,44} However, the estimated 25% mortality risk reduction compares well with estimates from other populations. A review⁴⁵ of 44 population-based cohort studies reported that adherence to the guideline was associated with a 20% to 30% reduction in all-causes mortality. Further reductions were observed at higher volumes of energy expenditure. Not only high baseline levels but also increments in physical activity level later in life are shown to be associated with lower mortality.^{46,47}

Alcohol

Although the protective effect of moderate alcohol consumption on cardiovascular risk has been sufficiently demonstrated in the general population cohorts,⁴⁸ for CAD patients there was concern about the adverse effects on the cardiovascular system, such as hypertension, arrhythmias, hemorrhagic stroke, and cardiomyopathy.⁴⁹ The presented studies are consistent in their finding that moderate alcohol consumption can improve the prognosis in CAD patients, even in patients with associated heart failure,²³ as long as the alcohol intake is moderate (2 to 3 U/d). The estimate of 20% mortality risk reduction in CAD patients is in range with a pooled estimate of 15% mortality reduction in cohort studies in middle-aged populations.⁵⁰ Of course, the benefits of moderate alcohol consumption should always be mentioned in relation to the potential risks of excessive alcohol consumption because there are still more deaths caused by alcohol than prevented.⁵¹

Saturated Fat

Reliable effect estimates could be provided for none of the individual dietary factors. The pooled effect estimates for saturated fat reduction were not statistically significant (for the 4 studies: RR, 0.98; 95% CI, 0.81 to 1.18) but agreed with the findings of 2 meta-analyses on fat modification combining the results of both primary and secondary prevention trials: RR, 0.94 (95% CI, 0.89 to 0.99; 17 trials)⁵² and RR, 0.98 (95% CI, 0.86 to 1.12; 11 trials).⁵³ In contrast to our study, these meta-analyses also included studies on total fat restriction, which might have attenuated the effect. They confirm our finding that a trend was seen toward a greater risk reduction in trials in which better adherence to the intervention is shown by a greater reduction in serum cholesterol.

Regular Fish (Oil) Consumption

There was heterogeneity between the studies, but the calculated pooled effect estimates for the trials (12% to 23% mortality risk reduction) are in agreement with an estimate of 20% all-causes mortality reduction in a meta-analysis by Bucher et al⁵⁴ based on 9 trials in CAD patients on the effects of dietary fish or fish oil supplementation in doses up to 10 g of ω -3 fatty acids per day. The pooled effect estimate from

the cohort studies in CAD patients was also 20%. Data on fish and all-causes mortality from population-based cohorts are inconsistent and vary from 0% to 30%.^{55–60} Null findings in some of the studies can possibly be explained by the adverse effects of the high mercury content of fish in some geographic areas^{56,61} or by the fact that the protective effect is specific for fatty fish and not for total fish consumption.⁶² The association with CAD mortality is more frequently studied than all-causes mortality, and significant risk reductions are reported.^{63–65}

For the remaining individual goals, studies on mortality were too few to provide effect estimates. This should not be interpreted as a lack of scientific support for these recommendations. The evidence from surrogate end point or clinical end point studies is reviewed elsewhere.^{66–77} Studies on all-causes mortality, however, are scarce, not only in CAD patients but also in other populations. Given the alarming signals^{78,79} on a high prevalence (80%) of overweight and obesity in CAD patients, it is surprising that no studies were found on the effect of intentional weight loss on mortality in CAD patients. Weight loss might be one of the mechanisms through which other lifestyle or dietary changes (eg, regular exercise or increased intake of whole grains and vegetables) might exert their protective effect, but few authors report on body weight changes.⁴⁰ Cohort studies in the general population have shown that mortality is 30% to 50% lower in normal-weight individuals than in their obese peers,⁸⁰ although this difference decreases with age.⁸¹ The effect that can be expected from weight reduction in patients already treated with preventive drugs is unclear. Some studies in CAD patients^{82–86} (not meeting our inclusion criteria) even suggest a prognostic benefit of obesity. These studies, however, are inconclusive because they often lack appropriate adjustments for confounding (eg, confounding by age because obese persons are generally 7 years younger at time of their first MI than normal-weight individuals), but they stress the need for high-quality additional research. Finally, population-based cohort studies that study all-causes mortality in relation to the intake of fruits and vegetables,^{87–90} whole grains,^{87,91,92} legumes,⁹³ nuts,^{94,95} or salt^{96–98} are scarce but are generally supportive of a protective effect of the recommendations.

The trials on combined dietary interventions showed impressive results, varying from 35% to 55% mortality reduction. Other intervention studies in CAD patients showed benefits of combined lifestyle and dietary changes on surrogate end points and cardiac events.^{99,100} The cohort study in 11 000 CAD patients by Barzi et al³⁶ showed an almost 50% lower mortality risk for those with the highest dietary quality score. Mortality risk reductions associated with dietary quality reported from other populations were generally smaller (15% to 25%), but a significant benefit was demonstrated in many studies.^{101–110} Two studies in elderly people^{101,104} showed a 60% to 70% lower mortality associated with a higher quality score for a combination of both lifestyle and dietary habits. Although the studies on combined changes are promising, they shed no light on the dominant mechanism and on the contribution of the individual lifestyle and dietary factors. More knowledge on the benefits of the 6 individual

TABLE 5. Approximate Mortality Reduction Potential of Preventive Drug Interventions After MI

Intervention	Mortality Risk Reduction, Mean (95% CI)
Low-dose aspirin ¹¹¹	18% (1%–30%)
Statins ¹¹²	21% (14%–28%)
β -Blockers ¹¹³	23% (15%–31%)
ACE inhibitors ¹¹⁴	26% (16%–35%)

dietary goals in particular is necessary for designing effective preventive strategies.

If the effect sizes of lifestyle and dietary changes in Table 4 reflect the true value, they compare favorably with effect size estimates for cardiopreventive drugs as shown in Table 5.^{111–114} In contrast to these pharmacological interventions, the prognostic effects of lifestyle and dietary changes are, however, less rigorously studied. For the future, well-designed and powered studies are needed to test the effect of dietary changes on prognosis. Second, because compliance with the recommendations is crucial, research is needed on strategies to enhance adaptation and maintenance of healthy lifestyle and dietary habits in CAD patients.

In conclusion, there is evidence from mortality studies in CAD patients that smoking cessation, physical activity, moderate alcohol consumption, and combined dietary changes improve prognosis. Effect size estimates for the lifestyle goals vary between 20% and 35% mortality reductions. Data on the benefits of individual dietary goals are limited. For the future, more and better-quality studies are needed to reduce the uncertainty that surrounds these effect size estimates.

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Circulation. 2005;112:924-934

doi: 10.1161/CIRCULATIONAHA.104.503995

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231

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Print ISSN: 0009-7322. Online ISSN: 1524-4539

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