Incidence and Prognostic Implications of Stable Angina Pectoris Among Women and Men

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Context  Stable angina pectoris in women has often been considered a “soft” diagnosis, with less-severe prognostic implications than in men, but large-scale population studies are lacking.

Objective  To determine sex differences in the incidence and prognosis of stable angina in a large ambulatory population.

Design  Prospective cohort study using linked national registers.

Setting  All municipal primary health care centers, hospital outpatient clinics, occupational health care services, and the private sector in Finland.

Participants  Among ambulatory patients aged 45 to 89 years who had no history of coronary disease, we defined new cases of “nitrate angina” based on nitrate prescription (56,441 women and 34,885 men) or “test-positive angina” based on abnormal invasive or noninvasive test results (11,391 women and 15,806 men). Potentially eligible patients were evaluated between January 1, 1996, and December 31, 1998. Follow-up ended in December 2001.

Main Outcome Measures  Coronary mortality at 4 years (n=7906 deaths) and fatal and nonfatal myocardial infarction at 1 year (n=3129 events).

Results  The age-standardized annual incidence per 100 population of all cases of angina was 2.03 in men and 1.89 in women, with a sex ratio of 1.07 (95% confidence interval [CI], 1.06-1.09). At every age, nitrate angina in women and men was associated with a similar increase in risk of coronary mortality relative to the general population. Women with test-positive angina who were younger than 75 years had higher coronary-standardized mortality ratios than men; for example, among those aged 55 to 64 years, it was 4.69 (95% CI, 3.60-6.11) in women compared with 2.40 (95% CI, 2.11-2.73) in men (P<.001 for interaction). There was a strong, graded relationship between amount of nitrates used and event rates; women using higher doses of nitrates had prognoses comparable with those of men. Among patients with diabetes and test-positive angina, age-standardized coronary event rates were 9.9 per 100 person-years in women vs 9.3 in men (P=.69), and the fully adjusted male-female sex ratio was 1.07 (95% CI, 0.81-1.41).

Conclusions  Women have a similarly high incidence of stable angina compared with men. Furthermore, stable angina in women is associated with increased coronary mortality relative to women in the general population and, among easily identifiable clinical subgroups, has similarly high absolute rates of prognostic outcomes compared with men.

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INCIDENCE AND PROGNOSTIC IMPLICATIONS OF STABLE ANGINA

“soft,” not reflecting coronary pathologic findings.

Population studies that might elucidate this paradox have been lacking, with no national or community-based surveillance programs reporting incidence and prognosis of angina in women compared with men. Epidemiological studies have recruited and followed up patients over the course of decades, precluding inferences about contemporary practice. Studies set in cardiologists’ outpatient clinics do not include the wider pool of patients presenting to internists or primary care. All studies have been limited by the small number of cases of angina and subsequent coronary events in women, as well as by exclusion of older patients. Sex disparities in access to specialist referral and investigation of angina have been widely demonstrated, yet no study has determined sex differences in the incidence and prognostic effect of angina patients with and without an investigation abnormality. Nor has any study investigated how the severity of incident angina or the presence of coexisting conditions might influence sex differences in prognosis.

Our objective was to determine sex differences in chronic stable angina with respect to (1) incidence in the general population, (2) coronary mortality compared with the general population, and (3) absolute coronary event rates, by angina severity and coexisting conditions. We used national linked registries in Finland, a country with a previously documented general population prevalence of angina similar to that of the United States (4.4% vs 6.3% in women and 4.4% vs 4.3% in men, respectively). Anonymized data and were approved by the Research Ethics Committee of STAKES, the National Research and Development Centre for Welfare and Health. STAKES (Sosiaali-ja Terveyden Tutkimus-ja Kehittamiskeskus) is a research institute funded by the national government as part of the Ministry of Social Affairs and Health. Under Finnish law, individual patient informed consent is not required for the analyses presented here.

Angina Case Definitions

Two mutually exclusive case definitions of incident, uncomplicated angina were used, based on linking records of reimbursement of charges for medications in the Social Insurance Institution during recruitment from January 1, 1996, to December 31, 1998. This register covers all prescriptions reimbursed by the mandatory national health insurance irrespective of the ambulatory care provider. All patients were identified in an ambulatory setting, which included municipal primary health care centers, hospital outpatient clinics, occupational health care services, and the private sector. To identify angina as the first symptomatic presentation of coronary disease, we excluded all patients with a prior special reimbursement right for coronary heart disease (CHD) or prior admission with acute myocardial infarction, unstable angina, or other coronary disease (International Classification of Diseases, Tenth Revision [ICD-10] codes 120-25; International Classification of Diseases, Ninth Revision codes 410-414) or for coronary revascularization during the 5 years before the date of angina.

The first case definition (“nitrated angina”) was based on reimbursement for dispensed (filled) prescriptions for glyceryl trinitrate, isosorbide dinitrate, and isosorbide mononitrate (including sublingual, aerosol, transdermal, and oral preparations) during the 3-year recruitment period. We excluded all patients who were taking a nitrate medication in the calendar year before recruitment. Nitrate use is a valid measure of angina in primary care, being a moderately sensitive (73%) and highly specific (96%) marker of a physician diagnosis of angina identified by case record review. The second case definition (“test-positive angina”) was based on a special reimbursement right requiring a medical certificate by the attending physician, usually an internist or a cardiologist, which was then reviewed and approved by a specialist physician at the Social Insurance Institution. Such a reimbursement right is awarded only to patients with chronic angina pectoris symptoms responding to antianginal medication in the presence of unequivocal electrocardiographic changes (on exercise or at rest) or angiographic coronary artery disease. Patients who made the transition from nitrate angina to test-positive angina at any time during the recruitment period were counted only once, as test-positive cases. We used the amount of reimbursed nitrate prescriptions filled during the year of incidence, expressed in defined daily doses, as a marker of angina severity. For example, the defined daily dose of sublingual glyceryl trinitrate is set at 2.5 mg; thus, a package containing thirty 0.25-mg tablets (total, 7.5 mg) corresponds to 3 defined daily doses. The defined daily dose of oral isosorbide dinitrate is 60 mg and that of isosorbide mononitrate is 40 mg.

Cardiovascular and Noncardiovascular Coexisting Conditions

The presence of coexisting conditions was ascertained from Social Insurance Institution data on entitlements to reimbursement of medicine costs according to a prespecified list of 43 chronic diseases at the time of angina diagnosis, each of which required confirmation by a specialist or hospital investi-
gations. This list included cardiovascular disorders (hypertension, diabetes, heart failure [ICD-10 codes I11.0, I13, I50, or I19.1], and arrhythmias [ICD-10 codes I47-149]) and noncardiovascular disorders, including respiratory (asthma and chronic obstructive pulmonary disease), musculoskeletal (rheumatoid arthritis and other systemic connective tissue disorders, gout), psychiatric (severe mental illness), and neoplastic. Coexisting condition codes validate well against hospital case records.32

**Mortality and Nonfatal Myocardial Infarction Follow-up**

All patients were linked to the Causes of Death Register at Statistics Finland, which provided details of the date and underlying cause of death, according to ICD-10 codes, until December 31, 2001 (median follow-up, 4 years). The postmortem examination rate in Finland during this period was approximately 60% among those younger than 65 years. Coronary heart disease mortality was defined by ICD-10 codes I20-I25, and 7906 coronary deaths occurred during follow-up. Details of nonfatal acute myocardial infarction (defined as ICD-10 codes I21-I22), percutaneous coronary intervention, and coronary artery bypass graft surgery were obtained from linkage to the hospital discharge register. The completeness and accuracy of the death and discharge registers for CHD have previously been demonstrated.33

**Statistical Analysis**

Annual incidence risks of angina were calculated as the ratio of the average number of new cases per year to the total 1996 Finnish population. To allow comparisons between sexes, incidence risks and the prevalence of coexisting conditions were adjusted for age using direct standardization to the entire Finnish population. Standardized mortality ratios (SMRs) were calculated as the ratio of observed to expected deaths. The expected number of deaths was calculated using age (5-year categories), sex, and calendar year–specific coronary mortality rates from the total Finnish population. When the observed number of deaths numbered fewer than 50, 95% confidence intervals (CIs) for the SMRs were calculated using the exact Poisson distribution, with an approximation used for larger numbers of deaths.

Absolute rates of the composite end point of fatal and nonfatal myocardial infarction at 1-year follow-up (n = 3129 events) were calculated per 100 person-years at risk. Entry into the register was defined by month and year for test-positive angina and by year for nitrate angina, and a midmonth or midyear date used for time-to-event and person-year analysis, respectively. When death occurred during the year of recruitment, entry was deemed to have occurred halfway between January 1 and the date of death. For nonfatal myocardial infarction and coronary revascularization, all patients were followed up for 1 calendar year after their incidence date.

Within the 2 angina case definitions, all-cause mortality and coronary event rates were compared between women and men with and without coexisting conditions using multivariable hazard ratios computed from Cox proportional hazards models, adjusting for the

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**Figure 1.** Age- and Sex-Specific Annual Incidence Risk* of Nitrater Angina and Test-Positive Angina and Sex Ratios Among Incident Cases

<table>
<thead>
<tr>
<th>Age Group, y</th>
<th>Women New Cases/Total Population</th>
<th>Men New Cases/Total Population</th>
<th>Incidence per 100 Population</th>
<th>Sex Ratio (95% CI)</th>
<th>More Common in Women</th>
<th>More Common in Men</th>
</tr>
</thead>
<tbody>
<tr>
<td>Test-Positive Angina</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>45-54</td>
<td>1034/376622</td>
<td>3377/376700</td>
<td>0.09 0.29</td>
<td>3.16 (2.95-3.40)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>55-64</td>
<td>2763/271357</td>
<td>5171/254182</td>
<td>0.34 0.68</td>
<td>2.00 (1.91-2.09)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>65-74</td>
<td>4929/250901</td>
<td>5172/184712</td>
<td>0.58 0.93</td>
<td>1.60 (1.54-1.67)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>75-84</td>
<td>2747/161718</td>
<td>1848/75957</td>
<td>0.57 0.81</td>
<td>1.43 (1.35-1.52)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>85-89</td>
<td>455/38519</td>
<td>238/13348</td>
<td>0.39 0.59</td>
<td>1.51 (1.29-1.76)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>All</td>
<td>11391/1099112</td>
<td>15806/915299</td>
<td>0.33 0.60</td>
<td>1.84 (1.78-1.90)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Total Angina Incidence</th>
<th>Women</th>
<th>Men</th>
<th>Incidence per 100 Population</th>
<th>Sex Ratio (95% CI)</th>
<th>More Common in Women</th>
<th>More Common in Men</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>67802/1099112</td>
<td>50691/915299</td>
<td>1.89 2.03</td>
<td>1.07 (1.06-1.09)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

CI indicates confidence interval. The size of the data markers represents the number of angina cases.

*Annual risk per 100 population, using estimated total population of Finland in 1996. Because the case definitions of angina are mutually exclusive, the same population denominator was used for each.

*Age-standardized to the combined (women and men) population.
potential confounders of age in the combined (women and men) population, education (<10, 10-11, or ≥12 years), marital status (married, divorced/separated, single, or widowed), nitrate type (none, glyceryl trinitrate, isosorbide mononitrate or isosorbide dinitrate, or both), nitrate use (0, 1-7, 8-30, 31-90, or >90 defined daily doses), number of noncardiovascular coexisting conditions (0, 1, or ≥2) and receipt of percutaneous coronary intervention or coronary artery bypass graft surgery during the first year of follow-up. We assessed the proportional hazards assumption by fitting exposure log time interaction terms and by examining the effects separately within each year of follow-up. These analyses showed that the proportionality assumption was robust. All P values are 2-tailed. All analyses were carried out in SAS software, version 8.2 (SAS Institute Inc, Cary, NC).

RESULTS
As shown in Figure 1, the age-standardized annual incidence of nitrate angina was higher in women than in men, but for test-positive angina the incidence was lower in women. The latter effect was most marked in the youngest age group, which included perimenopausal women. Among all cases combined, total incidence risks were similar in women (1.89 per 100) and men (2.03 per 100), with a sex ratio of 1.07 (95% CI, 1.06-1.09).

Into the ninth decade of life, age was strongly associated with higher incidence of nitrate angina (P < .001 for linear trend), but for test-positive angina, incidence declined after age 75 years (Figure 1). Among all cases of angina, women were less likely to be test-positive than men consistently within each age group (P < .001 for all), with proportions in women/men of 21%/41% at age 45 to 54 years, 21%/38% at 55 to 64 years, 18%/30% at 65 to 74 years, 13%/19% at 75 to 84 years, and 9%/13% at 85 to 89 years.

In every age group, nitrate angina in women was associated with increased coronary SMRs similar in magnitude to those observed in men (Figure 2). In contrast, women with test-positive angina aged 45 to 74 years had higher coronary SMRs than men (Figure 2). For example, among those aged 55 to 64 years, the SMR was 4.69 (95% CI, 3.60-6.11) in women and 2.40 (95% CI, 2.11-2.73) in men (P < .001 for interaction). Within strata defined by age and sex, associations with coronary mortality were stronger for test-positive angina than for nitrate angina.

As shown in Table 1, women with angina were older than men and, in age-adjusted analyses, were slightly more likely to be using short-acting nitrates.
and lower defined daily doses. Test-positive angina patients were prescribed more nitrates than those with nitrate angina, but there was little difference between sexes in amount used; 14.7% of women and 17.2% of men were taking no nitrates (but may have been taking other antianginal medication). Noncardiovascular coexisting conditions were more common among women and, in both sexes, were more common in nitrate angina cases than in test-positive cases.

Among nitrate angina cases in women and men, the amount of nitrates used showed a very strong, graded relationship with coronary event rates after adjustment for demographic factors, cardiovascular and noncardiovascular conditions, and receipt of coronary revascularization (Table 2). This dose-response effect was present among women who were taking short-acting nitrates only, with hazard ratios of 1.48 (95% CI, 1.31-1.67), 2.25 (95% CI, 1.84-2.73), and 2.72 (95% CI, 1.99-3.73) for 8 to 30, 31 to 90, and more than 90 defined daily doses, respectively (reference category, 1-7 defined daily doses).

In general, predictors of coronary events also tended to predict all-cause mortality. Absolute rates of fatal and nonfatal myocardial infarction tended to be lower in women than in men. However, women using higher doses of nitrates had comparable prognoses with men, and among test-positive cases, there were no sex differences in prognosis among patients with 2 or more noncardiovascular conditions. Diabetes was strongly associated with event rates, narrowing sex differences among cases of nitrate angina and abolishing them in test-positive angina. Among patients with diabetes and test-positive angina, age-standardized event rates were 9.9 per 100 person-years in women vs 9.3 in men (P = .69); in fully adjusted models, the male-to-female sex ratio for coronary events was 1.07 (95% CI, 0.81-1.41). Among women, the presence of heart failure was associated with increased coronary event rates, similar to those seen in men without these disorders.

**COMMENT**

To our knowledge, this study represents the first large-scale investigation of angina as an initial symptomatic manifestation of CHD. We found that...
overall incidence was similarly high in women and men among contemporary, unscreened patients in primary care. Angina in women was associated with increased coronary mortality relative to women in the general population and, in absolute terms, high coronary event rates. Indeed, among easily identifiable clinical subgroups, angina in women had similarly high absolute rates of prognostic outcomes compared with men.

The total incidence risk of angina in primary care reported herein is substantially (1 order of magnitude) higher than the rate of first admissions for acute myocardial infarction in Finland and in any of the age, sex, and race subgroups in the Atherosclerosis Risk in Communities study. Indeed, our estimates for angina may be conservative; not all angina is diagnosed and treated, particularly among women. Among those whose angina is treated, not all receive nitrates; furthermore, among those taking nitrates, not all pursue reimbursement. Finally, the general population denominator in this study inevitably included some cases of angina.

Women had a total incidence of angina that was similar to that of men, which is consistent with numerous population-based studies assessing angina prevalence with the Rose questionnaire. Taken together, these findings are likely to be robust, as the former is free of instrument and reporting biases and the latter is free of diagnostic and treatment biases. We found that women with nitrate angina had a markedly increased risk of coronary mortality compared with women in the general population, an effect similar in magnitude to that observed in men.

Women had a lower incidence than men of test-positive cases of angina, consistent with previous US studies that, although not based on primary care, report underuse of investigation in women with chest pain. This may relate to sex differences in symptom description or physician perception of risk. Of further concern was that these selected women had particularly high sex-specific coronary SMRs, exceeding those of men, up to age 75 years. This may reflect a combination of factors in women, including lower absolute rates of CHD mortality in the population, selection of sicker pa-

Table 2. Sex Differences in Prognostic Impact of the Severity of Angina and Coexisting Conditions on All-Cause Mortality and Fatal CHD and Nonfatal MI Among Angina Cases*

<table>
<thead>
<tr>
<th>Nitrate Angina</th>
<th>Test-Positive Angina</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All-Cause Mortality</td>
</tr>
<tr>
<td><strong>Women</strong></td>
<td></td>
</tr>
<tr>
<td>(9564 Deaths)</td>
<td>(8430 Events)</td>
</tr>
<tr>
<td>Mean age</td>
<td>1.07 (1.07-1.07)</td>
</tr>
<tr>
<td>Nitrate use, defined daily doses filled per year</td>
<td></td>
</tr>
<tr>
<td>1-7</td>
<td>1.00 (2.64)‡</td>
</tr>
<tr>
<td>8-30</td>
<td>1.28 (1.20-1.35)</td>
</tr>
<tr>
<td>31-90</td>
<td>1.71 (1.60-1.84)</td>
</tr>
<tr>
<td>&gt;90</td>
<td>2.07 (1.92-2.28)</td>
</tr>
<tr>
<td><strong>Cardiovascular conditions</strong></td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>1.00 (0.33)‡</td>
</tr>
<tr>
<td>Present</td>
<td>1.84 (1.74-1.94)</td>
</tr>
<tr>
<td>Hypertension</td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>1.00 (0.37)‡</td>
</tr>
<tr>
<td>Present</td>
<td>1.14 (1.10-1.19)</td>
</tr>
<tr>
<td>Heart failure</td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>1.00 (0.31)‡</td>
</tr>
<tr>
<td>Present</td>
<td>1.39 (1.33-1.48)</td>
</tr>
<tr>
<td>Arrhythmias</td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>1.00 (0.62)‡</td>
</tr>
<tr>
<td>Present</td>
<td>1.29 (1.19-1.40)</td>
</tr>
<tr>
<td>No. of coexisting noncardiovascular conditions</td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>1.00 (0.23)‡</td>
</tr>
<tr>
<td>1</td>
<td>1.37 (1.31-1.43)</td>
</tr>
<tr>
<td>2</td>
<td>1.80 (1.67-1.95)</td>
</tr>
</tbody>
</table>

Abbreviations: CHD, coronary heart disease; MI, myocardial infarction.
*Data are expressed as multivariable hazard ratios (95% confidence intervals) unless otherwise noted. Women without the coexisting condition or with the lowest use of nitrates are the reference category. All hazard ratios are adjusted for age in the combined (women and men) population, education (<10, 10-11, or >12 years), marital status (married, divorced/separated, single, or widowed), nitrate type, nitrate use, number of noncardiovascular coexisting conditions, and receipt of percutaneous coronary intervention or coronary artery bypass graft surgery during first year of follow-up.
†Hazard ratios for the effect of age are estimated per year of increase.
‡The age-standardized absolute event rate per 100 person-years is given in parentheses for each reference category.

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tients, and undertreatment. If there is a bias whereby men are more likely to be tested than women, it might explain the higher incidence of test-positive angina in men in contrast with the higher incidence of nitrate angina in women. The fact that long-term coronary mortality rates were higher in younger women with test-positive angina than in men suggests that sicker women were being tested—that is, there is a higher threshold for testing in women than in men. However, the similarity of the coronary SMRs in women and men with nitrate angina demonstrates that even if this bias exists, it is unlikely to have seriously affected our estimates of overall incidence.

The rate of coronary revascularization was higher in men than women, but adjustment for receipt of revascularization had no effect on sex differences in coronary event rates. Sex differences in secondary prevention are small in this population; in a companion study of 2650 patients carried out in 2001, we found that the proportion taking 3 agents (aspirin, a β-blocker, and a statin) was 49% for women and 51.6% for men (K.M., I.K., Antti Reunanen, MD, and Timo Klaukka, MD, PhD; unpublished data; 2006). In women and men older than 75 years, there were no sex differences in coronary SMRs and the incidence of test-positive angina declined, consistent with older age influencing access to testing.

We found a strong stepwise relationship between the amount of filled nitrate prescriptions over the year of incidence and subsequent coronary event rates. Angina follows an intermittent, relapsing-remitting course, and amount of nitrate use may thus be a valid marker of anginal severity over time. The prognostic clinical validity of a pragmatic measure of treated angina, demonstrated here, suggests a method of surveillance and identification of target populations in future randomized trials.

Absolute rates of coronary events in women were high when compared with thresholds for initiating secondary prevention treatment. Estimated 10-year risks of fatal and nonfatal myocardial infarction exceeded 10% (“moderately high”) for women with nitrate angina, even among those without cardiovascular or noncardiovascular comorbidity; absolute risks were considerably higher for women with test-positive angina. When compared with men, women overall tended to have lower coronary event rates. This effect was present among those with test-positive angina, suggesting that it is not explained by diagnostic error. However, the female advantage was diminished or absent among clinical subgroups. Women with diabetes and angina had particularly high event rates, reducing sex differences in prognosis in nitrate angina and eliminating them in test-positive angina.

Sex differences in the nature and severity of the underlying cardiac pathophysiology in angina may explain these prognostic differences. Further research is required to understand which patients with nitrate angina had never been investigated and which had been investigated and tested negative on conventional noninvasive ischemic testing or coronary angiography. Novel functional imaging studies suggest that among women with angina and nonobstructed coronary arteries (a finding considerably more common in women than in men with chest pain), nuclear magnetic resonance spectroscopy reveals hitherto undetected evidence of ischemia, which is associated with increased coronary event rates. Impaired coronary endothelial function in women with nonobstructive coronary disease is associated with adverse prognosis.

Randomized trials of angina select a large excess of men vs women (eg, with ratios of 3.8 in the ACTION [A Coronary Disease Trial Investigating Outcome With Nifedipine Gastrointestinal Therapeutic System], 4.2 in the TNT [Treating to New Targets], and 4.9 in the PEACE [Prevention of Events With Angiotensin Converting Enzyme Inhibition] trials). This does not reflect the sex burden of angina in the population, and influential trials may perpetuate the disadvantage of its underuse in women.

There have been no trials among incident cases of angina as the initial symptomatic manifestation of coronary disease; half or more of all patients in the existing angina trials have had previous myocardial infarction and many patients have already survived years since first presentation. In the absence of randomized comparisons of different investigational strategies for angina, formal methods of defining appropriate investigation and the prognostic consequences of its underuse in women are required.

The subject of long-standing debate, angina in women occurs in the general population as commonly as in men, and its prognostic impact suggests that it should not be discounted as a benign or soft diagnosis. These findings demonstrate the public health importance of angina in women and underscore the importance of both understanding the biological mechanisms of the angina-sex paradox and ensuring fair access to investigation and treatment services.

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Author Contributions: Dr Hemingway had full access to all of the data in the study and takes responsi-
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sibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Hemingway, McCallum, Manderbacka, Martikainen, Keskimäki.

Acquisition of data: Hemingway, Manderbacka, Martikainen, Keskimäki.

Analysis and interpretation of data: Hemingway, McCallum, Shipley, Manderbacka, Martikainen, Keskimäki.

Drafting of the manuscript: Hemingway, McCallum, Shipley, Manderbacka.

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Statistical analysis: Shipley, Martikainen.

Obtained funding: Hemingway, Manderbacka, Martikainen, Keskimäki.

Administrative, technical, or material support: McCallum, Keskimäki.

Study supervision: Hemingway, Martikainen, Keskimäki.

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Role of the Sponsors: The funders had no role in the design or conduct of the study; collection, management, analysis, and interpretation of the data; and preparation, review, and approval of the manuscript.

REFERENCES

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Obtained funding: Hollenbeck.

Administrative, technical, or material support: Hollenbeck.

Study supervision: Wei, Hollenbeck.

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Role of the Sponsor: The study sponsor had no role in the design and conduct of the study; collection, examination, analysis, and interpretation of the data; or preparation, review, or approval of the manuscript.


CORRECTIONS

Incorrect Unit of Measure: In the Original Contribution entitled “Effect of 6-Month Calorie Restriction on Biomarkers of Longevity, Metabolic Adaptation, and Oxidative Stress in Overweight Individuals: A Randomized Controlled Trial” published in the April 5, 2006, issue of JAMA (2006;295:1539-1548), an incorrect unit of measure was given for dehydroepiandrosterone sulfate (DHEAS). On page 1543 (Table 1) and page 1544 (Figure 3), the unit of measure for DHEAS should be μg/dl (not ng/ml).

Error in Byline: In the Original Contribution entitled “Incidence and Prognostic Implications of Stable Angina Pectoris Among Women and Men” published in the March 22/29, 2006, issue of JAMA (2006;295:1404-1411), the byline contained an incorrect academic degree. Alison McCallum should have been listed as having an MBChB, FPHP.

Incorrect Data: In the Original Contribution entitled “Frequency and Effect of Adjuvant Radiation Therapy Among Women With Stage I Endometrial Adenocarcinoma” published in the January 25, 2006, issue of JAMA (2006;295:389-397), incorrect data were reported in the “Results” section of the article. On page 391, the sentence “Within the RT cohort, 2551 patients (62.5%) had external beam radiation, 732 (17.9%) had vaginal brachytherapy, and 1078 (26.4%) received a combination of external beam radiation with vaginal brachytherapy” should read “Within the RT cohort, 2378 patients (58.3%) received external beam radiation, 962 (23.6%) received external beam and brachytherapy radiation, 654 (16.0%) received brachytherapy radiation alone, and for 86 (2.1%) the radiation modality was not specified.” The authors verified that this error did not have an impact on the data set or subsequent statistical analyses.

Incorrect Statements on Funding/Support and Role of the Sponsors and Incorrect and Incomplete Financial Disclosures: In the Review entitled “Anti-TNF Antibody Therapy in Rheumatoid Arthritis and the Risk of Serious Infections and Malignancies: Systematic Review and Meta-analysis of Rare Harmful Effects in Randomized Controlled Trials” published in the May 17, 2006, issue of JAMA (2006;295:2275-2285), the following errors appeared: After this issue was printed and mailed, JAMA was informed by the authors that information reported on page 2284 of the article was incorrect. The Funding/Support statement should have read “This study was supported by the Mayo Foundation. Additional data were provided by Abbott and Centocor. Data provided by Abbott were subject to a confidentiality agreement.” The Role of the Sponsors statement should have read “Abbott and Centocor did not have any role in the design and conduct of the study; the collection, management, analysis, and interpretation of the data; or the preparation or approval of the manuscript. The manuscript was sent to Abbott for review prior to submission for publication.” The Financial Disclosures statement should have read: “Dr Bongartz reported that he has given lectures for Abbott as part of seminars for study nurses and received honorarium in the form of a medical textbook for the Internal Medicine library; he received an educational grant from Amgen in February 2006 to perform the same type of analysis of harmful events under anti-TNF treatment for etanercept; and he received the 2005 Fellow’s Award of the American College of Rheumatology, which was supported by Amgen.” Dr Matteson reported that he has been a paid consultant for Centocor for work unrelated to this study and has been working with Wyeth and Amgen to perform a similar analysis for etanercept; he has been an Investigator for the American College of Rheumatology, Amgen, Asta, Biogen-IDEc, Burroughs-Wellcome, Centocor, Cypress, Endoocyte Inc, Genentech, Hoffmann-LaRoche, Human Genome Sciences, Immunex, Protein Design Laboratories, Nastech, Pharmacia & Upjohn, Schering, Wyeth, and Xoma Corp; he has received grant support from Amgen, Aventis, Centocor/Johnson & Johnson, Genentech, Immunex, Mayo Foundation, Novartis, and the National Institutes of Health; and he has been a consultant for Amgen, BoneandJoint.org, Burroughs-Wellcome, Centocor, Regeneron, Takeda, Upjohn, Watermark Research, and the Vascultis Foundation.”

This correction was published online on May 16, 2006. Because of the nature and extensiveness of this incorrect and incomplete reporting, JAMA has requested that the Mayo Clinic College of Medicine conduct an investigation. JAMA will publish another correction or clarification once the results of that investigation become available.