

Circulation

JOURNAL OF THE AMERICAN HEART ASSOCIATION



Evidence-Based Guidelines for Cardiovascular Disease Prevention in Women: 2007 Update

Lori Mosca, Carole L. Banka, Emelia J. Benjamin, Kathy Berra, Cheryl Bushnell, Rowena J. Dolor, Theodore G. Ganiats, Antoinette S. Gomes, Heather L. Gornik, Clarissa Gracia, Martha Gulati, Constance K. Haan, Debra R. Judelson, Nora Keenan, Ellie Kelepouris, Erin D. Michos, L. Kristin Newby, Suzanne Oparil, Pamela Ouyang, Mehmet C. Oz, Diana Petitti, Vivian W. Pinn, Rita F. Redberg, Rosalyn Scott, Katherine Sherif, Sidney C. Smith, Jr, George Sopko, Robin H. Steinhorn, Neil J. Stone, Kathryn A. Taubert, Barbara A. Todd, Elaine Urbina, Nanette K. Wenger and
for the Expert Panel/Writing Group

Circulation published online Feb 19, 2007;

DOI: 10.1161/CIRCULATIONAHA.107.181546

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75214

Copyright © 2007 American Heart Association. All rights reserved. Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:

<http://circ.ahajournals.org>

Subscriptions: Information about subscribing to *Circulation* is online at
<http://circ.ahajournals.org/subscriptions/>

Permissions: Permissions & Rights Desk, Lippincott Williams & Wilkins, 351 West Camden Street, Baltimore, MD 21202-2436. Phone 410-5280-4050. Fax: 410-528-8550. Email:
journalpermissions@lww.com

Reprints: Information about reprints can be found online at
<http://www.lww.com/static/html/reprints.html>

Evidence-Based Guidelines for Cardiovascular Disease Prevention in Women: 2007 Update

Lori Mosca, MD, MPH, PhD, Chair; Carole L. Banka, PhD; Emelia J. Benjamin, MD; Kathy Berra, MSN, NP; Cheryl Bushnell, MD; Rowena J. Dolor, MD, MHS; Theodore G. Ganiats, MD; Antoinette S. Gomes, MD; Heather L. Gornik, MD, MHS; Clarissa Gracia, MD, MSCE; Martha Gulati, MD, MS; Constance K. Haan, MD; Debra R. Judelson, MD; Nora Keenan, PhD; Ellie Kelepouris, MD; Erin D. Michos, MD; L. Kristin Newby, MD, MHS; Suzanne Oparil, MD; Pamela Ouyang, MD; Mehmet C. Oz, MD; Diana Petitti, MD, MPH; Vivian W. Pinn, MD; Rita F. Redberg, MD, MSc; Rosalyn Scott, MD; Katherine Sherif, MD; Sidney C. Smith, Jr, MD; George Sopko, MD, MPH; Robin H. Steinhorn, MD; Neil J. Stone, MD; Kathryn A. Taubert, PhD; Barbara A. Todd, MSN, CRNP; Elaine Urbina, MD; Nanette K. Wenger, MD; for the Expert Panel/Writing Group*

*Representing the following participating organizations and major cosponsors: the American Heart Association (L.M., C.L.B., E.J.B., K.B., C.B., R.J.D., A.S.G., H.L.G., E.K., E.D.M., L.K.N., S.O., P.O., M.C.O., R.F.R., R.H.S., N.J.S., K.A.T., E.U., N.K.W.), American Academy of Family Physicians (T.G.G.), American College of Obstetricians and Gynecologists (C.G.), American College of Cardiology Foundation (M.G.), Society of Thoracic Surgeons (C.K.H.), American Medical Women's Association (D.R.J.), Centers for Disease Control and Prevention (N.K.), Ad Hoc Writing Group Member (D.P.), Office of Research on Women's Health (V.W.P.), Association of Black Cardiologists (R.S.), American College of Physicians (K.S.),† World Heart Federation (S.C.S.), National Heart, Lung, and Blood Institute (G.S.), and American College of Nurse Practitioners (B.A.T.).

In addition, this report has been endorsed by the American Academy of Physician Assistants; American Association for Clinical Chemistry; American Association of Cardiovascular and Pulmonary Rehabilitation; American College of Chest Physicians; American College of Emergency Physicians; American Diabetes Association; American Geriatrics Society; American Society for Preventive Cardiology; American Society of Echocardiography; American Society of Nuclear Cardiology; Association of Women's Health, Obstetric and Neonatal Nurses; Global Alliance for Women's Health; The Mended Hearts, Inc; National Black Nurses Association; National Black Women's Health Imperative; National Women's Health Resource Center; North American Menopause Society; The Partnership for Gender-Specific Medicine at Columbia University; Preventive Cardiovascular Nurses Association; Society for Vascular Medicine and Biology; Society for Women's Health Research; Society of Geriatric Cardiology; Women in Thoracic Surgery; and WomenHeart: the National Coalition for Women with Heart Disease.

Worldwide, cardiovascular disease (CVD) is the largest single cause of death among women, accounting for one third of all deaths.¹ In many countries, including the United States, more women than men die every year of CVD, a fact largely unknown by physicians.^{2,3} The public health impact of CVD in women is not related solely to the mortality rate, given that advances in science and medicine allow many women to survive heart disease. For example, in the United States, 38.2 million women (34%) are living with CVD, and the population at risk is even larger.² In China, a country with a population of approximately 1.3 billion, the age-

standardized prevalence rates of dyslipidemia and hypertension in women 35 to 74 years of age are 53% and 25%, respectively, which underscores the enormity of CVD as a global health issue and the need for prevention of risk factors in the first place.⁴ As life expectancy continues to increase and economies become more industrialized, the burden of CVD on women and the global economy will continue to increase.⁵

The human toll and economic impact of CVD are difficult to overstate. In the United States alone, \$403 billion was estimated to be spent in 2006 on health care or in lost

†Representation does not imply endorsement by the American College of Physicians.

The online-only Data Supplement is available with this article at <http://circ.ahajournals.org/cgi/content/full/CIRCULATIONAHA.107.181546/DC1>.

The American Heart Association makes every effort to avoid any actual or potential conflicts of interest that may arise as a result of an outside relationship or a personal, professional, or business interest of a member of the writing panel. Specifically, all members of the writing group are required to complete and submit a Disclosure Questionnaire showing all such relationships that might be perceived as real or potential conflicts of interest.

This statement was approved by the American Heart Association Science Advisory and Coordinating Committee on January 9, 2007. A single reprint is available by calling 800-242-8721 (US only) or writing the American Heart Association, Public Information, 7272 Greenville Ave, Dallas, TX 75231-4596. Ask for reprint No. 71-0401. To purchase additional reprints: Up to 999 copies, call 800-611-6083 (US only) or fax 413-665-2671; 1000 or more copies, call 410-528-4121, fax 410-528-4264, or e-mail kelle.ramsay@wolterskluwer.com.

This article has been copublished in the March 20, 2007, issue of the *Journal of the American College of Cardiology*.

Expert peer review of AHA Scientific Statements is conducted at the AHA National Center. For more on AHA statements and guidelines development, visit <http://www.americanheart.org/presenter.jhtml?identifier=3023366>.

Permissions: Multiple copies, modification, alteration, enhancement, and/or distribution of this document are not permitted without the express permission of the American Heart Association. Instructions for obtaining permission are located at <http://www.americanheart.org/presenter.jhtml?Identifier=4431>. A link to the "Permission Request Form" appears on the right side of the page.

(*Circulation*. 2007;115:0000-0000.)

© 2007 American Heart Association, Inc.

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

DOI: 10.1161/CIRCULATIONAHA.107.181546

productivity as a result of CVD, compared with \$190 billion for cancer and \$29 billion for human immunodeficiency virus (HIV).² In addition to population-based and macroeconomic interventions, interventions in individual patients are key to reducing the incidence of CVD globally.⁶ Prevention of CVD is paramount to the health of every woman and every nation. Even modest control could have an enormous impact. It is projected that a reduction in the death rate due to chronic diseases by just 2% over 1 decade would prevent 36 million deaths.⁶

Fortunately, most CVD in women is preventable. In 1999, the American Heart Association (AHA) published a scientific statement titled "A Guide to Preventive Cardiology in Women," which was based on a 1997 review of the literature that documented unique aspects of risk factor management and the occurrence of CVD in women.^{7,8} Over the subsequent decade, many landmark clinical trials in the prevention of CVD altered the practice of medicine. In 2003, a systematic literature search was conducted to develop evidence-based guidelines for the prevention of CVD in women.⁹ Demand for clinical trial evidence increased in the wake of the Women's Health Initiative's discordant findings with observational studies of hormone therapy.¹⁰ Some commonly used preventive interventions lacked clinical trial data for women, and it was unclear whether results of studies conducted in men could be generalized to women. Since the 2003 literature review, numerous clinical trials that have a bearing on CVD prevention in women have been completed (see Appendix). These new research findings must be interpreted in the context of existing data and as-yet missing information so they can be translated appropriately into practice. With few exceptions (eg, the use of aspirin for primary prevention of heart disease), recommendations to prevent CVD in women do not differ from those for men. Healthcare providers should be aware that in some instances, the risk-reducing interventions recommended in these guidelines (eg, angiotensin-converting enzyme inhibitors and angiotensin receptor blockers for blood pressure control) are contraindicated in women contemplating pregnancy or in those who are pregnant.

This 2007 update provides the most current clinical recommendations for the prevention of CVD in women ≥ 20 years of age and is based on a systematic search of the highest-quality science, interpreted by experts in the fields of cardiology, epidemiology, family medicine, gynecology, internal medicine, neurology, nursing, public health, statistics, and surgery. These guidelines cover the primary and secondary prevention of chronic atherosclerotic vascular diseases. More acute management of vascular disease in the periprocedural or immediate posthospital settings and of valvular heart disease is covered in other AHA guidelines. Management of heart failure, atrial fibrillation for stroke prevention, and CVD risk factors during pregnancy is beyond the scope of the present document.

CVD Risk Assessment in Women

The 2004 guidelines emphasized the importance of recognizing the spectrum of CVD and thus classified women as being at high risk, intermediate risk, lower risk, and optimal risk. Classification was based on clinical criteria and/or the Fra-

TABLE 1. Classification of CVD Risk in Women

Risk Status	Criteria
High risk	Established coronary heart disease Cerebrovascular disease Peripheral arterial disease Abdominal aortic aneurysm End-stage or chronic renal disease Diabetes mellitus 10-Year Framingham global risk $>20\%^*$
At risk	≥ 1 major risk factors for CVD, including: Cigarette smoking Poor diet Physical inactivity Obesity, especially central adiposity Family history of premature CVD (CVD at <55 years of age in male relative and <65 years of age in female relative) Hypertension Dyslipidemia Evidence of subclinical vascular disease (eg, coronary calcification) Metabolic syndrome Poor exercise capacity on treadmill test and/or abnormal heart rate recovery after stopping exercise
Optimal risk	Framingham global risk $<10\%$ and a healthy lifestyle, with no risk factors

CVD indicates cardiovascular disease.

*Or at high risk on the basis of another population-adapted tool used to assess global risk.

mingham global risk score.¹¹ These criteria are still used to help guide lipid therapy. The 2007 update recommends a scheme for a general approach to the female patient that classifies her as at high risk, at risk, or at optimal risk (Table 1). The rationale for the change includes several factors: (1) The average lifetime risk for CVD in women is very high, approaching 1 in 2, so prevention is important in all women^{12,13}; (2) most clinical trial data used to formulate the recommendations included either women at high risk because of known CVD or apparently healthy women with a spectrum of risk, which allowed the current scheme to align the guidelines with the evidence; and (3) there has been a growing appreciation of the limitations of risk stratification with the Framingham risk function in diverse populations of women, including the narrow focus on short-term (10-year) risk of myocardial infarction and coronary heart disease death, lack of inclusion of family history, overestimation or underestimation of risk in nonwhite populations, and the documentation of subclinical disease among many women who score as being at low risk.¹⁴

The panel believed that a Framingham global risk score $>20\%$ could be used to identify a woman at high risk but that a lower score is not sufficient to ensure that an individual woman is at low risk. Even the presence of a single risk factor at 50 years of age is associated with a substantially increased lifetime absolute risk for CVD and shorter duration of

survival.¹³ Women who are at risk of CVD because they have ≥ 1 risk factor for heart disease, evidence of subclinical disease with or without risk factors, poor exercise capacity, or unhealthy lifestyles may have a broad range of risk for CVD. For example, a woman found to have coronary calcification or increased carotid intimal thickness may be at low absolute risk of CHD on the basis of the Framingham score, but she may actually be at intermediate or high risk of a future CVD event. Healthcare providers should take several factors into consideration, including medical and lifestyle history, Framingham risk score, family history of CVD, and other genetic conditions (eg, familial hypercholesterolemia), as they make decisions about the aggressiveness of preventive therapy. The optimal risk category has been maintained in the present update and emphasizes the importance of optimizing modifiable risk, especially with regard to maintaining a healthy lifestyle, and may reassure some women or motivate others.

The role that novel CVD risk factors (eg, high-sensitivity C-reactive protein) and novel screening technologies (eg, coronary calcium scoring) should play in guiding preventive interventions is not yet defined. Further research is needed on added benefits, risks, and costs associated with such strategies before they can be incorporated into guidelines. Unique opportunities to identify women's risk (eg, during pregnancy) also deserve further exploration. For example, preeclampsia may be an early indicator of CVD risk.^{15,16} Women with preeclampsia/eclampsia are significantly more likely to develop hypertension and cerebrovascular disease.^{15,16} In addition, maternal placental syndromes in combination with traditional cardiovascular risk factors, such as prepregnancy hypertension or diabetes mellitus, obesity, dyslipidemia, or metabolic syndrome, may be additive in defining CVD risk in women.¹⁶ Future research should evaluate the potential for events or medical contact during unique phases in a woman's lifespan, such as adolescence, pregnancy, and menopause, to identify women at high risk and to determine the effectiveness of preventive interventions during critical time periods.

Several important changes from the 2004 guidelines should be noted. First, the approach to risk stratification of women places greater emphasis on lifetime risk than on short-term absolute risk, defined by the Framingham global score, in part because of the limitations described above. The panel acknowledged that nearly all women are at risk for CVD, which underscores the importance of a heart-healthy lifestyle. Additionally, some women are at high risk of future events because of established CVD and/or multiple risk factors. These women are candidates for more aggressive preventive therapy. Second, more definitive data about menopausal therapy, aspirin therapy, and folic acid therapy have been published in recent years, and the guidelines have been revised accordingly. Of note is that aspirin therapy should be considered for all women for stroke prevention, depending on the balance of risks and benefits. Finally, an algorithm is provided to assist healthcare providers in evaluating CVD risk in women and prioritizing preventive interventions.

Methods

Selection of Expert Panel

The AHA Manuscript Oversight Committee commissioned the update of the guidelines and approved the chair of the

expert panel, who was a nonvoting member of the panel. The leadership of each AHA scientific council and interdisciplinary working group was asked to nominate a recognized expert in CVD prevention who had particular knowledge about women. Major professional or government organizations with a mission consistent with CVD prevention were solicited to serve as cosponsors and were each asked to nominate 1 representative with full voting rights to serve on the expert panel. Each panel member completed a conflict-of-interest statement and was asked to abstain from discussion of or voting on any recommendations they deemed to be a potential conflict of interest. Panelists also suggested diverse professional and community organizations to endorse the final document after its approval by the AHA Science Advisory and Coordinating Committee and cosponsoring organizations.

Selection of Topics and Systematic Search

The expert panel reviewed the list of recommendations in the 2004 guidelines and suggested additional topics to be researched to determine whether they warranted discussion or a clinical recommendation. The methods for the systematic search were similar to those for the research conducted in 2003 and described previously.⁹ The time period for the updated search was January 2003 through June 7, 2006. New topics were searched electronically on 3 databases from their inception (Medline, 1966 through June 7, 2006; CINAHL, 1982 through June 7, 2006; and PsychInfo, 1872 through June 7, 2006).

Briefly, studies were included if they were randomized clinical trials or large prospective cohort studies (>1000 subjects) of CVD risk-reducing interventions, meta-analyses that used a quantitative systematic review process, or surrogate end-point studies with at least 10 cases of major clinical CVD end points reported. The systematic search was conducted by the Duke Center for Clinical Health Policy Research, Durham, NC. Table 2 lists the number of articles included/excluded for each category of recommendation. A total of 5774 articles were initially identified; 828 were included for full-text screening, and 246 met the inclusion criteria and were included in the evidence tables. Some proposed new topics were searched but not included in the guidelines because the expert panel determined the data were insufficient to make clinical recommendations (eg, yoga/stress reduction) or because the topic had been covered in other recent guidelines (eg, treatment of atrial fibrillation for stroke prevention).^{17,18} The summary evidence used by the expert panel can be obtained online as a Data Supplement at <http://circ.ahajournals.org/cgi/content/full/CIRCULATIONAHA.107.181546/DC1>.

Evidence Rating and Recommendation Procedures

A series of conference calls to discuss recommendations was conducted. Primary and secondary reviewers were assigned to each recommendation to modify any wording and to ensure that the evidence tables were complete for that topic. Each expert received a final copy of the evidence tables and voted independently on the strength of the recommendation (Class I, IIa, IIb, or III) and level of evidence (A, B, or C) as outlined in Table 3. The final rating of evidence was determined by a

TABLE 2. Summary of Articles Identified From Systematic Literature Review, by Topic (2006)

Topic	Abstracts Identified	Articles Included for Full-Text Screening	Meta-Analyses Identified	Articles Included for Evidence Tables
Hyperlipidemia	166	27	5	9
Physical activity	298*	53†	1	11
Smoking	281	71	0	1
Antiplatelet therapy	402	95‡	7	12
Hypertension	78	32	1	10
β -Blocker therapy	234	17	1	4
Cardiac rehabilitation	298*	53†	3	3
ACE/ARB therapy	251	44	7	13
Weight management	52	4	0	1
Diabetes mellitus	119	14	2	8
Hormone replacement therapy/SERMs§	154	24	1	10
Diet modification	144	123‡	1	28
Warfarin, antiplatelet therapy,§ and antiarrhythmic therapy§ in atrial fibrillation	460	73	23	27
Aspirin for primary prevention	7	95†	2	1
Psychosocial§/depression	409	42	0	10
Antioxidant supplementation	48	13	3	5
Omega-3 fatty acid supplementation	87	23	3	4
Folic acid supplementation, vitamin B6,§ vitamin B12§	192	36	0	8
New search terms				
Alcohol	325	123‡	0	57
CHF rehabilitation	388	31	4	3
PVD rehabilitation	94	22	0	0
Yoga/stress reduction	83	20	2	6
Aldosterone blocker	239	7	0	4
Stroke rehabilitation	1263	57	11	11
Total	5774	828	77	246

ACE indicates angiotensin-converting enzyme; ARB, angiotensin receptor blocker; SERMs, selective estrogen-receptor modulators; CHF, congestive heart failure; and PVD, peripheral vascular disease.

*Physical activity and cardiac rehabilitation were combined during the initial literature search and full-text screening phase. This number reflects the total number of abstracts identified and articles included at full text as physical activity or cardiac rehabilitation.

†Antiplatelet therapy for coronary artery disease and aspirin for primary prevention were combined during the full-text screening phase. This number reflects the total number of articles included at full text as antiplatelet therapy for coronary artery disease or aspirin for primary prevention.

‡Diet modification and alcohol were combined during the full-text screening phase. This number reflects the total number of articles included at full text as diet modification or alcohol.

§New search term for 2006 combined with previous 2003 topic.

majority vote. Modifications to text and clinical recommendations were made on the basis of peer review comments and cosponsor reviews. The guidelines were then finalized and approved by the expert panel.

Clinical Recommendations and Limitations

Evidence-based recommendations for the prevention of CVD in women are listed in Table 4. Each recommendation is accompanied by the strength of recommendation and the level of evidence to support it. The strength of the recommendation is based not only on the level of evidence to support a clinical recommendation but also on other factors, such as the feasibility of conducting randomized controlled trials in women. Recommendations are grouped in the following categories: lifestyle interventions, major risk factor interventions, and preventive drug interventions. Table 5 lists Class III interventions that are not recommended for the

prevention of CVD, or myocardial infarction in particular, on the basis of current evidence.

The expert panel tried to simplify the guidelines as much as possible while attempting to preserve the integrity of the evidence-based process. This required the assumption of a class effect for most therapeutic interventions, and it should be noted that data are limited with regard to gender differences in any potential class effects. Although most agents in a single therapeutic class share similar efficacy in reducing CVD risk, the safety profiles and costs may vary significantly among agents; healthcare providers should take these factors into consideration as they prescribe pharmacotherapy to prevent CVD.

The panel also emphasizes that the effectiveness of therapies prescribed in the actual office or hospital setting may vary substantially from the efficacy and safety profiles observed in clinical trials because of wide variations in

TABLE 3. Classification and Levels of Evidence

Strength of Recommendation	
Classification	
Class I	Intervention is useful and effective.
Class IIa	Weight of evidence/opinion is in favor of usefulness/efficacy.
Class IIb	Usefulness/efficacy is less well established by evidence/opinion.
Class III	Intervention is not useful/effective and may be harmful.
Level of evidence	
A	Sufficient evidence from multiple randomized trials
B	Limited evidence from single randomized trial or other nonrandomized studies
C	Based on expert opinion, case studies, or standard of care

patient characteristics and adherence to therapy as prescribed. Guideline development has limitations related to the generalizability of results from one population to another. The net clinical impact of an intervention may not be reflected in the scope of CVD outcomes evaluated in these guidelines. Moreover, many studies used to formulate recommendations did not include older women, especially those >80 years of age, in whom CVD and comorbidities are common. Healthcare providers should use clinical judgment about the aggressiveness of preventive interventions in all women, especially older women.

Guideline Implementation

A suggested algorithm for the prevention of CVD in women that incorporates the updated guidelines is presented in the Figure. Although a comprehensive plan to maximize implementation of the guidelines in various practice settings is beyond the scope of this document, barriers to CVD prevention should be discussed with women. A previous study by the AHA has documented numerous barriers to heart health in women; chief among them was confusion by mixed messages from the media.²¹ Other barriers that healthcare providers can address were as follows: 36% of women did not perceive themselves to be at risk, 25% said their healthcare provider did not say heart health was important, and 1 in 5 said

healthcare providers did not clearly explain how they could change their risk status.²¹ Physicians have cited lack of insurance coverage as a barrier to assisting their patients with lifestyle changes.³

Widespread documentation of lack of adherence to CVD prevention guidelines is available, even among women at high risk of CVD in managed-care settings in the United States in which access and medication coverage are available.²² Policy makers, healthcare providers, and patients all have roles to play in maximizing adherence to preventive interventions and reducing the burden of CVD. It is also important to recognize that although the causes of CVD are common to all parts of the world, the approaches to its prevention at the societal or individual level will differ among countries for cultural, social, medical, and economic reasons.²³

Research Needs and Future Directions

The expert panel suggested several gaps in knowledge related to the prevention of CVD that must be addressed to optimize the cardiovascular health of women. More rigorous testing of the impact of guidelines themselves on prevention of risk factors, slowing the progression of risk factors, and reducing the burden of CVD is needed. The development and testing of effective methods to implement guidelines in various healthcare settings, at work sites, and in communities are also research priorities. The role of communication of risk and barriers to CVD prevention should be studied and incorporated into creative methods to disseminate and implement guidelines among diverse populations of women.

The role of genetics in risk stratification and in the responsiveness to preventive interventions is an active and important area of research. Likewise, the role of gender and sex hormones requires further study to understand how they affect outcomes after interventions and how female sex may modify the prognostic value of new biomarkers and measures of subclinical CVD.

Population-wide strategies are necessary to combat the pandemic of CVD in women, because individually tailored interventions alone are likely insufficient to maximally prevent and control CVD. Public policy as an intervention to reduce gender-based disparities in CVD preventive care and improve cardiovascular outcomes among women must become an integral strategy to reduce the global burden of CVD.

TABLE 4. Guidelines for Prevention of CVD in Women: Clinical Recommendations**Lifestyle interventions****Cigarette smoking**

Women should not smoke and should avoid environmental tobacco smoke. Provide counseling, nicotine replacement, and other pharmacotherapy as indicated in conjunction with a behavioral program or formal smoking cessation program (*Class I, Level B*).

Physical activity

Women should accumulate a minimum of 30 minutes of moderate-intensity physical activity (eg, brisk walking) on most, and preferably all, days of the week (*Class I, Level B*).

Women who need to lose weight or sustain weight loss should accumulate a minimum of 60 to 90 minutes of moderate-intensity physical activity (eg, brisk walking) on most, and preferably all, days of the week (*Class I, Level C*).

Rehabilitation

A comprehensive risk-reduction regimen, such as cardiovascular or stroke rehabilitation or a physician-guided home- or community-based exercise training program, should be recommended to women with a recent acute coronary syndrome or coronary intervention, new-onset or chronic angina, recent cerebrovascular event, peripheral arterial disease (*Class I, Level A*), or current/prior symptoms of heart failure and an LVEF <40% (*Class I, Level B*).

Dietary intake

Women should consume a diet rich in fruits and vegetables; choose whole-grain, high-fiber foods; consume fish, especially oily fish,* at least twice a week; limit intake of saturated fat to <10% of energy, and if possible to <7%, cholesterol to <300 mg/d, alcohol intake to no more than 1 drink per day,† and sodium intake to <2.3 g/d (approximately 1 tsp salt). Consumption of *trans*-fatty acids should be as low as possible (eg, <1% of energy) (*Class I, Level B*).

Weight maintenance/reduction

Women should maintain or lose weight through an appropriate balance of physical activity, caloric intake, and formal behavioral programs when indicated to maintain/achieve a BMI between 18.5 and 24.9 kg/m² and a waist circumference ≤35 in (*Class I, Level B*).

Omega-3 fatty acids

As an adjunct to diet, omega-3 fatty acids in capsule form (approximately 850 to 1000 mg of EPA and DHA) may be considered in women with CHD, and higher doses (2 to 4 g) may be used for treatment of women with high triglyceride levels (*Class IIb, Level B*).

Depression

Consider screening women with CHD for depression and refer/treat when indicated (*Class IIa, Level B*).

Major risk factor interventions**Blood pressure—optimal level and lifestyle**

Encourage an optimal blood pressure of <120/80 mm Hg through lifestyle approaches such as weight control, increased physical activity, alcohol moderation, sodium restriction, and increased consumption of fresh fruits, vegetables, and low-fat dairy products (*Class I, Level B*).

Blood pressure—pharmacotherapy

Pharmacotherapy is indicated when blood pressure is ≥140/90 mm Hg or at an even lower blood pressure in the setting of chronic kidney disease or diabetes (≥130/80 mm Hg). Thiazide diuretics should be part of the drug regimen for most patients unless contraindicated or if there are compelling indications for other agents in specific vascular diseases. Initial treatment of high-risk women‡ should be with β-blockers and/or ACE inhibitors/ARBs, with addition of other drugs such as thiazides as needed to achieve goal blood pressure (*Class I, Level A*).

Lipid and lipoprotein levels—optimal levels and lifestyle

The following levels of lipids and lipoproteins in women should be encouraged through lifestyle approaches: LDL-C <100 mg/dL, HDL-C >50 mg/dL, triglycerides <150 mg/dL, and non-HDL-C (total cholesterol minus HDL cholesterol) <130 mg/dL (*Class I, Level B*). If a woman is at high risk‡ or has hypercholesterolemia, intake of saturated fat should be <7% and cholesterol intake <200 mg/d (*Class I, Level B*).

Lipids—pharmacotherapy for LDL lowering, high-risk women

Utilize LDL-C-lowering drug therapy simultaneously with lifestyle therapy in women with CHD to achieve an LDL-C <100 mg/dL (*Class I, Level A*) and similarly in women with other atherosclerotic CVD or diabetes mellitus or 10-year absolute risk >20% (*Class I, Level B*).

A reduction to <70 mg/dL is reasonable in very-high-risk women§ with CHD and may require an LDL-lowering drug combination (*Class IIa, Level B*).

Lipids—pharmacotherapy for LDL lowering, other at-risk women

Utilize LDL-C-lowering therapy if LDL-C level is ≥130 mg/dL with lifestyle therapy and there are multiple risk factors and 10-year absolute risk 10% to 20% (*Class I, Level B*).

Utilize LDL-C-lowering therapy if LDL-C level is ≥160 mg/dL with lifestyle therapy and multiple risk factors even if 10-year absolute risk is <10% (*Class I, Level B*).

Utilize LDL-C-lowering therapy if LDL ≥190 mg/dL regardless of the presence or absence of other risk factors or CVD on lifestyle therapy (*Class I, Level B*).

Lipids—pharmacotherapy for low HDL or elevated non-HDL, high-risk women

Utilize niacin|| or fibrate therapy when HDL-C is low or non-HDL-C is elevated in high-risk women|| after LDL-C goal is reached (*Class IIa, Level B*).

Lipids—pharmacotherapy for low HDL or elevated non-HDL, other at-risk women

Consider niacin|| or fibrate therapy when HDL-C is low or non-HDL-C is elevated after LDL-C goal is reached in women with multiple risk factors and a 10-year absolute risk 10% to 20% (*Class IIb, Level B*).

Diabetes mellitus

Lifestyle and pharmacotherapy should be used as indicated in women with diabetes (*Class I, Level B*) to achieve an HbA_{1c} <7% if this can be accomplished without significant hypoglycemia (*Class I, Level C*).

TABLE 4. Continued

Preventive drug interventions**Aspirin, high risk**

Aspirin therapy (75 to 325 mg/d)[¶] should be used in high-risk[‡] women unless contraindicated (*Class I, Level A*).

If a high-risk[‡] woman is intolerant of aspirin therapy, clopidogrel should be substituted (*Class I, Level B*).

Aspirin—other at-risk or healthy women

In women ≥ 65 years of age, consider aspirin therapy (81 mg daily or 100 mg every other day) if blood pressure is controlled and benefit for ischemic stroke and MI prevention is likely to outweigh risk of gastrointestinal bleeding and hemorrhagic stroke (*Class IIa, Level B*) and in women < 65 years of age when benefit for ischemic stroke prevention is likely to outweigh adverse effects of therapy (*Class IIb, Level B*).

 β -Blockers

β -Blockers should be used indefinitely in all women after MI, acute coronary syndrome, or left ventricular dysfunction with or without heart failure symptoms, unless contraindicated (*Class I, Level A*).

ACE inhibitors/ARBs

ACE inhibitors should be used (unless contraindicated) in women after MI and in those with clinical evidence of heart failure or an LVEF $\leq 40\%$ or with diabetes mellitus (*Class I, Level A*). In women after MI and in those with clinical evidence of heart failure or an LVEF $\leq 40\%$ or with diabetes mellitus who are intolerant of ACE inhibitors, ARBs should be used instead (*Class I, Level B*).

Aldosterone blockade

Use aldosterone blockade after MI in women who do not have significant renal dysfunction or hyperkalemia who are already receiving therapeutic doses of an ACE inhibitor and β -blocker, and have LVEF $\leq 40\%$ with symptomatic heart failure (*Class I, Level B*).

LVEF indicates left ventricular ejection fraction; BMI, body mass index; EPA, eicosapentaenoic acid; DHA, docosahexaenoic acid; CHD, coronary heart disease; ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; CVD, cardiovascular disease; and MI, myocardial infarction.

*Pregnant and lactating women should avoid eating fish potentially high in methylmercury (eg, shark, swordfish, king mackerel, or tile fish) and should eat up to 12 oz/wk of a variety of fish and shellfish low in mercury and check the Environmental Protection Agency and the US Food and Drug Administration's Web sites for updates and local advisories about safety of local catch.

†A drink equivalent is equal to a 12-oz bottle of beer, a 5-oz glass of wine, or a 1.5-oz shot of 80-proof spirit.

‡Criteria for high risk include established CHD, cerebrovascular disease, peripheral arterial disease, abdominal aortic aneurysm, end-stage or chronic renal disease, diabetes mellitus, and 10-year Framingham risk $> 20\%$.

§Criteria for very high risk include established CVD plus any of the following: multiple major risk factors, severe and poorly controlled risk factors, diabetes mellitus.¹⁹

||Dietary supplement niacin should not be used as a substitute for prescription niacin.

¶After percutaneous intervention with stent placement or coronary artery bypass grafting within previous year and in women with noncoronary forms of CVD, use current guidelines for aspirin and clopidogrel.²⁰

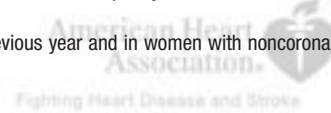


TABLE 5. Class III Interventions (Not Useful/Effective and May Be Harmful) for CVD or MI Prevention in Women

Menopausal therapy

Hormone therapy and selective estrogen-receptor modulators (SERMs) should not be used for the primary or secondary prevention of CVD (*Class III, Level A*).

Antioxidant supplements

Antioxidant vitamin supplements (eg, vitamin E, C, and beta carotene) should not be used for the primary or secondary prevention of CVD (*Class III, Level A*).

Folic acid*

Folic acid, with or without B6 and B12 supplementation, should not be used for the primary or secondary prevention of CVD (*Class III, Level A*).

Aspirin for MI in women < 65 years of age[†]

Routine use of aspirin in healthy women < 65 years of age is not recommended to prevent MI (*Class III, Level B*).

CVD indicates cardiovascular disease; MI, myocardial infarction.

*Folic acid supplementation should be used in the childbearing years to prevent neural tube defects.

†For recommendation for aspirin to prevent CVD in women ≥ 65 years of age or stroke in women < 65 years of age, please see Table 4.

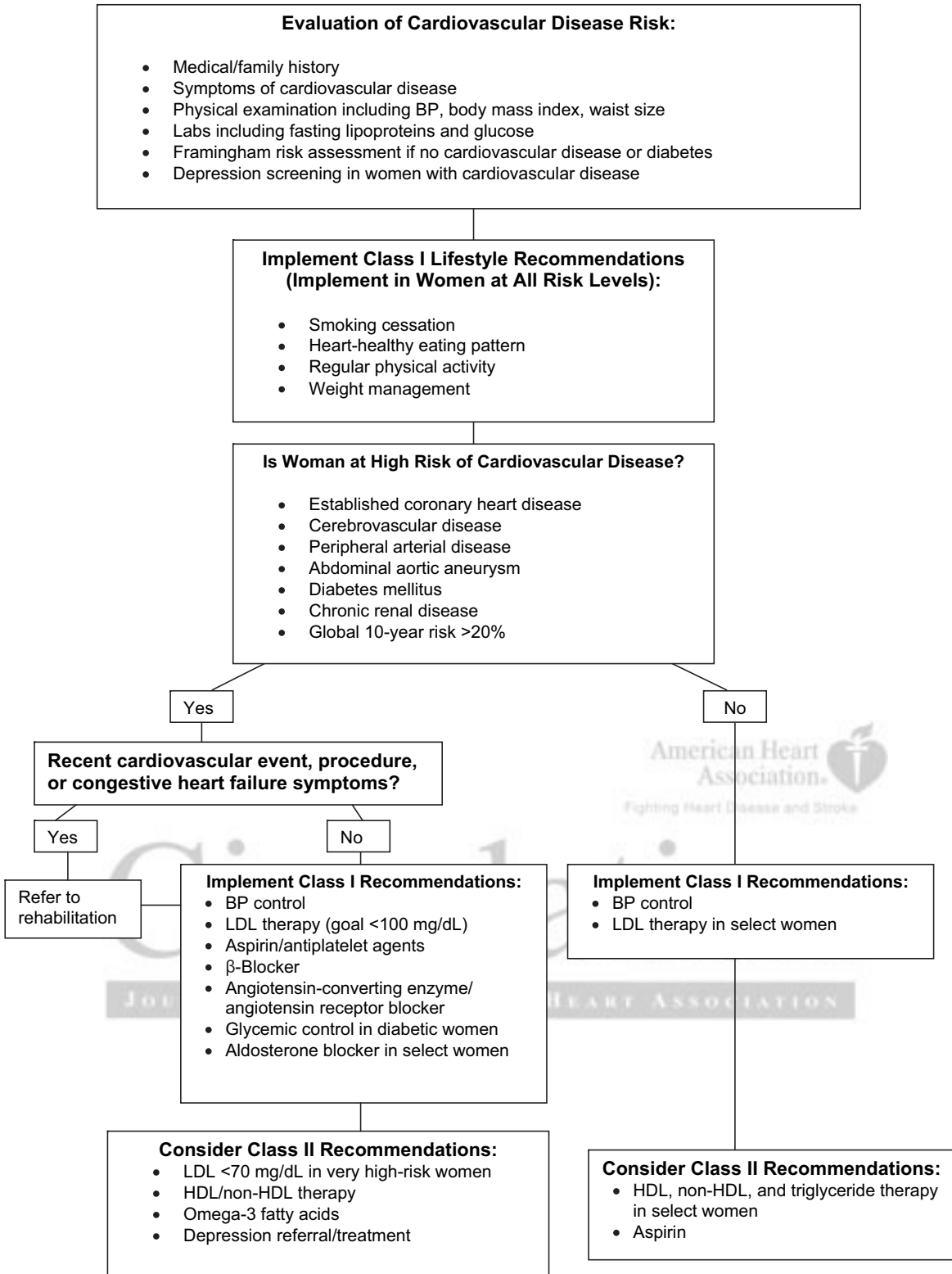


Figure. Algorithm for CVD preventive care in women. Labs indicates laboratory tests; BP, blood pressure; LDL, low-density lipoprotein cholesterol; and HDL, high-density lipoprotein cholesterol.

References

1. Women. World Heart Federation Web site. Available at: <http://www.worldheart.org/awareness-women.php>. Accessed October 6, 2006.
2. Thom T, Haase N, Rosamond W, Howard VJ, Rumsfeld J, Manolio T, Zheng ZJ, Flegal K, O'Donnell C, Kittner S, Lloyd-Jones D, Goff DC Jr, Hong Y, Adams R, Friday G, Furie K, Gorelick P, Kissela B, Marler J, Meigs J,

Sidney S, Sorlie P, Steinberger J, Wasserthiel-Smoller S, Wilson M, Wolf P; American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Heart disease and stroke statistics—2006 update: a report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee [published corrections appear in *Circulation*. 2006;113:e696 and *Circulation*. 2006;114:e630]. *Circulation*. 2006;113:e85–e151.

3. Mosca L, Linfante AH, Benjamin EJ, Berra K, Hayes SN, Walsh BW, Fabunmi RP, Kwan J, Mills T, Simpson SL. National study of physician awareness and adherence to cardiovascular disease prevention guidelines in the United States. *Circulation*. 2005;111:499–510.
4. Gu D, Gupta A, Muntner P, Hu S, Duan X, Chen J, Reynolds RF, Whelton PK, He J. Prevalence of cardiovascular disease risk factor clustering among the adult population of China: results from the International Collaborative Study of Cardiovascular Disease in Asia (InterAsia). *Circulation*. 2005;112:658–665.
5. Yusuf S, Reddy S, Ounpuu S, Anand S. Global burden of cardiovascular diseases: part I: general considerations, the epidemiologic transition, risk factors, and impact of urbanization. *Circulation*. 2001;104:2746–2753.
6. Strong K, Mathers C, Leeder S, Beaglehole R. Preventing chronic diseases: how many lives can we save? *Lancet*. 2005;366:1578–1582.
7. Mosca L, Grundy SM, Judelson D, King K, Limacher M, Oparil S, Pasternak R, Pearson TA, Redberg RF, Smith SC Jr, Winston M, Zinberg S. Guide to preventive cardiology for women: AHA/ACC Scientific Statement Consensus Panel statement. *Circulation*. 1999;99:2480–2484.
8. Mosca L, Manson JE, Sutherland SE, Langer RD, Manolio T, Barrett-Connor E. Cardiovascular disease in women: a statement for healthcare professionals from the American Heart Association. *Circulation*. 1997;96:2468–2482.
9. Mosca L, Appel LJ, Benjamin EJ, Berra K, Chandra-Stobos N, Fabunmi RP, Grady D, Haan CK, Hayes SN, Judelson DR, Keenan NL, McBride P, Oparil S, Ouyang P, Oz MC, Mendelsohn ME, Pasternak RC, Pinn VW, Robertson RM, Schenck-Gustafsson K, Sila CA, Smith SC Jr, Sopko G, Taylor AL, Walsh BW, Wenger NK, Williams CL; American Heart Association. Evidence-based guidelines for cardiovascular disease prevention in women. *Circulation*. 2004;109:672–692.
10. Rossouw JE, Anderson GL, Prentice RL, LaCroix AZ, Kooperberg C, Stefanick ML, Jackson RD, Beresford SA, Howard BV, Johnson KC, Kotchen JM, Ockene J; Writing Group for the Women's Health Initiative Investigators. Risks and benefits of estrogen plus progestin in healthy postmenopausal women: principal results from the Women's Health Initiative randomized controlled trial. *JAMA*. 2002;288:321–333.
11. National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). Third report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. *Circulation*. 2002;106:3143–3421.
12. Lloyd-Jones DM, Larson MG, Beiser A, Levy D. Lifetime risk of developing coronary heart disease. *Lancet*. 1999;353:89–92.
13. Lloyd-Jones DM, Leip EP, Larson MG, D'Agostino RB, Beiser A, Wilson PW, Wolf PA, Levy D. Prediction of lifetime risk for cardiovascular disease by risk factor burden at 50 years of age. *Circulation*. 2006;113:791–798.
14. Sibley C, Blumenthal RS, Bairey Merz CN, Mosca L. Limitations of current cardiovascular disease risk assessment strategies in women. *J Womens Health (Larchmt)*. 2006;15:54–56.
15. Wilson BJ, Watson MS, Prescott GJ, Sunderland S, Campbell DM, Hannaford P, Smith WC. Hypertensive diseases of pregnancy and risk of hypertension and stroke in later life: results from cohort study. *BMJ*. 2003;326:845–852.
16. Ray JG, Vermeulen MJ, Schull MJ, Redelmeier DA. Cardiovascular Health After Maternal Placental Syndromes (CHAMPS): population-based retrospective cohort study. *Lancet*. 2005;366:1797–1803.
17. Goldstein LB, Adams R, Alberts MJ, Appel LJ, Brass LM, Bushnell CD, Culebras A, Degraba TJ, Gorelick PB, Guyton JR, Hart RG, Howard G, Kelly-Hayes M, Nixon JV, Sacco RL; American Heart Association/American Stroke Association Stroke Council; Atherosclerotic Peripheral Vascular Disease Interdisciplinary Working Group; Cardiovascular Nursing Council; Clinical Cardiology Council; Nutrition, Physical Activity, and Metabolism Council; Quality of Care and Outcomes Research Interdisciplinary Working Group; American Academy of Neurology. Primary prevention of ischemic stroke: a guideline from the American Heart Association/American Stroke Association Stroke Council. *Stroke*. 2006;37:1583–1633.
18. Fuster V, Ryden LE, Cannon DS, Crijns HJ, Curtis AB, Ellenbogen KA, Halperin JL, Le Heuzey JY, Kay GN, Lowe JE, Olsson SB, Prystowsky EN, Tamargo JL, Wann S, Smith SC Jr, Jacobs AK, Adams CD, Anderson JL, Antman EM, Halperin JL, Hunt SA, Nishimura R, Ornato JP, Page RL, Riegel B, Priori SG, Blanc JJ, Budaj A, Camm AJ, Dean V, Deckers JW, Despres C, Dickstein K, Lekakis J, McGregor K, Metra M, Morais J, Osterspey A, Tamargo JL, Zamorano JL; American College of Cardiology/American Heart Association Task Force on Practice Guidelines; European Society of Cardiology Committee for Practice Guidelines; European Heart Rhythm Association; Heart Rhythm Society. ACC/AHA/ESC 2006 guidelines for the management of patients with atrial fibrillation: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the European Society of Cardiology Committee for Practice Guidelines (Writing Committee to Revise the 2001 Guidelines for the Management of Patients With Atrial Fibrillation): developed in collaboration with the European Heart Rhythm Association and the Heart Rhythm Society. *Circulation*. 2006;114:e257–e354.
19. Grundy SM, Cleeman JI, Merz CN, Brewer HB Jr, Clark LT, Hunninghake DB, Pasternak RC, Smith SC Jr, Stone NJ; National Heart, Lung, and Blood Institute; American College of Cardiology Foundation; American Heart Association. Implications of recent clinical trials for the National Cholesterol Education Program Adult Treatment Panel III guidelines [published correction appears in *Circulation*. 2004;110:763]. *Circulation*. 2004;110:227–239.
20. Smith SC Jr, Allen J, Blair SN, Bonow RO, Brass LM, Fonarow GC, Grundy SM, Hiratzka L, Jones D, Krumholz HM, Mosca L, Pasternak RC, Pearson T, Pfeffer MA, Taubert KA; AHA/ACC; National Heart, Lung, and Blood Institute. AHA/ACC guidelines for secondary prevention for patients with coronary and other atherosclerotic vascular disease: 2006 update [published correction appears in *Circulation*. 2006; 113:e847]. *Circulation*. 2006;113:2363–2372.
21. Mosca L, Mochari H, Christian AH, Berra K, Taubert K, Mills T, Burdick KA, Simpson SL. National study of women's awareness, preventive action, and barriers to cardiovascular health. *Circulation*. 2006;113:525–534.
22. Mosca L, Bairey-Merz N, Blumenthal RS, Cziraky MJ, Fabunmi RP, Sarawate C, Watson K, Willey VJ, Stanek EJ. Opportunity for intervention to achieve American Heart Association guidelines for optimal lipid levels in high-risk women in a managed care setting. *Circulation*. 2005;111:488–493.
23. Smith SC Jr, Jackson R, Pearson TA, Fuster V, Yusuf S, Faergeman O, Wood DA, Alderman M, Horgan J, Home P, Hunn M, Grundy SM. Principles for national and regional guidelines on cardiovascular disease prevention: a scientific statement from the World Heart and Stroke Forum. *Circulation*. 2004;109:3112–3121.

Appendix—Bibliography by Topic

Hyperlipidemia

- Brophy JM, Brassard P, Bourgault C. The benefit of cholesterol-lowering medications after coronary revascularization: a population study. *Am Heart J*. 2005;150:282–286.
- Foody JM, Rathore SS, Galusha D, Masoudi FA, Havranek EP, Radford MJ, Krumholz HM. Hydroxymethylglutaryl-CoA reductase inhibitors in older persons with acute myocardial infarction: evidence for an age-statin interaction. *J Am Geriatr Soc*. 2006;54:421–430.
- Keech A, Colquhoun D, Best J, Kirby A, Simes RJ, Hunt D, Hague W, Beller E, Arulchelvam M, Baker J, Tonkin A; LIPID Study Group. Secondary prevention of cardiovascular events with long-term pravastatin in patients with diabetes or impaired fasting glucose: results from the LIPID trial. *Diabetes Care*. 2003;26:2713–2721.
- Keough-Ryan TM, Kiberd BA, Dipchand CS, Cox JL, Rose CL, Thompson KJ, Clase CM. Outcomes of acute coronary syndrome in a large Canadian cohort: impact of chronic renal insufficiency, cardiac interventions, and anemia. *Am J Kidney Dis*. 2005;46:845–855.
- Koren MJ, Hunninghake DB; ALLIANCE Investigators. Clinical outcomes in managed-care patients with coronary heart disease treated aggressively in lipid-lowering disease management clinics: the Alliance Study. *J Am Coll Cardiol*. 2004;44:1772–1779.
- Liem AH, van Boven AJ, Veeger NJ, Withagen AJ, Robles de Medina RM, Tijssen JG, van Veldhuisen DJ; Folic Acid on Risk Diminishment After Acute Myocardial Infarction Study Group. Efficacy of folic acid when added to statin therapy in patients with hypercholesterolemia following acute myocardial infarction: a randomized pilot trial. *Int J Cardiol*. 2004;93:175–179.
- Pan W, Pintar T, Anton J, Lee VV, Vaughn WK, Collard CD. Statins are associated with a reduced incidence of perioperative mortality after coronary artery bypass graft surgery. *Circulation*. 2004;110(suppl 1):II-45–II-49.
- Sever PS, Poulter NR, Dahlof B, Wedel H, Collins R, Beevers G, Caulfield M, Kjeldsen SE, Kristinsson A, McInnes GT, Mehlsen J, Nieminen M, O'Brien E. Reduction in cardiovascular events with atorvastatin in 2,532 patients with type 2 diabetes: Anglo-Scandinavian Cardiac Outcomes Trial-Lipid-Lowering Arm (ASCOT-LLA). *Diabetes Care*. 2005;28:1151–1157.
- Smith CS, Cannon CP, McCabe CH, Murphy SA, Bentley J, Braunwald E. Early initiation of lipid-lowering therapy for acute coronary syndromes improves compliance with guideline recommendations: observations from the Orbofiban in Patients with Unstable Coronary Syndromes (OPUS-TIMI 16) trial. *Am Heart J*. 2005;149:444–450.

Hyperlipidemia Meta-Analyses

- Baigent C, Keech A, Kearney PM, Blackwell L, Buck G, Pollicino C, Kirby A, Sourjina T, Peto R, Collins R, Simes R; Cholesterol Treatment Trialists' (CTT) Collaborators. Efficacy and safety of cholesterol-lowering treatment: prospective meta-analysis of data from 90,056 participants in 14 randomised trials of statins [published correction appears in *Lancet*. 2005;366:1358]. *Lancet*. 2005;366:1267–1278.
- Chen JT, Wesley R, Shamburek RD, Pucino F, Csako G. Meta-analysis of natural therapies for hyperlipidemia: plant sterols and stanols versus policosanols. *Pharmacotherapy*. 2005;25:171–183.
- Corvol JC, Bouzamondo A, Sirol M, Hulot JS, Sanchez P, Lechat P. Differential effects of lipid-lowering therapies on stroke prevention: a meta-analysis of randomized trials. *Arch Intern Med*. 2003;163:669–676.
- Tonelli M, Isles C, Curhan GC, Tonkin A, Pfeffer MA, Shepherd J, Sacks FM, Furberg C, Cobbe SM, Simes J, Craven T, West M. Effect of pravastatin on cardiovascular events in people with chronic kidney disease. *Circulation*. 2004;110:1557–1563.
- Vrečer M, Turk S, Drinovec J, Mrhar A. Use of statins in primary and secondary prevention of coronary heart disease and ischemic stroke: meta-analysis of randomized trials. *Int J Clin Pharmacol Ther*. 2003;41:567–577.

Physical Activity

- Blumenthal JA, Babyak MA, Carney RM, Huber M, Saab PG, Burg MM, Sheps D, Powell L, Taylor CB, Kaufmann PG. Exercise, depression, and mortality after myocardial infarction in the ENRICH trial. *Med Sci Sports Exerc*. 2004;36:746–755.
- Conroy MB, Cook NR, Manson JE, Buring JE, Lee IM. Past physical activity, current physical activity, and risk of coronary heart disease. *Med Sci Sports Exerc*. 2005;37:1251–1256.
- Hambrecht R, Walther C, Mobius-Winkler S, Gielen S, Linke A, Conradi K, Erbs S, Kluge R, Kendziorra K, Sabri O, Sick P, Schuler G. Percutaneous coronary angioplasty compared with exercise training in patients with stable coronary artery disease: a randomized trial. *Circulation*. 2004;109:1371–1378.
- Hillsdon M, Thorogood M, Murphy M, Jones L. Can a simple measure of vigorous physical activity predict future mortality? Results from the OXCHECK study. *Public Health Nutr*. 2004;7:557–562.
- Knoops KT, de Groot LC, Kromhout D, Perrin AE, Moreiras-Varela O, Menotti A, van Staveren WA. Mediterranean diet, lifestyle factors, and 10-year mortality in elderly European men and women: the HALE project. *JAMA*. 2004;292:1433–1439.
- Lee IM, Sesso HD, Oguma Y, Paffenbarger RS Jr. Relative intensity of physical activity and risk of coronary heart disease. *Circulation*. 2003;107:1110–1116.
- Li TY, Rana JS, Manson JE, Willett WC, Stampfer MJ, Colditz GA, Rexrode KM, Hu FB. Obesity as compared with physical activity in predicting risk of coronary heart disease in women. *Circulation*. 2006;113:499–506.
- Noda H, Iso H, Toyoshima H, Date C, Yamamoto A, Kikuchi S, Koizumi A, Kondo T, Watanabe Y, Wada Y, Inaba Y, Tamakoshi A; JACC Study Group. Walking and sports participation and mortality from coronary heart disease and stroke. *J Am Coll Cardiol*. 2005;46:1761–1767.
- Sjol A, Thomsen KK, Schroll M, Andersen LB. Secular trends in acute myocardial infarction in relation to physical activity in the general Danish population. *Scand J Med Sci Sports*. 2003;13:224–230.
- Sundquist K, Qvist J, Johansson SE, Sundquist J. The long-term effect of physical activity on incidence of coronary heart disease: a 12-year follow-up study. *Prev Med*. 2005;41:219–225.
- Yu S, Yarnell JW, Sweetnam PM, Murray L. What level of physical activity protects against premature cardiovascular death? The Caerphilly study. *Heart*. 2003;89:502–506.

Physical Activity Meta-Analysis

- McGrath PD. Review: exercise-based cardiac rehabilitation reduces all-cause and cardiac mortality in coronary heart disease. *ACP J Club*. 2004;141:62–63.

Smoking

- Godtfredsen NS, Osler M, Vestbo J, Andersen I, Prescott E. Smoking reduction, smoking cessation, and incidence of fatal and non-fatal myocardial infarction in Denmark 1976–1998: a pooled cohort study. *J Epidemiol Community Health*. 2003;57:412–416.

Smoking Meta-Analyses

None reported.

Antiplatelet Therapy

- Yusuf S, Mehta SR, Zhao F, Gersh BJ, Commerford PJ, Blumenthal M, Budaj A, Wittlinger T, Fox KA; Clopidogrel in Unstable angina to prevent Recurrent Events Trial Investigators. Early and late effects of clopidogrel in patients with acute coronary syndromes. *Circulation*. 2003;107:966–972.
- Bhatt DL, Fox KA, Hacke W, Berger PB, Black HR, Boden WE, Cacoub P, Cohen EA, Creager MA, Easton JD, Flather MD, Haffner SM, Hamm CW, Hankey GJ, Johnston SC, Mak KH, Mas JL, Montalescot G, Pearson TA, Steg PG, Steinhilber SR, Weber MA, Brennan DM, Fabry-Ribaud L, Booth J, Topol EJ; CHARISMA Investigators. Clopidogrel and aspirin versus aspirin alone for the prevention of atherothrombotic events. *N Engl J Med*. 2006;354:1706–1717.
- Collet JP, Montalescot G, Blanchet B, Tanguy ML, Golmard JL, Choussat R, Beygui F, Payot L, Vignolles N, Metzger JP, Thomas D. Impact of prior use or recent withdrawal of oral antiplatelet agents on acute coronary syndromes. *Circulation*. 2004;110:2361–2367.
- Frilling B, Schiele R, Gitt AK, Zahn R, Schneider S, Glunz HG, Gieseler U, Jagodzinski E, Senges J; Maximal Individual Therapy in Acute Myocardial Infarction Study Group. Too little aspirin for secondary prevention after acute myocardial infarction in patients at high risk for cardiovascular events: results from the MITRA study. *Am Heart J*. 2004;148:306–311.
- Herlitz J, Holm J, Peterson M, Karlson BW, Evander MH, Erhardt L; LoWASA Study Group. Factors associated with development of stroke long-term after myocardial infarction: experiences from the LoWASA trial. *J Intern Med*. 2005;257:201–207.
- Herlitz J, Holm J, Peterson M, Karlson BW, Haglid Evander M, Erhardt L; LoWASA Study Group. Effect of fixed low-dose warfarin added-aspirin in the long term after acute myocardial infarction: the LoWASA Study. *Eur Heart J*. 2004;25:232–239.
- Lee SW, Park SW, Hong MK, Lee CW, Kim YH, Park JH, Kang SJ, Han KH, Kim JJ, Park SJ. Comparison of cilostazol and clopidogrel after successful coronary stenting. *Am J Cardiol*. 2005;95:859–862.
- Maresta A, Balducci M, Latini R, Bernardi G, Moccetti T, Sosa C, Barlera S, Varani E, Ribeiro da Silva EE, Monici Preti A, Maggioni AP; STARC II Investigators. Starc II, a multicenter randomized placebo-controlled double-blind clinical trial of trapiidil for 1-year clinical events and angiographic restenosis reduction after coronary angioplasty and stenting. *Catheter Cardiovasc Interv*. 2005;64:375–382.
- Mueller C, Roskamm H, Neumann FJ, Hunziker P, Marsch S, Perruchoud A, Buettner HJ. A randomized comparison of clopidogrel and aspirin versus ticlopidine and aspirin after the placement of coronary artery stents. *J Am Coll Cardiol*. 2003;41:969–973.
- Pekdemir H, Cin VG, Camsari A, Cicek D, Akkus MN, Doven O, Parmaksiz TA. Comparison of 1-month and 6-month clopidogrel therapy on clinical and angiographic outcome after stent implantation. *Heart Vessels*. 2003;18:123–129.
- Quinn MJ, Aronow HD, Califf RM, Bhatt DL, Sapp S, Kleiman NS, Harrington RA, Kong DF, Kandzari DE, Topol EJ. Aspirin dose and six-month outcome after an acute coronary syndrome. *J Am Coll Cardiol*. 2004;43:972–978.
- Segiguchi M, Hoshizaki H, Adachi H, Ohshima S, Taniguchi K, Kurabayashi M. Effects of antiplatelet agents on subacute thrombosis and restenosis after successful coronary stenting: a randomized comparison of ticlopidine and cilostazol. *Circ J*. 2004;68:610–614.

Antiplatelet Therapy Meta-Analyses

- Cosmi B, Rubboli A, Castelvetti C, Milandri M. Ticlopidine versus oral anticoagulation for coronary stenting. *Cochrane Database Syst Rev*. 2001;(4):CD002133.
- Rothberg MB, Celestin C, Fiore LD, Lawler E, Cook JR. Warfarin plus aspirin after myocardial infarction or the acute coronary syndrome: meta-analysis with estimates of risk and benefit. *Ann Intern Med*. 2005;143:241–250.
- Casella G, Ottani F, Pavesi PC, Sangiorgio P, Rubboli A, Galvani M, Fontanelli A, Bracchetti D. Safety and efficacy evaluation of clopidogrel compared with ticlopidine after stent implantation: an updated meta-analysis. *Ital Heart J*. 2003;4:677–684.
- De Schryver ELLM, Algra A, van Gijn J. Dipyridamole for preventing stroke and other vascular events in patients with vascular disease. *Cochrane Database Syst Rev*. 2006;(2):CD001820.
- Lim E, Ali Z, Ali A, Routledge T, Edmonds L, Altman DG, Large S. Indirect comparison meta-analysis of aspirin therapy after coronary surgery [published correction appears in *BMJ*. 2004;328:147]. *BMJ*. 2003;327:1309.
- Rubboli A, Milandri M, Castelvetti C, Cosmi B. Meta-analysis of trials comparing oral anticoagulation and aspirin versus dual antiplatelet therapy after coronary stenting: clues for the management of patients with an

indication for long-term anticoagulation undergoing coronary stenting. *Cardiology*. 2005;104:101–106.

Schleinitz MD, Olkin I, Heidenreich PA. Cilostazol, clopidogrel or ticlopidine to prevent sub-acute stent thrombosis: a meta-analysis of randomized trials. *Am Heart J*. 2004;148:990–997.

Hypertension

Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial Collaborative Research Group. Diuretic versus alpha-blocker as first-step antihypertensive therapy: final results from the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT). *Hypertension*. 2003;42:239–246.

Almgren T, Persson B, Wilhelmsen L, Rosengren A, Andersson OK. Stroke and coronary heart disease in treated hypertension: a prospective cohort study over three decades. *J Intern Med*. 2005;257:496–502.

Bakris GL, Gaxiola E, Messerli FH, Mancia G, Erdine S, Cooper-DeHoff R, Pepine CJ; INVEST Investigators. Clinical outcomes in the diabetes cohort of the International Verapamil SR-Trandolapril study. *Hypertension*. 2004;44:637–642.

Benetos A, Thomas F, Bean KE, Guize L. Why cardiovascular mortality is higher in treated hypertensives versus subjects of the same age, in the general population. *J Hypertens*. 2003;21:1635–1640.

Blacher J, Evans A, Arveiler D, Amouyel P, Ferrieres J, Bingham A, Yarnell J, Haas B, Montaye M, Ruidavets JB, Ducimetiere P; PRIME Study Group. Residual coronary risk in men aged 50–59 years treated for hypertension and hyperlipidemia in the population: the PRIME study. *J Hypertens*. 2004;22:415–423.

Black HR, Elliott WJ, Grandits G, Grambsch P, Lucente T, White WB, Neaton JD, Grimm RH Jr, Hansson L, Lacourciere Y, Muller J, Sleight P, Weber MA, Williams G, Wittes J, Zanchetti A, Anders RJ. Principal results of the Controlled Onset Verapamil Investigation of Cardiovascular End Points (CONVINCE) Trial. *JAMA*. 2003;289:2073–2082.

Pepine CJ, Handberg EM, Cooper-DeHoff RM, Marks RG, Kowey P, Messerli FH, Mancia G, Cangiano JL, Garcia-Barreto D, Keltai M, Erdine S, Bristol HA, Kolb HR, Bakris GL, Cohen JD, Parmley WW. A calcium antagonist versus a non-calcium antagonist hypertension treatment strategy for patients with coronary artery disease: the International Verapamil-Trandolapril Study (INVEST): a randomized controlled trial. *JAMA*. 2003;290:2805–2816.

Rahman M, Pressel S, Davis BR, Nwachuku C, Wright JT Jr, Whelton PK, Barzilay J, Batuman V, Eckfeldt JH, Farber MA, Franklin S, Henriquez M, Kopyt N, Louis GT, Saklayen M, Stanford C, Walworth C, Ward H, Wiegmann T. Cardiovascular outcomes in high-risk hypertensive patients stratified by baseline glomerular filtration rate. *Ann Intern Med*. 2006;144:172–180.

Rodgers A, Chapman N, Woodward M, Liu LS, Colman S, Lee A, Chalmers J, MacMahon S. Perindopril-based blood pressure lowering in individuals with cerebrovascular disease: consistency of benefits by age, sex and region. *J Hypertens*. 2004;22:653–659.

Staessen JA, Thijs L, Fagard R, Celis H, Birkenhager WH, Bulpitt CJ, de Leeuw PW, Fletcher AE, Forette F, Leonetti G, McCormack P, Nachev C, O'Brien E, Rodicio JL, Rosenfeld J, Sarti C, Tuomilehto J, Webster J, Yodanis Y, Zanchetti A; Systolic Hypertension in Europe (Syst-Eur) Trial Investigators. Effects of immediate versus delayed antihypertensive therapy on outcome in the Systolic Hypertension in Europe Trial. *J Hypertens*. 2004;22:847–857.

Hypertension Meta-Analysis

Mulrow C, Lau J, Cornell J, Brand M. Pharmacotherapy for hypertension in the elderly. *Cochrane Database Syst Rev*. 2000;(2):CD000028.

β-Blocker Therapy

Bunch TJ, Muhlestein JB, Bair TL, Renlund DG, Lappe DL, Jensen KR, Horne BD, Carter MA, Anderson JL; Intermountain Heart Collaborative Study Group. Effect of beta-blocker therapy on mortality rates and future myocardial infarction rates in patients with coronary artery disease but no history of myocardial infarction or congestive heart failure. *Am J Cardiol*. 2005;95:827–831.

Ellis K, Tcheng JE, Sapp S, Topol EJ, Lincoff AM. Mortality benefit of beta blockade in patients with acute coronary syndromes undergoing coronary intervention: pooled results from the Epic, Epilog, Epistent, Capture and Rapport trials. *J Interv Cardiol*. 2003;16:299–305.

Harjai KJ, Stone GW, Boura J, Grines L, Garcia E, Brodie B, Cox D, O'Neill WW, Grines C. Effects of prior beta-blocker therapy on clinical outcomes after primary coronary angioplasty for acute myocardial infarction. *Am J Cardiol*. 2003;91:655–660.

Janosi A, Ghali JK, Herlitz J, Czuringa I, Klibaner M, Wikstrand J, Hjalmarson A; MERIT-HF Study Group. Metoprolol CR/XL in postmyocardial infarction

patients with chronic heart failure: experiences from MERIT-HF. *Am Heart J*. 2003;146:721–728.

β-Blocker Therapy Meta-Analysis

Wikstrand J, Wedel H, Ghali J, Deedwania P, Fagerberg B, Goldstein S, Gottlieb S, Hjalmarson A, Kjekshus J, Waagstein F. How should subgroup analyses affect clinical practice? Insights from the Metoprolol Succinate Controlled-Release/Extended-Release Randomized Intervention Trial in Heart Failure (MERIT-HF). *Card Electrophysiol Rev*. 2003;7:264–275.

Cardiac Rehabilitation

Kovoor P, Lee AK, Carrozzi F, Wiseman V, Byth K, Zecchin R, Dickson C, King M, Hall J, Ross DL, Uther JB, Denniss AR. Return to full normal activities including work at two weeks after acute myocardial infarction. *Am J Cardiol*. 2006;97:952–958.

Lisspers J, Sundin O, Ohman A, Hofman-Bang C, Ryden L, Nygren A. Long-term effects of lifestyle behavior change in coronary artery disease: effects on recurrent coronary events after percutaneous coronary intervention. *Health Psychol*. 2005;24:41–48.

Murchie P, Campbell NC, Ritchie LD, Simpson JA, Thain J. Secondary prevention clinics for coronary heart disease: four year follow up of a randomised controlled trial in primary care. *BMJ*. 2003;326:84.

Cardiac Rehabilitation Meta-Analyses

Jolliffe JA, Rees K, Taylor RS, Thompson D, Oldridge N, Ebrahim S. Exercise-based rehabilitation for coronary heart disease. *Cochrane Database Syst Rev*. 2001;(1):CD001800.

Clark AM, Hartling L, Vandermeer B, McAlister FA. Meta-analysis: secondary prevention programs for patients with coronary artery disease. *Ann Intern Med*. 2005;143:659–672.

Taylor RS, Brown A, Ebrahim S, Jolliffe J, Noorani H, Rees K, Skidmore B, Stone JA, Thompson DR, Oldridge N. Exercise-based rehabilitation for patients with coronary heart disease: systematic review and meta-analysis of randomized controlled trials. *Am J Med*. 2004;116:682–692.

Angiotensin-Converting Enzyme/Angiotensin Receptor Blocker Therapy

Braunwald E, Domanski MJ, Fowler SE, Geller NL, Gersh BJ, Hsia J, Pfeffer MA, Rice MM, Rosenberg YD, Rouleau JL; PEACE Trial Investigators. Angiotensin-converting-enzyme inhibition in stable coronary artery disease. *N Engl J Med*. 2004;351:2058–2068.

Buch P, Rasmussen S, Abildstrom SZ, Kober L, Carlsen J, Torp-Pedersen C; TRACE investigators. The long-term impact of the angiotensin-converting enzyme inhibitor trandolapril on mortality and hospital admissions in patients with left ventricular dysfunction after a myocardial infarction: follow-up to 12 years. *Eur Heart J*. 2005;26:145–152.

Daly CA, Fox KM, Remme WJ, Bertrand ME, Ferrari R, Simoons ML; EUROPA Investigators. The effect of perindopril on cardiovascular morbidity and mortality in patients with diabetes in the EUROPA study: results from the PERSUADE substudy. *Eur Heart J*. 2005;26:1369–1378.

Demers C, McMurray JJ, Swedberg K, Pfeffer MA, Granger CB, Olofsson B, McKelvie RS, Ostergren J, Michelson EL, Johansson PA, Wang D, Yusuf S; CHARM Investigators. Impact of candesartan on nonfatal myocardial infarction and cardiovascular death in patients with heart failure. *JAMA*. 2005;294:1794–1798.

Fox KM; EUROPEAN trial On reduction of cardiac events with Perindopril in stable coronary Artery disease Investigators. Efficacy of perindopril in reduction of cardiovascular events among patients with stable coronary artery disease: randomised, double-blind, placebo-controlled, multicenter trial (the EUROPA study). *Lancet*. 2003;362:782–788.

Gottlieb S, Leor J, Shotan A, Harpaz D, Boyko V, Rott D, Mandelzweig L, Behar S; Working Group on Intensive Cardiac Care, Israel Heart Society. Comparison of effectiveness of angiotensin-converting enzyme inhibitors after acute myocardial infarction in diabetic versus nondiabetic patients. *Am J Cardiol*. 2003;92:1020–1025.

Kjoller-Hansen L, Steffensen R, Grande P. Extended follow-up of patients randomly assigned in the Angiotensin-converting enzyme inhibition Post-Revascularization Study (APRES). *Am Heart J*. 2004;148:475–480.

Kondo J, Sone T, Tsuboi H, Mukawa H, Morishima I, Uesugi M, Kono T, Kosaka T, Yoshida T, Numaguchi Y, Matsui H, Murohara T, Okumura K. Effects of low-dose angiotensin II receptor blocker candesartan on cardiovascular events in patients with coronary artery disease. *Am Heart J*. 2003;146:1022–1027.

Nissen SE, Tuzcu EM, Libby P, Thompson PD, Ghali M, Garza D, Berman L, Shi H, Buebendorf E, Topol EJ. Effect of antihypertensive agents on cardiovascular events in patients with coronary disease and normal blood pressure: the CAMELOT study: a randomized controlled trial. *JAMA*. 2004;292:2217–2226.

- Pfeffer MA, McCurray JJ, Velazquez EJ, Rouleau JL, Kober L, Maggioni AP, Solomon SD, Swedberg K, Van de Werf F, White H, Leimberger JD, Henis M, Edwards S, Zelenkofske S, Sellers MA, Califf RM. Valsartan, captopril, or both in myocardial infarction complicated by heart failure, left ventricular dysfunction, or both. *N Engl J Med*. 2003;349:1893–1906.
- Suzuki H, Kanno Y; Efficacy of Candesartan on Outcome in Saitama Trial (E-COST) Group. Effects of candesartan on cardiovascular outcomes in Japanese hypertensive patients [published correction appears in *Hypertens Res*. 2005;28:553]. *Hypertens Res*. 2005;28:307–314.
- Tardif JC, Ducharme A, Yu H, Wogen J, Guertin MC. Retrospective longitudinal cohort study comparing the effects of angiotensin-converting enzyme inhibitors and long-acting calcium channel blockers on total and cardiovascular mortality in patients with hypertension. *Clin Ther*. 2004;26:1073–1083.
- Ueshima K, Fukami K, Hiramori K, Hosoda S, Kishida H, Kato K, Fujita T, Tsutani K, Sakuma A; Japanese Acute Myocardial Infarction Prospective Study Group. Is angiotensin-converting enzyme inhibitor useful in a Japanese population for secondary prevention after acute myocardial infarction? A final report of the Japanese Acute Myocardial Infarction Prospective (JAMP) study. *Am Heart J*. 2004;148:292–299.

Angiotensin-Converting Enzyme/Angiotensin Receptor Blocker Therapy Meta-Analyses

- Al-Mallah MH, Tleyjeh IM, Abdel-Latif AA, Weaver WD. Angiotensin-converting enzyme inhibitors in coronary artery disease and preserved left ventricular systolic function: a systematic review and meta-analysis of randomized controlled trials. *J Am Coll Cardiol*. 2006;47:1576–1583.
- Danchin N, Cucherat M, Thuillez C, Durand E, Kadri Z, Steg PG. Angiotensin-converting enzyme inhibitors in patients with coronary artery disease and absence of heart failure or left ventricular systolic dysfunction: an overview of long-term randomized controlled trials. *Arch Intern Med*. 2006;166:787–796.
- Lee VC, Rhew DC, Dylan M, Badamgarav E, Braunstein GD, Weingarten SR. Meta-analysis: angiotensin-receptor blockers in chronic heart failure and high-risk acute myocardial infarction [published correction appears in *Ann Intern Med*. 2005;142:391]. *Ann Intern Med*. 2004;141:693–704.
- McDonald MA, Simpson SH, Ezekowitz JA, Gyenes G, Tsuyuki RT. Angiotensin receptor blockers and risk of myocardial infarction: systematic review. *BMJ*. 2005;331:873.
- Rodriguez EJ, Eisenberg MJ, Pilote L. Effects of early and late administration of angiotensin-converting enzyme inhibitors on mortality after myocardial infarction. *Am J Med*. 2003;115:473–479.
- Staessen JA, Wang JG, Thijs L. Cardiovascular prevention and blood pressure reduction: a quantitative overview updated until 1 March 2003. *J Hypertens*. 2003;21:1055–1076.
- Verdecchia P, Reboldi G, Angeli F, Gattobigio R, Bentivoglio M, Thijs L, Staessen JA, Porcellati C. Angiotensin-converting enzyme inhibitors and calcium channel blockers for coronary heart disease and stroke prevention. *Hypertension*. 2005;46:386–392.

Weight Management

- Li TY, Rana JS, Manson JE, Willett WC, Stampfer MJ, Colditz GA, Rexrode KM, Hu FB. Obesity as compared with physical activity in predicting risk of coronary heart disease in women. *Circulation*. 2006;113:499–506.

Weight Management Meta-Analyses

None reported.

Diabetes Mellitus

- Choi D, Kim SK, Choi SH, Ko YG, Ahn CW, Jang Y, Lim SK, Lee HC, Cha BS. Preventative effects of rosiglitazone on restenosis after coronary stent implantation in patients with type 2 diabetes. *Diabetes Care*. 2004;27:2654–2660.
- Dormandy JA, Charbonnel B, Eckland DJ, Erdmann E, Massi-Benedetti M, Moules IK, Skene AM, Tan MH, Lefebvre PJ, Murray GD, Standl E, Wilcox RG, Wilhelmsen L, Betteridge J, Birkeland K, Golay A, Heine RJ, Koranyi L, Laakso M, Mokan M, Norkus A, Pirags V, Podar T, Scheen A, Scherbaum W, Schernthaner G, Schmitz O, Skrha J, Smith U, Taton J; PROactive Investigators. Secondary prevention of macrovascular events in patients with type 2 diabetes in the PROactive Study (PROspective pioglitazone Clinical Trial In macroVascular Events): a randomised controlled trial. *Lancet*. 2005;366:1279–1289.
- Gaede P, Vedel P, Larsen N, Jensen GV, Parving HH, Pedersen O. Multifactorial intervention and cardiovascular disease in patients with type 2 diabetes. *N Engl J Med*. 2003;348:383–393.
- Malmberg K, Ryden L, Wedel H, Birkeland K, Bootsma A, Dickstein K, Efendic S, Fisher M, Hamsten A, Herlitz J, Hildebrandt P, MacLeod K,

Laakso M, Torp-Pedersen C, Waldenstrom A; DIGAMI 2 Investigators. Intense metabolic control by means of insulin in patients with diabetes mellitus and acute myocardial infarction (DIGAMI 2): effects on mortality and morbidity. *Eur Heart J*. 2005;26:650–661.

- Murcia AM, Hennekens CH, Lamas GA, Jimenez-Navarro M, Rouleau JL, Flaker GC, Goldman S, Skali H, Braunwald E, Pfeffer MA. Impact of diabetes on mortality in patients with myocardial infarction and left ventricular dysfunction. *Arch Intern Med*. 2004;164:2273–2279.
- Nishio K, Sakurai M, Kusuyama T, Shigemitsu M, Fukui T, Kawamura K, Itoh S, Konno N, Katagiri T. A randomized comparison of pioglitazone to inhibit restenosis after coronary stenting in patients with type 2 diabetes. *Diabetes Care*. 2006;29:101–106.
- Takagi T, Yamamuro A, Tamita K, Yamabe K, Katayama M, Mizoguchi S, Ibuki M, Tani T, Tanabe K, Nagai K, Shiratori K, Morioka S, Yoshikawa J. Pioglitazone reduces neointimal tissue proliferation after coronary stent implantation in patients with type 2 diabetes mellitus: an intravascular ultrasound scanning study. *Am Heart J*. 2003;146:366.
- Wang G, Wei J, Guan Y, Jin N, Mao J, Wang X. Peroxisome proliferator-activated receptor-gamma agonist rosiglitazone reduces clinical inflammatory responses in type 2 diabetes with coronary artery disease after coronary angioplasty. *Metabolism*. 2005;54:590–597.

Diabetes Mellitus Meta-Analyses

- Genuth S. Exogenous insulin administration and cardiovascular risk in non-insulin-dependent and insulin-dependent diabetes mellitus. *Ann Intern Med*. 1996;124(pt 2):104–109.
- Hanefeld M, Cagatay M, Petrowitsch T, Neuser D, Petzinna D, Rupp M. Acarbose reduces the risk for myocardial infarction in type 2 diabetic patients: meta-analysis of seven long-term studies. *Eur Heart J*. 2004;25:10–16.

Hormone Replacement Therapy/Selective Estrogen-Receptor Modulators

- Anderson GL, Limacher M, Assaf AR, Bassford T, Beresford SA, Black H, Bonds D, Brunner R, Brzyski R, Caan B, Chlebowski R, Curb D, Gass M, Hays J, Heiss G, Hendrix S, Howard BV, Hsia J, Hubbell A, Jackson R, Johnson KC, Judd H, Kotchen JM, Kuller L, LaCroix AZ, Lane D, Langer RD, Lasser N, Lewis CE, Manson J, Margolis K, Ockene J, O'Sullivan MJ, Phillips L, Prentice RL, Ritenbaugh C, Robbins J, Rossouw JE, Sarto G, Stefanick ML, Van Horn L, Wactawski-Wende J, Wallace R, Wassertheil-Smoller S; Women's Health Initiative Steering Committee. Effects of conjugated equine estrogen in postmenopausal women with hysterectomy: the Women's Health Initiative randomized controlled trial. *JAMA*. 2004;291:1701–1712.
- Barrett-Connor E, Mosca L, Collins P, Geiger MJ, Grady D, Kornitzer M, McNabb MA, Wenger NK. Effects of raloxifene on cardiovascular events and breast cancer in postmenopausal women. *N Engl J Med*. 2006;355:125–137.
- Grodstein F, Manson JE, Stampfer MJ. Hormone therapy and coronary heart disease: the role of time since menopause and age at hormone initiation. *J Womens Health (Larchmt)*. 2006;15:35–44.
- Hsia J, Langer RD, Manson JE, Kuller L, Johnson KC, Hendrix SL, Pettinger M, Heckbert SR, Greep N, Crawford S, Eaton CB, Kostis JB, Caralis P, Prentice R; Women's Health Initiative Investigators. Conjugated equine estrogens and coronary heart disease: the Women's Health Initiative. *Arch Intern Med*. 2006;166:357–365.
- Lokkegaard E, Jovanovic Z, Heitmann BL, Keiding N, Ottesen B, Pedersen AT. The association between early menopause and risk of ischemic heart disease: influence of hormone therapy. *Maturitas*. 2006;53:226–233.
- Manson JE, Hsia J, Johnson KC, Rossouw JE, Assaf AR, Lasser NL, Trevisan M, Black HR, Heckbert SR, Detrano R, Strickland OL, Wong ND, Crouse JR, Stein E, Cushman M; Women's Health Initiative Investigators. Estrogen plus progestin and the risk of coronary heart disease. *N Engl J Med*. 2003;349:523–534.
- Nordenskjold B, Rosell J, Rutqvist LE, Malmstrom PO, Bergh J, Bengtsson NO, Hatschek T, Wallgren A, Carstensen J. Coronary heart disease mortality after 5 years of adjuvant tamoxifen therapy: results from a randomized trial. *J Natl Cancer Inst*. 2005;97:1609–1610.
- Parsons E, Newby LK, Bhapkar MV, Alexander KP, White HD, Shah SH, Bushnell CD, Califf RM; Symphony and 2nd Symphony Investigators. Postmenopausal hormone use in women with acute coronary syndromes. *J Womens Health (Larchmt)*. 2004;13:863–871.
- Pentti K, Honkanen R, Tuppurainen MT, Sandini L, Kroger H, Saarikoski S. Hormone replacement therapy and mortality in 52- to 70-year-old women: the Kuopio Osteoporosis Risk Factor and Prevention Study. *Eur J Endocrinol*. 2006;154:101–107.
- Simon JA, Lin F, Vittinghoff E, Bittner V. The relation of postmenopausal hormone therapy to serum uric acid and the risk of coronary heart disease

events: the Heart and Estrogen-Progestin Replacement Study (HERS). *Ann Epidemiol.* 2006;16:138–145.

Hormone Replacement Therapy/Selective Estrogen-Receptor Modulators Meta-Analysis

Magliano DJ, Rogers SL, Abramson MJ, Tonkin AM. Hormone therapy and cardiovascular disease: a systematic review and meta-analysis. *BJOG.* 2006;113:5–14.

Diet Modification

Abbott RD, Ando F, Masaki KH, Tung KH, Rodriguez BL, Petrovitch H, Yano K, Curb JD. Dietary magnesium intake and the future risk of coronary heart disease (the Honolulu Heart Program). *Am J Cardiol.* 2003;92:665–669.

Al-Delaimy WK, Rimm E, Willett WC, Stampfer MJ, Hu FB. A prospective study of calcium intake from diet and supplements and risk of ischemic heart disease among men. *Am J Clin Nutr.* 2003;77:814–818.

Bazzano LA, He J, Ogden LG, Loria CM, Whelton PK; National Health and Nutrition Examination Survey I Epidemiologic Follow-up Study. Dietary fiber intake and reduced risk of coronary heart disease in US men and women: the National Health and Nutrition Examination Survey I Epidemiologic Follow-up Study. *Arch Intern Med.* 2003;163:1897–1904.

Boniface DR, Tefft ME. Dietary fats and 16-year coronary heart disease mortality in a cohort of men and women in Great Britain. *Eur J Clin Nutr.* 2002;56:786–792.

Dauchet L, Ferrieres J, Arveiler D, Yarnell JW, Gey F, Ducimetiere P, Ruidavets JB, Haas B, Evans A, Bingham A, Amouyel P, Dallongeville J. Frequency of fruit and vegetable consumption and coronary heart disease in France and Northern Ireland: the PRIME study. *Br J Nutr.* 2004;92:963–972.

Ellingsen I, Hjermann I, Abdelnoor M, Hjerkin EM, Tonstad S. Dietary and antismoking advice and ischemic heart disease mortality in men with normal or high fasting triacylglycerol concentrations: a 23-year follow-up study. *Am J Clin Nutr.* 2003;78:935–940.

Erkkila AT, Booth SL, Hu FB, Jacques PF, Manson JE, Rexrode KM, Stampfer MJ, Lichtenstein AH. Phylloquinone intake as a marker for coronary heart disease risk but not stroke in women. *Eur J Clin Nutr.* 2005;59:196–204.

Howard BV, Van Horn L, Hsia J, Manson JE, Stefanick ML, Wassertheil-Smoller S, Kuller LH, LaCroix AZ, Langer RD, Lasser NL, Lewis CE, Limacher MC, Margolis KL, Mysiw WJ, Ockene JK, Parker LM, Perri MG, Phillips RL, Prentice RL, Robbins J, Rossouw JE, Sarto GE, Schatz IJ, Snetselaar LG, Stevens VJ, Tinker LF, Trevisan M, Vitamins MZ, Anderson GL, Assaf AR, Bassford T, Beresford SA, Black HR, Brunner RL, Brzyski RG, Caan B, Chlebowski RT, Gass M, Granek I, Greenland P, Hays J, Heber D, Heiss G, Hendrix SL, Hubbell FA, Johnson KC, Kotchen JM. Low-fat dietary pattern and risk of cardiovascular disease: the Women's Health Initiative Randomized Controlled Dietary Modification Trial. *JAMA.* 2006;295:655–666.

Hu FB, Rimm EB, Stampfer MJ, Ascherio A, Spiegelman D, Willett WC. Prospective study of major dietary patterns and risk of coronary heart disease in men. *Am J Clin Nutr.* 2000;72:912–921.

Hu FB, Stampfer MJ, Manson JE, Rimm E, Colditz GA, Speizer FE, Hennekens CH, Willett WC. Dietary protein and risk of ischemic heart disease in women. *Am J Clin Nutr.* 1999;70:221–227.

Hu FB, Stampfer MJ, Manson JE, Rimm EB, Wolk A, Colditz GA, Hennekens CH, Willett WC. Dietary intake of alpha-linolenic acid and risk of fatal ischemic heart disease among women. *Am J Clin Nutr.* 1999;69:890–897.

Jensen MK, Koh-Banerjee P, Hu FB, Franz M, Sampson L, Gronbaek M, Rimm EB. Intakes of whole grains, bran, and germ and the risk of coronary heart disease in men. *Am J Clin Nutr.* 2004;80:1492–1499.

Knoops KT, de Groot LC, Kromhout D, Perrin AE, Moreiras-Varela O, Menotti A, van Staveren WA. Mediterranean diet, lifestyle factors, and 10-year mortality in elderly European men and women: the HALE project. *JAMA.* 2004;292:1433–1439.

Kromhout D, Bloemberg BP, Feskens EJ, Hertog MG, Menotti A, Blackburn H. Alcohol, fish, fiber and antioxidant vitamins intake do not explain population differences in coronary heart disease mortality. *Int J Epidemiol.* 1996;25:753–759.

Lee DH, Folsom AR, Harnack L, Halliwell B, Jacobs DR Jr. Does supplemental vitamin C increase cardiovascular disease risk in women with diabetes? *Am J Clin Nutr.* 2004;80:1194–1200.

Liu S, Manson JE, Lee IM, Cole SR, Hennekens CH, Willett WC, Buring JE. Fruit and vegetable intake and risk of cardiovascular disease: the Women's Health Study. *Am J Clin Nutr.* 2000;72:922–928.

Liu S, Sesso HD, Manson JE, Willett WC, Buring JE. Is intake of breakfast cereals related to total and cause-specific mortality in men? *Am J Clin Nutr.* 2003;77:594–599.

McCullough ML, Feskanich D, Stampfer MJ, Rosner BA, Hu BF, Hunter DJ, Variyam JN, Colditz GA, Willett WC. Adherence to the Dietary Guidelines for Americans and risk of major chronic disease in women. *Am J Clin Nutr.* 2000;72:1214–1222.

Mukamal KJ, Maclure M, Muller JE, Sherwood JB, Mittleman MA. Caffeinated coffee consumption and mortality after acute myocardial infarction. *Am Heart J.* 2004;147:999–1004.

Nestel PJ, Baghurst K, Colquhoun DM, Simes RJ, Mehalski K, White HD, Tonkin AM, Kirby A, Pollicino C. Relation of diet to cardiovascular disease risk factors in subjects with cardiovascular disease in Australia and New Zealand: analysis of the Long-Term Intervention with Pravastatin in Ischemic Disease trial. *Am J Clin Nutr.* 2005;81:1322–1329.

Osler M, Helms Andreassen A, Heitmann B, Hoidrup S, Gerdes U, Mørch Jørgensen L, Schroll M. Food intake patterns and risk of coronary heart disease: a prospective cohort study examining the use of traditional scoring techniques. *Eur J Clin Nutr.* 2002;56:568–574.

Sesso HD, Gaziano JM, Liu S, Buring JE. Flavonoid intake and the risk of cardiovascular disease in women. *Am J Clin Nutr.* 2003;77:1400–1408.

Steffen LM, Jacobs DR Jr, Stevens J, Shahar E, Carithers T, Folsom AR. Associations of whole-grain, refined-grain, and fruit and vegetable consumption with risks of all-cause mortality and incident coronary artery disease and ischemic stroke: the Atherosclerosis Risk in Communities (ARIC) Study. *Am J Clin Nutr.* 2003;78:383–390.

Trichopoulou A, Bamia C, Trichopoulos D. Mediterranean diet and survival among patients with coronary heart disease in Greece. *Arch Intern Med.* 2005;165:929–935.

Trichopoulou A, Costacou T, Bamia C, Trichopoulos D. Adherence to a Mediterranean diet and survival in a Greek population. *N Engl J Med.* 2003;348:2599–2608.

van der ADL, Peeters PH, Grobbee DE, Marx JJ, van der Schouw YT. Dietary haem iron and coronary heart disease in women. *Eur Heart J.* 2005;26:257–262.

van der Schouw YT, Kreijkamp-Kaspers S, Peeters PH, Keinan-Boker L, Rimm EB, Grobbee DE. Prospective study on usual dietary phytoestrogen intake and cardiovascular disease risk in Western women. *Circulation.* 2005;111:465–471.

Yano K, Rhoads GG, Kagan A. Coffee, alcohol and risk of coronary heart disease among Japanese men living in Hawaii. *N Engl J Med.* 1977;297:405–409.

Diet Modification Meta-Analysis

Huxley RR, Neil HA. The relation between dietary flavonol intake and coronary heart disease mortality: a meta-analysis of prospective cohort studies. *Eur J Clin Nutr.* 2003;57:904–908.

Warfarin, Antiplatelet Therapy, and Antiarrhythmic Therapy in Atrial Fibrillation

Albers GW, Diener HC, Frison L, Grind M, Nevinson M, Partridge S, Halperin JL, Horrow J, Olsson SB, Petersen P, Vahanian A; SPORTIF Executive Steering Committee for the SPORTIF V Investigators. Ximelagatran versus warfarin for stroke prevention in patients with nonvalvular atrial fibrillation: a randomized trial. *JAMA.* 2005;293:690–698.

Bhatt DL, Fox KA, Hacke W, Berger PB, Black HR, Boden WE, Cacoub P, Cohen EA, Creager MA, Easton JD, Flather MD, Haffner SM, Hamm CW, Hankey GJ, Johnston SC, Mak KH, Mas JL, Montalescot G, Pearson TA, Steg PG, Steinhilber SR, Weber MA, Brennan DM, Fabry-Ribaud L, Booth J, Topol EJ; CHARISMA Investigators. Clopidogrel and aspirin versus aspirin alone for the prevention of atherothrombotic events. *N Engl J Med.* 2006;354:1706–1717.

Bousser MG, Eschwege E, Haguenu M, Lefauconnier JM, Thibault N, Touboul D, Touboul PJ. "AICLA" controlled trial of aspirin and dipyridole in the secondary prevention of athero-thrombotic cerebral ischemia. *Stroke.* 1983;14:5–14.

Coleman CI, Perkerson KA, Gillespie EL, Kluger J, Gallagher R, Horowitz S, White CM. Impact of prophylactic postoperative beta-blockade on post-cardiothoracic surgery length of stay and atrial fibrillation. *Ann Pharmacother.* 2004;38:2012–2016.

Corley SD, Epstein AE, DiMarco JP, Domanski MJ, Geller N, Greene HL, Josephson RA, Kellen JC, Klein RC, Krahn AD, Mickel M, Mitchell LB, Nelson JD, Rosenberg Y, Schron E, Shemanski L, Waldo AL, Wyse DG; AFFIRM Investigators. Relationships between sinus rhythm, treatment, and survival in the Atrial Fibrillation Follow-Up Investigation of Rhythm Management (AFFIRM) Study. *Circulation.* 2004;109:1509–1513.

Diener HC, Bogousslavsky J, Brass LM, Cimminiello C, Csiba L, Kaste M, Leys D, Matias-Guiu J, Rupprecht HJ; MATCH Investigators. Aspirin and

- clopidogrel compared with clopidogrel alone after recent ischemic stroke or transient ischemic attack in high-risk patients (MATCH): randomised, double-blind, placebo-controlled trial. *Lancet*. 2004;364:331–337.
- Edvardsson N, Juul-Moller S, Omblus R, Pehrsson K. Effects of low-dose warfarin and aspirin versus no treatment on stroke in a medium-risk patient population with atrial fibrillation. *J Intern Med*. 2003;254:95–101.
- Fang MC, Singer DE, Chang Y, Hylek EM, Henault LE, Jensvold NG, Go AS. Gender differences in the risk of ischemic stroke and peripheral embolism in atrial fibrillation: the AnTicoagulation and Risk factors In Atrial fibrillation (ATRIA) study. *Circulation*. 2005;112:1687–1691.
- Fox KA, Mehta SR, Peters R, Zhao F, Lakkis N, Gersh BJ, Yusuf S; Clopidogrel in Unstable angina to prevent Recurrent ischemic Events Trial. Benefits and risks of the combination of clopidogrel and aspirin in patients undergoing surgical revascularization for non-ST-elevation acute coronary syndrome: the Clopidogrel in Unstable angina to prevent Recurrent ischemic Events (CURE) Trial. *Circulation*. 2004;110:1202–1208.
- Go AS, Hylek EM, Chang Y, Phillips KA, Henault LE, Capra AM, Jensvold NG, Selby JV, Singer DE. Anticoagulation therapy for stroke prevention in atrial fibrillation: how well do randomized trials translate into clinical practice? *JAMA*. 2003;290:2685–2692.
- Gorelick PB, Richardson D, Kelly M, Ruland S, Hung E, Harris Y, Kittner S, Leurgans S; African American Antiplatelet Stroke Prevention Study Investigators. Aspirin and ticlopidine for prevention of recurrent stroke in black patients: a randomized trial. *JAMA*. 2003;289:2947–2957.
- Ito E, Takahashi A, Yamamoto H, Kuzuhara S, Uchiyama S, Nakajima M; Tokai Panalidine Aspirin Long-Term Study (TOPALS). Ticlopidine alone versus ticlopidine plus aspirin for preventing recurrent stroke. *Intern Med*. 2003;42:793–799.
- Kizer JR, Dahlof B, Kjeldsen SE, Julius S, Beevers G, de Faire U, Fyhrquist F, Ibsen H, Kristianson K, Lederballe-Pedersen O, Lindholm LH, Nieminen MS, Omvik P, Oparil S, Wedel H, Wachtell K, Edelman JM, Snapinn SM, Harris KE, Devereux RB. Stroke reduction in hypertensive adults with cardiac hypertrophy randomized to losartan versus atenolol: the Losartan Intervention For End point reduction in hypertension study. *Hypertension*. 2005;45:46–52.
- Kluger J, White CM. Amiodarone prevents symptomatic atrial fibrillation and reduces the risk of cerebrovascular accidents and ventricular tachycardia after open heart surgery: results of the Atrial Fibrillation Suppression Trial (AFIST). *Card Electrophysiol Rev*. 2003;7:165–167.
- Olsson SB; Executive Steering Committee on behalf of the SPORTIF III Investigators. Stroke prevention with the oral direct thrombin inhibitor ximelagatran compared with warfarin in patients with non-valvular atrial fibrillation (SPORTIF III): randomised controlled trial. *Lancet*. 2003;362:1691–1698.
- Perkerson KA, Gillespie EL, White CM, Kluger J, Takata H, Kardas M, Ismaili A, Coleman CI. Impact of prophylactic amiodarone on length of hospital stay, stroke, and atrial fibrillation after cardiothoracic surgery. *Pharmacotherapy*. 2005;25:320–324.
- Peters RJ, Mehta SR, Fox KA, Zhao F, Lewis BS, Kopecky SL, Diaz R, Commerford PJ, Valentin V, Yusuf S; Clopidogrel in Unstable angina to prevent Recurrent Events (CURE) Trial Investigators. Effects of aspirin dose when used alone or in combination with clopidogrel in patients with acute coronary syndromes: observations from the Clopidogrel in Unstable angina to prevent Recurrent Events (CURE) study. *Circulation*. 2003;108:1682–1687.
- Sacco RL, Sivenius J, Diener HC. Efficacy of aspirin plus extended-release dipyridamole in preventing recurrent stroke in high-risk populations. *Arch Neurol*. 2005;62:403–408.
- Sherman DG, Kim SG, Boop BS, Corley SD, Dimarco JP, Hart RG, Haywood LJ, Hoyte K, Kaufman ES, Kim MH, Nasco E, Waldo AL; National Heart, Lung, and Blood Institute AFFIRM Investigators. Occurrence and characteristics of stroke events in the Atrial Fibrillation Follow-up Investigation of Sinus Rhythm Management (AFFIRM) study. *Arch Intern Med*. 2005;165:1185–1191.
- Singh BN, Singh SN, Reda DJ, Tang XC, Lopez B, Harris CL, Fletcher RD, Sharma SC, Atwood JE, Jacobson AK, Lewis HD Jr, Raisch DW, Ezekowitz MD; Sotalol Amiodarone Atrial Fibrillation Efficacy Trial (SAFE-T) Investigators. Amiodarone versus sotalol for atrial fibrillation. *N Engl J Med*. 2005;352:1861–1872.
- Sivenius J, Riekkinen PJ, Laakso M, Smets P, Lowenthal A. European Stroke Prevention Study (ESPS): antithrombotic therapy is also effective in the elderly. *Acta Neurol Scand*. 1993;87:111–114.
- Sivenius J, Riekkinen PJ, Lowenthal A, Smets P, Laakso M. Antiplatelet therapy is effective in primary prevention of myocardial infarction in patients with a previous cerebrovascular ischemic event. *Arch Neurol*. 1993;50:710–713.
- Steinhuyl SR, Berger PB, Mann JT III, Fry ET, DeLago A, Wilmer C, Topol EJ; CREDO Investigators. Clopidogrel for the Reduction of Events During Observation. Early and sustained dual oral antiplatelet therapy following percutaneous coronary intervention: a randomized controlled trial [published correction appears in *JAMA*. 2003;289:987]. *JAMA*. 2002;288:2411–2420.
- Wachtell K, Lehto M, Gerds E, Olsen MH, Hornestam B, Dahlof B, Ibsen H, Julius S, Kjeldsen SE, Lindholm LH, Nieminen MS, Devereux RB. Angiotensin II receptor blockade reduces new-onset atrial fibrillation and subsequent stroke compared with atenolol: the Losartan Intervention For End Point Reduction in Hypertension (LIFE) study. *J Am Coll Cardiol*. 2005;45:712–719.
- Wyse DG, Slee A, Epstein AE, Gersh BJ, Rocco T Jr, Vidaillet H, Volgman A, Weiss R, Shemanski L, Greene HL; AFFIRM Investigators. Alternative endpoints for mortality in studies of patients with atrial fibrillation: the AFFIRM study experience. *Heart Rhythm*. 2004;1:531–537.
- Wyse DG, Waldo AL, DiMarco JP, Domanski MJ, Rosenberg Y, Schron EB, Kellen JC, Greene HL, Mickel MC, Dalquist JE, Corley SD; Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) Investigators. A comparison of rate control and rhythm control in patients with atrial fibrillation. *N Engl J Med*. 2002;347:1825–1833.
- Yusuf S, Mehta SR, Zhao F, Gersh BJ, Commerford PJ, Blumenthal M, Budaj A, Wittlinger T, Fox KA; Clopidogrel in Unstable angina to prevent Recurrent Events Trial Investigators. Early and late effects of clopidogrel in patients with acute coronary syndromes. *Circulation*. 2003;107:966–972.

Warfarin, Antiplatelet Therapy, and Antiarrhythmic Therapy in Atrial Fibrillation Meta-Analyses

- Aasbo JD, Lawrence AT, Krishnan K, Kim MH, Trohman RG. Amiodarone prophylaxis reduces major cardiovascular morbidity and length of stay after cardiac surgery: a meta-analysis. *Ann Intern Med*. 2005;143:327–336.
- Aguilar M, Hart R. Antiplatelet therapy for preventing stroke in patients with non-valvular atrial fibrillation and no previous history of stroke or transient ischemic attacks. *Cochrane Database Syst Rev*. 2005;(4):CD001925.
- Aguilar M, Hart R. Oral anticoagulants for preventing stroke in patients with non-valvular atrial fibrillation and no previous history of stroke or transient ischemic attacks. *Cochrane Database Syst Rev*. 2005;(3):CD001927.
- Antithrombotic Trialists' Collaboration. Collaborative meta-analysis of randomised trials of antiplatelet therapy for prevention of death, myocardial infarction, and stroke in high risk patients [published correction appears in *BMJ*. 2002;324:141]. *BMJ*. 2002;324:71–86.
- Birman-Deych E, Radford MJ, Nilasena DS, Gage BF. Use and effectiveness of warfarin in Medicare beneficiaries with atrial fibrillation. *Stroke*. 2006;37:1070–1074.
- Connolly SJ. Prevention of vascular events in patients with atrial fibrillation: evidence, guidelines, and practice. *J Cardiovasc Electrophysiol*. 2003;14(suppl):S52–S55.
- Costa J, Ferro JM, Matias-Guiu J, Alvarez-Sabin J, Torres F. Triflusal for preventing serious vascular events in people at high risk. *Cochrane Database Syst Rev*. 2005;(3):CD004296.
- Crystal E, Connolly SJ, Sleik K, Ginger TJ, Yusuf S. Interventions on prevention of postoperative atrial fibrillation in patients undergoing heart surgery: a meta-analysis. *Circulation*. 2002;106:75–80.
- de Denuis S, Sanoski CA, Carlsson J, Opolski G, Spinler SA. Rate versus rhythm control in patients with atrial fibrillation: a meta-analysis. *Arch Intern Med*. 2005;165:258–262.
- De Schryver ELLM, Algra A, van Gijn J. Cochrane review: dipyridamole for preventing major vascular events in patients with vascular disease. *Stroke*. 2003;34:2072–2080.
- De Schryver ELLM, Algra A, van Gijn J. Dipyridamole for preventing stroke and other vascular events in patients with vascular disease. *Cochrane Database Syst Rev*. 2006;(2):CD001820.
- Diener HC; Executive Steering Committee on behalf of the SPORTIF III and V Investigators. Stroke prevention using the oral direct thrombin inhibitor ximelagatran in patients with non-valvular atrial fibrillation: pooled analysis from the SPORTIF III and V studies. *Cerebrovasc Dis*. 2006;21:279–293.
- Gillespie EL, Coleman CI, Sander S, Kluger J, Gryskiewicz KA, White CM. Effect of prophylactic amiodarone on clinical and economic outcomes after cardiothoracic surgery: a meta-analysis. *Ann Pharmacother*. 2005;39:1409–1415.
- Hankey GJ, Sudlow CLM, Dunbabin DW. Thienopyridine derivatives (ticlopidine, clopidogrel) versus aspirin for preventing stroke and other serious vascular events in high vascular risk patients. *Cochrane Database Syst Rev*. 2000;(2):CD001246.
- Hankey GJ, Sudlow CLM, Dunbabin DW. Thienopyridines or aspirin to prevent stroke and other serious vascular events in patients at high risk of vascular disease? A systematic review of the evidence from randomized trials. *Stroke*. 2000;31:1779–1784.
- Hart RG, Pearce LA, Koudestaal PJ. Transient ischemic attacks in patients with atrial fibrillation: implications for secondary prevention: the European

- Atrial Fibrillation Trial and Stroke Prevention in Atrial Fibrillation III trial. *Stroke*. 2004;35:948–951.
- Leonardi-Bee J, Bath PM, Bousser MG, Davalos A, Diener HC, Guiraud-Chaumeil B, Sivenius J, Yatsu F, Dewey ME; Dipyridamole in Stroke Collaboration (DISC). Dipyridamole for preventing recurrent ischemic stroke and other vascular events: a meta-analysis of individual patient data from randomized controlled trials. *Stroke*. 2005;36:162–168.
- Perret-Guillaume C, Wahl DG. Low-dose warfarin in atrial fibrillation leads to more thromboembolic events without reducing major bleeding when compared with adjusted-dose: a meta-analysis. *Thromb Haemost*. 2004;91:394–402.
- Redman AR; Ryan GJ. Analysis of trials evaluating combinations of acetylsalicylic acid and dipyridamole in the secondary prevention of stroke. *Clin Ther*. 2001;23:1391–1408.
- Reynolds MW, Fahrback K, Hauch O, Wygant G, Estok R, Cella C, Nalysnyk L. Warfarin anticoagulation and outcomes in patients with atrial fibrillation: a systematic review and metaanalysis. *Chest*. 2004;126:1938–1945.
- Saxena R, Koustaal P. Anticoagulants versus antiplatelet therapy for preventing stroke in patients with nonrheumatic atrial fibrillation and a history of stroke or transient ischemic attack. *Cochrane Database Syst Rev*. 2004;(4):CD000187.
- Testa L, Biondi-Zoccai GG, Dello Russo A, Bellocchi F, Andreotti F, Crea F. Rate-control versus rhythm-control in patients with atrial fibrillation: a meta-analysis. *Eur Heart J*. 2005;26:2000–2006.
- Zimmer J, Pezzullo J, Choucair W, Southard J, Kokkinos P, Karasik P, Greenberg MD, Singh SN. Meta-analysis of antiarrhythmic therapy in the prevention of postoperative atrial fibrillation and the effect on hospital length of stay, costs, cerebrovascular accidents, and mortality in patients undergoing cardiac surgery. *Am J Cardiol*. 2003;91:1137–1140.

Aspirin for Primary Prevention

- Ridker PM, Cook NR, Lee IM, Gordon D, Gaziano JM, Manson JE, Hennekens CH, Buring JE. A randomized trial of low-dose aspirin in the primary prevention of cardiovascular disease in women. *N Engl J Med*. 2005;352:1293–1304.

Aspirin for Primary Prevention Meta-Analyses

- Berger JS, Roncaglioni MC, Avanzini F, Pangrazzi I, Tognoni G, Brown DL. Aspirin for the primary prevention of cardiovascular events in women and men: a sex-specific meta-analysis of randomized controlled trials. *JAMA*. 2006;295:306–313.
- Eidelman RS, Hebert PR, Weisman SM, Hennekens CH. An update on aspirin in the primary prevention of cardiovascular disease. *Arch Intern Med*. 2003;163:2006–2010.

Psychosocial/Depression

- Blumenthal JA, Babyak MA, Carney RM, Huber M, Saab PG, Burg MM, Sheps D, Powell L, Taylor CB, Kaufmann PG. Exercise, depression, and mortality after myocardial infarction in the ENRICH trial. *Med Sci Sports Exerc*. 2004;36:746–755.
- Carney RM, Blumenthal JA, Freedland KE, Youngblood M, Veith RC, Burg MM, Cornell C, Saab PG, Kaufmann PG, Czajkowski SM, Jaffe AS; ENRICH Investigators. Depression and late mortality after myocardial infarction in the Enhancing Recovery in Coronary Heart Disease (ENRICH) study. *Psychosom Med*. 2004;66:466–474.
- Eng PM, Rimm EB, Fitzmaurice G, Kawachi I. Social ties and change in social ties in relation to subsequent total and cause-specific mortality and coronary heart disease incidence in men. *Am J Epidemiol*. 2002;155:700–709.
- Jenkinson CM, Madeley RJ, Mitchell JR, Turner ID. The influence of psychosocial factors on survival after myocardial infarction. *Public Health*. 1993;107:305–317.
- Monster TB, Johnsen SP, Olsen ML, McLaughlin JK, Sorensen HT. Antidepressants and risk of first-time hospitalization for myocardial infarction: a population-based case-control study. *Am J Med*. 2004;117:732–737.
- Reed D, McGee D, Yano K, Feinleib M. Social networks and coronary heart disease among Japanese men in Hawaii. *Am J Epidemiol*. 1983;117:384–396.
- Sauer WH, Berlin JA, Kimmel SE. Effect of antidepressants and their relative affinity for the serotonin transporter on the risk of myocardial infarction. *Circulation*. 2003;108:32–36.
- Schlienger RG, Fischer LM, Jick H, Meier CR. Current use of selective serotonin reuptake inhibitors and risk of acute myocardial infarction. *Drug Saf*. 2004;27:1157–1165.
- Schneiderman N, Saab PG, Catellier DJ, Powell LH, DeBusk RF, Williams RB, Carney RM, Raczynski JM, Cowan MJ, Berkman LF, Kaufmann PG; ENRICH Investigators. Psychosocial treatment within sex by ethnicity subgroups in the Enhancing Recovery in Coronary Heart Disease clinical trial. *Psychosom Med*. 2004;66:475–483.

- Taylor CB, Youngblood ME, Catellier D, Veith RC, Carney RM, Burg MM, Kaufmann PG, Shuster J, Mellman T, Blumenthal JA, Krishnan R, Jaffe AS; ENRICH Investigators. Effects of antidepressant medication on morbidity and mortality in depressed patients after myocardial infarction. *Arch Gen Psychiatry*. 2005;62:792–798.

Psychosocial/Depression Meta-Analyses

None reported.

Antioxidant Supplementation

- Arad Y, Spadaro LA, Roth M, Newstein D, Guerci AD. Treatment of asymptomatic adults with elevated coronary calcium scores with atorvastatin, vitamin C, and vitamin E: the St. Francis Heart Study randomized clinical trial. *J Am Coll Cardiol*. 2005;46:166–172.
- Dauchet L, Ferrières J, Arveiler D, Yarnell JW, Gey F, Ducimetiere P, Ruidavets JB, Haas B, Evans A, Bingham A, Amouyel P, Dallongeville J. Frequency of fruit and vegetable consumption and coronary heart disease in France and Northern Ireland: the PRIME study. *Br J Nutr*. 2004;92:963–972.
- Lee DH, Folsom AR, Harnack L, Halliwell B, Jacobs DR Jr. Does supplemental vitamin C increase cardiovascular disease risk in women with diabetes? *Am J Clin Nutr*. 2004;80:1194–1200.
- Osganian SK, Stampfer MJ, Rimm E, Spiegelman D, Hu FB, Manson JE, Willett WC. Vitamin C and risk of coronary heart disease in women. *J Am Coll Cardiol*. 2003;42:246–252.
- Tornwall ME, Virtamo J, Korhonen PA, Virtanen MJ, Taylor PR, Albanes D, Huttunen JK. Effect of alpha-tocopherol and beta-carotene supplementation on coronary heart disease during the 6-year post-trial follow-up in the ATBC study. *Eur Heart J*. 2004;25:1171–1178.

Antioxidant Supplementation Meta-Analyses

- Eidelman RS, Hollar D, Hebert PR, Lamas GA, Hennekens CH. Randomized trials of vitamin E in the treatment and prevention of cardiovascular disease. *Arch Intern Med*. 2004;164:1552–1556.
- Knekt P, Ritz J, Pereira MA, O'Reilly EJ, Augustsson K, Fraser GE, Goldbourt U, Heitmann BL, Hallmans G, Liu S, Pietinen P, Spiegelman D, Stevens J, Virtamo J, Willett WC, Rimm EB, Ascherio A. Antioxidant vitamins and coronary heart disease risk: a pooled analysis of 9 cohorts. *Am J Clin Nutr*. 2004;80:1508–1520.
- Shekelle PG, Morton SC, Jungvig LK, Udani J, Spar M, Tu W, Suttrop MJ, Coulter I, Newberry SJ, Hardy M. Effect of supplemental vitamin E for the prevention and treatment of cardiovascular disease. *J Gen Intern Med*. 2004;19:380–389.

Omega-3 Fatty Acid Supplementation

- Albert CM, Oh K, Whang W, Manson JE, Chae CU, Stampfer MJ, Willett WC, Hu FB. Dietary alpha-linolenic acid intake and risk of sudden cardiac death and coronary heart disease. *Circulation*. 2005;112:3232–3238.
- Iso H, Kobayashi M, Ishihara J, Sasaki S, Okada K, Kita Y, Kokubo Y, Tsugane S; JPHC Study Group. Intake of fish and n3 fatty acids and risk of coronary heart disease among Japanese: the Japan Public Health Center-Based (JPHC) Study Cohort I. *Circulation*. 2006;113:195–202.
- Mozaffarian D, Ascherio A, Hu FB, Stampfer MJ, Willett WC, Siscovick DS, Rimm EB. Interplay between different polyunsaturated fatty acids and risk of coronary heart disease in men. *Circulation*. 2005;111:157–164.
- Mozaffarian D, Lemaitre RN, Kuller LH, Burke GL, Tracy RP, Siscovick DS; Cardiovascular Health Study. Cardiac benefits of fish consumption may depend on the type of fish meal consumed: the Cardiovascular Health Study. *Circulation*. 2003;107:1372–1377.

Omega-3 Fatty Acid Supplementation Meta-Analyses

- Brouwer IA, Katan MB, Zock PL. Dietary alpha-linolenic acid is associated with reduced risk of fatal coronary heart disease, but increased prostate cancer risk: a meta-analysis. *J Nutr*. 2004;134:919–922.
- Whelton SP, He J, Whelton PK, Muntner P. Meta-analysis of observational studies on fish intake and coronary heart disease. *Am J Cardiol*. 2004;93:1119–1123.
- Yzebe D, Lievre M. Fish oils in the care of coronary heart disease patients: a meta-analysis of randomized controlled trials. *Fundam Clin Pharmacol*. 2004;18:581–592.

Folic Acid Supplementation/Vitamin B6/Vitamin B12

- Anderson JL, Jensen KR, Carlquist JF, Bair TL, Home BD, Muhlestein JB. Effect of folic acid fortification of food on homocysteine-related mortality. *Am J Med*. 2004;116:158–164.

- Bonaa KH, Njolstad I, Ueland PM, Schirmer H, Tverdal A, Steigen T, Wang H, Nordrehaug JE, Arnesen E, Rasmussen K; NORVIT Trial Investigators. Homocysteine lowering and cardiovascular events after acute myocardial infarction. *N Engl J Med*. 2006;354:1578–1588.
- Lange H, Suryapranata H, De Luca G, Borner C, Dille J, Kallmayer K, Pasalary MN, Scherer E, Dambrink JH. Folate therapy and in-stent restenosis after coronary stenting. *N Engl J Med*. 2004;350:2673–2681.
- Liem A, Reynierse-Buitenwerf GH, Zwinderman AH, Jukema JW, van Veldhuisen DJ. Secondary prevention with folic acid: effects on clinical outcomes. *J Am Coll Cardiol*. 2003;41:2105–2113.
- Lonn E, Yusuf S, Arnold MJ, Sheridan P, Pogue J, Micks M, McQueen MJ, Probstfield J, Fodor G, Held C, Genest J Jr; Heart Outcomes Prevention Evaluation (HOPE) 2 Investigators. Homocysteine lowering with folic acid and B vitamins in vascular disease. *N Engl J Med*. 2006;354:1567–1577.
- Schnyder G, Roffi M, Flammer Y, Pin R, Hess OM. Effect of homocysteine-lowering therapy with folic acid, vitamin B12, and vitamin B6 on clinical outcome after percutaneous coronary intervention: the Swiss Heart study: a randomized controlled trial. *JAMA*. 2002;288:973–979.
- Schnyder G, Roffi M, Pin R, Flammer Y, Lange H, Eberli FR, Meier B, Turi ZG, Hess OM. Decreased rate of coronary restenosis after lowering of plasma homocysteine levels. *N Engl J Med*. 2001;345:1593–1600.
- Toole JF, Malinow MR, Chambless LE, Spence JD, Pettigrew LC, Howard VJ, Sides EG, Wang CH, Stampfer M. Lowering homocysteine in patients with ischemic stroke to prevent recurrent stroke, myocardial infarction, and death: the Vitamin Intervention for Stroke Prevention (VISP) randomized controlled trial. *JAMA*. 2004;291:565–575.

Folic Acid Supplementation/Vitamin B6/Vitamin B12 Meta-Analyses

None reported.

Alcohol

- Regular alcohol intake decreased risk of coronary heart disease events but not total mortality in men. *Evid Based Nurs*. 1999;2:130. Comment.
- Albert CM, Manson JE, Cook NR, Ajani UA, Gaziano JM, Hennekens CH. Moderate alcohol consumption and the risk of sudden cardiac death among US male physicians. *Circulation*. 1999;100:944–950.
- Blackwelder WC, Yano K, Rhoads GG, Kagan A, Gordon T, Palesch Y. Alcohol and mortality: the Honolulu Heart Study. *Am J Med*. 1980;68:164–169.
- Boffetta P, Garfinkel L. Alcohol drinking and mortality among men enrolled in an American Cancer Society prospective study. *Epidemiology*. 1990;1:342–348.
- Camargo CA Jr, Stampfer MJ, Glynn RJ, Grodstein F, Gaziano JM, Manson JE, Buring JE, Hennekens CH. Moderate alcohol consumption and risk for angina pectoris or myocardial infarction in US male physicians. *Ann Intern Med*. 1997;126:372–375.
- Doll R, Peto R, Hall E, Wheatley K, Gray R. Mortality in relation to consumption of alcohol: 13 years' observations on male British doctors. *BMJ*. 1994;309:911–918.
- Ebbert JO, Janney CA, Sellers TA, Folsom AR, Cerhan JR. The association of alcohol consumption with coronary heart disease mortality and cancer incidence varies by smoking history. *J Gen Intern Med*. 2005;20:14–20.
- Emberson JR, Shaper AG, Wannamethee SG, Morris RW, Whincup PH. Alcohol intake in middle age and risk of cardiovascular disease and mortality: accounting for intake variation over time. *Am J Epidemiol*. 2005;161:856–863.
- Farchi G, Fidanza F, Mariotti S, Menotti A. Alcohol and mortality in the Italian rural cohorts of the Seven Countries Study. *Int J Epidemiol*. 1992;21:74–81.
- Garg R, Wagener DK, Madans JH. Alcohol consumption and risk of ischemic heart disease in women. *Arch Intern Med*. 1993;153:1211–1216.
- Gaziano JM, Gaziano TA, Glynn RJ, Sesso HD, Ajani UA, Stampfer MJ, Manson JE, Hennekens CH, Buring JE. Light-to-moderate alcohol consumption and mortality in the Physicians' Health Study enrollment cohort. *J Am Coll Cardiol*. 2000;35:96–105.
- Gronbaek M, Becker U, Johansen D, Gottschau A, Schnohr P, Hein HO, Jensen G, Sorensen TI. Type of alcohol consumed and mortality from all causes, coronary heart disease, and cancer. *Ann Intern Med*. 2000;133:411–419.
- Gronbaek M, Johansen D, Becker U, Hein HO, Schnohr P, Jensen G, Vestbo J, Sorensen TI. Changes in alcohol intake and mortality: a longitudinal population-based study. *Epidemiology*. 2004;15:222–228.
- Hart CL, Smith GD, Hole DJ, Hawthorne VM. Alcohol consumption and mortality from all causes, coronary heart disease, and stroke: results from a prospective cohort study of Scottish men with 21 years of follow up. *BMJ*. 1999;318:1725–1729.
- Hein HO, Suadcani P, Gyntelberg F. Alcohol consumption, serum low density lipoprotein cholesterol concentration, and risk of ischemic heart disease: six year follow up in the Copenhagen male study [published correction appears in *BMJ*. 1996;312:1007]. *BMJ*. 1996;312:736–741.
- Kauhanen J, Kaplan GA, Goldberg DE, Salonen JT. Beer drinking and mortality: results from the Kuopio ischemic heart disease risk factor study, a prospective population based study. *BMJ*. 1997;315:846–851.
- Keil U, Chambless LE, Doring A, Filipiak B, Stieber J. The relation of alcohol intake to coronary heart disease and all-cause mortality in a beer-drinking population. *Epidemiology*. 1997;8:150–156.
- Kitamura A, Iso H, Sankai T, Naito Y, Sato S, Kiyama M, Okamura T, Nakagawa Y, Iida M, Shimamoto T, Komachi Y. Alcohol intake and premature coronary heart disease in urban Japanese men. *Am J Epidemiol*. 1998;147:59–65.
- Kittner SJ, Garcia-Palmieri MR, Costas R Jr, Cruz-Vidal M, Abbott RD, Havlik RJ. Alcohol and coronary heart disease in Puerto Rico. *Am J Epidemiol*. 1983;117:538–550.
- Kivela SL, Nissinen A, Ketola A, Punsar S, Puska P, Karvonen M. Alcohol consumption and mortality in aging or aged Finnish men [published correction appears in *J Clin Epidemiol*. 1989;42:701]. *J Clin Epidemiol*. 1989;42:61–68.
- Klatsky AL, Armstrong MA, Friedman GD. Alcohol and mortality. *Ann Intern Med*. 1992;117:646–654.
- Klatsky AL, Armstrong MA, Friedman GD. Risk of cardiovascular mortality in alcohol drinkers, ex-drinkers and nondrinkers. *Am J Cardiol*. 1990;66:1237–1242.
- Kozarevic D, Demirovic J, Gordon T, Kaelber CT, McGee D, Zukel WJ. Drinking habits and coronary heart disease: the Yugoslavia cardiovascular disease study. *Am J Epidemiol*. 1982;116:748–758.
- Lazarus NB, Kaplan GA, Cohen RD, Leu DJ. Change in alcohol consumption and risk of death from all causes and from ischemic heart disease. *BMJ*. 1991;303:553–556.
- Mukamal KJ, Chung H, Jenny NS, Kuller LH, Longstreth WT Jr, Mittleman MA, Burke GL, Cushman M, Psaty BM, Siscovick DS. Alcohol consumption and risk of coronary heart disease in older adults: the Cardiovascular Health Study. *J Am Geriatr Soc*. 2006;54:30–37.
- Mukamal KJ, Chung H, Jenny NS, Kuller LH, Longstreth WT Jr, Mittleman MA, Burke GL, Cushman M, Beauchamp NJ Jr, Siscovick DS. Alcohol use and risk of ischemic stroke among older adults: the Cardiovascular Health Study. *Stroke*. 2005;36:1830–1834.
- Mukamal KJ, Conigrave KM, Mittleman MA, Camargo CA Jr, Stampfer MJ, Willett WC, Rimm EB. Roles of drinking pattern and type of alcohol consumed in coronary heart disease in men. *N Engl J Med*. 2003;348:109–118.
- Mukamal KJ, Girotra S, Mittleman MA. Alcohol consumption, atherosclerotic progression, and prognosis among patients with coronary artery bypass grafts. *Am Heart J*. 2006;151:368–372.
- Mukamal KJ, Jensen MK, Gronbaek M, Stampfer MJ, Manson JE, Pischon T, Rimm EB. Drinking frequency, mediating biomarkers, and risk of myocardial infarction in women and men. *Circulation*. 2005;112:1406–1413.
- Mukamal KJ, Maclure M, Muller JE, Mittleman MA. Binge drinking and mortality after acute myocardial infarction. *Circulation*. 2005;112:3839–3845.
- Mukamal KJ, Maclure M, Muller JE, Sherwood JB, Mittleman MA. Prior alcohol consumption and mortality following acute myocardial infarction. *JAMA*. 2001;285:1965–1970.
- Muntwyler J, Hennekens CH, Buring JE, Gaziano JM. Mortality and light to moderate alcohol consumption after myocardial infarction. *Lancet*. 1998;352:1882–1885.
- Palmer AJ, Fletcher AE, Bulpitt CJ, Beevers DG, Coles EC, Ledingham JG, Petrie JC, Webster J, Dollery CT. Alcohol intake and cardiovascular mortality in hypertensive patients: report from the Department of Health Hypertension Care Computing Project. *J Hypertens*. 1995;13:957–964.
- Paunio M, Virtamo J, Gref CG, Heinonen OP. Serum high density lipoprotein cholesterol, alcohol, and coronary mortality in male smokers. *BMJ*. 1996;312:1200–1203.
- Rehm JT, Bondy SJ, Sempos CT, Vuong CV. Alcohol consumption and coronary heart disease morbidity and mortality. *Am J Epidemiol*. 1997;146:495–501.
- Renaud SC, Gueguen R, Conard P, Lanzmann-Petithory D, Orgogozo JM, Henry O. Moderate wine drinkers have lower hypertension-related mortality: a prospective cohort study in French men. *Am J Clin Nutr*. 2004;80:621–625.
- Rimm EB, Giovannucci EL, Willett WC, Colditz GA, Ascherio A, Rosner B, Stampfer MJ. Prospective study of alcohol consumption and risk of coronary disease in men. *Lancet*. 1991;338:464–468.
- Romelsjo A, Leifman A. Association between alcohol consumption and mortality, myocardial infarction, and stroke in 25 year follow up of 49 618 young Swedish men. *BMJ*. 1999;319:821–822.

- Rosengren A, Wilhelmsen L, Wedel H. Separate and combined effects of smoking and alcohol abuse in middle-aged men. *Acta Med Scand.* 1988;223:111–118.
- Salonen JT, Puska P, Nissinen A. Intake of spirits and beer and risk of myocardial infarction and death: a longitudinal study in Eastern Finland. *J Chronic Dis.* 1983;36:533–543.
- Shaper AG, Wannamethee SG. Alcohol intake and mortality in middle aged men with diagnosed coronary heart disease. *Heart.* 2000;83:394–399.
- Simons LA, McCallum J, Friedlander Y, Simons J. Alcohol intake and survival in the elderly: a 77 month follow-up in the Dubbo study. *Aust N Z J Med.* 1996;26:662–670.
- Solomon CG, Hu FB, Stampfer MJ, Colditz GA, Speizer FE, Rimm EB, Willett WC, Manson JE. Moderate alcohol consumption and risk of coronary heart disease among women with type 2 diabetes mellitus. *Circulation.* 2000;102:494–499.
- Stampfer MJ, Colditz GA, Willett WC, Speizer FE, Hennekens CH. A prospective study of moderate alcohol consumption and the risk of coronary disease and stroke in women. *N Engl J Med.* 1988;319:267–273.
- Suh I, Shaten BJ, Cutler JA, Kuller LH. Alcohol use and mortality from coronary heart disease: the role of high-density lipoprotein cholesterol: the Multiple Risk Factor Intervention Trial Research Group. *Ann Intern Med.* 1992;116:881–887.
- Suhonen O, Aromaa A, Reunanen A, Knekt P. Alcohol consumption and sudden coronary death in middle-aged Finnish men. *Acta Med Scand.* 1987;221:335–341.
- Tanasescu M, Hu FB, Willett WC, Stampfer MJ, Rimm EB. Alcohol consumption and risk of coronary heart disease among men with type 2 diabetes mellitus. *J Am Coll Cardiol.* 2001;38:1836–1842.
- Trevisan M, Schisterman E, Mennotti A, Farchi G, Conti S; Risk Factor And Life Expectancy Research Group. Drinking pattern and mortality: the Italian Risk Factor and Life Expectancy pooling project. *Ann Epidemiol.* 2001;11:312–319.
- Tsugane S, Fahey MT, Sasaki S, Baba S. Alcohol consumption and all-cause and cancer mortality among middle-aged Japanese men: seven-year follow-up of the JPHC study Cohort I: Japan Public Health Center. *Am J Epidemiol.* 1999;150:1201–1207.
- Walsh CR, Larson MG, Evans JC, Djousse L, Ellison RC, Vasan RS, Levy D. Alcohol consumption and risk for congestive heart failure in the Framingham Heart Study. *Ann Intern Med.* 2002;136:181–191.
- Wannamethee SG, Shaper AG. Lifelong teetotallers, ex-drinkers and drinkers: mortality and the incidence of major coronary heart disease events in middle-aged British men. *Int J Epidemiol.* 1997;26:523–531.
- Wannamethee SG, Shaper AG. Patterns of alcohol intake and risk of stroke in middle-aged British men. *Stroke.* 1996;27:1033–1039.
- Wannamethee SG, Shaper AG. Taking up regular drinking in middle age: effect on major coronary heart disease events and mortality. *Heart.* 2002;87:32–36.
- Wannamethee SG, Shaper AG. Type of alcoholic drink and risk of major coronary heart disease events and all-cause mortality. *Am J Public Health.* 1999;89:685–690.
- Wellmann J, Heidrich J, Berger K, Doring A, Heuschmann PU, Keil U. Changes in alcohol intake and risk of coronary heart disease and all-cause mortality in the MONICA/KORA-Augsburg cohort 1987–97. *Eur J Cardiovasc Prev Rehabil.* 2004;11:48–55.
- Whiteman D, Muir J, Jones L, Murphy M, Key T. Dietary questions as determinants of mortality: the OXCHECK experience. *Public Health Nutr.* 1999;2:477–487.
- Yang T, Doherty TM, Wong ND, Detrano RC. Alcohol consumption, coronary calcium, and coronary heart disease events. *Am J Cardiol.* 1999;84:802–806.

Alcohol Meta-Analyses

None reported.

Chronic Heart Failure Rehabilitation

- Belardinelli R, Georgiou D, Cianci G, Purcaro A. Randomized, controlled trial of long-term moderate exercise training in chronic heart failure: effects on functional capacity, quality of life, and clinical outcome. *Circulation.* 1999;99:1173–1182.
- Koelling TM, Johnson ML, Cody RJ, Aaronson KD. Discharge education improves clinical outcomes in patients with chronic heart failure. *Circulation.* 2005;111:179–185.
- Stromberg A, Martensson J, Fridlund B, Levin LA, Karlsson JE, Dahlstrom U. Nurse-led heart failure clinics improve survival and self-care behavior in patients with heart failure: results from a prospective, randomised trial. *Eur Heart J.* 2003;24:1014–1023.

Chronic Heart Failure Rehabilitation Meta-Analyses

- Lloyd-Williams F, Mair FS, Leitner M. Exercise training and heart failure: a systematic review of current evidence. *Br J Gen Pract.* 2002;52:47–55.
- Piepoli MF, Davos C, Francis DP, Coats AJ; ExTraMATCH Collaborative. Exercise training meta-analysis of trials in patients with chronic heart failure (ExTraMATCH). *BMJ.* 2004;328:189.
- Rees K, Taylor RS, Singh S, Coats AJS, Ebrahim S. Exercise based rehabilitation for heart failure. *Cochrane Database Syst Rev.* 2004;(3):CD003331.
- Smart N, Marwick TH. Exercise training for patients with heart failure: a systematic review of factors that improve mortality and morbidity. *Am J Med.* 2004;116:693–706.

Peripheral Vascular Disease Rehabilitation

None reported.

Peripheral Vascular Disease Rehabilitation Meta-Analyses

None reported.

Yoga/Stress Reduction

- Appels A, Bar F, Lasker J, Flamm U, Kop W. The effect of a psychological intervention program on the risk of a new coronary event after angioplasty: a feasibility study. *J Psychosom Res.* 1997;43:209–217.
- Frasure-Smith N, Prince R. The ischemic heart disease life stress monitoring program: impact on mortality. *Psychosom Med.* 1985;47:431–445.
- Krucoff MW, Crater SW, Gallup D, Blankenship JC, Cuffe M, Guarneri M, Krieger RA, Kshetry VR, Morris K, Oz M, Pichard A, Sketch MA Jr, Koenig HG, Mark D, Lee KL. Music, imagery, touch, and prayer as adjuncts to interventional cardiac care: the Monitoring and Actualisation of Noetic Trainings (MANTRA) II randomised study. *Lancet.* 2005;366:211–217.
- Patel C, Marmot MG, Terry DJ, Carruthers M, Hunt B, Patel M. Trial of relaxation in reducing coronary risk: four year follow up. *Br Med J (Clin Res Ed).* 1985;290:1103–1106.
- van Dixhoorn J, Duivenvoorden HJ, Staal JA, Pool J, Verhage F. Cardiac events after myocardial infarction: possible effect of relaxation therapy. *Eur Heart J.* 1987;8:1210–1214.
- van Dixhoorn JJ, Duivenvoorden HJ. Effect of relaxation therapy on cardiac events after myocardial infarction: a 5-year follow-up study. *J Cardiopulm Rehabil.* 1999;19:178–185.

Yoga/Stress Reduction Meta-Analyses

- Nunes EV, Frank KA, Kornfeld DS. Psychological treatment for the type A behavior pattern and for coronary heart disease: a meta-analysis of the literature. *Psychosom Med.* 1987;49:159–173.
- Ornish D, Scherwitz LW, Doody RS, Kesten D, McLanahan SM, Brown SE, DePuey E, Sonnemaker R, Haynes C, Lester J, McAllister GK, Hall RJ, Burdine JA, Gotto AM Jr. Effects of stress management training and dietary changes in treating ischemic heart disease. *JAMA.* 1983;249:54–59.

Aldosterone Blocker

- Pitt B, Remme W, Zannad F, Neaton J, Martinez F, Roniker B, Bittman R, Hurley S, Kleiman J, Gatlin M; Eplerenone Post-Acute Myocardial Infarction Heart Failure Efficacy and Survival Study Investigators. Eplerenone, a selective aldosterone blocker, in patients with left ventricular dysfunction after myocardial infarction [published correction appears in *N Engl J Med.* 2003;348:2271]. *N Engl J Med.* 2003;348:1309–1321.
- Pitt B, White H, Nicolau J, Martinez F, Gheorghiadu M, Aschermann M, van Veldhuisen DJ, Zannad F, Krum H, Mukherjee R, Vincent J; EPHEUS Investigators. Eplerenone reduces mortality 30 days after randomization following acute myocardial infarction in patients with left ventricular systolic dysfunction and heart failure. *J Am Coll Cardiol.* 2005;46:425–431.
- Pitt B, Zannad F, Remme WJ, Cody R, Castaigne A, Perez A, Palensky J, Wittes J. The effect of spironolactone on morbidity and mortality in patients with severe heart failure: Randomized Aldactone Evaluation Study Investigators. *N Engl J Med.* 1999;341:709–717.
- Sligl W, McAllister FA, Ezekowitz J, Armstrong PW. Usefulness of spironolactone in a specialized heart failure clinic. *Am J Cardiol.* 2004;94:443–447.

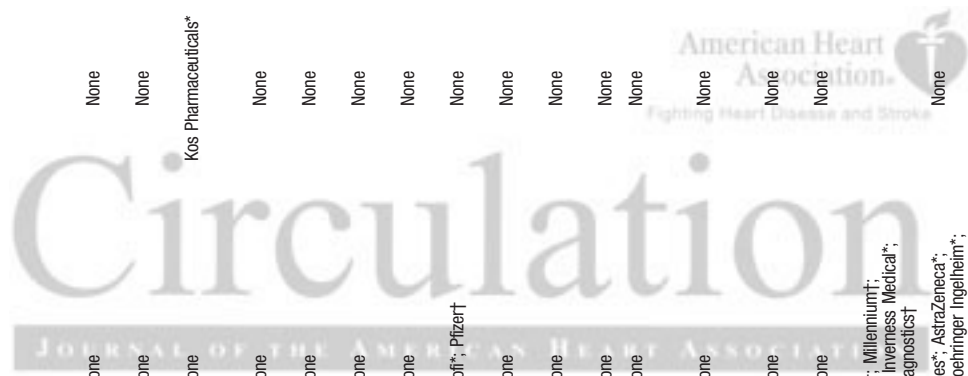
Aldosterone Blocker Meta-Analyses

None reported.

Disclosures

Writing Group Disclosures

Writing Group Member	Employment	Research Grant	Other Research Support	Speakers' Bureau/ Honoraria	Ownership Interest	Consultant/Advisory Board	Other
Lori Mosca	Columbia University	NIH (Pfizer) (no salary)	Cholestech (in kind)*; Didexus (in kind)*; Lipo Science Inc (in kind)*	Abbott*; Formier*; Kos*; Merck*; Schering-Plough*	None	Eli Lilly†; McNeil†; NIH†; Novartis*; Pfizer*; Sanofi-Aventis*; Schering-Plough*†; Unilever*; Waterfront Media*	Educational grants to Columbia University from Cholestech*; Fact Foundation†; Organon†; Pfizer†; Reliant†; Unilever*; Waterfront Media*
Carole L. Banka	La Jolla Institute for Molecular Medicine	None	None	None	None	None	None
Emelia J. Benjamin	Boston University School of Medicine	None	None	None	None	None	None
Kathy Berra	Stanford Center for Research & Disease Prevention	None	Kos Pharmaceuticals*	None	None	None	None
Cheryl Bushnell	Duke University Medical Center	None	None	None	None	None	None
Rowena J. Dolor	Duke University Medical Center	None	None	None	None	Pfizer*, Wyeth*	None
Theodore G. Ganiats	University of California, San Diego	None	None	None	None	Pfizer	None
Antoninette S. Gomes	University of California at Los Angeles	None	None	None	None	None	None
Heather L. Gornik	The Cleveland Clinic Foundation	BMS-Sanofi†; Pfizer†	None	None	None	None	None
Clarissa Gracia	University of Pennsylvania	None	None	None	None	None	None
Martha Gulati	Northwestern University	None	None	None	None	None	None
Constance K. Haan	University of Florida	None	None	None	None	None	None
Debra R. Judelson	Cardiovascular Medical Group of Southern California Centers for Disease Control and Prevention	None	None	Biovail†; Kos*; Novartis*; Pfizer*	None	Novartis*, Pfizer*	Expert Witness*
Nora Keenan	Temple University School of Medicine	None	None	None	None	None	None
Ellie Kalepouris	Johns Hopkins School of Medicine	None	None	None	None	None	None
L. Kristin Newby	Duke University Medical Center	BMS-Sanofi†; Millennium†; Schering-Plough†; Inverness Medical*; Roche Diagnostics†	None	BMS-Sanofi*; Millennium*	None	Biosite*; Eli Lilly*; Inverness Medical*; Proctor & Gamble*; Johnson & Johnson*	None
Suzanne Oparil	University of Alabama, Birmingham	Abbott Laboratories*; AstraZeneca*; Aventis*; Biovail†; Boehringer Ingelheim*; Bristol-Myers Squibb*; Forest Laboratories*; GlaxoSmithKline*; Novartis*; Merck & Co*; Pfizer*; Sankyo Pharma*; Sanofi-Synthelabo*; Schering-Plough*	None	None	None	Bristol-Myers Squibb*; Merck & Co*; Pfizer*; Sanofi*; Novartis*; The Salt Institute*	Encysive Pharmaceuticals BOD*
Pamela Ouyang	Johns Hopkins Bayview Medical Center	None	None	None	None	CV Therapeutics*	None
Mehmet C. Oz	Columbia University	None	None	None	None	None	None



Writing Group Disclosures Continued

Writing Group Member	Employment	Research Grant	Other Research Support	Speakers' Bureau/ Honoraria	Ownership Interest	Consultant/Advisory Board	Other
Diana Pettiti, Ad Hoc Member	Kaiser Permanente Southern California	National Institutes of Health*	None	None	None	None	None
Vivian W. Plinn	Department of Health and Human Services (NIH)	None	None	None	None	None	None
Rita F. Redberg	University of California at San Francisco Medical Center	None	None	Estrasorb*	None	CV Therapeutics*	None
Rosalyn Scott	Drew Medical Center, Los Angeles, Calif	None	None	ABC Center for Women's Health Annual Symposium*	None	ABC Center for Women's Health*	None
Katherine Sheriff†	Drexel University College of Medicine	Novartis†	None	Novartis*	None	None	None
Sidney C. Smith, Jr	University of North Carolina, Chapel Hill	None	None	Bayer*; BMS*; Sanofi*	None	Eli Lilly*; GlaxoSmithKline*; Merck*; Pfizer*; Sanofi-Aventis*	AstraZeneca (DSMB)*
George Sopko	National Heart, Lung, and Blood Institute	None	None	None	None	None	None
Robin H. Steinhorn	Children's Memorial Hospital, Chicago, Ill	None	None	None	None	INO Therapeutics*	None
Neil J. Stone	Northwestern University, Chicago, Ill	None	None	Abbott*; AstraZeneca*; Merck*; Pfizer*; Sanofi*; Schering-Plough*	None	Abbott*; AstraZeneca*; Merck*; Pfizer*; Reliant*; Schering-Plough*; Sonosite*	None
Kathryn A. Taubert	American Heart Association	None	None	None	None	None	None
Barbara A. Todd	University of Pennsylvania	None	None	None	None	None	None
Elaine Urbina	Cincinnati Children's Hospital	None	None	None	None	None	None
Nanette K. Wenger	Emory University School of Medicine	Eli Lilly†; AstraZeneca*; Pfizer*	None	Bristol-Myers Squibb; Eli Lilly; Merck*; NitroMed*; Novartis*; Pfizer*	None	BMS*; CV Therapeutics†; Eli Lilly*; GSK; Kos Pharmaceuticals; Merck*; NitroMed*; Pfizer*; Sanofi-Aventis*; Schering-Plough*	None

This table represents the relationships of writing group members that may be perceived as actual or reasonably perceived conflicts of interest as reported on the Disclosure Questionnaire, which all members of the writing group are required to complete and submit. A relationship is considered to be "significant" if (1) the person receives \$10 000 or more during any 12-month period, or 5% or more of the person's gross income; or (2) the person owns 5% or more of the voting stock or share of the entity, or owns \$10 000 or more of the fair market value of the entity. A relationship is considered to be "modest" if it is less than "significant" under the preceding definition.

*Modest.
†Significant.
‡Representation does not imply endorsement by the American College of Physicians.

Reviewer Disclosures

Reviewer	Representation	Research Grant	Other Research Support	Speakers' Bureau/ Honoraria	Ownership Interest	Consultant/ Advisory Board	Other
Jeffrey L. Anderson	American College of Cardiology Foundation Clinical Expert Consensus Document Task Force	None	None	Bristol-Myers Squibb*; Merck*	None	None	None
Vera Bitner	American College of Cardiology Foundation Prevention Committee	National Heart, Lung, and Blood Institute; Pfizer; Atherogenics†; National Institutes of Health/Kost†	None	None	None	Pfizer*; Reliant*; CV Therapeutics*	None
Roger S. Blumenthal	American College of Cardiology Foundation Prevention Committee, American Heart Association	None	AstraZeneca†; Kos†; Merck†; Pfizer†	None	None	General Electric†; Pfizer†	None
Ann Bolger	American Heart Association	None	None	None	None	None	None
Charles Bridges	Society for Thoracic Surgeons	None	None	None	None	None	None
Doug Campos-Outcalt	American Academy of Family Physicians	None	None	None	None	None	None
Vincent F. Carr	American College of Cardiology Foundation Board of Governors	None	None	None	None	None	None
James I. Cleeman	National Heart, Lung and Blood Institute	None	None	None	None	None	None
Darla E. Danford	National Heart, Lung and Blood Institute	None	None	None	None	None	None
Karen A. Donato	National Heart, Lung and Blood Institute	None	None	None	None	None	None
Mark J. Eisenberg	American College of Cardiology Foundation Clinical Expert Consensus Document Task Force	None	None	None	None	None	None
Victor Ferraris	Society for Thoracic Surgeons	Aventis*; THG Med Co*†; Bayer†; BioMarin†; Guilford†; Medtronic†	None	AstraZeneca*; Bayer*; NATA*; THG Med Co*	None	None	None
Valentin Fuster	World Heart Federation	None	None	None	None	Kereos*; Vasogen*	GlaxoSmithKline Research & Education Foundation for Cardiovascular Disease*
Deborah Grady	American College of Physicians	Eli Lilly*	None	None	None	None	None
Sharonne Hayes	American Heart Association	None	None	None	None	None	None
David Herrington	American Heart Association	None	None	None	None	None	None
Mark Hlaty	American College of Cardiology Foundation Board of Trustees	None	None	None	None	None	None
Suzanne Hughes	American College of Cardiology Foundation Board of Trustees	None	None	Biosite*; Kos*; Pfizer*	None	Guidant*; Johnson & Johnson*; Merck*	Associate editor, Cardiosource
Darwin Labarthe	Centers for Disease Control and Prevention	None	None	None	None	None	None
Robert Lichtenberg	American College of Cardiology Foundation Board of Trustees	None	None	None	None	None	None
Edward J. Rocella	National Heart, Lung and Blood Institute	None	None	None	None	None	None
Samuel J. Shubrooks, Jr	American College of Cardiology Foundation Clinical Expert Consensus Document Task Force	None	None	None	None	None	None
Cynthia Tracy	American College of Cardiology Foundation Clinical Expert Consensus Document Task Force	None	None	None	None	None	None
Janet S. Wright	American College of Cardiology Foundation Board of Trustees	None	None	None	None	None	None
Stanley Zinberg	American College of Obstetricians and Gynecologists	None	None	None	None	None	None

This table represents the relationships of reviewers that may be perceived as actual or reasonably perceived conflicts of interest as reported on the Disclosure Questionnaire, which all reviewers are required to complete and submit.

*Modest.

†Significant.



Stroke Rehabilitation

- Drummond AE, Pearson B, Lincoln NB, Berman P. Ten year follow-up of a randomized controlled trial of care in a stroke rehabilitation unit. *BMJ*. 2005;331:491–492.
- Fagerberg B, Claesson L, Gosman-Hedstrom G, Blomstrand C. Effect of acute stroke unit care integrated with care continuum versus conventional treatment: a randomized 1-year study of elderly patients: the Goteborg 70+ Stroke Study. *Stroke*. 2000;31:2578–2584.
- Kalra L, Eade J. Role of stroke rehabilitation units in managing severe disability after stroke. *Stroke*. 1995;26:2031–2034.
- Kalra L, Evans A, Perez I, Knapp M, Donaldson N, Swift CG. Alternative strategies for stroke care: a prospective randomised controlled trial. *Lancet*. 2000;356:894–899.
- Kalra L, Evans A, Perez I, Melbourn A, Patel A, Knapp M, Donaldson N. Training carers of stroke patients: randomised controlled trial. *BMJ*. 2004;328:1099–1101.
- Langhammer B, Stanghelle JK. Bobath or motor relearning program? A follow-up one and four years post stroke. *Clin Rehabil*. 2003;17:731–734.
- Musico M, Emberti L, Nappi G, Caltagirone C; Italian Multicenter Study on Outcomes of Rehabilitation of Neurological Patients. Early and long-term outcome of rehabilitation in stroke patients: the role of patient characteristics, time of initiation, and duration of interventions. *Arch Phys Med Rehabil*. 2003;84:551–558.
- Ronning OM, Guldvog B. Outcome of subacute stroke rehabilitation: a randomized controlled trial. *Stroke*. 1998;29:779–784.
- Rudd AG, Wolfe CD, Tilling K, Beech R. Randomized controlled trial to evaluate early discharge scheme for patients with stroke. *BMJ*. 1997;315:1039–1044.
- Sulch D, Perez I, Melbourn A, Kalra L. Randomized controlled trial of integrated (managed) care pathway for stroke rehabilitation. *Stroke*. 2000;31:1929–1934.
- Thorsen AM, Holmqvist LW, de Pedro-Cuesta J, von Koch L. A randomized controlled trial of early supported discharge and continued rehabilitation at home after stroke: five-year follow-up of patient outcome. *Stroke*. 2005;36:297–303.

Stroke Rehabilitation Meta-Analyses

- Langhorne P, Williams BO, Gilchrist W, Howie K. Do stroke units save lives? *Lancet*. 1993;342:395–398.
- Langhorne P, Taylor G, Murray G, Dennis M, Anderson C, Bautz-Holter E, Dey P, Indredavik B, Mayo N, Power M, Rodgers H, Ronning OM, Rudd A, Suwanwela N, Widen-Holmqvist L, Wolfe C. Early supported discharge services for stroke patients: a meta-analysis of individual patients' data. *Lancet*. 2005;365:501–506.

- Evans RL, Connis RT, Hendricks RD, Haselkorn JK. Multidisciplinary rehabilitation versus medical care: a meta-analysis. *Soc Sci Med*. 1995;40:1699–1706.
- Early Supported Discharge Trialists. Services for reducing duration of hospital care for acute stroke patients. *Cochrane Database Syst Rev*. 2005;(2):CD000443.
- Anderson C, Ni Mhurchu C, Brown PM, Carter K. Stroke rehabilitation services to accelerate hospital discharge and provide home-based care: an overview and cost analysis. *Pharmacoeconomics*. 2002;20:537–552.
- Foley NC, Teasell RW, Bhogal SK, Doherty T, Speechley MR. The efficacy of stroke rehabilitation: a qualitative review. *Top Stroke Rehabil*. 2003;10:1–18.
- Langhorne P, Duncan P. Does the organization of postacute stroke care really matter? *Stroke*. 2001;32:268–274.
- Lincoln NB, Husbands S, Trescoli C, Drummond AE, Gladman JR, Berman P. Five year follow up of a randomised controlled trial of a stroke rehabilitation unit. *BMJ*. 2000;320:549.
- Outpatient Service Trialists. Therapy-based rehabilitation services for stroke patients at home. *Cochrane Database Syst Rev*. 2003;(1):CD002925.
- Walker MF, Leonardi-Bee J, Bath P, Langhorne P, Dewey M, Corr S, Drummond A, Gilbertson L, Gladman JR, Jongbloed L, Logan P, Parker C. Individual patient data meta-analysis of randomized controlled trials of community occupational therapy for stroke patients. *Stroke*. 2004;35:2226–2232.

Acknowledgments

We are grateful to the Duke Center for Clinical Health Policy Research, Durham, NC, for conducting and summarizing the systematic literature searches. Persons from Duke who contributed to this project include: Rowena J. Dolor, MD, MHS, L. Kristin Newby, MD, MHS; Lori A. Bastian, MD, MPH; Jeffrey S. Berger, MD, MS; Laura Leigh Fitzpatrick, MD, MPH; Camille G. Frazier, MD; R. Julian Irvine, MSM; Radha Goel Kachhy, MD; Wanda Lakey, MD; Lillian F. Lien, MD; Chiara Melloni, MD; Viranga Pathiraja, MPH; John L. Petersen, MD; Zainab Samad, MD; Svati H. Shah, MD, MHS; Tracy Y. Wang, MD, MS; and Karen L. Ziegler, RN, MSN, FNP. The chair also thanks Donna Stephens for her assistance in coordinating the expert panel and Lisa Rehm for assisting with the preparation of the manuscript. The Expert Panel appreciated the thoughtful comments from peer reviewers and sponsoring and endorsing organizations.

KEY WORDS: AHA Scientific Statements ■ women ■ cardiovascular diseases ■ prevention ■ risk factors