Using Nontraditional Risk Factors in Coronary Heart Disease Risk Assessment: U.S. Preventive Services Task Force Recommendation Statement

U.S. Preventive Services Task Force

Description: New recommendation from the U.S. Preventive Services Task Force (USPSTF) on the use of nontraditional, or novel, risk factors in assessing the coronary heart disease (CHD) risk of asymptomatic persons.

Methods: Systematic reviews were conducted of literature since 1996 on 9 proposed nontraditional markers of CHD risk: high-sensitivity C-reactive protein, ankle–brachial index, leukocyte count, fasting blood glucose, periodontal disease, carotid intima–media thickness, coronary artery calcification score on electron-beam computed tomography, homocysteine, and lipoprotein(a). The reviews followed a hierarchical approach aimed at determining which factors could practically and definitively reassign persons assessed as intermediate-risk according to their Framingham score to either a high-risk or low-risk strata, and thereby improve outcomes by means of aggressive risk-factor modification in those newly assigned to the high-risk stratum.

Recommendation: The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of using the nontraditional risk factors studied to screen asymptomatic men and women with no history of CHD to prevent CHD events. (I statement).

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* For a list of the members of the USPSTF, see the **Appendix** (available at www.annals.org).

The U.S. Preventive Services Task Force (USPSTF) makes recommendations about preventive care services for patients without recognized signs or symptoms of the target condition.

It bases its recommendations on a systematic review of the evidence of the benefits and harms and an assessment of the net benefit of the service.

The USPSTF recognizes that clinical or policy decisions involve more considerations than this body of evidence alone. Clinicians and policymakers should understand the evidence but individualize decision making to the specific patient or situation.

Summary of Recommendation and Evidence

The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of using the nontraditional risk factors discussed in this statement to screen asymptomatic men and women with no history of coronary heart disease (CHD) to prevent CHD events. This is an I statement.

The nontraditional risk factors included in this recommendation are high-sensitivity C-reactive protein (hs-CRP), ankle–brachial index (ABI), leukocyte count, fasting blood glucose level, periodontal disease, carotid intima–media thickness (carotid IMT), coronary artery calcification (CAC) score on electron-beam computed tomography (EBCT), homocysteine level, and lipoprotein(a) level.

See the Clinical Considerations section for suggestions for practice concerning the Insufficient Evidence statement.

See the **Figure** for a summary of the recommendation and suggestions for clinical practice.

See **Table 1** for a description of the USPSTF grades and **Table 2** for a description of the USPSTF classification of levels of certainty about net benefit.

See also:

Print
Related articles 483, 496
Summary for Patients. I-38

Web-Only
Appendix
CME quiz
Conversion of graphics into slides
Downloadable recommendation summary

Rationale

Importance

Coronary heart disease is the most common cause of mortality in adults in the United States. Treatment to prevent CHD events by modifying risk factors is currently based on the Framingham risk model, which sorts individuals into low-, intermediate-, or high-risk groups. If the risk model could be improved, treatment might be bet-

ter targeted, thereby maximizing screening benefits and minimizing harms. The most likely opportunity to improve the model is use of additional risk factors to reclassify those in the intermediate-risk group to either high- or low-risk.

Detection

There is insufficient evidence to determine the percentage of persons with an intermediate CHD risk who would be reclassified by screening with nontraditional risk factors other than hs-CRP and ABI.

About 11% of men with an intermediate CHD risk would be reclassified into the high-risk category by hs-CRP screening, and about 12% of men would be reclassified into the low-risk category. National estimates of the number of women who would be reclassified by hs-CRP screening are not reliable because of small study samples. The available meta-analysis of individual data on ABI does not yield a clear picture on the proportion of intermediate-risk men who would be reclassified but does suggest that approximately 10% of women would be reclassified from intermediate to high risk for CHD.

Benefits of Screening and Additional Risk Assessment

The evidence is insufficient to determine the magnitude of any reduction in CHD events and CHD-related deaths obtained by using nontraditional risk factors in CHD screening. This constitutes a critical gap in the evidence for benefit from screening.

Harms of Screening and Additional Risk Assessment

Little evidence is available to determine the harms of using nontraditional risk factors in CHD screening. Harms include lifelong use of medications without proof of benefit but with expense and potential side effects. Statins are the class of medication most commonly used; these medications have been demonstrated to be safe but are associated with the rare but serious side effect of rhabdomyolysis (1). Psychological and other harms may result from being put into a higher risk category for CHD events.

USPSTF Assessment

The USPSTF concludes that the evidence is insufficient to determine the balance between benefits and harms of using nontraditional risk factors in screening for CHD risk.

Although using hs-CRP and ABI to screen men and women with intermediate Framingham CHD risk would reclassify some into the low-risk group and others into the high-risk group, the evidence is insufficient to determine the ultimate effect on the occurrence of CHD events and CHD-related deaths.

Clinical Considerations

Patient Population Under Consideration

The USPSTF intends this recommendation for asymptomatic men and women with no history of CHD, diabetes, or any CHD risk equivalent.

Suggestions for Practice Regarding the I Statement

Clinicians should use the Framingham model to assess CHD risk and to guide risk-based therapy until further evidence is obtained. (See the Other Considerations section for a discussion of risk calculators.)

Because adding nontraditional risk factors to CHD assessment requires additional patient and clinical staff time and effort, routinely screening with nontraditional risk factors could result in lost opportunities for provision of other important health services of proven benefit.

Assessment of Risk

This recommendation is to be used for those who fall into a 10% to 20% (intermediate) 10-year risk category after being screened for CHD risk by using traditional CHD risk factors. Using a risk assessment tool is a key step in managing CHD risk in patients. One validated method of assessing CHD risk is the Framingham model. Persons with low (<10%) Framingham risk scores do not benefit from aggressive risk factor modification, whereas those with high (>20%) Framingham risk scores do benefit. Examples of persons who fall into the intermediate-risk category include a 60-year-old male smoker with untreated hypertension or a 60-year-old female with untreated hypertension and hyperlipidemia. The current recommendation used the Adult Treatment Panel III (ATP III) Framingham risk calculator (available at http://hp2010.nhlbihin.net/atpiii/calculator.asp?usertype=prof) and does not include diabetic populations.

Treatment

About 31% of asymptomatic U.S. men and 7% of asymptomatic U.S. women age 40 to 79 years without diabetes will fall into the intermediate-risk category. No evidence or consensus is available regarding how to treat and counsel these persons.

Useful Resources

Other USPSTF recommendations (1–5) provide guidance for preventing CHD events.

Other Considerations

Costs

Because of limitations in the evidence of effectiveness, little information is available on the cost-effectiveness of using nontraditional risk factors in CHD screening. When the evidence for effectiveness is clearer, evaluating cost-effectiveness will be a research priority.

Research Needs and Gaps

For hs-CRP, ABI, and EBCT, high priority should be given to determining the benefits and harms of aggressive treatment of persons reclassified from intermediate to high risk on the basis of additional information obtained from these tests.

For hs-CRP and ABI, future priority should be given to studies that assess the health effect of reclassifying those

at high and intermediate risk for CHD events into lower-risk categories on the basis of this assessment. Similar studies for EBCT would be useful.

The predictive value and prevalence of periodontal disease, carotid IMT, and lipoprotein(a) should be examined in conjunction with traditional Framingham risk factors for predicting CHD events and death.

Various risk models for CHD are available. Some consider diabetes as a CHD equivalent and others use it as a risk factor for CHD. The predictive value and prevalence of nontraditional risk factors for predicting CHD events and death should be examined specifically in diabetic populations.

Several risk calculators are available that use data from the Framingham studies; 2 of the most commonly used are the ATP III and the traditional Framingham risk calculator (available at www.intmed.mcw.edu/clincalc/heartrisk.html). Evidence for this recommendation relied on the risk estimation from the ATP III calculator.

Discussion

Burden of Disease

In the United States, CHD is the leading cause of death, accounting for 27% of all deaths in 2004 (6). The decision to adopt preventive interventions as well as the intensity of these interventions are guided by a person's 10-year risk for myocardial infarction (MI) or death from CHD. Several risk calculators are available for this purpose, including the ATP III and traditional Framingham calculators (7, 8). The ATP III of the National Cholesterol Education Program algorithm categorizes adults without CHD, diabetes, or noncardiac vascular disease into 3 risk categories, low (<10% risk over 10 years), intermediate (10% to 20% risk over 10 years), and high (>20% risk over 10 years), on the basis of age, sex, systolic blood pressure, serum total cholesterol level, high-density lipoprotein cholesterol level, and cigarette smoking. The traditional Framingham risk calculator uses these risk factors plus diastolic blood pressure and diabetes. Neither risk calculator takes hs-CRP, ABI, leukocyte count, fasting blood glucose, periodontal disease, carotid intimal thickness, EBCT, homocysteine, or lipoprotein(a) into account.

In the United States, approximately 31% of asymptomatic men and 7% of asymptomatic women fall into the intermediate-risk category. It would be useful if those in the intermediate category could be recategorized into the low-risk category to be reassured or into the high-risk category to be prescribed more aggressive medical management (such as treatment to lower low-density lipoprotein level or blood pressure or chemoprophylactic aspirin administration) or possibly invasive interventions (such as coronary catheterization or bypass) if such management were judged beneficial for reclassified persons.

Scope of Review

For this review, the USPSTF addressed the health benefits, including reduction in CHD events, CHD mortality, and overall mortality, of applying nontraditional risk factors to those identified as intermediate-risk by the Framingham CHD risk algorithm. The nontraditional risk factors addressed in this recommendation include ABI, leukocyte count, fasting glucose level, periodontal disease, carotid IMT, EBCT, homocysteine level, lipoprotein(a) level, and hs-CRP level. In addition to direct evidence for benefit, the USPSTF evaluated indirect evidence for the independent predictive value of these risk factors for MI and death from cardiovascular disease (CVD), the prevalence of such risk factors in intermediate- and low-risk persons, the frequency with which those in the low- and intermediate-risk groups would be restratified into high-risk groups, the benefit of aggressive medical management or other treatments of groups identified as high-risk by using these risk factors, and the harms and burdens of risk restratification resulting from use of these risk factors (9).

Effectiveness, in Terms of Health Outcomes, of Using Nontraditional Risk Factors

The USPSTF found no evidence that risk stratification with any of these risk factors, either independently or in addition to Framingham risk scoring, reduces MI or CVD mortality compared with risk stratification and treatment on the basis of Framingham scoring alone. Therefore, the USPSTF examined the evidence for the independent and additive predictive value of each nontraditional risk factor in assessing 10-year risk for MI and CHD mortality. For those risk factors for which evidence for independent or additive predictive value is available, the USPSTF evaluated the evidence for the effect such factors may have on recategorizing intermediate-risk persons into low- or high-risk groups.

Independent Predictive Value of Each Risk Factor

ABI

A recent well-conducted meta-analysis of 16 population-based cohort studies concluded that lower ABI is associated with an increased risk for CVD events and mortality, independent of Framingham risk score (10). However, because of particular aspects of the meta-analysis, this evidence cannot provide an unbiased determination of how many asymptomatic men without known vascular disease would be reclassified from the intermediate classification obtained by using Framingham factors alone to a higher cardiac risk stratum. This analysis did provide an unbiased estimate that approximately 10% of women would be reclassified from intermediate to high CHD risk.

Leukocyte Count

Three good- and 3 fair-quality cohort studies and 1 meta-analysis examined the value of leukocyte count in predicting CHD risk, independent of Framingham risk factors, in participants without known coronary disease

(9). The results of these studies are conflicting: 4 of the studies found an independent predictive value for leukocyte count, whereas the others did not. The USPSTF concluded that there is at least fair evidence of no association between leukocyte count and the risk for coronary events.

Impaired Fasting Glucose

Fair-quality evidence indicates that impaired fasting serum glucose (defined as levels of 5.55 and 6.94 mmol/L [100 and 125 mg/dL]) is a weak predictor of CHD, independent of Framingham risk factors, in persons without diabetes. Two good- and 5 fair-quality studies had conflicting results. One good-quality study showed a weak association between fasting glucose level and CHD after 4 years of follow-up (hazard ratio, 1.09 [95% CI, 1.02 to 1.16] per 0.72-mmol/L [13-mg/dL] increase in fasting glucose level), after adjusting for Framingham risk score without diabetes (11), and the other good-quality study found no association after 8 years of follow-up (adjusted hazard ratio, 1.05 [CI, 0.94 to 1.17]) (12). The remaining fair-quality cohort studies compared patients with elevated fasting glucose level with those with normal fasting glucose level and found no significant increased risk for CHD (13).

Periodontal Disease

Fair-quality evidence indicates that periodontal disease can predict CHD risk independent of Framingham risk factors. A meta-analysis performed by Humphrey and colleagues (14) examined the results from 3 good and 4 fair-quality cohort studies in North America and Finland, which included from 175 to more than 100 000 men and women and had follow-up that ranged from 5 to 21 years; pooled data from 6 of these studies showed a risk ratio of 1.24 (CI, 1.01 to 1.51) for any CHD or CVD event. Of note, these studies did not consistently define periodontal disease or CHD outcomes.

Periodontal bone loss was an important risk factor for subsequent CHD, with 2 studies showing statistically significant relative risks that ranged from 1.36 to 1.90. A meta-analysis of 4 cohort studies showed that tooth loss, a component of periodontal disease, predicts CVD events independent of Framingham risk factors. Investigators observed a 41% increased risk for CHD or CVD events among those with 0 to 10 teeth at baseline, compared with those who had 25 to 32 teeth (combined risk estimate, 1.41 [CI, 1.22 to 1.63]) (14). No information was available about prevalence or applicability in populations at intermediate risk for CHD events.

Carotid IMT

Fair-quality evidence indicates, on the basis of 1 fair- and 2 good-quality population-based longitudinal studies in the United States and the Netherlands, that carotid IMT predicts CHD independent of Framingham risk factors in asymptomatic persons (1300 to 16 000 men and women who showed a relative risk of 1.19 to 3.80) (15–17). Adding carotid IMT scores to a risk prediction equation based on traditional risk factors modestly improved the prediction of subsequent CHD among healthy adults, particularly for men (18). However, the studies that show an association of carotid IMT with CHD outcome have all been done in research settings, and the ability to conduct carotid IMT with precision in nonresearch settings has not been established. No information is available about the prevalence or applicability of carotid IMT to populations at intermediate risk for CHD events.

CAC Score on EBCT

Poor- to fair-quality evidence indicates that higher CAC scores on EBCT predict CHD events independent of Framingham risk factors, on the basis of a systematic review of 8 cohort studies. Three good-quality population cohort studies and 5 fair-quality studies reported that the highest CAC score groups had significantly greater relative risk estimates than the lowest score groups (19–26). Although 3 of the studies met the technical requirements for a good-quality rating, none of them make a convincing case that CAC adds information about intermediate-risk persons. One of the 3 included only low-risk persons. Another study, from the Rotterdam Coronary Calcification Study, used self-selected participants who were classified into 2 categories (10-year Framingham risk of >20% or <20%), and results for the intermediate-risk group (10% to 20%) were therefore not reported separately. Several features of the third study, from the South Bay Heart Watch, limit its applicability to an intermediate risk group. The predictive value of a high CAC score was inconsistent; for example, participants with a Framingham risk score of 11% to 15% and participants with a risk score of 16% to 20% had the same baseline risk (7%). The CAC score also seemed to be imprecise; among participants who had a high CAC score, those with a pretest Framingham risk score of 10% to 15% had a higher posttest risk (19%) than those with a pretest score of 16% to 20%. Finally, participants were potentially self-selected.

The 5 studies rated as fair quality were primarily limited by their use of proxy measures to control for Framingham risk factors or their recruitment of self-selected participants.

In summary, although the 8 included studies consistently reported statistically significant relative risks for coronary events with increasing CAC scores, no study uniformly met all 3 of the following conditions: addressed an intermediate-risk cohort, was population-based or free of selection bias, and appropriately measured or controlled for traditional risk factors (13).

Homocysteine Level

Fair-quality evidence indicates that elevated homocysteine levels predict CHD events after adjustment for

some Framingham risk factors; however, no studies calculated a Framingham risk score, assessed predictive value beyond Framingham risk scoring, or assessed whether homocysteine levels contribute to reclassification from intermediate to another risk category (27). Results from 21 studies in 20 cohorts were conflicting; 16 found a positive association and 5 found no association or a negative association. When all good- or fair-quality studies in participants without previous coronary disease were pooled, each 5-μmol/L increase in homocysteine level was associated with an 18% increase in the risk for coronary events (1.21 [CI, 1.10 to 1.32]) (27). However, none of the studies addressed the prevalence and applicability of homocysteine level in intermediate-risk participants.

Lipoprotein(a) Level

Fair-quality evidence indicates that lipoprotein(a) level predicts CHD events after adjustment for some Framingham risk factors, but no studies calculated a Framingham risk score, assessed predictive value beyond Framingham risk scoring, or assessed whether lipoprotein(a) contributes to reclassification from intermediate to another risk category. In a systematic review and meta-analysis of 4 good- and 11 fair-quality studies, 12 of the 15 found a positive association (13). A meta-analysis of the 15 fair- and good-quality studies that excluded baseline CHD and CVD showed an increased relative risk of 1.59 (CI, 1.29 to 1.97) when comparing lipoprotein(a) levels of 300 mg/L or greater with levels less than 300 mg/L (13). The pooled estimate was similar among men and women, and the association between lipoprotein(a) level and CHD was greater in studies with follow-up times of more than 10 years. No studies attempted to evaluate the prevalence and applicability of lipoprotein(a) level in intermediate-risk participants.

hs-CRP Level

Ten good-quality studies, 13 fair-quality studies, and 2 meta-analyses provide fair-to-good evidence that an elevated hs-CRP level predicts a higher risk for CHD events independent of Framingham risk factors (28). For studies that adjusted for all Framingham risk variables (including diabetes), the summary estimate of relative risk for incident CHD was 1.58 (CI, 1.37 to 1.83) for an hs-CRP level greater than 3.0 mg/L, compared with a level of less than 1.0 mg/L. No trials directly addressed application of hs-CRP in the intermediate-risk population.

Effectiveness of Treatment in Groups Identified as High-Risk by Nontraditional Risk Factors

ABI

The USPSTF found no evidence that using ABI in addition to Framingham-based risk assessment to guide risk factor treatment reduces CVD events more than using Framingham risk assessment alone to guide treatment.

Homocysteine Level

The USPSTF found no evidence that treating persons with a high homocysteine level improves outcomes. In several well-conducted trials (29, 30), homocysteine therapy did not prevent CHD events in persons with known heart disease. Trials are currently under way to evaluate the strategy of treating elevated homocysteine levels for primary prevention of CHD (31, 32).

Periodontal Disease

The USPSTF found no evidence regarding the efficacy of preventive dental care or treatment for periodontal disease in reducing CHD events.

Carotid IMT

Lipid-lowering therapy has been shown to be associated with slowing of carotid IMT.

CAC Score on EBCT

Statins have not been shown to decrease mortality in patients screened and found to have elevated CAC scores, and evidence conflicts about whether statins produce the intermediate outcome of reduction in CAC scores (33, 34).

hs-CRP Level

JUPITER (Justification for the Use of Statins in Prevention: an Intervention Trial Evaluating Rosuvastatin) (35) did not address the issue of whether using hs-CRP in addition to Framingham risk assessment would reduce CVD events beyond the use of Framingham risk assessment alone, and no other treatment studies answer this question. However, there are observational studies or small controlled trials showing that weight loss, exercise training, or both have been associated with reductions in hs-CRP level (36). Intervention trials in those with MI have shown that statins decrease hs-CRP level (as well as low-density lipoprotein cholesterol level), and that this reduction is independently associated with slower atherosclerotic progression (37).

Potential Harms of Risk Assessment

The USPSTF found no studies that addressed the harms of assessing nontraditional risk factors and using this information for risk assessment. Electron-beam computed tomography uses the equivalent radiation of 10 chest x-rays. Potential adverse effects of using these risk factors include false-positive test results and labeling, resulting in unnecessary invasive diagnostic procedures (such as coronary angiography), and side effects of aggressive risk factor management (such as the adverse effects of antihypertensive and lipid-lowering drugs). In particular, the potential harm associated with the long-term decrease of low-density lipoprotein cholesterol to very low levels is cause for concern.

Estimate of Magnitude of Net Benefit

C-reactive protein is the only risk marker for which magnitude of benefit could be estimated by modeling based on sufficient information about predictive value and prevalence among persons at intermediate risk. Buckley and colleagues include analyses in their review (28) that model the additive benefit of hs-CRP to traditional Framingham risk factors in those at intermediate risk. The model predicts that 11% of men in the intermediate group would be reclassified as high-risk; if those reclassified men are provided intensive risk-reduction therapy, it could avert 47.8 CHD events over 10 years per 1000 among men age 40 to 79 years. The net benefit of hs-CRP testing was felt to be of uncertain magnitude because of the lack of information on harms of testing and the unknown effect of intensive therapy on those who are defined as high-risk by virtue of hs-CRP testing.

RECOMMENDATIONS OF OTHERS

The American Heart Association encourages Framingham risk assessment in asymptomatic persons, advises against CAC assessment by EBCT in asymptomatic persons at low and high risk (those at <10% and >20% 10-year risk, respectively), and states that "it may be reasonable to consider use of CAC measurement in such patients based on available evidence that demonstrates incremental risk prediction information in this selected (intermediate-risk) patient group. This conclusion is based on the possibility that such patients might be reclassified to a higher-risk status based on high CAC score, and that subsequent patient management may be modified" (38).

A joint statement by the American Heart Association and the Centers for Disease Control and Prevention recommends against the use of hs-CRP as a risk marker in the general population and against the use of other inflammatory markers or acute-phase reactants for CHD risk prediction (Class III, Level of Evidence C). The recommendation states that "measurement of hs-CRP is an independent marker of risk and, in those judged at intermediate risk by global risk assessment (10 to 20% risk of CHD per 10 years), at the discretion of the physician, may help direct further evaluation and therapy in the primary prevention of CVD. The benefits of such therapy based on this strategy remain uncertain. (Class IIa, Level of Evidence B)" (39).

The ATP III states that homocysteine level, hs-CRP level, carotid IMT, and CAC score on EBCT may be useful in certain circumstances but does not recommend incorporating any emerging risk factors into risk assessment for all persons receiving primary prevention risk assessment (40).

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Requests for Single Reprints: Reprints are available from the USPSTF Web site (www.preventiveservices.ahrq.gov).

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Figure. **Using Nontraditional Risk Factors in Coronary Heart Disease Risk Assessment: Clinical Summary of U.S. Preventive Services Task Force Recommendation.**

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USPSTF

USING NONTRADITIONAL RISK FACTORS IN CORONARY HEART DISEASE RISK ASSESSMENT CLINICAL SUMMARY OF U.S. PREVENTIVE SERVICES TASK FORCE RECOMMENDATION

Population	**Asymptomatic men and women with no history of coronary heart disease (CHD), diabetes, or any CHD risk equivalent**
I statement: Insufficient Evidence	**No recommendation because of insufficient evidence**

Risk Assessment	This recommendation applies to adult men and women classified at intermediate 10-year risk for CHD (10% to 20%) by traditional risk factors.
Importance	Coronary heart disease (CHD) is the most common cause of death in adults in the United States. Treatment to prevent CHD events by modifying risk factors is currently based on the Framingham risk model. If the classification of individuals at intermediate risk could be improved by using additional risk factors, treatment to prevent CHD might be targeted more effectively. Risk factors not currently part of the Framingham model (nontraditional risk factors) include high-sensitivity C-reactive protein (hs-CRP), ankle–brachial index (ABI), leukocyte count, fasting blood glucose level, periodontal disease, carotid intima–media thickness, coronary artery calcification score on electron-beam computed tomography, homocysteine level, and lipoprotein(a) level.
Rationale for No Recommendation	There is insufficient evidence to determine the percentage of intermediate-risk individuals who would be reclassified by screening with nontraditional risk factors, other than hs-CRP and ABI. For individuals reclassified as high-risk on the basis of hs-CRP or ABI scores, data are not available to determine whether they benefit from additional treatments. Little evidence is available to determine the harms of using nontraditional risk factors in screening. Potential harms include lifelong use of medications without proven benefit and psychological and other harms from being misclassified in a higher risk category.
Considerations for Practice	Clinicians should continue to use the Framingham model to assess CHD risk and guide risk-based preventive therapy. Adding nontraditional risk factors to CHD assessment would require additional patient and clinical staff time and effort. Routinely screening with nontraditional risk factors could result in lost opportunities to provide other important health services of proven benefit.
Relevant USPSTF Recommendations	USPSTF recommendations on risk assessment for CHD, the use of aspirin to prevent cardiovascular disease, and screening for high blood pressure can be accessed at www.preventiveservices.ahrq.gov.

For a summary of the evidence systematically reviewed in making these recommendations, the full recommendation statement, and supporting documents, please go to www.preventiveservices.ahrq.gov.

Table 1. **What the USPSTF Grades Mean and Suggestions for Practice**

Grade	Definition	Suggestions for Practice
A	The USPSTF recommends the service. There is high certainty that the net benefit is substantial.	Offer/provide this service.
B	The USPSTF recommends the service. There is high certainty that the net benefit is moderate or there is moderate certainty that the net benefit is moderate to substantial.	Offer/provide this service.
C	The USPSTF recommends against routinely providing the service. There may be considerations that support providing the service in an individual patient. There is moderate or high certainty that the net benefit is small.	Offer/provide this service only if other considerations support offering or providing the service in an individual patient.
D	The USPSTF recommends against the service. There is moderate or high certainty that the service has no net benefit or that the harms outweigh the benefits.	Discourage the use of this service.
I statement	The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of the service. Evidence is lacking, of poor quality, or conflicting, and the balance of benefits and harms cannot be determined.	Read the clinical considerations section of the USPSTF Recommendation Statement. If the service is offered, patients should understand the uncertainty about the balance of benefits and harms.

Table 2. **USPSTF Levels of Certainty Regarding Net Benefit**

Level of Certainty*	Description
High	The available evidence usually includes consistent results from well-designed, well-conducted studies in representative primary care populations. These studies assess the effects of the preventive service on health outcomes. This conclusion is therefore unlikely to be strongly affected by the results of future studies.
Moderate	The available evidence is sufficient to determine the effects of the preventive service on health outcomes, but confidence in the estimate is constrained by such factors as: the number, size, or quality of individual studies inconsistency of findings across individual studies limited generalizability of findings to routine primary care practice lack of coherence in the chain of evidence. As more information becomes available, the magnitude or direction of the observed effect could change, and this change may be large enough to alter the conclusion.
Low	The available evidence is insufficient to assess effects on health outcomes. Evidence is insufficient because of: the limited number or size of studies important flaws in study design or methods inconsistency of findings across individual studies gaps in the chain of evidence findings that are not generalizable to routine primary care practice a lack of information on important health outcomes. More information may allow an estimation of effects on health outcomes.

* The USPSTF defines *certainty* as "likelihood that the USPSTF assessment of the net benefit of a preventive service is correct." The net benefit is defined as benefit minus harm of the preventive service as implemented in a general primary care population. The USPSTF assigns a certainty level based on the nature of the overall evidence available to assess the net benefit of a preventive service.

Appendix: U.S. Preventive Services Task Force

Members of the U.S. Preventive Services Task Force at the time this recommendation was finalized† were Ned Calonge, MD, MPH, *Chair* (Colorado Department of Public Health and Environment, Denver, Colorado); Diana B. Petitti, MD, MPH, *Vice Chair* (Arizona State University, Phoenix, Arizona); Thomas G. DeWitt, MD (Children's Hospital Medical Center, Cincinnati, Ohio); Kimberly D. Gregory, MD, MPH (Cedars-Sinai Medical Center, Los Angeles, California); Russell Harris, MD, MPH (University of North Carolina School of Medicine, Chapel Hill, North Carolina); George Isham, MD, MS (HealthPartners, Minneapolis, Minnesota); Michael L. LeFevre, MD, MSPH (University of Missouri School of Medicine, Columbia, Missouri); Carol Loveland-Cherry, PhD, RN (University of Michigan School of Nursing, Ann Arbor, Michigan); Lucy N. Marion, PhD, RN (Medical College of Georgia, Augusta, Georgia); Virginia A. Moyer, MD, MPH (Baylor College of Medicine, Houston, Texas); Judith K. Ockene, PhD (University of Massachusetts Medical School, Worcester, Massachusetts); George F. Sawaya, MD (University of California, San Francisco, San Francisco, California); Albert L. Siu, MD, MSPH (Mount Sinai Medical Center, New York, New York); Steven M. Teutsch, MD, MPH (Merck & Company, West Point, Pennsylvania); and Barbara P. Yawn, MD, MSc (Olmsted Medical Center, Rochester, Minnesota).

† For a list of current Task Force members, go to www.ahrq.gov/clinic/uspstfab.htm.