Epidemiology and Prevention

Association of Diet, Exercise, and Smoking Modification With Risk of Early Cardiovascular Events After Acute Coronary Syndromes

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Background—Although preventive drug therapy is a priority after acute coronary syndrome, less is known about adherence to behavioral recommendations. The aim of this study was to examine the influence of adherence to behavioral recommendations in the short term on risk of cardiovascular events.

Methods and Results—The study population included 18 809 patients from 41 countries enrolled in the Organization to Assess Strategies in Acute Ischemic Syndromes (OASIS) 5 randomized clinical trial. At the 30-day follow-up, patients reported adherence to diet, physical activity, and smoking cessation. Cardiovascular events (myocardial infarction, stroke, cardiovascular death) and all-cause mortality were documented to 6 months. About one third of smokers persisted in smoking. Adherence to neither diet nor exercise recommendations was reported by 28.5%, adherence to either diet or exercise by 41.6%, and adherence to both by 29.9%. In contrast, 96.1% of subjects reported antiplatelet use, 78.9% reported statin use, and 72.4% reported angiotensin-converting enzyme/angiotensin receptor blocker use. Quitting smoking was associated with a decreased risk of myocardial infarction compared with persistent smoking (odds ratio, 0.57; 95% confidence interval, 0.36 to 0.89). Diet and exercise adherence was associated with a decreased risk of myocardial infarction compared with nonadherence (odds ratio, 0.52; 95% confidence interval, 0.4 to 0.69). Patients who reported persistent smoking and nonadherence to diet and exercise had a 3.8-fold (95% confidence interval, 2.5 to 5.9) increased risk of myocardial infarction/stroke/death compared with never smokers who modified diet and exercise.

Conclusions—Adherence to behavioral advice (diet, exercise, and smoking cessation) after acute coronary syndrome was associated with a substantially lower risk of recurrent cardiovascular events. These findings suggest that behavioral modification should be given priority similar to other preventive medications immediately after acute coronary syndrome.

Clinical Trial Registration Information—URL: http://clinicaltrials.gov/ct2/show/NCT00139815. Unique identifier: NCT00139815. (Circulation. 2010;121:750-758.)

Key Words: acute coronary syndrome ■ cardiovascular diseases ■ diet ■ exercise ■ prevention ■ smoking

Smoking, poor diet, and lack of exercise are important risk factors for coronary heart disease.1 Population studies attribute a substantial proportion of the decline in cardiovascular diseases seen in some high-income countries (HICs) in recent decades to falling rates of smoking secondary to aggressive policy interventions and improved diets as a consequence of specific food policies, improved trade, and increased availability of fruit and vegetables.2-6 Smoking cessation is effective in the secondary prevention of coronary heart disease. A recent systematic review found that smoking cessation in persons with known coronary heart disease was associated with an ≈30% lower crude risk rate of death and myocardial infarction (MI) during the subsequent 3 to 7 years.7 However, many of these studies enrolled persons with established coronary heart disease (not presenting with acute events), had limited information on confounding factors (such as risk factors or secondary preventive treatments), and did not examine whether benefits occurred early after an acute event. Some small studies have indicated that benefits may occur as early as 1 year after acute coronary syndrome (ACS) presentation, but they have not been large enough to evaluate whether such benefits persist after controlling for risk factors.
or the use of proven pharmacological or interventional therapies.\textsuperscript{8,9} Certain dietary recommendations (eg, Mediterranean diet) and exercise have also shown to be effective in the secondary prevention of coronary heart disease.\textsuperscript{10,11} Cardiac rehabilitation programs that target health behaviors and adherence to drugs have also been associated with better outcomes.\textsuperscript{12} Some of these benefits may occur early, but this is unclear.\textsuperscript{13}

**Clinical Perspective on p 758**

The main aim of these analyses was to examine the influence of adherence to behavioral recommendations on risk for short-term (<6 months after the index event) cardiovascular outcomes and whether there is incremental benefit in modifying multiple lifestyle behaviors after controlling for the use of pharmacological secondary prevention measures.

**Methods**

The Organization to Assess Strategies in Acute Ischemic Syndromes (OASIS) 5 was a randomized, double-blind, double-dummy trial in which fondaparinux was compared with enoxaparin in patients with unstable angina or MI without ST-segment elevation.\textsuperscript{14} In total, 20 078 patients from 576 centers in 41 countries were recruited between April 9, 2003 and May 30, 2005; 11 558 came from HICs and 8520 came from low- and middle-income countries (LMICs) (http://web-worldbank.org). Patients were eligible if they met at least 2 of the 3 criteria: age of at least 60 years, an elevated level of troponin or creatine kinase-MB isoenzyme, or ECG changes indicative of ischemia. Patients with contraindications to low-molecular-weight heparin, recent hemorrhagic stroke, indications for anticoagulation other than an ACS, or a serum creatinine level of at least 3 mg/dL (265 μmol/L) were excluded. Further details are reported elsewhere.\textsuperscript{15}

At baseline, data on demographics, risk factors, and comorbidities were collected. At follow-up visits at 30, 90, and 180 days, the following simple questions on behavioral modification were included: Smoking was assessed with the question, “Is the patient currently smoking?” Answer options were “yes” and “no.” Current smoking was defined as smoking at least 1 cigarette (or cigar or pipe) per day within the last month. Those who used only chewing tobacco were recorded as never smokers. Exercise was assessed with the question, “Is the patient exercising regularly (>30 minutes 3 times a week)?” Answer options were “yes” and “no.” Exercise was noted to include walking uninterrupted or as part of an exercise program. Details on type of exercise or exercise intensity were not recorded. Diet was assessed with the question, “Has patient received counseling for dietary modification?” Answer options were “yes” and “no.” If the response was affirmative, then the follow-up question was, “Is the patient compliant?” Answer options were “yes” and “no.” Diet counseling was described as formal counseling individually, in a group with a dietitian or professional nutritionist, or at a secondary rehabilitation clinic. Details on the nature of the dietary advice or intensity of the program attended were not recorded.

Use of drugs and treatments of percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG) were recorded at baseline, discharge, and 30, 90, and 180 days. Patients were followed up for 180 days, and the outcomes of MI, death, and stroke were systematically recorded. All of the events were adjudicated by a central committee according to standardized operational definitions. In brief, stroke was defined as the presence of a new focal neurological deficit thought to be vascular in origin with signs or symptoms lasting >24 hours. MI was defined as either pathological findings or a typical rise in enzymes with at least 1 of the following: ischemic symptoms, new Q waves, ECG changes indicative of ischemia (ST elevation or depression), or coronary artery interven-

<p>| Table 1. Adherence to Secondary Preventive Medications at 30-Day and 6-Month Follow-Up |
|-----------------------------------------------|-----------------|-----------------|-----------------|</p>
<table>
<thead>
<tr>
<th>Medication</th>
<th>At Discharge, n (%)</th>
<th>At 30 Days, n (%)</th>
<th>At 6 Months, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antiplatelet</td>
<td>18 145 (96.5)</td>
<td>18 069 (96.1)</td>
<td>17 106 (94.7)</td>
</tr>
<tr>
<td>Statin</td>
<td>14 820 (78.8)</td>
<td>14 792 (78.0)</td>
<td>13 389 (90.5)</td>
</tr>
<tr>
<td>ACE/ARB</td>
<td>13 705 (72.9)</td>
<td>13 643 (72.5)</td>
<td>12 251 (89.8)</td>
</tr>
<tr>
<td>β-blocker</td>
<td>15 506 (82.4)</td>
<td>9100 (48.4)</td>
<td>7110 (78.1)</td>
</tr>
</tbody>
</table>

Percentage adherence compared with previous visit.

**Analysis**

Patients included in this analysis were those who survived >30 days and reported information on lifestyle behaviors at the 30-day follow-up visit. Smoking status was classified according to self-report into 4 categories: never smokers, former smokers (ex-smokers who quit before entry into the OASIS 5 study), recent quitters (those who reported not smoking at the 30-day follow-up visit but who were current smokers at study entry), or persistent smokers (those who were smokers at study entry and reported smoking at the 30-day follow-up).

Diet/exercise program adherers were classified into 3 categories: no diet/exercise (those who responded “no” to regular exercise and diet questions at the 30-day follow-up, either diet or exercise (those who responded “yes” to exercise or diet questions), or both diet and exercise (those who responded “yes” to all exercise and diet questions). Unadjusted subject characteristics are reported by these groups.

The associations between smoking status and outcomes and diet/exercise and outcomes were examined in separate age- and sex-adjusted logistic regression models and in multivariable logistic regression models. For multivariable analysis, a forward variable selection procedure was used. The final model included factors that increased the area under the curve of the model and decreased the Akaike information criteria of the model or were known strong predictors of outcomes. The final model included baseline risk factors of age, sex, region of origin, history of hypertension, history of diabetes, body mass index, creatinine, and history of prior MI;
PCI/CABG interventions before 30 days; and reported use of secondary preventive medications at 30 days, including β-blockers, statins, antiplatelets, and angiotensin-converting enzyme/angiotensin receptor blocker (ACE/ARB) use. Total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, and triglycerides were not included in final models because they were available in only about half of the subjects. Occupation also was not included because the majority of participants (77%) were retired and prior occupation information for this group was not collected.

In sensitivity analyses, adjustment for total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, triglycerides, unemployment, occupation, history of cancer, heart failure, and peak creatine kinase resulted in minor changes to the adjusted odds ratio (OR) for each outcome. Among these parameters, the greatest increase in area under the curve for the total model occurred with addition of low-density lipoprotein cholesterol. For example, the area under the curve of the final model predicting MI including all risk factors increased by 3% from 0.726 to 0.748 with the addition of low-density lipoprotein cholesterol. All of the analyses were performed with the statistical software Stata/SE 10 (StataCorp LP, College Station, Tex) and repeated with SAS version 9.1 for Unix (SAS Institute Inc, Cary, NC).

Results

Patient Characteristics, Medications, and Lifestyles

Of the 20,078 persons enrolled in the OASIS study, 18,809 persons were alive and reported on behaviors at the 30-day follow-up visit. The average age of this group was 66.8 years (range, 21.4 to 97.8 years); 38.2% were women; 54.6% had MI without ST elevation and 45.4% had unstable angina at study entry; and 37.5% had PCI and 9.9% had CABG before discharge or within 30 days of the event. Adherence to secondary preventive drugs at the 30-day and 6-month follow-up was generally better (Table 1) than adherence to behavioral modification (Figure 1&2).

Variations by Region and Country

Economic Classification

In HICs and LMICs and across all regions, the use of antiplatelet medication was similarly high (Tables 2 and 3). However, variations existed for other medication use. Use

BMI indicates body mass index; CAD, coronary artery disease; CK, creatine kinase; and BP, blood pressure. Values are mean (SD) or frequency (%) as appropriate.
Adherence to diet advice was reported more frequently by smokers compared with quitters and persistent smokers. Participants from LMICs versus HICs, but regular exercise was higher in HICs versus LMICs. Both PCI and CABG were more frequent in HICs, particularly North America.

Adherence to diet advice was more frequent by individuals in LMICs versus HICs, but regular exercise was higher in HICs versus LMICs. Participants from India had the highest rate of dietary adherence (88.1%); participants from South Africa had the lowest rate (39.0%). The highest rate of exercise was in Australia (60.7%), and lowest was in South Africa (25.7%). The highest rates of smoking cessation were in Latin America (81.5%) and India (90.5%), whereas the lowest was in Western Europe (38.8%).

General Characteristics of Behavior Modifiers Versus Nonmodifiers

Smoking Categories

Nonsmokers and former smokers were older at presentation compared with quitters and persistent smokers. Persistent smokers and recent quitters were generally similar; however, quitters reported higher rates of dietary adherence (60.8% versus 47.2%) and exercise (49.9% versus 42.2%) (Table 4).
Diet and Exercise Categories
Adherers to both diet and exercise were younger than nonadherers. Length of hospital stay was similar across categories, but prevalence of heart failure was lower in adherers. Rates of never smoking were similar across groups, but recent quitting was more common in adherers to diet and exercise. Use of aspirin, β-blockers, and ACE/ARB was similar across groups, but statin use was higher in adherers despite lipid levels being similar. There was a significant trend to increased weight loss in the first 30 days in adherers to diet/exercise compared with other groups (Table 5).

Relationship Between Behavioral Change and Cardiovascular Outcomes
Among the study population that survived to 30 days after ACS presentation, 455 (2.4%) had a subsequent MI, 120 (0.6%) had a subsequent stroke, and 481 (2.6%) died by the end of the 6-month follow-up period.

Event Rates in Relationship to Smoking Behavior
Compared with persistent smokers, quitters had an OR (from fully adjusted models) of 0.57 (95% confidence interval [CI], 0.36 to 0.89; P=0.0145) for MI and an OR of 0.74 (95% CI, 0.53 to 1.02; P=0.0698) for MI/stroke/death (Table 6).

Diet and Physical Activity Behaviors
Compared with nonadherers to either diet or exercise, people who were adherent to either diet or exercise had an OR of 0.46 (95% CI, 0.38 to 0.57; P<0.0001) (Table 7). ORs calculated from fully

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Never Smokers</th>
<th>Former Smokers</th>
<th>Recent Quitters</th>
<th>Persistent Smokers</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>8534 (45.4)</td>
<td>5944 (31.6)</td>
<td>2802 (14.9)</td>
<td>1522 (8.1)</td>
<td></td>
</tr>
<tr>
<td>Women, n (%)</td>
<td>5095 (59.7)</td>
<td>1132 (19)</td>
<td>598 (21.3)</td>
<td>353 (23.2)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Unemployed, n (%)</td>
<td>396 (4.6)</td>
<td>339 (5.7)</td>
<td>218 (7.8)</td>
<td>217 (14.3)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Age, y</td>
<td>70 (9.6)</td>
<td>67.9 (9.8)</td>
<td>59.2 (10.5)</td>
<td>58.3 (10.8)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>27.4 (4.5)</td>
<td>27.7 (4.4)</td>
<td>27 (4.4)</td>
<td>26.9 (4.8)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Diabetes, n (%)</td>
<td>6396 (74.9)</td>
<td>3992 (67.2)</td>
<td>1406 (50.2)</td>
<td>790 (51.9)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>1416 (16.6)</td>
<td>1312 (22.1)</td>
<td>645 (23)</td>
<td>438 (28.8)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Previous MI, n (%)</td>
<td>2005 (23.5)</td>
<td>1985 (33.4)</td>
<td>412 (14.7)</td>
<td>361 (23.7)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Previous stroke, n (%)</td>
<td>535 (6.3)</td>
<td>406 (6.8)</td>
<td>116 (4.1)</td>
<td>68 (4.5)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Previous cancer, n (%)</td>
<td>474 (5.6)</td>
<td>453 (7.6)</td>
<td>91 (3.2)</td>
<td>67 (4.4)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Creatinine, mmol/L</td>
<td>92.5 (28.3)</td>
<td>98.3 (30.9)</td>
<td>88.9 (24.9)</td>
<td>88.7 (27)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Total cholesterol, mmol/L</td>
<td>5.3 (1.4)</td>
<td>5.1 (1.6)</td>
<td>5.5 (2)</td>
<td>5.4 (1.4)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>LDL cholesterol, mmol/L</td>
<td>3.3 (1.1)</td>
<td>3.1 (1.2)</td>
<td>3.5 (1.1)</td>
<td>3.3 (1.1)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>HDL cholesterol, mmol/L</td>
<td>1.3 (0.4)</td>
<td>1.2 (0.5)</td>
<td>1.2 (0.5)</td>
<td>1.2 (0.4)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Triglycerides, mmol/L</td>
<td>1.8 (1.2)</td>
<td>1.9 (1.5)</td>
<td>2 (1.8)</td>
<td>2.1 (1.6)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Hospital stay, mean, d</td>
<td>10.4 (6.2)</td>
<td>9.8 (6.5)</td>
<td>9.6 (5.9)</td>
<td>8.2 (4.8)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Heart failure at admission, n (%)</td>
<td>1495 (17.5)</td>
<td>840 (14.1)</td>
<td>308 (11)</td>
<td>183 (12)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Total CK</td>
<td>229.4 (317.6)</td>
<td>239 (322.8)</td>
<td>328.8 (448.6)</td>
<td>307.2 (481.2)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>PCI in first 30 d, n (%)</td>
<td>2618 (30.7)</td>
<td>2421 (40.7)</td>
<td>1326 (47.3)</td>
<td>681 (44.7)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>CABG in first 30 d, n (%)</td>
<td>740 (8.7)</td>
<td>709 (11.9)</td>
<td>374 (13.3)</td>
<td>45 (3)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Secondary prevention, 30 d, n (%)</td>
<td>7850 (92)</td>
<td>5511 (92.7)</td>
<td>2672 (95.4)</td>
<td>1433 (94.2)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Aspirin</td>
<td>8146 (95.5)</td>
<td>5714 (96.1)</td>
<td>2733 (97.5)</td>
<td>1470 (96.6)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Antiplatelet</td>
<td>4509 (52.8)</td>
<td>2791 (47)</td>
<td>1145 (40.9)</td>
<td>654 (43)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>ACE/ARB</td>
<td>6382 (74.8)</td>
<td>4351 (73.2)</td>
<td>1885 (67.3)</td>
<td>1020 (67)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Any BP lowering</td>
<td>8062 (94.5)</td>
<td>5573 (93.8)</td>
<td>2576 (91.9)</td>
<td>1392 (91.5)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Statin</td>
<td>6445 (75.5)</td>
<td>4827 (81.2)</td>
<td>2335 (83.3)</td>
<td>1182 (77.7)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Dietary compliance</td>
<td>5177 (60.7)</td>
<td>3448 (58)</td>
<td>1705 (60.8)</td>
<td>719 (47.2)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Regular exercise</td>
<td>3280 (38.4)</td>
<td>2703 (45.5)</td>
<td>1399 (49.9)</td>
<td>642 (42.2)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>PCI &gt;30 d to 6 mo</td>
<td>421 (4.9)</td>
<td>380 (6.5)</td>
<td>198 (7.1)</td>
<td>71 (4.7)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>CABG &gt;30 d to 6 mo</td>
<td>279 (3.3)</td>
<td>236 (4.0)</td>
<td>133 (4.8)</td>
<td>34 (2.2)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Abbreviations as in Table 1.
adjusted models were not materially different from those calculated by age- and sex-adjusted models. Analyses were repeated with a hierarchical model to control for country within region and center within country, and results were similar to those reported here.

**Effects of Multiple Lifestyle Changes**

For each category of smoker, change in diet and exercise had additive effects in decreasing risk of cardiovascular events. Persistent smokers who did not modify diet or exercise had the highest risk of a repeat cardiovascular event (fully adjusted OR, 3.77; 95% CI, 2.40 to 5.91; Figure 3).

**Discussion**

This study found that adherence to recommendations regarding smoking, diet, and exercise at 30 days after ACS is associated with a substantially lower rate of short-term major cardiovascular outcomes and all-cause mortality. Compared with persistent smokers, recent quitters had a lower risk of MI and a marginally lower risk of the composite outcome. Adherers to diet and exercise had a 50% lower risk for all major events in 6 months compared with nonadherers. The risk associated with diet alone or exercise alone was similar for MI and stroke, but for death, exercise may be more

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### Table 5. Characteristics of ACS Patients According to Health Behaviors

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>No Diet/Exercise Modification</th>
<th>Either Diet or Exercise Modification</th>
<th>Both Diet and Exercise Modification</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>5356 (28.5)</td>
<td>7829 (41.6)</td>
<td>5624 (29.9)</td>
<td>...</td>
</tr>
<tr>
<td>Baseline</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Women, n (%)</td>
<td>2323 (43.4)</td>
<td>3131 (40.0)</td>
<td>1728 (30.7)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Unemployed, n (%)</td>
<td>400 (7.5)</td>
<td>433 (5.5)</td>
<td>338 (6.0)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Age, y</td>
<td>68.7 (10.8)</td>
<td>67.2 (10.6)</td>
<td>64.3 (10.8)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>27.3 (4.6)</td>
<td>27.4 (4.5)</td>
<td>27.5 (4.4)</td>
<td>0.0149</td>
</tr>
<tr>
<td>Diabetes, n (%)</td>
<td>1396 (26.1)</td>
<td>1975 (25.2)</td>
<td>1270 (22.6)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>3679 (68.7)</td>
<td>5315 (67.9)</td>
<td>3595 (63.9)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Family history of CAD, n (%)</td>
<td>1046 (19.5)</td>
<td>1641 (21.0)</td>
<td>1126 (20.0)</td>
<td>0.1141</td>
</tr>
<tr>
<td>Previous MI, n (%)</td>
<td>1480 (27.6)</td>
<td>2041 (26.1)</td>
<td>1246 (22.2)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Previous stroke, n (%)</td>
<td>371 (6.9)</td>
<td>482 (6.2)</td>
<td>273 (4.9)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Previous cancer, n (%)</td>
<td>374 (7.0)</td>
<td>450 (5.7)</td>
<td>261 (4.6)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Total cholesterol, mmol/L</td>
<td>5.2 (1.5)</td>
<td>5.3 (1.6)</td>
<td>5.3 (1.7)</td>
<td>0.0003</td>
</tr>
<tr>
<td>LDL cholesterol, mmol/L</td>
<td>3.2 (1.1)</td>
<td>3.3 (1.2)</td>
<td>3.3 (1.1)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>HDL cholesterol, mmol/L</td>
<td>1.2 (0.4)</td>
<td>1.2 (0.5)</td>
<td>1.2 (0.5)</td>
<td>0.0772</td>
</tr>
<tr>
<td>Triglycerides, mmol/L</td>
<td>1.8 (1.3)</td>
<td>1.9 (1.6)</td>
<td>1.9 (1.4)</td>
<td>0.1545</td>
</tr>
<tr>
<td>Creatinine, mmol/L</td>
<td>94.6 (30.4)</td>
<td>93.8 (29.6)</td>
<td>92 (25.9)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Never smoker, n (%)</td>
<td>2533 (47.3)</td>
<td>3545 (45.3)</td>
<td>2456 (43.7)</td>
<td>0.0007</td>
</tr>
<tr>
<td>Former smoker, n (%)</td>
<td>1627 (30.4)</td>
<td>2574 (32.9)</td>
<td>1818 (32.3)</td>
<td>0.0085</td>
</tr>
<tr>
<td>Current smoker, n (%)</td>
<td>1195 (22.3)</td>
<td>1709 (21.8)</td>
<td>1350 (24)</td>
<td>0.0098</td>
</tr>
<tr>
<td>In hospital</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hospital stay, mean, d</td>
<td>10.2 (6.7)</td>
<td>10 (6.3)</td>
<td>9.5 (5.4)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Total CK</td>
<td>230.7 (324.3)</td>
<td>257.2 (363.6)</td>
<td>271.4 (383.6)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Heart failure at admission, n (%)</td>
<td>896 (16.7)</td>
<td>1219 (15.6)</td>
<td>711 (12.6)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>PCI in first 30 d, n (%)</td>
<td>1847 (34.4)</td>
<td>2841 (36.3)</td>
<td>2360 (42.0)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>CABG in first 30 d, n (%)</td>
<td>510 (9.5)</td>
<td>800 (10.2)</td>
<td>560 (10.0)</td>
<td>0.4222</td>
</tr>
<tr>
<td>Secondary prevention, 30 d, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aspirin</td>
<td>4910 (91.7)</td>
<td>7251 (92.6)</td>
<td>5311 (94.4)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Antiplatelet</td>
<td>5085 (94.9)</td>
<td>7506 (95.9)</td>
<td>5478 (97.4)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>( \beta )-blocker</td>
<td>2635 (49.2)</td>
<td>3921 (50.1)</td>
<td>2544 (45.2)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>ACE/ARB</td>
<td>3917 (73.1)</td>
<td>5717 (73.0)</td>
<td>4009 (71.2)</td>
<td>0.0425</td>
</tr>
<tr>
<td>Any BP lowering</td>
<td>5042 (94.1)</td>
<td>7316 (93.4)</td>
<td>5251 (93.4)</td>
<td>0.1836</td>
</tr>
<tr>
<td>Statin</td>
<td>3981 (74.3)</td>
<td>6166 (78.8)</td>
<td>4645 (82.6)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Recently quit (% overall)</td>
<td>676 (12.6)</td>
<td>1148 (14.7)</td>
<td>978 (17.4)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Weight loss between baseline and 30 d, mean (SD), kg*</td>
<td>0.503 (2.66)</td>
<td>0.789 (2.83)</td>
<td>0.888 (3.13)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>PCI &gt;30 d to 6 mo</td>
<td>278 (5.5)</td>
<td>435 (5.9)</td>
<td>353 (5.5)</td>
<td>0.7348</td>
</tr>
<tr>
<td>CABG &gt;30 d to 6 mo</td>
<td>140 (2.8)</td>
<td>288 (3.9)</td>
<td>240 (3.9)</td>
<td>0.0016</td>
</tr>
</tbody>
</table>

*Weight data at baseline and 30 days were available for 4211 in the no modification group, 6654 in the either modification group, and 5039 in the both modifications group.

Abbreviations as in Table 1.
important. Persistent smokers who did not diet or exercise had an \( \approx 4 \)-fold risk of cardiovascular events compared with never smokers who dieted and exercised. Excess risk for all of the categories was apparent after accounting for multiple confounders, including drug treatments, PCI, and CABG, suggesting that the benefits of adherence to lifestyle modification are additional to the benefits conferred by drugs and interventions.

Our study suggests that these benefits accrue early (by 6 months). Smoking cessation may lead to early benefit through reversal of platelet activation, coronary artery spasm, and ventricular arrhythmias.\(^{16}\) Diet and exercise may have early benefits through risk factor control,\(^ {12,17}\) improved plaque stabilization in response to less oxidative stress damage, and fewer arrhythmias resulting from membrane stabilization.\(^{18,19}\)

An important potential explanation for the benefits seen in adherers is that adherence per se is a marker of adherence to other beneficial treatments and healthy behaviors in unmeasured ways. That is, the effects seen with lifestyle behaviors here are not a true effect of diet and exercise per se but are related to characteristics of adherers. This study did not demonstrate substantial differences in characteristics or drug treatments in adherers to diet/exercise or smoking cessation compared with nonadherers. We also examined whether those who do not change behavior are more or less compliant with medications and did not identify a relationship (analyses not shown). Supportive of the above notion is that good lifestyle behaviors appear to cluster (eg, persons who quit smoking had higher rates of adherence to diet and exercise). Randomized studies have found that those with improved adherence to either study drug or placebo are relatively protected compared with nonadherers and postulate that this may be due to other unmeasured health attitudinal characteristics.\(^ {20}\)

Although it is not clear what the cause of the decreased risk is in adherers to lifestyle recommendations, this study adds to the body of evidence that behavior modification is associated with substantial benefits. This study highlights the early benefits of lifestyle modification and the incremental benefits of multiple behavior changes and underscores the relatively poor adherence to lifestyle recommendations (compared with preventive drug therapy) in a well-treated clinical trial population.

The strengths of this study are its large size and its inclusion of patients with ACS from a wide range of centers in multiple countries. The study had detailed records of the use of secondary preventive medications at follow-up visits, enabling us to assess the effect of this important potential confounder. An additional strength is the rigorous, systematic reporting of events and highly complete follow-up resulting from the study being principally a large clinical trial.

Potential limitations of this study are that information on secondary preventive lifestyle behaviors was collected with simple self-report questions. The definitions of quitting and persistent smoking relied on self-report and were not validated by cotinine measurements. Similarly, we did not collect details on actual diet or exercise and hence cannot quantify them or describe which elements of diet or exercise programs are associated with the lower risk.

We acknowledge that unmeasured baseline characteristics may have had an impact on subsequent events (eg, socioeconomic status, physical disability). Reporting of compliance may vary substantially according to geographic region or cultural traditions. There could be a potential for misclassification because adherers/nonadherers were categorized at the 30-day follow-up; however, such misclassifications would tend to minimize real differences between groups, so our data may be an underestimate of the true benefits of behavioral change after ACS.

This study found that individuals who change their behavior (quit smoking and modify diet and exercise) after ACS are

### Table 6. Relationship Between Diet/Exercise Modification and Repeat Cardiovascular Events in Patients With ACS

<table>
<thead>
<tr>
<th>Category</th>
<th>Risk of MI</th>
<th>P</th>
<th>Risk of Stroke</th>
<th>P</th>
<th>Risk of Death</th>
<th>P</th>
<th>Risk of Death/MI/Stroke</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>No diet/exercise</td>
<td>Reference</td>
<td></td>
<td>Reference</td>
<td></td>
<td>Reference</td>
<td></td>
<td>Reference</td>
<td></td>
</tr>
<tr>
<td>Diet only</td>
<td>0.93 (0.74–1.16)</td>
<td>0.5137</td>
<td>0.84 (0.54–1.31)</td>
<td>0.4357</td>
<td>0.91 (0.73–1.13)</td>
<td>0.3986</td>
<td>0.91 (0.77–1.07)</td>
<td>0.2605</td>
</tr>
<tr>
<td>Exercise only</td>
<td>0.78 (0.56–1.11)</td>
<td>0.1547</td>
<td>0.94 (0.52–1.68)</td>
<td>0.8256</td>
<td>0.61 (0.42–0.88)</td>
<td>0.0091</td>
<td>0.69 (0.54–0.89)</td>
<td>0.0037</td>
</tr>
<tr>
<td>Both diet and exercise</td>
<td>0.52 (0.40–0.69)</td>
<td>&lt;0.0001</td>
<td>0.46 (0.26–0.82)</td>
<td>0.0079</td>
<td>0.45 (0.33–0.60)</td>
<td>&lt;0.0001</td>
<td>0.46 (0.38–0.57)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Models were adjusted for age; sex; region; history of hypertension, diabetes, and prior MI; body mass index; creatinine; PCI/CABG before 30 days; and use of \( \beta \)-blockers, statins, antiplatelets, and ACE/ARB drugs at 30 days.

### Table 7. Relationship Between Smoking and Repeat Cardiovascular Events in Patients With ACS

<table>
<thead>
<tr>
<th>Category</th>
<th>Risk of MI</th>
<th>P</th>
<th>Risk of Stroke</th>
<th>P</th>
<th>Risk of Death</th>
<th>P</th>
<th>Risk of Death/MI/Stroke</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Persistent smoker</td>
<td>Reference</td>
<td></td>
<td>Reference</td>
<td></td>
<td>Reference</td>
<td></td>
<td>Reference</td>
<td></td>
</tr>
<tr>
<td>Quitter</td>
<td>0.57 (0.36–0.89)</td>
<td>0.0145</td>
<td>0.40 (0.14–1.17)</td>
<td>0.0930</td>
<td>0.93 (0.59–1.46)</td>
<td>0.7594</td>
<td>0.74 (0.53–1.02)</td>
<td>0.0698</td>
</tr>
<tr>
<td>Ex-smoker</td>
<td>0.68 (0.48–0.98)</td>
<td>0.3990</td>
<td>0.79 (0.36–1.74)</td>
<td>0.5547</td>
<td>0.65 (0.44–0.97)</td>
<td>0.0360</td>
<td>0.68 (0.51–0.90)</td>
<td>0.0067</td>
</tr>
<tr>
<td>Never smoker</td>
<td>0.49 (0.34–0.71)</td>
<td>0.0002</td>
<td>0.83 (0.38–1.82)</td>
<td>0.6397</td>
<td>0.59 (0.40–0.89)</td>
<td>0.0108</td>
<td>0.59 (0.44–0.78)</td>
<td>0.0002</td>
</tr>
</tbody>
</table>

Models were adjusted for age; sex; region; history of hypertension, diabetes, and prior MI; body mass index; creatinine; PCI/CABG before 30 days; and use of \( \beta \)-blockers, statins, antiplatelets, and ACE/ARB drugs at 30 days.
at substantially lower risk of repeat cardiovascular events. These benefits are seen early (<6 months), and the benefits from each behavior modification are additive. These results indicate that adherence to behavioral recommendations in the immediate postevent care of patients with ACS should be given as high a priority by physicians and caregivers as other secondary preventive medications and invasive strategies and justify a significant investment in establishing programs that systematically enhance early lifestyle modification and secondary prevention.

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Disclosures

None.

References

Although preventive drug therapy is a priority after myocardial infarction (MI), less is known about adherence to behavioral recommendations. The aim of this study was to examine the influence of adherence to behavioral recommendations on the risk for repeat MI. The study population included 18,809 patients from 41 countries enrolled in the Organization to Assess Strategies in Acute Ischemic Syndromes (OASIS) 5 randomized clinical trial. One month after presenting with MI, 28.5% reported nonadherence to diet and exercise recommendations, and about one third of smokers persisted in smoking. In models adjusted for known risk factors and medical treatments, quitting smoking was associated with about half the risk of repeat MI compared with persistent smoking (odds ratio, 0.57; 95% confidence interval, 0.36 to 0.89), and diet and exercise adherence was associated with about half the risk of repeat MI compared with nonadherence (odds ratio, 0.52; 95% confidence interval, 0.4 to 0.69). Persistent smoking and nonadherence to diet and exercise were associated with a 3.8-fold (95% confidence interval, 2.5 to 5.9) increased risk of cardiovascular events (MI, stroke, and death) compared with risks in never smokers who modified diet and exercise. These analyses highlight the relatively poor adherence to behavioral advice (diet, exercise, and smoking cessation) after MI and suggest that behavioral modification should be given priority similar to other preventive medications immediately after MI because they are associated with substantial benefits in the prevention of repeat events.

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