Screening Asymptomatic Adults With Resting or Exercise Electrocardiography: A Review of the Evidence for the U.S. Preventive Services Task Force

Roger Chou, MD; Bhaskar Arora, MD; Tracy Dana, MLS; Rongwei Fu, PhD; Miranda Walker, MA; and Linda Humphrey, MD

Background: Coronary heart disease is the leading cause of death in adults. Screening for abnormalities by using resting or exercise electrocardiography (ECG) might help identify persons who would benefit from interventions to reduce cardiovascular risk.

Purpose: To update the 2004 U.S. Preventive Services Task Force evidence review on screening for resting or exercise ECG abnormalities in asymptomatic adults.

Data Sources: MEDLINE (2002 through January 2011), the Cochrane Library database (through the fourth quarter of 2010), and reference lists.

Study Selection: Randomized, controlled trials and prospective cohort studies.

Data Extraction: Investigators abstracted details about the study population, study design, data analysis, follow-up, and results and assessed quality by using predefined criteria.

Data Synthesis: No study evaluated clinical outcomes or use of risk-reducing therapies after screening versus no screening. No study estimated how accurately resting or exercise electrocardiography classified participants into high-, intermediate-, or low-risk groups, compared with traditional risk factor assessment alone. Sixty-three prospective cohort studies evaluated abnormalities on resting or exercise ECG as predictors of cardiovascular events after adjustment for traditional risk factors. Abnormalities on resting ECG (ST-segment or T-wave abnormalities, left ventricular hypertrophy, bundle branch block, or left-axis deviation) or exercise ECG (ST-segment depression with exercise, chronotropic incompetence, abnormal heart rate recovery, or decreased exercise capacity) were associated with increased risk (pooled hazard ratio estimates, 1.4 to 2.1). Evidence on harms was limited, but direct harms seemed minimal (for resting ECG) or small (for exercise ECG). No study estimated harms from subsequent testing or interventions, although rates of angiography after exercise ECG ranged from 0.6% to 2.9%.

Limitations: Only English-language studies were included. Statistical heterogeneity was present in several of the pooled analyses.

Conclusion: Abnormalities on resting or exercise ECG are associated with an increased risk for subsequent cardiovascular events after adjustment for traditional risk factors, but the clinical implications of these findings are unclear.

Primary Funding Source: Agency for Healthcare Research and Quality.


For author affiliations, see end of text.

Coronary heart disease (CHD) is the leading cause of death in U.S. adults (1, 2). Many persons do not experience symptoms before a major first CHD event, such as sudden cardiac arrest, myocardial infarction, congestive heart failure, or unstable angina (3). Traditional Framingham risk factors (age, sex, blood pressure, serum total or low-density lipoprotein cholesterol concentration, high-density lipoprotein cholesterol concentration, cigarette smoking, and diabetes) can help predict future CHD events but do not explain all of the excess risk (4, 5). Supplementing traditional risk factor assessment with other methods, including resting or exercise electrocardiography (ECG), might help better guide use of risk-reduction therapies in asymptomatic persons without known CHD (6).

In 2004, the U.S. Preventive Services Task Force (USPSTF) recommended against screening with resting or exercise ECG in adults at low risk for CHD (D recommendation) and found insufficient evidence for a recommendation in adults at increased risk (I recommendation) (7). To update its recommendations, the USPSTF commissioned a new evidence review in 2009 to systematically evaluate the current evidence on screening with resting or exercise ECG. Our report differs from earlier USPSTF reviews because we focused on studies that adjusted for traditional cardiovascular risk factors, performed meta-analysis, and evaluated whether screening with ECG in improves risk reclassification. The key questions, analytic framework (Appendix Figure, available at www.annals.org), and scope were developed in accordance with previously published USPSTF processes and methods. The key questions were as follows:

1. What are the benefits of screening for abnormalities on resting or exercise electrocardiography compared with no screening on coronary heart disease outcomes?
Context
What are the potential benefits of screening electrocardiography (ECG)?

Contribution
Studies included in this systematic review showed that some abnormalities found on resting or exercise ECG were independent predictors of future cardiovascular events. No study compared clinical outcomes or use of risk-reducing therapies between persons who did and did not receive screening ECG. No studies assessed whether ECG findings better classified patients into meaningful risk groups than did traditional risk factor assessment alone.

Implication
Some abnormalities on ECG are risk factors for cardiovascular events, but the benefits and clinical implications of routine ECG screening are not clear.

—The Editors

2. How does the identification of high-risk persons via resting or exercise electrocardiography affect use of treatments to reduce cardiovascular risk?

3. What is the accuracy of resting or exercise electrocardiography for stratifying persons into high-, intermediate- and low-risk groups?

4. What are the harms of screening with resting or exercise electrocardiography?

METHODS
We followed a standard protocol for this review. Detailed search strategies, selection criteria, evidence tables, quality assessments, and forest plots are available in a technical report available at the Agency for Healthcare Research and Quality (AHRQ) Web site (8).

Data Sources
We searched MEDLINE from 2002 through January 2011 and the Cochrane Library database through the fourth quarter of 2010 to identify relevant English-language articles. We also reviewed reference lists of relevant articles and included studies from the previous USPSTF review that met inclusion criteria.

Study Selection
We included studies that evaluated persons without symptoms of CHD, reported results separately for asymptomatic persons, or had fewer than 10% of participants with symptoms. Randomized, controlled trials and controlled observational studies were included if they evaluated the effects of screening with resting or exercise ECG versus no screening on clinical outcomes (benefits or harms) or the use of lipid-lowering therapy or aspirin (interventions for which recommended use varies by assessed cardiovascular risk). Prospective cohort studies that reported rates of cardiovascular outcomes and controlled for at least 5 of the 7 Framingham cardiovascular risk factors (male sex, age, tobacco use, diabetes, hypertension, total or low-density lipoprotein cholesterol concentration, and high-density lipoprotein cholesterol concentration) by means of restriction (such as by enrolling only male participants) or adjustment were also included. Two reviewers independently evaluated each study to determine inclusion eligibility. Only published studies were included.

Data Extraction and Quality Assessment
One investigator abstracted details about the population, study design, analysis, and duration of follow-up; the Framingham risk factors and other adjusted confounding factors; and results. A second investigator reviewed the data abstraction for accuracy. Two investigators independently applied criteria developed by the USPSTF (9) to rate the quality of each study as good, fair, or poor. Discrepancies in quality ratings were resolved by consensus.

Data Synthesis and Analysis
Using methods developed by the USPSTF, we assessed the aggregate internal validity (quality) of the body of evidence for each key question as good, fair, or poor, on the basis of the number, quality, and size of the studies; consistency of results between studies; and directness of evidence (9). To evaluate the benefits of screening for asymptomatic CHD, we focused on (in order of preference) death from CHD, death from cardiovascular disease, nonfatal myocardial infarction, all-cause mortality, stroke, other cardiovascular outcomes (such as congestive heart failure), and composite cardiovascular outcomes. The accuracy of screening with ECG for identifying the presence or degree of asymptomatic atherosclerosis was not evaluated because of its unclear clinical implications. Participant anxiety, labeling, and rates and consequences of subsequent tests and procedures were evaluated to assess the harms of screening. Other USPSTF reviews (10, 11) have evaluated adverse outcomes associated with lipid-lowering therapy and aspirin.

Several methods were used to assess the incremental value of resting or exercise ECG (12). We evaluated how adding screening with ECG to traditional risk factor assessment affects reclassification of persons as being at high (10-year risk for CHD events >20%), medium (10% to 20%), or low (<10%) risk compared with classification on the basis of traditional risk factors alone (13). The recent literature (13–16) has emphasized understanding the frequency and accuracy by which people are reclassified into different risk categories, which can have an important effect on clinical decisions (6, 17). We also evaluated how adding resting or exercise ECG to traditional risk factor assessment changed the c-statistic (which measures how accurately a risk assessment method separates persons with from those without a disease or outcome [18]), when this was reported, and whether screening with ECG improves calibration (the degree to which predicted and observed risk estimates agree [15]).
Most studies did not provide sufficient data to estimate the degree and accuracy of reclassification. They instead provided an estimate of risk associated with the presence (vs. the absence) of abnormalities on ECG after adjustment for traditional risk factors. We used Stata/IC, version 11.1 (StataCorp, College Station, Texas), to conduct meta-analyses of abnormalities on ECG that were evaluated by at least 3 studies of (in order of preference) adjusted estimates of risk for CHD death, death from cardiovascular disease, nonfatal myocardial infarction, all-cause mortality, or composite cardiovascular outcomes, using the Dersimonian–Laird random-effects model (19). Heterogeneity was estimated by using the $I^2$ statistic (20). If at least 5 studies evaluated an electrocardiographic abnormality, potential sources of heterogeneity were assessed by stratifying studies according to the outcome evaluated, study quality, and use of different definitions for the abnormality being evaluated. Sensitivity analyses were performed that excluded outlier studies, if present. Meta-regression was also performed on the proportion of men enrolled in the study, the number of traditional risk factors adjusted for (range, 5 to 7), and the duration of follow-up.

**Role of the Funding Source**

Our study was funded by AHRQ under a contract to support the work of the USPSTF. Staff at AHRQ and members of the USPSTF helped to develop the scope of the work and reviewed draft manuscripts. Approval from AHRQ was required before manuscript could be submitted for publication, but the authors are solely responsible for the content and the decision to submit it for publication.

**RESULTS**

The **Figure** shows the results of the evidence search and selection process.

---

**Figure. Summary of evidence search and selection.**

Abstracts of potentially relevant articles identified through Ovid MEDLINE, Cochrane databases*, or other sources† ($n = 979$)

- Excluded ($n = 662$)
  - Abstracts excluded ($n = 252$)
    - Contextual only: 24
    - Wrong population: 45
    - Wrong intervention: 33
    - Wrong outcome: 63
    - Wrong study design for KQ: 24
    - Wrong publication type (review article, editorial, results reported elsewhere, or no original data): 21
    - Not in English, but otherwise relevant: 3
  - Statistical adjustment for <5 Framingham risk factors: 39

- Full-text articles reviewed with inclusion and exclusion criteria for the KQs ($n = 317$)
  - Included articles for KQ 1: Screening outcomes ($n = 0$)
  - Included articles for KQ 2: Use of treatment ($n = 0$)
  - Included articles for KQ 3: Stratifying individuals ($n = 63$)
    - Studies evaluating risk reclassification: 0
    - Prospective cohort studies addressing ECG findings and risk for cardiovascular events: 63 (2 studies assessed both resting and exercise ECG)
  - Included articles for KQ 4: Harms ($n = 2$)

ECG = electrocardiography; KQ = key question.

* Includes the Cochrane Central Register of Controlled Trials and the Cochrane Database of Systematic Reviews.
† Includes studies identified from reference lists or suggested by experts.
Screening Asymptomatic Adults With Resting or Exercise Electrocardiography

Key Question 1
What are the benefits of screening for abnormalities on resting or exercise electrocardiography compared with no screening on coronary heart disease outcomes?

Similar to the previous USPSTF reviewers (21), we found no randomized, controlled trials or prospective cohort studies on the effects of screening asymptomatic adults with resting or exercise ECG versus no screening on clinical outcomes.

Key Question 2
How does the identification of high-risk persons via resting or exercise electrocardiography affect use of treatments to reduce cardiovascular risk?

Like the previous USPSTF reviewers (21), we identified no studies that evaluated how screening affects use of lipid-lowering therapy or aspirin.

Key Question 3
What is the accuracy of resting or exercise electrocardiography for stratifying persons into high-, intermediate- and low-risk groups?

No study estimated how accurately resting or exercise electrocardiography classified participants into high-, intermediate-, or low-risk groups compared with traditional risk factor assessment alone, or provided sufficient data for constructing risk-stratification tables (13). One study in women (22) found that adding resting ECG findings to the Framingham risk score increased the c-statistic for prediction of future CHD events from 0.69 to 0.74, but the CIs for the estimates overlapped substantially. Another study in men and women (23) reported a c-statistic of 0.73 for traditional risk factor assessment by using the European Systematic Coronary Risk Evaluation (SCORE) alone versus 0.76 for SCORE plus exercise ECG variables (CIs not reported).

Twenty-seven prospective cohort studies of resting ECG, reported in 28 publications (22, 24–50), and 38 prospective cohort studies of exercise ECG (23, 24, 34, 51–85) evaluated abnormalities on baseline ECG and risk for subsequent cardiovascular events; 2 studies (24, 34) evaluated both resting and exercise ECG (Supplement Tables 1 and 2, available at www.annals.org). Excluding double-counted populations, we evaluated resting ECG in 173,710 participants and exercise ECG in 91,746 participants. Duration of follow-up ranged from 3 years (31, 79) to 56 years (27). Ten studies of resting ECG (22, 24, 29, 30, 32, 34, 36, 44, 45, 50) and 19 studies of exercise ECG (24, 34, 51, 52, 54–58, 60, 63, 67–69, 72, 75, 78, 80, 83) were rated good-quality; the rest were rated fair-quality. The most common methodological shortcomings were no description of handling of participants with interpretable ECG results (43 of 62 studies), loss to follow-up (39 of 62 studies), or race in reports of baseline demographic characteristics (31 of 62 studies). Three studies (70, 71, 79), discussed separately, only enrolled persons with diabetes mellitus or impaired fasting glucose.

Several abnormalities on resting ECG were associated with an increased risk for subsequent cardiovascular events (Table 1). The pooled adjusted hazard ratio (HR) was 1.9 (95% CI, 1.4 to 2.5; I² = 62%) for persons with resting ST-segment abnormalities (5 studies [27, 29, 33, 36, 39]), 1.6 (CI, 1.3 to 1.8; I² = 56%) for those with T-wave abnormalities (6 studies [27, 29, 33, 36, 39, 45]), and 1.9 (CI, 1.6 to 2.4; I² = 50%) for persons with either ST-segment or T-wave abnormalities (7 studies [28, 31, 33, 41, 42, 49, 50]).

Left ventricular hypertrophy (LVH), left-axis deviation, and bundle branch block on resting ECG were each associated with a similar risk for subsequent cardiovascular events. The pooled adjusted HR was 1.6 (CI, 1.1 to 1.9; I² = 0%) for left-axis deviation (3 studies [29, 41, 50]), and 1.5 (CI, 0.98 to 2.3; I² = 46%) for bundle branch block (4 studies [29, 39, 41, 42]).

Six studies (22, 29, 37, 38, 41, 50) evaluated major or minor abnormalities on resting ECG and subsequent cardiovascular events, but the results could not be pooled.

**Table 1.** Summary of Pooled Risk Estimates for Subsequent Cardiovascular Events With Abnormalities on Resting or Exercise ECG

<table>
<thead>
<tr>
<th>Type of ECG and Abnormality</th>
<th>Studies (References), n</th>
<th>Pooled Adjusted HR (95% CI)</th>
<th>I² Value, %</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Resting ECG</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ST-segment abnormalities</td>
<td>5 (27, 29, 33, 36, 39)</td>
<td>1.9 (1.4–2.5)</td>
<td>62</td>
</tr>
<tr>
<td>T-wave abnormalities</td>
<td>6 (27, 29, 33, 39, 45)</td>
<td>1.6 (1.3–1.8)</td>
<td>56</td>
</tr>
<tr>
<td>ST-segment or T-wave abnormals</td>
<td>7 (28, 31, 33, 41, 42, 49, 50)</td>
<td>1.9 (1.6–2.4)</td>
<td>50</td>
</tr>
<tr>
<td>Left ventricular hypertrophy</td>
<td>8 (24, 25, 29, 35, 36, 39, 41, 50)</td>
<td>1.6 (1.3–2.0)</td>
<td>46</td>
</tr>
<tr>
<td>Bundle branch block</td>
<td>4 (29, 39, 41, 42, 67, 68, 69)</td>
<td>1.5 (0.98–2.3)</td>
<td>46</td>
</tr>
<tr>
<td>Left-axis deviation</td>
<td>3 (29, 41, 50)</td>
<td>1.5 (1.1–1.9)</td>
<td>0</td>
</tr>
<tr>
<td><strong>Exercise ECG</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ST-segment depression with exercise</td>
<td>12 (23, 24, 52, 55, 56, 58, 59, 63, 69, 72, 76, 81)</td>
<td>2.1 (1.6–2.9)</td>
<td>71</td>
</tr>
<tr>
<td>Chronotropic incompetence</td>
<td>4 (51, 52, 66, 72)</td>
<td>1.4 (1.3–1.6)</td>
<td>0</td>
</tr>
<tr>
<td>Abnormal heart rate recovery*</td>
<td>3 (23, 54, 74)</td>
<td>1.5 (1.3–1.9)</td>
<td>0</td>
</tr>
<tr>
<td>Decreased exercise capacity or fitness</td>
<td>6 (23, 53, 61, 69, 77, 85)</td>
<td>Range, 1.7–3.1 (could not be pooled)</td>
<td>–</td>
</tr>
</tbody>
</table>

EGC = electrocardiography; HR = hazard ratio.
* Estimate is for all-cause mortality; cardiovascular-specific outcomes could not be pooled.
because the definitions of major and minor varied (Table 2). Two studies (29, 41) reported an association between presence of a major abnormality on resting ECG and CHD death over 10 years (HR, 2.3 [CI, 1.5 to 3.7] and 3.1 [CI, 1.9 to 5.1], respectively), and a third (22) reported an association with CHD events over 5 years (HR, 3.0 [CI, 2.0 to 4.5]). In each study, the risk estimate for minor abnormalities was weaker than the estimate for major abnormalities. For example, 1 study (41) reported HRs of 1.8 (CI, 1.3 to 2.5) for minor abnormalities and subsequent CHD death and 3.1 (CI, 1.9 to 5.1) for major abnormalities. In some studies (29, 50), the association between minor abnormalities and subsequent CHD events did not reach statistical significance.

Other abnormalities on resting ECG have been evaluated, including prolonged QT interval, ischemic changes, atrial fibrillation, right-axis deviation, Q waves, ventricular premature contractions, and high resting heart rate (26, 32, 34, 38–40, 42, 46–48, 86), but these were evaluated in too few studies or were too variably defined to draw firm conclusions about their usefulness as predictors. Several studies were not included in the meta-analyses because they evaluated nonpooled outcomes or electrocardiographic abnormalities. One study (43) found ST-segment abnormalities (but not T-wave abnormalities or LVH) associated with increased risk for stroke over 0 to 30 years of follow-up (HR, 3.4 [CI, 2.1 to 5.4]), and another (32) found an association between ST-segment or T-wave abnormalities and incident congestive heart failure (HR, 1.6 [CI, 1.3 to 2.1]). In 1 study, incomplete bundle branch block (HR, 1.4 [CI, 1.0 to 2.0]) and complete bundle branch block (HR, 1.7 [CI, 1.3 to 2.4]) were associated

Table 2. Major and Minor Abnormalities on ECG as Predictors of Cardiovascular Events

<table>
<thead>
<tr>
<th>Study, Year (Reference)</th>
<th>Study Name</th>
<th>Sample Size, n</th>
<th>Mean Age (Range), y</th>
<th>Men, %</th>
<th>Mean Duration of Follow-up, y</th>
<th>Definition (Prevalence) of ECG Abnormalities</th>
<th>HR for Events With Major or Minor ECG Abnormalities Compared With No Abnormalities (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>De Bacquer et al, 1998 (29)</td>
<td>Belgian Inter-University Research on Nutrition and Health</td>
<td>9954</td>
<td>48 (25–74)</td>
<td>52</td>
<td>10</td>
<td>Minnesota code 4.1, 4.2, 5.1, 5.2, 6.1, 6.2, 7.1, 7.2, 8.1, or 8.3 (29%)</td>
<td>CHD death: major, 2.3 (1.5–3.7); minor, 1.1 (0.77–1.7)</td>
</tr>
<tr>
<td>Denes et al, 2007 (22)</td>
<td>Women’s Health Initiative</td>
<td>14 749</td>
<td>63 (50–79)</td>
<td>0</td>
<td>5.2</td>
<td>Novacode 1.4, 1.5, 1.7, 1.8, 1.9, 2.3.1, 2.3.2, 2.4, 3.1.0, 3.1.1, 3.2.0, 3.3.0, 3.3.1, 5.1, 5.2, 5.3, 5.4, 5.5, 5.6, 6.1.1, 6.1.4, 6.1.7, or 6.1.8 (6.2%)</td>
<td>CHD death: minor, 1.8 (0.2–4.5); CVD death: major, 2.3 (1.8–3.0); minor, 1.4 (1.1–1.7)</td>
</tr>
<tr>
<td>Liao et al, 1988 (37)</td>
<td>The Chicago Heart Association Detection Project in Industry</td>
<td>17 633</td>
<td>51</td>
<td>55</td>
<td>11.5</td>
<td>Minnesota code 6.1 or 6.2, 7.1, 7.2, or 7.4, 8.3, 8.1, 4.1, or 5.1 or 5.2 (11.1%)</td>
<td>CHD death: major, 3.7 for men and 1.9 for women; minor, 2.1 for men and 1.5 for women CVD death: major, 3.4 for men and 2.1 for women; minor, 2.1 for men and 1.5 for women All-cause mortality: major, 2.4 for men and 1.4 for women; minor, 1.7 for men and 1.2 for women</td>
</tr>
<tr>
<td>Macfarlane et al, 2007 (38)</td>
<td>West of Scotland Coronary Prevention Study</td>
<td>5835</td>
<td>55</td>
<td>100</td>
<td>4.9</td>
<td>Not assessed</td>
<td>CHD death or nonfatal myocardial infarction: minor, 1.7 (1.3–2.3) All-cause mortality: minor, 2.1 (1.5–3.1)</td>
</tr>
<tr>
<td>Menotti et al, 2001 (41), and Menotti and Secchiarlicia, 1997 (42)</td>
<td>The FINE Study</td>
<td>1785</td>
<td>Not reported (65–84)</td>
<td>100</td>
<td>10</td>
<td>Minnesota code 1.1, 4.1, 5.1, 6.8, 7.1, 7.4, or 8.3 (8%)</td>
<td>CHD death: major, 3.1 (1.9–5.1); minor, 1.8 (1.3–2.5)†</td>
</tr>
<tr>
<td>Sutherland et al, 1993 (50)</td>
<td>Charleston Heart Study</td>
<td>993</td>
<td>48 (35–74)</td>
<td>100</td>
<td>30</td>
<td>Minnesota code 4.1, 4.2, 5.1, 5.2, 7.1, 7.2, 7.4, 8.1, or 8.3 (9%)</td>
<td>CHD death: major, 2.7 (1.5–5.0) for white men and 2.0 (0.93–4.1) for black men; minor, 1.3 (0.74–2.1) for white men and 0.58 (0.24–1.4) for black men All-cause mortality: major, 2.1 (1.4–3.1) for white men and 1.4 (0.91–2.1) for black men; minor, 1.2 (0.92–1.7) for white men and 0.79 (0.52–1.2) for black men</td>
</tr>
</tbody>
</table>

CHD = coronary heart disease; CVD = cardiovascular disease; ECG = electrocardiography; FINE = Finland, Italy, and the Netherlands; HR = hazard ratio.

* No CIs were reported.
† Compared with absent or marginal abnormalities.
with greater risk for congestive heart failure than no bundle branch block (30). Another study (44) found new or incident LVH on 6-year follow-up ECG to be associated with increased risk for CHD death.

Several abnormalities on exercise ECG were also associated with an increased risk for subsequent cardiovascular events (Table 1). The most frequently evaluated abnormality, ST-segment depression with exercise (12 studies [23, 24, 52, 55, 56, 58, 59, 63, 69, 72, 76, 81]), was associated with an adjusted pooled HR of 2.1 (CI, 1.6 to 2.9).

In 4 studies (51, 52, 66, 72), chronotropic incompetence on exercise ECG (defined as inability to reach 85% or 90% of maximum predicted heart rate) was associated with a pooled adjusted HR of 1.4 (CI, 1.3 to 1.6; $I^2 = 0\%$) for subsequent cardiovascular events. Abnormal heart rate recovery (defined as a decrease of $<12$ beats/min from peak heart rate 1 minute into recovery or of $<42$ beats/min after 2 minutes) was associated with a pooled adjusted HR for all-cause mortality of 1.5 (CI, 1.3 to 1.9; $I^2 = 0\%$) in 3 studies (23, 54, 74). Studies that were excluded from the meta-analysis because they evaluated ECG findings as multicategory or continuous variables also found that lower maximum heart rate (24, 34, 84) and slower return to baseline heart rate were associated with increased risk (34).

Decreased exercise capacity or fitness (on the basis of metabolic equivalents or watts achieved or exercise duration) was consistently associated with increased risk for subsequent cardiovascular events or mortality in 9 studies (23, 53, 60, 61, 69, 77, 81, 82, 85), but results could not be pooled because of the different methods of measurement and analysis. In 6 studies (23, 53, 61, 69, 77, 85), adjusted HRs for subsequent cardiovascular events or all-cause mortality ranged from 1.7 to 3.1 for lower versus higher exercise capacity categories. In 5 studies (23, 60, 69, 81, 82), lower exercise capacity was also predictive when analyzed as a continuous variable.

Two studies (63, 72) found ventricular ectopy during or after exercise ECG to be associated with increased risk for cardiovascular events (HR, 2.5 [CI, 1.6 to 3.9] and 1.7 [CI, 1.1 to 2.6], respectively). One study each found decreased peak oxygen pulse (53), lower Duke treadmill score (60), and “abnormal” (undefined) exercise ECG (53) associated with increased risk for cardiovascular events. Finally, 1 study (73) found that having both low heart rate recovery and low metabolic equivalents was a stronger predictor of death from cardiovascular disease than having either abnormality alone.

Stratifying the studies in the meta-analyses by type of cardiovascular outcome assessed, study quality, or restriction to men resulted in estimates that were similar to the overall pooled estimates and did not reduce observed statistical heterogeneity. An exception was LVH on resting ECG, for which estimates were lower for the 4 studies rated good-quality (HR, 1.2 [CI, 0.9 to 1.7]; $I^2 = 31\%$) (24, 29, 36, 50) than for the 4 rated fair-quality (HR, 2.0 [CI, 1.6 to 2.5]; $I^2 = 0\%$; $P$ for difference = 0.03) (25, 35, 39, 41). Variability in the proportion of men, duration of follow-up, or number of traditional risk factors adjusted for also did not explain the between-study variance in estimates. Excluding the outlier trials (23, 72) from the meta-analysis of ST-segment depression on exercise ECG did not reduce statistical heterogeneity or result in different estimates. In studies that stratified results by sex (26, 29, 33, 37, 39, 42, 52, 53, 73, 85), estimates of risk associated with various abnormalities in resting and exercise ECG were either similar for men and women or had overlapping CIs.

Two studies (70, 79) evaluated exercise ECG in diabetic participants. One study (70) found that 1-mm ST-segment depression or elevation with exercise was associated with increased risk for CHD death (HR, 2.1 [CI, 1.3 to 3.3]). The second study (79) also found that exercise-induced ST-segment depression was associated with increased risk for CHD events, but the sample size was small (86 participants) and the CI was very wide (HR, 21 [CI, 2 to 204]). One other study (71) found higher fitness on exercise ECG (on the basis of maximum exercise duration and metabolic equivalents) was associated with a lower risk for all-cause mortality than low fitness (HR, about 0.65 for either moderate or high fitness) in women with impaired fasting glucose or undiagnosed diabetes.

**Key Question 4**

What are the harms of screening with resting or exercise electrocardiography testing?

**Direct Harms**

No studies reported harms directly associated with resting ECG. For exercise ECG, 1 study with 377 participants (87), included in the previous USPSTF review, reported no complications as a direct result of screening. Survey data that included symptomatic participants undergoing exercise ECG reported arrhythmia in fewer than 0.2%, acute myocardial infarction in 0.04%, and sudden cardiac death in 0.01% (88). The overall risk for experiencing sudden death or an event that requires hospitalization has been estimated to be 1 per 10 000 tests (88).

**Harms Associated With Subsequent Tests or Interventions**

We identified no studies on harms associated with follow-up testing or interventions after a screening resting or exercise ECG. In 9 studies (87, 89–96), summarized in the previous USPSTF evidence review (97), rates of subsequent angiography in primarily asymptomatic participants after an abnormal exercise ECG ranged from 0.6% to 2.9%, excluding an outlier study of hypertensive veterans (94) with a 13% angiography rate. Two subsequent studies of screening exercise ECG (23, 55), comprising 4605 participants, found that 0.6% and 1.7% of the total sample subsequently had angiography, and 0.1% (4 of 3554) and
Table 3. Summary of Evidence

<table>
<thead>
<tr>
<th>Key Question</th>
<th>Studies, n</th>
<th>Overall Quality Rating</th>
<th>Summary of Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. What are the benefits of screening for abnormalities on resting or exercise electrocardiography compared with no screening on coronary heart disease outcomes?</td>
<td>None</td>
<td>–</td>
<td>No randomized, controlled trials or controlled observational studies of screening asymptomatic adults for CHD with resting or exercise ECG versus no screening were identified.</td>
</tr>
<tr>
<td>2. How does the identification of high-risk persons via resting or exercise electrocardiography affect use of treatments to reduce cardiovascular risk?</td>
<td>None</td>
<td>–</td>
<td>No studies were identified that evaluated how screening patients for CHD by using resting or exercise ECG affects use of interventions to reduce cardiovascular risk.</td>
</tr>
<tr>
<td>3. What is the accuracy of resting or exercise electrocardiography for stratifying persons into high-, intermediate- and low-risk groups?</td>
<td>None on risk reclassification, 2 on changes in the c-statistic, and 63 on risk associated with abnormalities on ECG</td>
<td>Fair</td>
<td>No study estimated how accurately resting or exercise ECG plus traditional risk factor assessment classified patients into high-, intermediate-, or low-risk groups compared with classification on the basis of traditional risk factor assessment alone, or provided sufficient data for risk stratification tables to estimate risk reclassification rates. Two studies found resting or exercise ECG findings plus traditional risk factor assessment resulted in a slight increase in the c-statistic compared with traditional risk factor assessment alone. Pooled analyses showed that abnormalities on resting ECG (ST-segment or T-wave abnormalities, left ventricular hypertrophy, bundle branch block, or left-axis deviation) or exercise ECG (ST-segment depression with exercise, failure to reach maximum target heart rate, or low exercise capacity) are associated with an increased risk (pooled hazard ratio estimates from 1.4 to 2.1) for subsequent cardiovascular events, after adjustment for traditional risk factors.</td>
</tr>
<tr>
<td>4. What are the harms of screening with resting or exercise electrocardiography?</td>
<td>2 studies</td>
<td>Poor</td>
<td>No studies reported harms directly associated with screening with resting ECG. One study (included in the previous report) found no complications in 377 patients who had screening with exercise ECG. No studies reported downstream harms associated with follow-up testing or interventions after screening with resting or exercise ECG.</td>
</tr>
</tbody>
</table>

CHD = coronary heart disease; ECG = electrocardiography.

0.5% (5 of 1051), respectively, had a subsequent revascularization procedure.

None of these studies estimated complications associated with angiography or revascularization procedures. On the basis of large, population-based registries that include symptomatic persons (98), the risk for any serious adverse event as a result of angiography is about 1.7%; this includes risk for death (0.1%), myocardial infarction (0.05%), stroke (0.07%), and arrhythmia (0.4%).

Coronary angiography, computed tomography angiography, and myocardial perfusion imaging are associated with radiation exposure that could increase cancer risk. Coronary angiography is associated with an average effective radiation dose of 7 mSv and myocardial perfusion imaging with a dose of 15.6 mSv (99).

Persons who have an abnormal screening result and undergo additional testing, but do not have coronary artery disease, are subjected to potential harms without the possibility of benefit. One study included in the previous USPSTF review (96) found severe coronary artery disease in 15% of participants who had angiography; another (89) found that 55% of participants who underwent angiography had greater than 50% occlusion and 37% had greater than 70% occlusion in at least 1 coronary artery. A recent, large (nearly 400,000 participants) study (100) of a primarily symptomatic population (70%) who had angiography found that 39% had no coronary artery disease (defined as <20% stenosis).

**Discussion**

Table 3 summarizes our results. Like the previous USPSTF reviewers, we found no studies that evaluated clinical outcomes or use of lipid-lowering therapy or aspirin after screening with resting or exercise ECG compared with no screening. Another critical research gap is that no studies directly evaluated the incremental value of adding screening with ECG to traditional risk factor assessment for accurately classifying persons into different risk categories. The lack of information on reclassification is critical from a clinical perspective because decisions regarding therapies for reducing cardiovascular risk are often based on whether a person is classified as having low (<10% risk over the next 10 years), intermediate, or high (>20%) risk for future CHD events. On the basis of current data, we cannot determine the degree to which resting or exercise ECG accurately moves a person from one risk category to another, rather than yielding a more precise estimate in a risk category (which is less clinically useful). For example, in populations at very low (<5%) risk for CHD events,
such as most young adults, even a doubling of risk would not move a person from a lower to a higher risk category. Similarly, abnormalities on resting or exercise ECG are unlikely to change management decisions for persons who are already at high risk on the basis of traditional risk factor assessment. The greatest potential benefits of screening with ECG would be for intermediate-risk persons, because the presence of abnormalities would shift such persons into a high-risk group for whom additional interventions might be warranted. Two studies (22, 23) evaluated the effect on a high-risk group for whom additional interventions might be indicated as high-, intermediate-, or low-risk (13).

Most of the available evidence evaluated the association between abnormalities on resting ECG (ST-segment abnormalities, T-wave abnormalities, LVH, left-axis deviation, or bundle branch block) or exercise ECG (ST-segment depression with exercise, chronotropic incompetence, impaired heart rate recovery, or decreased exercise capacity) and risk for subsequent cardiovascular events, after adjustment for traditional Framingham risk factors. The adjusted pooled HRs ranged from around 1.4 to around 2.1 for various abnormalities on resting or exercise ECG. Despite strong evidence that such abnormalities are associated with increased risk beyond that accounted for by assessment of traditional risk factors, understanding the usefulness of screening requires additional information on the reclassification that would result and on whether such reclassification would lead to clinical actions that improve patient outcomes (6).

Evidence on harms associated with screening ECG is limited. However, serious direct harms seem to be minimal with resting ECG (other than possible anxiety or labeling) and small or rare with exercise ECG (for example, ischemia or injuries associated with exercise), assuming appropriate attention to contraindications to exercise testing and adherence to standard safety precautions. However, the potential downstream harms from additional testing or interventions that result from screening could be of greater concern. Some patients have angiography after a screening ECG and are therefore exposed to the potential harms related to that procedure, which include bleeding, radiation exposure, and contrast allergy or nephropathy. Patients who receive lipid-lowering therapy or aspirin because of screening ECG are exposed to the harms related to those interventions. Evidence on downstream harms associated with screening is not available, although data indicate that 0.6% to 1.7% of patients subsequently have angiography. A small proportion (<1%) of patients have revascularization with coronary artery bypass graft surgery or a percutaneous coronary intervention after screening exercise ECG, despite the risks of these interventions and their lack of benefits in asymptomatic persons (23, 55).

Our evidence review has limitations. We included only English-language studies, which could have resulted in language bias. A random-effects model was used to perform meta-analysis, because studies that evaluated the risk associated with various rest or exercise ECG abnormalities varied in quality and duration of follow-up, assessed different patient populations and cardiovascular outcomes, and used different methods to define the abnormalities. Although statistical heterogeneity was present in several of the meta-analyses, stratified analyses and meta-regression had little effect on estimates and conclusions. Referral bias could have resulted in underestimates of risk if identification of electrocardiographic abnormalities led to increased use of treatments effective at reducing cardiovascular risk.

Studies are needed to directly evaluate how screening with resting or exercise ECG affects clinical outcomes compared with no screening. Any screening study should also evaluate harms, including downstream harms related to additional testing and therapies. Although randomized trials would be desirable, well-conducted, nonrandomized prospective studies could also be informative. In the absence of direct evidence on the clinical effects of screening, data from future studies on risk prediction should enable estimates of reclassification, from which potential benefits of screening might be extrapolated on the basis of the known efficacy of interventions in high-risk populations. Decisions to allocate resources to update this or similar reviews on the usefulness of screening ECG might be predicated on the availability of such evidence, identified by using literature scans or other methods. Many of the studies included in our review evaluated large sample sizes over long periods, and the information needed to assess reclassification rates in these databases probably already exists. Reanalyzing preexisting databases would therefore be a more efficient method for obtaining information on reclassification than would initiating new studies.

From the Oregon Evidence-based Practice Center, Oregon Health & Science University, and Portland Veterans Affairs Medical Center, Portland, Oregon.

Acknowledgment: The authors thank AHRQ Medical Officer Tracy Wolff, MD, MPH; USPSTF Leads Susan Curry, PhD, Michael LeFevre, MD, MSPH, Joy Melnikow, MD, MPH, and Sanford (Sandy) Schwartz, MD, for their contributions to this report; and Christina Bougatsos, BS, Oregon Evidence-based Practice Center, for her assistance in preparing this report.


Potential Conflicts of Interest: Dr. Chou: Grant: Agency for Healthcare Research and Quality; Consultancy: Consumers Union. Dr. Arora: Support for travel to meetings for the study or other purposes: Agency for Healthcare Research and Quality. Ms. Dana, Dr. Fu, and Ms. Walker:
References


Screening Asymptomatic Adults With Resting or Exercise Electrocardiography


82. Savonen KP, Lakka TA, Laukkanen JA, Rauramaa TH, Salonen JT, Rauramaa R. Effectiveness of workload at the heart rate of 100 beats/min in predicting cardiovascular mortality in men aged 42, 48, 54, or 60 years at baseline. Am J Cardiol. 2007;100:563-8. [PMID: 17697806]


86. Moller CS, Byberg L, Sundstrom J, Lind L. T wave abnormalities, high body mass index, current smoking and high lipoprotein (a) levels predict the development of major abnormal Q/QS patterns 20 years later. A population-based study. BMC Cardiovasc Disord. 2006;6:10. [PMID: 16519804]


Appendix Figure. Analytic framework and key questions.

Asymptomatic adults

- Assess cardiac risk on the basis of traditional risk factors: age, sex, total and high-density lipoprotein cholesterol concentration, systolic blood pressure, diabetes, and smoking

- History, physical examination, and assessment of risk on the basis of traditional risk factors
  - Low risk
  - Intermediate risk
  - High risk

- Perform screening test for CAD

- New risk after screening test
  - Low risk
  - Intermediate risk
  - High risk

- Change in CHD risk-reducing treatment

- Change in CHD health outcomes

- Harms

KQ 1

KQ 2

KQ 3

KQ 4

CAD = coronary artery disease; CHD = coronary heart disease; ECG = electrocardiography; KQ = key question.