

Screening for Atrial Fibrillation

Updated Evidence Report and Systematic Review for the US Preventive Services Task Force

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IMPORTANCE Atrial fibrillation (AF), the most common arrhythmia, increases the risk of stroke.

OBJECTIVE To review the evidence on screening for AF in adults without prior stroke to inform the US Preventive Services Task Force.

DATA SOURCES PubMed, Cochrane Library, and trial registries through October 5, 2020; references, experts, and literature surveillance through October 31, 2021.

STUDY SELECTION Randomized clinical trials (RCTs) of screening among asymptomatic persons without known AF or prior stroke; test accuracy studies; RCTs of anticoagulation among persons with AF; systematic reviews; and observational studies reporting harms.

DATA EXTRACTION AND SYNTHESIS Two reviewers assessed titles/abstracts, full-text articles, and study quality and extracted data; when at least 3 similar studies were available, meta-analyses were conducted.

MAIN OUTCOMES AND MEASURES Detection of undiagnosed AF, test accuracy, mortality, stroke, stroke-related morbidity, and harms.

RESULTS Twenty-six studies (N = 113 784) were included. In 1 RCT (n = 28 768) of twice-daily electrocardiography (ECG) screening for 2 weeks, the likelihood of a composite end point (ischemic stroke, hemorrhagic stroke, systemic embolism, all-cause mortality, and hospitalization for bleeding) was lower in the screened group over 6.9 years (hazard ratio, 0.96 [95% CI, 0.92-1.00]; *P* = .045), but that study had numerous limitations. In 4 RCTs (n = 32 491), significantly more AF was detected with intermittent and continuous ECG screening compared with no screening (risk difference range, 1.0%-4.8%). Treatment with warfarin over a mean of 1.5 years in populations with clinical, mostly persistent AF was associated with fewer ischemic strokes (pooled risk ratio [RR], 0.32 [95% CI, 0.20-0.51]; 5 RCTs; n = 2415) and lower all-cause mortality (pooled RR, 0.68 [95% CI, 0.50-0.93]) compared with placebo. Treatment with direct oral anticoagulants was also associated with lower incidence of stroke (adjusted odds ratios range, 0.32-0.44) in indirect comparisons with placebo. The pooled RR for major bleeding for warfarin compared with placebo was 1.8 (95% CI, 0.85-3.7; 5 RCTs; n = 2415), and the adjusted odds ratio for major bleeding for direct oral anticoagulants compared with placebo or no treatment ranged from 1.38 to 2.21, but CIs did not exclude a null effect.

CONCLUSIONS AND RELEVANCE Although screening can detect more cases of unknown AF, evidence regarding effects on health outcomes is limited. Anticoagulation was associated with lower risk of first stroke and mortality but with increased risk of major bleeding, although estimates for this harm are imprecise; no trials assessed benefits and harms of anticoagulation among screen-detected populations.

JAMA. 2022;327(4):368-383. doi:10.1001/jama.2021.21811

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Atrial fibrillation (AF) is the most common arrhythmia and may be symptomatic or asymptomatic.¹ Increasing age is a risk for AF,² and persons with AF have an increased risk for thromboembolic stroke and related morbidity and mortality.³ The treatment for people with symptomatic AF involves rate and rhythm control; anticoagulation for stroke prevention may also be warranted when benefits outweigh the harms.^{4,5}

The primary rationale for screening for AF is to identify asymptomatic persons before a thromboembolic event occurs. In 2018, the US Preventive Services Task Force (USPSTF) concluded that the evidence was insufficient to assess the balance of benefits and harms of screening for AF with electrocardiography (ECG) in older adults (I statement).⁶ This updated review evaluated the current evidence on screening for AF for populations and settings relevant to primary care in the US to inform an updated recommendation by the USPSTF.

Methods

Scope of the Review

The analytic framework and key questions (KQs) that guided the review are shown in [Figure 1](#). Detailed methods, evidence tables, and contextual information are available in the full evidence report.⁷

Data Sources and Searches

PubMed and the Cochrane Library were searched for English-language articles published from May 1, 2017, through October 5, 2020. ClinicalTrials.gov and the World Health Organization International Clinical Trials Registry Platform were also searched. To supplement systematic electronic searches (eMethods page 1 in the [Supplement](#)), reference lists of pertinent articles and studies suggested by reviewers were searched. Article alerts and targeted searches of journals to identify major studies published in the interim that may affect the conclusions or understanding of the evidence and the related USPSTF recommendation were used as part of ongoing surveillance. The last surveillance was conducted on October 31, 2021.

Study Selection

Two investigators independently reviewed titles, abstracts, and full-text articles using prespecified inclusion criteria for each KQ (eMethods page 16 in the [Supplement](#)); disagreements were resolved by discussion or by a third reviewer. English-language studies that met all study selection criteria, were fair or good methodological quality, and were conducted in countries categorized as very highly developed by the 2018 United Nations Human Development Index⁸ were eligible. Studies included in the prior 2018 review for the USPSTF were reassessed against the study selection and methodological quality criteria for this update. Studies performed in emergency department, inpatient, and procedural settings were excluded.

For KQ1, KQ2, and KQ4, the focus was on unselected or explicitly asymptomatic adults 50 years or older without known AF or history of prior stroke or transient ischemic attack. For these KQs, randomized clinical trials (RCTs) or nonrandomized controlled intervention studies of screening (compared with no screening or nonsystematic screening) that reported health outcomes (KQ1), detection of AF (KQ2), or harms of screening (KQ4) were included. For screening accuracy (KQ3), case-control studies were excluded because these designs have a high risk of bias, and studies for which

persons who were symptomatic or who had known AF comprised the majority of the population were excluded. For KQs 1 through 4, studies assessing index tests feasible for use in or referable from primary care including single-point-in-time tests typically conducted in an office setting (eg, single- or 12-lead ECG, automated heart rhythm assessment built into oscillometric blood pressure monitors or devices using photoplethysmography such as pulse oximeters), intermittent or continuous ambulatory strategies using ECG or other technologies, and 2-stage screening approaches were included. Pulse palpation and other components of a standard physical examination (eg, heart auscultation) were not eligible because the USPSTF considers these usual care. For KQ1 and KQ2, a no-screening or usual care (which could include pulse palpation) comparator was required. For KQ3, studies were required to use 1 of the following reference tests: 12-lead ECG interpreted by a cardiologist, continuous ambulatory ECG interpreted by a cardiologist, or implantable cardiac monitor.

For treatment effectiveness (KQ5) and harms (KQ6), RCTs and nonrandomized controlled intervention studies or systematic reviews of RCTs comparing anticoagulation with placebo or no treatment that reported health outcomes or harms were included. The scopes of these KQs were revised for this update to remove antiplatelet therapy as an eligible treatment because it is no longer standard practice for primary stroke prevention in AF. For harms (KQ6), large prospective cohort studies or systematic reviews of prospective cohort studies were also included.

Data Extraction and Quality Assessment

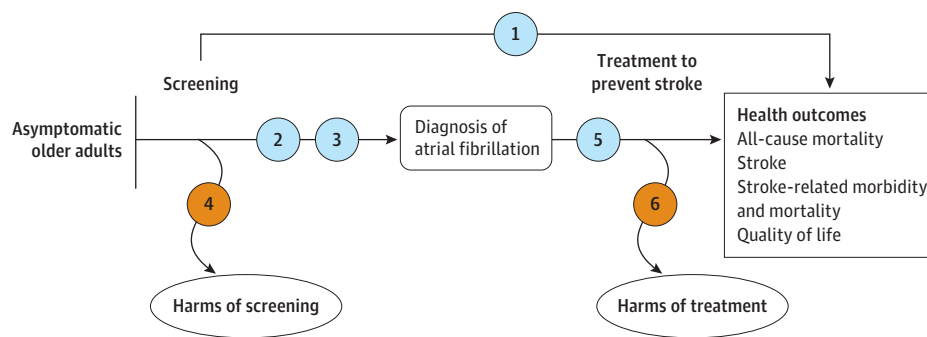
For each included study, 1 reviewer abstracted relevant study characteristics (ie, population, intervention, comparator) and data for eligible outcomes into a structured form. A second reviewer checked all data for completeness and accuracy. Two senior reviewers independently assessed each study's methodological quality using predefined criteria established by the USPSTF (eMethods page 19 in the [Supplement](#)) and others.^{9,10} Disagreements in study quality ratings were resolved through discussion or by a third senior reviewer. Detailed study quality assessments are provided in eTables 1 through 21 in the [Supplement](#).

Data Synthesis and Analysis

Data were synthesized in tabular and narrative forms. When at least 3 similar studies were available, a quantitative synthesis was performed using random-effects models with the inverse-variance weighted method of DerSimonian and Laird in Stata version 16 (StataCorp) to generate pooled estimates of the relative risk ratio (RR).¹¹ The I^2 statistic was calculated to assess statistical heterogeneity in effects.^{12,13} Significance testing was based on the exclusion of the null value by the 95% CI around the pooled estimate; all testing was 2-sided.

The strength of evidence was assessed as high, moderate, low, or insufficient using methods developed for the USPSTF and the Agency for Healthcare Research and Quality Evidence-based Practice Center program.¹⁴ These methods specify the assessment of methodological quality of studies, consistency of results between studies, precision of findings, risk of reporting bias, and limitations of the body of evidence for each intervention/comparison and major outcome of interest. Two senior reviewers independently developed initial assessments of strength of evidence; disagreements were resolved through discussion or input of a third senior reviewer.

Figure 1. Analytic Framework: Screening for Atrial Fibrillation



Key questions

- 1 Does screening for AF with selected tests improve health outcomes (ie, reduce all-cause mortality, reduce morbidity or mortality from stroke, or improve quality of life) in asymptomatic older adults?
 - a. Does improvement in health outcomes vary for subgroups defined by stroke risk, age, sex, or race and ethnicity?
- 2 Does systematic screening for AF with selected tests identify older adults with previously undiagnosed AF more effectively than usual care?
- 3 What is the accuracy of selected screening tests for diagnosing AF in asymptomatic adults?
- 4 What are the harms of screening for AF with selected tests in older adults?
 - a. Do the harms of screening vary for subgroups defined by stroke risk, age, sex, or race and ethnicity?
- 5 What are the benefits of anticoagulation therapy on health outcomes in asymptomatic, screen-detected older adults with AF?
 - a. Do the benefits of anticoagulation vary for subgroups defined by stroke or bleeding risk, age, sex, race and ethnicity, or AF burden (ie, number of episodes, duration of episodes, and proportion of time spent in AF)?
- 6 What are the harms of anticoagulation therapy in asymptomatic, screen-detected older adults with AF?
 - a. Do the harms of anticoagulation therapy vary for subgroups defined by stroke risk or bleeding risk, age, sex, race and ethnicity, or AF burden?

AF indicates atrial fibrillation.

Results

Twenty-six studies (N = 113 784) from 33 publications were included (Figure 2).^{4,15-42} Twelve of these studies were new to this update.³³⁻⁴⁶ Three RCTs reported on the benefits of screening (KQ1); 8 RCTs reported on the diagnostic yield of screening (KQ2); 9 studies reported on the accuracy of various screening strategies (KQ3); 4 RCTs and 1 cohort study reported on the harms of screening (KQ4); 5 RCTs and 5 systematic reviews reported on the health benefits of treatment with anticoagulation (KQ5); and 5 RCTs, 6 systematic reviews, and 1 cohort study reported on the harms of treatment with anticoagulation (KQ6). A list of full-text articles screened but excluded is provided in the Supplement (page 101).

Benefits of Screening

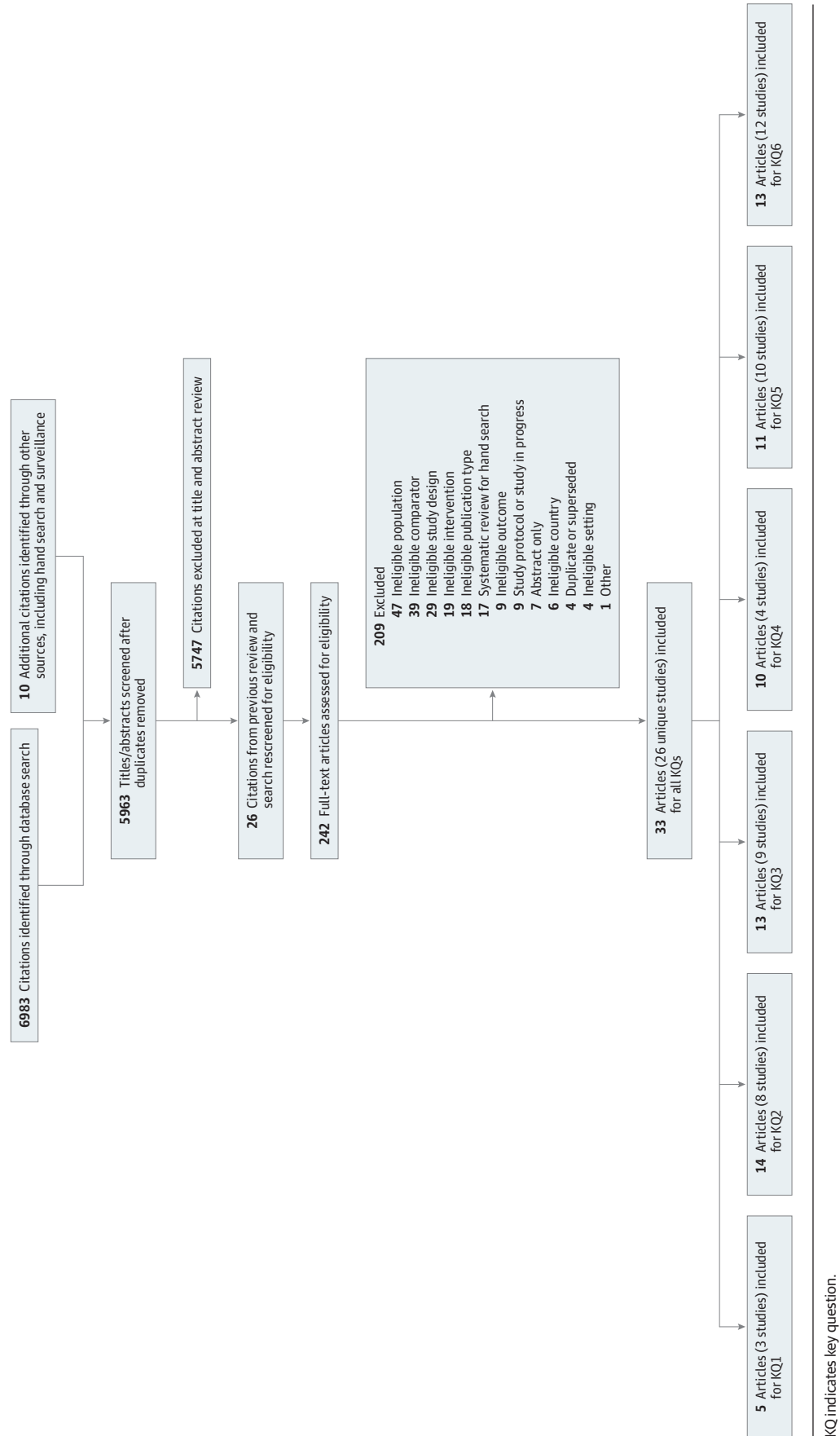
Key Question 1. Does screening for AF with selected tests improve health outcomes (ie, reduce all-cause mortality, reduce morbidity or mortality from stroke, or improve quality of life) in asymptomatic older adults?

Key Question 1a. Does improvement in health outcomes vary for subgroups defined by stroke risk, age, sex, or race and ethnicity?

Three RCTs randomized persons to screening vs no screening; however, only 1 of these studies was designed and powered for evaluating health outcomes.^{44,45,47} Although the other 2 RCTs were powered for evaluating differences in the detection of AF (a KQ2 outcome), they reported a limited amount of information related to health outcomes, but events were rare.^{32,43} Findings from these 2 RCTs are reported in eTables 22 through 25 in the Supplement.

The fair-quality STROKESTOP study randomized adults aged 75 or 76 years living in 2 regions of Sweden to an invitation to screening (n = 14 387) or to a control group that did not receive an invitation to screening (n = 14 381).^{44,45,47} At baseline, 12.1% of the intervention group and 12.8% of the control group had known AF.⁴⁴ Of those invited to screening, 51.3% participated in the screening intervention, which was 2 weeks of twice-daily intermittent single-lead ECG monitoring with a handheld device for 30 seconds.^{44,45,47} The intervention was not masked, and outcome ascertainment was through national health registry data; outcome assessment was not formally masked, and outcomes were not centrally adjudicated. The primary outcome was originally specified as ischemic stroke but was changed by study investigators in 2017 before any data analysis to a composite end point that included ischemic stroke, hemorrhagic stroke, systemic embolism, bleeding leading to hospitalization, and

Figure 2. Literature Search Flow Diagram: Screening for Atrial Fibrillation



all-cause mortality. At a median follow-up of 6.9 years, the rate of composite end point events was significantly lower in the invitation-to-screening group (5.45 events/100 person-years) compared with the control group (5.68 events/100 person-years) with an unadjusted hazard ratio (HR) of 0.96 (95% CI, 0.92-1.00; $P = .045$).⁴⁴ No significant differences were observed between the invitation-to-screening group and the control group for any of the individual outcomes contributing to the composite end point (eTable 25 in the Supplement).⁴⁴ No findings were reported for the subgroup of participants without known AF at baseline.

Detection of AF

Key Question 2. Does systematic screening for AF with selected tests identify older adults with previously undiagnosed AF more effectively than usual care?

Eight fair-quality RCTs in 14 articles ($n = 86\,590$) were included^{15-19,29,32,33,36,41,43-45,47}; 5 RCTs were new to this update.^{33,36,41,43-45,47} Study, population, and intervention characteristics are reported in Table 1, with detailed characteristics reported in eTables 22 through 24 in the Supplement. Six trials^{32,33,36,41,43-45,47} compared ECG screening with no screening, 1 trial²⁹ compared ECG screening with pulse palpation chart reminders, and 1 trial¹⁵⁻¹⁹ compared both. Four trials^{15-19,29,36,41} used a 1-time approach to screening (eg, single-lead ECG during an office visit), 2 trials evaluated intermittent screening with a handheld ECG twice daily for 2 weeks^{44,45,47} or for 1 year,³² and 2 trials^{33,43} used 2 rounds of a continuous patch ECG patch for 2 weeks; 1 of these trials also included twice-daily blood pressure screening with automated AF detection.^{32,43}

Across studies, the detection of previously unknown AF was reported at 4 to 12 months of follow-up. Findings are summarized in Figure 3 and in eTable 25 in the Supplement. Screening identified numerically more cases of AF compared with no screening in the 3 cluster-randomized trials using 1-time approaches to screening compared with no screening (absolute risk difference range, 0.06-0.60 percentage points; RR range, 1.04-1.58)^{15-19,36,41}; however, this difference was statistically significant only in the Screening for Atrial Fibrillation in the Elderly (SAFE) trial ($n = 14\,802$).¹⁵⁻¹⁹ In 2 of these trials, only 10.7%³⁶ and 44.5%⁴¹ of eligible participants at intervention practices received the screening test. Detection of previously unknown AF was significantly higher in the 4 trials comparing intermittent or continuous ECG screening approaches with no screening, with absolute risk differences ranging from 1.0% to 4.8% and RRs ranging from 1.1 to 11.2.^{32,33,43-45,47} Intervention fidelity ranged from 51.3% to 74.0% in the intermittent screening trials and from 65.0% to 79.0% in the continuous screening trials.^{15,29,32,33}

Accuracy of Screening Tests

Key Question 3. What is the accuracy of selected screening tests for diagnosing AF in asymptomatic adults?

Nine studies published in 13 articles^{15,34,37-43} ($n = 4978$) reported on the accuracy of primary care-feasible screening tests; population, index test, and reference test characteristics are summarized in Table 2, with details reported in eTables 26 through 28 in the Supplement. All are new to this update because this KQ was not included in the previous report.

The sensitivity and specificity of various screening tests varied and are summarized in Table 3, with details reported in eTable 29 in the Supplement. The 1 study⁴³ using a continuous ECG reference stan-

dard reported a lower sensitivity (0.35) compared with the studies that used a 1-time 12-lead ECG interpreted by a cardiologist, likely a result of increased detection of paroxysmal AF. In a population of 1000 persons with a prevalence of undiagnosed AF of 1.3%,⁷ there would be between 4 and 13 true-positive test results, 0 to 237 false-positive results, 0 to 9 false-negative results, and 750 to 987 true-negative results based on extrapolation of the accuracy data reported by included studies.

Harms of Screening

Key Question 4. What are the harms of screening for AF with selected tests in older adults?

Key Question 4a. Do the harms of screening vary for subgroups defined by stroke risk, age, sex, or race and ethnicity?

Four RCTs (SAFE,¹⁵⁻¹⁹ SCREEN-AF,⁴³ STROKESTOP,^{45,47,48} and mHealth Screening to Prevent Strokes [mStoPS]³³) reported harms of screening; all were described in the KQ1 and KQ2 sections of this article and are included in Table 1. SAFE¹⁵⁻¹⁹ was included in the prior review for the USPSTF; the rest are new to this update. The mStoPS RCT also included a prospective cohort component that reported relevant outcomes.³³ Detailed study characteristics and results are reported in eTables 30 and 31 in the Supplement.

SAFE reported no difference in anxiety scores between those screened with ECG compared with pulse palpation reminders.¹⁵⁻¹⁹ In STROKESTOP, the rate of hemorrhagic stroke was 0.16 events per 100 person-years in the invitation-to-screening group compared with 0.18 in the control group (HR, 0.88 [95% CI, 0.70-1.11]).⁴⁴ The rate of hospitalization for major bleeding was 1.71 events per 100 person-years in the invitation-to-screening group, compared with 1.74 in the control group (HR, 0.98 [95% CI, 0.91-1.06]). In SCREEN-AF, authors reported 0 intracranial hemorrhages.⁴³ The 2 RCTs evaluating continuous patch ECG screening reported an incidence of skin irritation ranging from 1.2% to 1.5%^{33,43} and an incidence of non-AF arrhythmias ranging from 0% to 3.9% depending on the arrhythmia, although the clinical consequences of this detection are not known. In the mStoPS cohort study ($n = 5214$), the frequency of initiation of anticoagulation, antiarrhythmics, and procedures was higher among the cohort that got screened compared with the matched cohort that did not get screened. In the SCREEN-AF trial, no statistically significant differences were reported for emergency department visits, hospitalizations, or pacemaker implantations, although all of these events were rare in both the screening and control groups.⁴³ No studies reported on variation in harms by subgroups.

Benefits of Anticoagulation

Key Question 5. What are the benefits of anticoagulation therapy on health outcomes in asymptomatic, screen-detected older adults with AF?

Key Question 5a. Do the benefits of anticoagulation vary for subgroups defined by stroke or bleeding risk, age, sex, race and ethnicity, or AF burden (ie, number of episodes, duration of episodes, and proportion of time spent in AF)?

Although the aim of this KQ was to determine the benefits of treatment in screen-detected older adults with AF, no trials or systematic reviews that focused solely on this population were identified. Five fair-quality RCTs of anticoagulation in persons with clinically detected AF were identified²¹⁻²⁶; none were new to this update. Most study participants had long-standing, persistent AF; few had

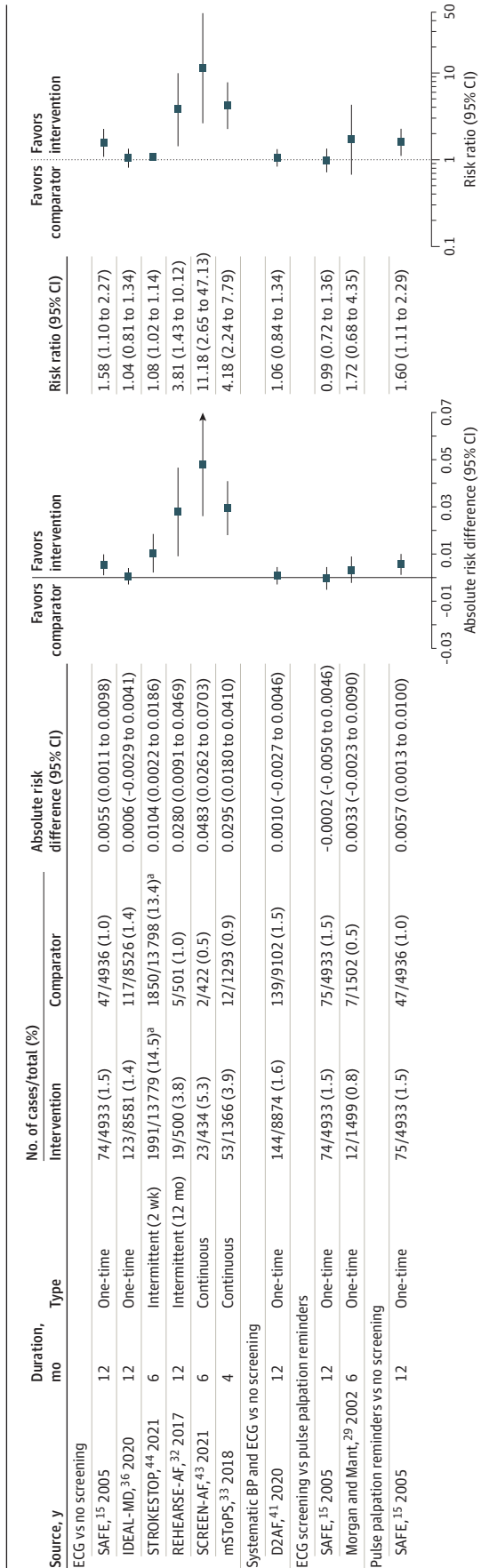
Table 1. Study Characteristics of Randomized Clinical Trials of Screening Reporting Detection of Atrial Fibrillation (Key Question 2)

Study, source	Study design (country)	Recruitment setting	Age, mean (SD), y	Women, No. (%)	Intervention groups (No. participants randomized)	Study duration, mo	Study quality
REHEARSE-AF Halcox et al, ³² 2017	Parallel-group RCT (UK)	General practices (No. unknown)	72.6 (5.4)	535 (53)	No screening, care as usual (501) Twice-weekly 30-s, single-lead ECG with handheld device (AliveCor Heart Monitor), plus additional recordings if symptomatic (500)	12	Fair
SAFE Hobbs et al, ¹⁵ 2005 Fitzmaurice et al, ¹⁷ 2007 Fitzmaurice et al, ¹⁶ 2014 Mant et al, ¹⁸ 2007 Swanncutt et al, ¹⁹ 2004	Cluster-group RCT (UK)	50 Primary care practices	75.3 (7.2)	8500 (57.4)	No screening, care as usual (4936) Reminder for pulse palpation in the chart; clinicians encouraged to record pulse during routine visits; patients with irregular pulses invited to attend a nurse-led screening clinic and have 12-lead ECG (4933) Patients invited to attend a nurse-led screening clinic for pulse palpation and 12-lead ECG (4933)	12	Fair
IDEAL-MD Kaasenbrood et al, ³⁶ 2020	Cluster-group RCT (the Netherlands)	31 General practices	Intervention: 74.3 (7.3) Control: 74.5 (7.3)	Intervention: 4680 (54.5) Control: 4610 (54.1)	No screening, care as usual (8526) Practices instructed to screen persons ≥65 y without AF during visits using a single-lead ECG; implementation left to the discretion of practices (8581)	12	Fair
Morgan and Mant, ²⁹ 2002	Parallel-group RCT (UK)	4 General practices	75.5 (NR)	1756 (58.8)	Reminder for pulse palpation in the chart; clinicians encouraged to record pulse during routine visits (1502) Patients invited to attend a nurse-led screening clinic for pulse palpation and single-lead ECG (1499)	6	Fair
mSToPS Steinhubl et al, ³³ 2018	Parallel-group RCT (US)	Siteless trial with health plan members recruited by mail	72.4 (7.3)	1026 (38.6)	Delayed screening initiated 4 mo after enrollment date (1293) Single-use, 14-d, ambulatory ECG skin patch for 2 wk on enrollment and a second patch 3 mo later for another 2 wk (1366)	4	Fair
D2AF Uittenboogaart et al, ⁴¹ 2020	Cluster-group RCT (the Netherlands)	96 General practices	Intervention: 75.2 (6.8) Control: 75.0 (6.9)	10 248 (53.4)	No screening, care as usual (9789) Reminder in chart of eligible patients randomly selected at each practice to conduct pulse palpation, oscillometric blood pressure monitor with AF detection feature, and single-lead handheld ECG with optional Holter monitoring if all 3 test results negative (9400)	12	Fair

Abbreviations: AF, atrial fibrillation; D2AF, Detecting and Diagnosing Atrial Fibrillation; ECG, electrocardiograph; IDEAL-MD, Improving Detection of Atrial Fibrillation in Primary Care With the MyDiagnostick; mSToPS, mHealth Screening to Prevent Strokes; NR, not reported; RCT, randomized clinical trial; REHEARSE-AF, Remote Heart

Rhythm Sampling Using the AliveCor Heart Monitor to Screen for Atrial Fibrillation; SAFE, Screening for Atrial Fibrillation in the Elderly.

Figure 3. Comparative Detection of Atrial Fibrillation From RCTs of Screening (KQ2)



To calculate the absolute risk difference in percentage points, multiply value by 100 (eg, 0.0010 multiplied by 100 = 0.1 percentage points). BP indicates blood pressure; D2AF, Detecting and Diagnosing Atrial Fibrillation; ECG, electrocardiography; IDEAL-MD, Improving Detection of Atrial Fibrillation in

Primary Care With the MyDiagnostick; KQ, key question; mSToPS, mHealth Screening to Prevent Strokes; RCT, randomized clinical trial; REHEARSE-AF, Remote Heart Rhythm Sampling Using the AliveCor Heart Monitor to Screen for Atrial Fibrillation; SAFE, Screening for Atrial Fibrillation in the Elderly.

Table 2. Characteristics of Included Test Accuracy Studies (Key Question 3)

Study, source	Recruitment setting (total No.)	Inclusion criteria	Age, mean (SD), y	Female, No. (%)	Index test(s)	Reference test(s)	Study quality
Himmelreich et al, ³⁷ 2019	10 General practices in the Netherlands (106)	Age ≥18 y with 12-lead ECG ordered for nonacute indications	69.3 (10.7)	62 (58)	Single-lead, handheld ECG (KardiaMobile) with automated AF detection during an office visit ^a	12-Lead ECG independently interpreted by 2 cardiologists	Good
SAFE Hobbs et al, ¹⁵ 2005	25 General practices in the UK (1452)	Age ≥65 y	75.3 (7.2) ^b	8500 (57.4)	(1) General practitioner-interpreted 12-lead ECG (2) General practitioner-interpreted limb-lead II ECG (3) General practitioner-interpreted thoracic-lead ECG	12-Lead ECG independently interpreted by 2 cardiologists	Good
Kearley et al, ³⁸ 2014	6 General practices in the UK (999)	Age ≥75 y	79.7 (NR)	507 (50.7) ^c	(1) Modified oscillometric BP monitor (Microlife WatchBP) with automated AF detection during an office visit ^d (2) Single-lead ECG (OMRON model HCG-801) with and without automated AF detection during an office visit ^e	12-Lead ECG interpreted by 2 cardiologists	Fair
Marazzi et al, ⁴⁰ 2012	Hypertension clinic in Italy (383)	None specified	67 (10.5)	230 (46)	(1) Oscillometric BP monitor (Microlife BP A200 Plus) with automated AF detection during an office visit (2) Oscillometric BP monitor (OMRON M6) with automated AF detection during an office visit	12-Lead ECG interpreted by cardiologist	Good
Philippson et al, ³⁴ 2017	Diabetes and cardiology outpatient clinics in Denmark (82)	Age ≥65 y and treatment for diabetes and hypertension with stable medications	71 (4)	30 (37) ^c	2-Channel, 72-hour Holter monitor adjudicated by 2 cardiologists AF defined as at least 1 episode lasting ≥30 s	Continuous ECG with an insertable cardiac monitor (median, 588 d), with AF defined as at least 1 episode lasting ≥2 min	Good
Sabar et al, ⁴² 2019	Outpatient hospital cardiology clinic (632)	Age ≥18 y attending outpatient cardiology for routine 12-lead ECGs or other appointments	66 (range 18-97)	384 (51)	6-lead ECG (RhythmPad, Cadiocity) with automated detection during an office visit	12-Lead ECG independently interpreted by 2 cardiologists	Fair
Uittenbogaart et al, ⁴¹ 2020	96 Primary care practices in the Netherlands (742)	Age ≥65 y	75 ^b	NR (53.4) ^b	Combined approach that included pulse palpation, oscillometric blood pressure monitor with automated AF detection (WatchBP Home A, Microlife), and single-lead handheld ECG (MyDiagnostick)	12-Lead ECG interpreted by cardiologists (only 10% random sample of participants with negative index test results received reference test)	Fair
Wiesel et al, ³⁹ 2014	2 Outpatient cardiology clinics in the US (148)	Age ≥50 y	74 (NR)	75 (41) ^c	(1) Oscillometric blood pressure monitor (OMRON M6 Comfort) with automated irregular rhythm detection during an office visit (2) Oscillometric blood pressure monitor (Microlife BP A 200) with automated AF detection during an office visit ^f	12-Lead ECG interpreted by a cardiologist	Fair

Abbreviations: AF, atrial fibrillation; BP, blood pressure; ECG, electrocardiograph; KQ, key question; NR, not reported; SAFE, Screening for Atrial Fibrillation in the Elderly.

^a Rhythms classified by algorithm as AF, normal, unreadable, or no classification. For this analysis, screening was considered positive for any "possible AF" tracings and was considered negative for all other tracings. The AF classification refers to both atrial fibrillation and atrial flutter.

^b For entire study population; not all study participants from the trial were included in the KQ3 analyses.

^c Calculated value.

^d Inconclusive results treated as "positive."

^e "Analysis impossible" and "inconclusive results" were counted as positive test results.

^f Test result is considered positive if at least 2 of the 3 readings are positive for AF.

Table 3. Results From Included Test Accuracy Studies (Key Question 3)

Source	Device/method	Sensitivity (95% CI)	Specificity (95% CI)	Results per 1000 tests (1.3% prevalence of AF)	
				False-negative	False-positive
Oscillometric BP monitor with automated AF detection vs 12-lead ECG interpreted by cardiologist					
Kearley et al, ³⁸ 2014	Microlife Watch BP Home A	0.95 (0.88-0.99)	0.90 (0.88-0.92)	1	99
Marazzi et al, ⁴⁰ 2012	Microlife BP A200	0.92 (NR)	Calculated: 0.95	1	49
Marazzi et al, ⁴⁰ 2012	OMRON M6	1.0 (NR)	0.94 (NR)	0	59
Wiesel et al, ³⁹ 2014	Microlife BP A200	1.0 (0.86-1.0) ^a	0.92 (0.86-0.96)	0	79
Wiesel et al, ³⁹ 2014	OMRON M6	0.30 (0.15-0.49) ^a	0.97 (0.93-0.99)	9	30
Single-lead ECG with automated AF detection vs 12-lead ECG interpreted by cardiologist					
Himmelreich et al, ³⁷ 2019	KardiaMobile	0.88 (0.47-1.0)	1.0 (0.96-1.0)	2	0
Kearley et al, ³⁸ 2014	OMRON	0.99 (0.93-1.0)	0.76 (0.73-0.79)	<1	237
6-lead ECG with automated AF detection vs 12-lead ECG interpreted by cardiologist					
Sabar et al, ⁴² 2019	6-Lead ECG	0.95 (NR)	0.99 (NR)	1	10
General practitioner-interpreted ECG vs 12-lead ECG interpreted by cardiologist					
SAFE, ¹⁵ 2005	12-lead ECG	0.80 (0.71-0.87)	0.92 (0.90-0.93)	3	79
	Single limb lead	0.83 (0.75-0.88)	0.88 (0.87-0.90)	2	118
	Single thoracic lead	0.85 (0.79-0.91)	0.86 (0.84-0.88)	2	138
Combined pulse palpation, oscillometric BP, and single-lead ECG both with automated AF detection vs 12-lead ECG interpreted by cardiologist					
D2AF, ⁴¹ 2020	MyDiagnostick device and Microlife Watch BP Home A	ND ^b	ND ^b	ND ^b	ND ^b
72-h continuous Holter monitoring vs continuous ECG monitoring with insertable cardiac monitor over median 588 d^c					
Philippson et al, ³⁴ 2017		Calculated: 0.12	Calculated: 1	NA	NA

Abbreviations: AF, atrial fibrillation; BP, blood pressure; D2AF, Detecting and Diagnosing Atrial Fibrillation; ECG, electrocardiograph; KQ, key question; NA, not available; ND, not determinable; NR, not reported; SAFE, Screening for Atrial Fibrillation in the Elderly.

^a The author of this study disclosed holding a patent for the AF detection algorithm present in the Microlife BP device; the sensitivity of the OMRON oscillometric device was markedly lower in this study when compared with the estimate for Microlife and when compared with the OMRON device reported in the study by Marazzi et al.⁴⁰

^b The study only performed a 12-lead referent test on a random sample of participants who tested negative on the index screening test; thus, data to determine sensitivity and specificity were not available. However, based on data reported, the positive predictive value is 6% and the negative predictive value is 100%, suggesting a test with very high sensitivity but poor specificity.

^c Holter monitoring occurred approximately 1 month after placement of implantable cardiac monitor. When limited to the same 72-hour monitoring window, sensitivity was 1.0.

a history of transient ischemic attack or stroke (<8%). All trials evaluated titrated doses of warfarin. Study characteristics are detailed in eTables 32 and 33 in the [Supplement](#).

In pooled analysis of the 5 RCTs (n = 2145), warfarin treatment over a mean of 1.5 years was significantly associated with reductions in all-cause mortality (pooled RR, 0.68 [95% CI, 0.50-0.93]; $I^2 = 0\%$), ischemic stroke (pooled RR, 0.32 [95% CI, 0.20-0.51]; $I^2 = 0\%$), and moderately to severely disabling stroke (pooled RR, 0.38 [95% CI, 0.19-0.78]; $I^2 = 0\%$), compared with controls (**Figure 4**). For a population with a baseline annual stroke risk of 4%, such as patients with CHA₂DS₂-VASc scores of 3 or 4, warfarin would be associated with a number needed to treat of 24 (95% CI, 17-36) to prevent 1 ischemic stroke over 1.5 years. Individual study results are detailed in eTable 34 in the [Supplement](#).

Results of 5 previously included systematic reviews (including 2 individual patient data meta-analyses) evaluating warfarin compared with placebo or control were consistent with the findings from the pooled analysis of included studies and are summarized in eTables 13 and 36 in the [Supplement](#).^{4,20,28,30,31} Authors of a network meta-analysis of 21 RCTs (n = 96 017) reported statistically significant associations for reductions in stroke or systemic embolism and all-cause mortality for 4 direct oral anticoagulants compared with placebo (adjusted odds ratios ranged from 0.32 to 0.44; eTable 36 in the [Supplement](#)).³⁰

With respect to subgroup findings, an individual patient data meta-analysis³¹ reported lower stroke risk with warfarin in male patients (relative risk reduction, 60% [95% CI, 35%-76%]) and in female patients (relative risk reduction, 84% [95% CI, 55%-95%]), but the difference between male and female patients was not statistically significant.³¹ In another individual patient data meta-analysis,²⁰ warfarin was associated with reduced risk for ischemic stroke for all ages, with no statistically significant interaction with increasing age.²⁰

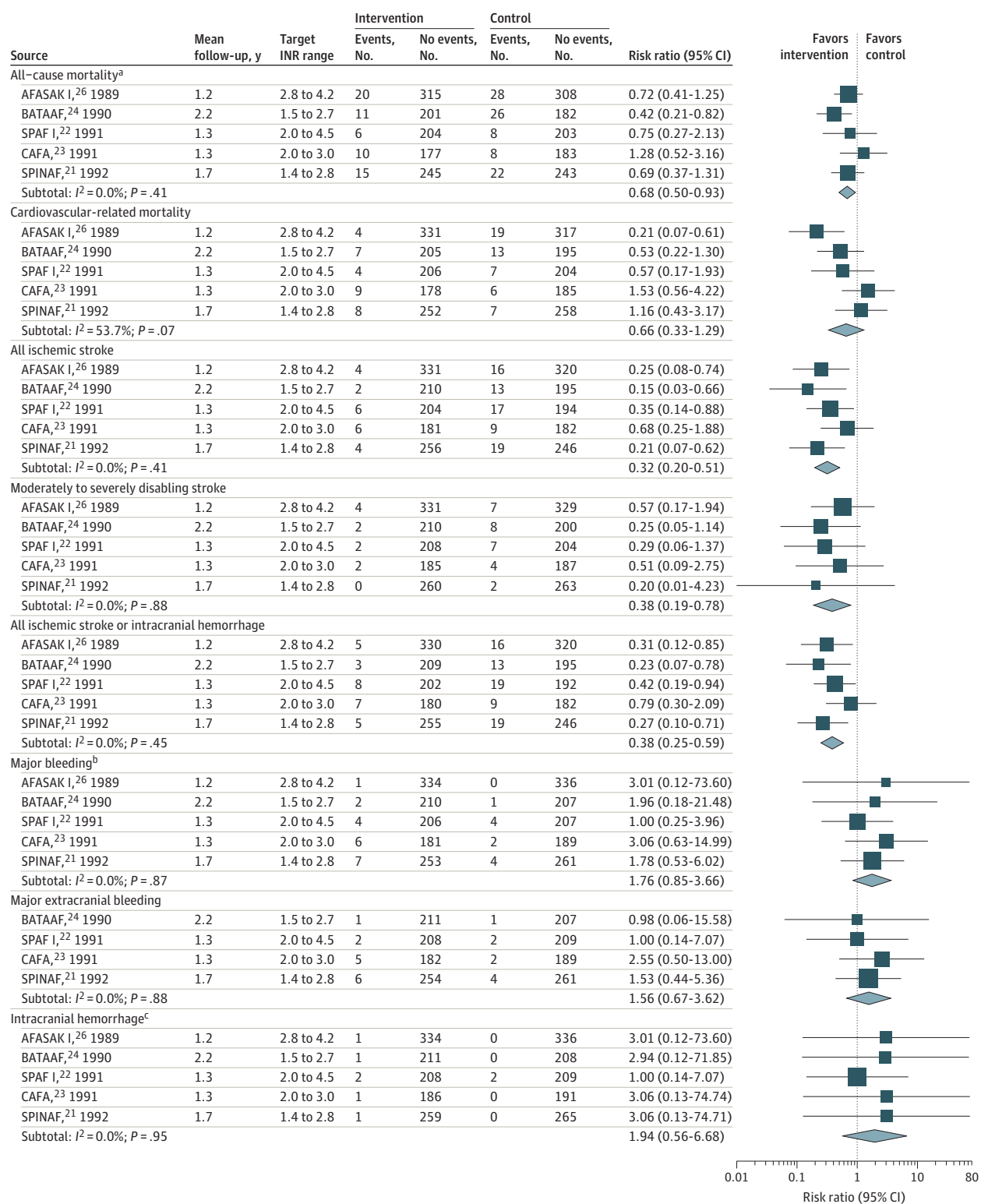
Harms of Anticoagulation

Key Question 6. What are the harms of anticoagulation therapy in asymptomatic, screen-detected older adults with AF?

Key Question 6a. Do the harms of anticoagulation therapy vary for subgroups defined by stroke risk or bleeding risk, age, sex, race and ethnicity, or AF burden?

Although the aim was to determine the harms of anticoagulation treatment for screen-detected older adults with AF, no trials or systematic reviews that focused solely on this population were identified. The same 5 RCTs included for KQ5 also reported on harms of anticoagulation.²¹⁻²⁶ One new observational study (n = 28 628) was identified for this update; the Global Anticoagulant Registry in the Field-Atrial Fibrillation (GARFIELD-AF) study is a fair-quality, ongoing prospective registry of persons with newly diagnosed AF from more than 1000 primary and specialty care clinics in 32 countries.³⁵

Figure 4. Benefits and Harms of Warfarin for Stroke Prevention Compared With Placebo or Control



^a SPINAF includes only those without history of stroke. AFASAK includes data from a published meta-analysis obtained from the original study authors. ^b AFASAK did not specify severity of most bleeding events; it reported 1 fatal intracerebral hemorrhage in the warfarin group and only reported bleeding events leading to withdrawal from study (warfarin, 21; placebo, 0). BAATAF defines major bleeding as intracranial bleeding, fatal bleeding, or bleeding that led to transfusion (≥ 4 units within 48 h);

SPAF I, as bleeding that involved the central nervous system, management requiring hospitalization with transfusion and/or surgery, or permanent residual impairment; CAFA, as life-threatening bleeding; SPINAF, as bleeding that required transfusion, emergency procedure, or removal of a hematoma or that led to ICU admission. ^c SPAF I included 1 fatal intracerebral hemorrhage and 1 subdural hematoma with full recovery (warfarin) and 2 subdural hematomas with full recovery (placebo).

In a pooled analysis of the 5 RCTs (2415 participants), major bleeding events occurred in 20 participants from the warfarin groups and 11 participants from the placebo/control groups over 1.5 years (pooled RR, 1.8 [95% CI, 0.85-3.70]; $I^2 = 0\%$). Additional bleeding outcomes are reported in Figure 4 and in eTable 35 in the [Supplement](#). Results of 6 previously included systematic reviews were consistent with the findings from the analysis of the primary studies and are summarized in eTable 36 in the [Supplement](#).^{4,20,27,28,30,31} Authors of the previously described network meta-analysis of 21 RCTs (n = 96 017) reported adjusted odds ratios for major bleeding ranging from 1.38 to 2.21 in indirect comparisons of 4 direct oral anticoagulants compared with placebo; the CIs around these estimates were wide, and findings were not statistically significant (eTable 36 in the [Supplement](#)).³⁰

In the GARFIELD-AF observational study, the adjusted HR for first occurrence of major bleeding was 1.73 (95% CI, 1.33-2.25) for participants receiving any anticoagulation treatment (warfarin, direct oral anticoagulant, antiplatelets, or combination), compared with participants receiving no treatment (eTable 35 in the [Supplement](#)).³⁵

With respect to subgroups, an individual patient data meta-analysis³¹ reported a higher mean age for patients with intracranial hemorrhage (73 years) compared with those without bleeding (69 years), but bleeding events were rare, and this difference was not statistically significant.³¹ The other individual patient data meta-analysis²⁰ reported that no statistical interaction between age and risk of serious hemorrhage associated with warfarin was found.²⁰

Discussion

This updated evidence review examined screening for AF in older adults without a history of stroke; the evidence is summarized in [Table 4](#).

STROKESTOP is the only included trial of screening that was designed and powered to evaluate health outcomes.^{44,45,47} Authors reported a small but statistically significant difference favoring the screening group in the intention-to-treat analysis using a composite end point that included both benefit and harm outcomes, despite uptake of screening by only 51% of those randomized to the invitation to screening. However, this study had numerous limitations; the outcomes evaluated were diagnosed through routine clinical care, without formal masking, and were not based on standard diagnostic criteria with central, blinded adjudication. Whether benefit and harm end points should be combined into a "net benefit" composite is an area of debate and violates assumptions recommended for composite end points.⁴⁹⁻⁵¹ This study enrolled persons with known AF, many of whom were already taking oral anticoagulants, limiting applicability to screening among persons without known AF. The other 2 studies reporting health outcomes from screening compared with no screening were not powered for such outcomes; events were rare or absent in these studies. The potential for reporting bias is also present because 1 of the studies reporting KQ2 outcomes designated major cardiovascular events and all-cause mortality as secondary outcomes, but these have not been reported.³⁶ Several ongoing studies comparing screening with no screening may provide additional evidence for this KQ in the future (eTable 37 in the [Supplement](#)).

Screening with intermittent or continuous ECG can identify more cases of AF compared with no screening. When 1-time ECG screen-

ing was compared with pulse palpation reminders, no significant difference in cases identified was observed. The variation in sensitivity and specificity of various 1-time screening strategies based on ECG or oscillometric blood pressure monitor with automated AF detection may be the result of differences in the underlying populations tested, differences in thresholds used for defining positive index or reference tests, or the fidelity with which screening was conducted. The clinical importance of this variation is uncertain. Given the relatively low prevalence of undiagnosed AF, 1-time spot screening will generate more false-positive results relative to true-positives and relative to false-negatives. Estimates of these results across various AF prevalences are provided in eTable 38 in the [Supplement](#).

For harms of screening, 1 RCT reported that anxiety was not significantly different between participants who received ECG screening and participants whose clinicians received pulse palpation reminders, but a direct comparison of screened with not screened participants was not reported. Data from SCREEN-AF and STROKESTOP suggested no increased risk of serious bleeding events, including hemorrhagic stroke, but such events were rare, and estimates were imprecise, precluding a definitive conclusion about bleeding harms from screening. Although this review identified evidence to estimate the potential number of screening tests with inaccurate results (ie, false-positive and false-negative results), evidence is limited with respect to the consequences of those inaccurate screening results. Potential harms could result from unnecessary stress tests and angiographies initiated to follow up on ECG abnormalities later determined to be false-positives or unnecessary treatment resulting from overdiagnosis. A study using a database from a US hospital that evaluated 2298 ECGs (from 1085 patients) with a computerized interpretation of AF found that ECGs from 382 patients (35%) had been misinterpreted; physicians did not correct the computerized misinterpretation and initiated inappropriate and potentially harmful treatments, and they pursued unnecessary additional testing for 92 patients (9%).⁵² However, potential benefits could result from appropriate care provided for medically actionable findings other than AF (eg, high-degree atrioventricular block, ventricular tachycardia).

Among trials enrolling persons with clinical AF without a prior history of stroke, consistent evidence suggests that the risk for stroke and all-cause mortality is reduced with anticoagulation compared with placebo or control. The same body of evidence suggests a possible increased risk for major bleeding, but estimates are imprecise. It is uncertain whether the benefits and harms of treatment are applicable to screen-detected populations, particularly persons with brief episodes of AF.

Limitations

This review has several limitations. First, it was restricted to fair- or good-quality studies conducted in very highly developed countries and published in English. Second, it did not consider screening approaches that are not feasible in or referable from primary care. Third, non-AF findings resulting from screening were considered harms (eg, because treatment and procedures have inherent disutility, inconvenience, and costs and may be harmful in the setting of false-positive screening results and overdiagnosis). However, treatment offered for medically actionable non-AF findings may provide benefit for some persons. Fourth, the comparative effectiveness of anticoagulation treatments was not evaluated.

Table 4. Summary of Evidence for Screening for Atrial Fibrillation

No. of studies/study designs (No. of participants)	Summary of findings	Consistency and precision	Limitations	Strength of evidence	Applicability
QK1: Benefits of screening					
1 RCT (27 975) ^{44,45,47} Designed to address QK1	Intermittent screening ECG twice daily for 2 wk compared with no screening (1 RCT) ^{44,45,47} Composite benefit/harm end point ^a : Events/100 person-years, 5.45 (95% CI, 5.29-5.61) vs 5.68 (95% CI, 5.52-5.85); HR, 0.96 (95% CI, 0.92-1.00); P = .045 Secondary outcomes: Ischemic stroke: HR, 0.92 (95% CI, 0.83-1.01) All-cause mortality: HR, 0.96 (95% CI, 0.92-1.01) Systemic embolism: HR, 1.10 (95% CI, 0.76-1.59) Ischemic stroke or systemic embolism: HR, 0.92 (95% CI, 0.84-1.02), as randomized; 0.76 (0.67-0.85), as treated ^b	Consistent; imprecise ^c	Fair-quality studies; in largest trial, ≈12% had known AF at baseline and only 51.3% of persons randomized to screening participated, with no formal outcome assessment masking or central adjudication; primary outcome changed to a composite end point that included both benefit and harm outcomes; the other 2 trials were designed for QK2 and not powered for health outcomes, were not masked, and had some measurement bias; reporting bias detected (1 of the KQ2 studies was also designed to report KQ1 outcomes per trial registry entry but no results published)	Insufficient for addressing question of direct benefits of screening in persons without known AF differences between participants and nonparticipants that make predicting the bias from poor fidelity challenging	Adults with mean age in 70s and 80s, with stroke risks in range recommended for anticoagulation if no contraindication; unclear applicability to screening in persons in primary care practice settings, given population recruitment in only trial powered for health outcomes with clear differences between participants and nonparticipants that make predicting the bias from poor fidelity challenging
2 RCTs (1857) ^{32,43} Not designed to address QK1 but reported some health outcomes	Intermittent screening ECG twice weekly for 12 mo compared with no screening (1 RCT) ³² Composite of stroke, TIA, or systemic embolism: 6 (screened) vs 10 (not screened) events; HR, 0.61 (95% CI, 0.22-1.69) Continuous ECG for 2 weeks, twice (total 4 weeks) compared with no screening (1 RCT) ⁴³ : 1 death (no screening), 2 ischemic strokes (screening), 1 TIA (screening), 0 systemic embolism	Consistent; imprecise ^{d,e}	Fair quality, study inclusion/exclusion criteria focused on persons without known AF but most did not routinely assess for potential symptoms at study entry; fidelity low to modest in intervention groups	Moderate for increased detection, with higher detection seen with intermittent and continuous approaches	Applicable to older adults without known AF for various screening modalities (1-time ECG, intermittent ECG, continuous patch ECG, pulse palpation combined with 1-time ECG and oscillometric BP with AF detection). ^f
QK2: Identifying new cases of AF					
7 RCTs (74 386) ^{15-19,32,33,36-41,43-45,47}	Various ECG screening compared with no screening: 1-time (3 RCTs): ARDs, 0.06%-0.60% Intermittent (2 RCTs): ARDs, 1.0%-2.8% Continuous (2 RCTs): ARDs, 3.0%-4.8%	Consistent; imprecise	Fair quality; fidelity of pulse assessment was 29% in 1 trial and 69% in the other trial; fidelity of ECG screening was 73% in 1 trial and 53% in the other trial	Low for no difference in detection	Applicable to 1-time ECG screening only, reminders in either paper charts or electronic records
2 RCTs (12 867) ^{15-19,29}	ECG screening vs pulse palpation reminders: ARD, -0.02% in 1 trial and 0.3% in other trial (not statistically significant in either)	Consistent; imprecise	Fair quality; fidelity of pulse palpation in response to reminders was 69%	Low for increased detection	Older adults; reminders in either paper charts or electronic records
1 RCT (9869) ¹⁵⁻¹⁹	Pulse palpation reminders vs no screening: ARD, 0.6% (95% CI, 0.1%-1.0%)	Single study, consistency unknown; precise	Fair quality; fidelity of pulse palpation in response to reminders was 69%	Low for increased detection	Older adults; reminders in either paper charts or electronic records
QK3: Accuracy of screening tests⁹					
7 studies (4544) ^{15,34,37-42}	Various screening strategies compared with 12-lead ECG interpreted by cardiologist Sensitivity range: 0.80-1.0h Specificity range: 0.76-1.0	Consistent; precise ^h	Four studies were fair quality because of concerns about applicability and selection bias related to method of enrollment in 2 studies, and lack of masking of index and reference test results in other used 1-time reference standard in 1 study; most studies underestimate the prevalence of paroxysmal AF	Moderate to low depending on screening approach	Applicable to adults and for the following screening modalities: 6-lead ECG, general practitioner-interpreted ECG (12-lead or <12-lead), oscillometric BP monitor with automatic AF detection, single-lead ECG with automatic AF detection
1 study (399) ⁴³	Oscillometric BP monitor with AF detection feature compared with continuous ECG (4 wk) Sensitivity, 0.35; specificity, 0.81	Consistent; precise	Four studies were fair quality because of concerns about applicability and selection bias related to method of enrollment in 2 studies, and lack of masking of index and reference test results in other used 1-time reference standard in 1 study; most studies underestimate the prevalence of paroxysmal AF	Moderate to low depending on screening approach	Applicable to adults and for the following screening modalities: 6-lead ECG, general practitioner-interpreted ECG (12-lead or <12-lead), oscillometric BP monitor with automatic AF detection, single-lead ECG with automatic AF detection

(continued)

Table 4. Summary of Evidence for Screening for Atrial Fibrillation (continued)

No. of studies/study designs (No. of participants)	Summary of findings	Consistency and precision	Limitations	Strength of evidence	Applicability
KQ4: Harms of screening 4 RCTs (43 633) ^{1,5-19,33,43-45,47} 1 cohort (5214) ^k	Anxiety (1 RCT): Mean scores not significantly different for invitation to ECG screening compared with pulse palpation reminders Bleeding outcomes (2 RCTs): 0 intracranial hemorrhages or major bleeding events after 6 mo in the smaller of the RCTs HR, 0.88 (95% CI, 0.70-1.11) for hemorrhagic stroke and HR, 0.98 (95% CI, 0.91-1.06) for hospitalization for major bleeding in a larger RCT after a median follow-up of 6.9 y Non-AF arrhythmias (1 RCT and 1 cohort): detected in 2.6% of participants who received screening in cohort study and between 0 and 3.9% in the RCT depending on the type of arrhythmia; arrhythmias were considered clinically actionable in both studies. Initiation of anticoagulation, antiarrhythmics, and procedures (2 RCTs and 1 cohort): generally higher among participants who received screening compared with controls who did not get screened but only statistically significant for higher oral anticoagulant use in 2 of the 3 studies ^m Skin irritation from patch (2 RCTs): 1.2% (95% CI, 0.5%-2.7%) to 1.5% (95% CI, 1.1%-2.0%) of participants	Consistent; imprecise Consistency unknown; imprecise Consistent; precise Consistent; imprecise Consistent; precise	Fair quality; anxiety scores not reported for comparison of invitation to ECG screening vs no screening Fair quality; no centralized outcome adjudication, studies underpowered for rare events Fair quality; no masking Fair quality, no masking Fair quality; not masked, methods of ascertainment of skin irritation not reported	Insufficient for anxiety Insufficient for bleeding outcomes Moderate for increased detection, clinical consequences unknown ^l Low for increased initiation, clinical consequences unknown ^l Moderate for increased skin irritation	Applicable to older adults for the following screening modalities: general practitioner-interpreted ECG (anxiety), continuous ECG monitoring patch (non-AF arrhythmias, initiation of oral anticoagulants and procedures, and skin irritation), intermittent ECG (initiation of oral anticoagulants and procedures, bleeding outcomes)
KQ5: Benefits of anticoagulation treatment 5 RCTs (2415) ²¹⁻²⁶ 5 Systematic reviews ^{4,20,28,30,31}	Warfarin (mean, 1.5 y) vs placebo/control: Reduced all-cause mortality: pooled RR, 0.68 (95% CI, 0.50-0.93) Reduced ischemic stroke: pooled RR, 0.32 (95% CI, 0.20-0.51) Previously published systematic reviews: Similar findings reported for warfarin compared with placebo In a network meta-analysis, 4 direct oral anticoagulants were also more effective than placebo/control (adjusted ORs, 0.32-0.44). ⁿ	Consistent; precise	All warfarin trials were fair quality and stopped early; 3 of the 5 trials were open-label; 4 of the 5 trials had inadequate or unclear methods of allocation concealment Reporting bias not detected Limitations of the network meta-analysis included (1) the lack of sensitivity analyses removing the studies with greater focus on secondary prevention, (2) limited ability to adjust for population characteristics (because some included studies were older and did not report CHADS ₂ scores, and they were estimated from baseline characteristics), and (3) heterogeneity of doses in intervention and control groups	Moderate for benefit Moderate for benefit Moderate for increased skin irritation	Adults with AF and no history of stroke or TIA; uncertain whether the results are applicable to asymptomatic screen-detected persons with AF Most participants had AF for more than 1 year, and few had paroxysmal AF Estimates for lifelong treatment are not available

(continued)

Table 4. Summary of Evidence for Screening for Atrial Fibrillation (continued)

No. of studies/study designs (No. of participants)	Summary of findings	Consistency and precision	Limitations	Strength of evidence	Applicability
K06: Harms of anticoagulation treatment					
5 RCTs (2415) ²¹⁻²⁶	Warfarin (mean, 1.5 Y) vs placebo/control: Major bleeding: pooled RR, 1.8 (95% CI, 0.85-3.7) Intracranial hemorrhage: pooled RR, 1.9 (95% CI, 0.56-6.7)	Consistent, imprecise ^p	All warfarin trials were fair quality and stopped early; 3 of the 5 trials were open label; 4 of the 5 trials had inadequate or unclear methods of allocation concealment; reporting bias not detected	Moderate for harm ^q	Adults with AF and no history of stroke or TIA
6 Systematic reviews ^{4,20,27,28,30,31}	Previously published systematic reviews, similar findings reported for warfarin compared with placebo		Limitations of the network meta-analysis included (1) the lack of sensitivity analyses removing the studies with greater focus on secondary prevention, (2) limited ability to adjust for population characteristics (because some included studies were older and did not report CHADS ₂ scores, and they were estimated from baseline characteristics), and (3) heterogeneity of doses in intervention and control groups		
1 prospective cohort study (26628) ³⁵	In a network meta-analysis, the adjusted ORs for major bleeding comparing 4 direct oral anticoagulants with placebo/controls ranged from 1.38 to 2.21; CIs were wide and included the null ^o . Anticoagulation compared with no anticoagulation over 2 Y in cohort study: first bleeding event adjusted HR, 1.73 (95% CI, 1.33-2.25)				
	Abbreviations: AF, atrial fibrillation; ARD, absolute risk difference; BP, blood pressure; CHADS ₂ , Congestive heart failure, Hypertension, Age \geq 75 years, Diabetes mellitus, Prior stroke or TIA or thromboembolism; ECG, electrocardiogram; HR, hazard ratio; IQ, key question; NA, not applicable; OR, odds ratio; RCT, randomized clinical trial; RR, risk ratio; TIA, transient ischemic attack.				
	^a Includes both benefit and harm outcomes: ischemic stroke, hemorrhagic stroke, systemic arterial embolism, all-cause death, and bleeding leading to hospitalization.				
	^b When nonparticipants in the invitation to screening group were excluded (ie, the as-treated analysis), a larger net benefit is observed; however, nonparticipants, compared with participants, had worse socioeconomic status and lower education, higher alcohol use, and higher prevalence of comorbidities that increase both stroke risk and risk for major bleeding. Thus, the as-treated analysis, while mitigating for poor intervention fidelity, could overestimate the benefit because participants were, on average, slightly younger and healthier.				
	^c For detecting a small benefit; based on optimal information size criteria would require a trial with 36 896 participants to detect a relative risk reduction of 20% (RR, 0.80) given incidence in comparator group (2%) using 2-tailed $\alpha = .05$, power = 0.8. Even more participants would be required to detect a smaller risk reduction.				
	^d Study was rated consistent because of consistency in detection based on duration and intensity of screening strategy.				
	^e Study was rated imprecise because the number of events (ie, cases detected) was low across all studies, and the estimates for some individual studies were imprecise. Further, based on optimal information size criteria for average detection rate in no-screening group (1.2%), a single trial would require a sample size of 74 668 to detect a 20% relative increase in AF detection, 2-tailed $\alpha = .05$, power = 0.8, and even more participants to detect a smaller increase in detection.				
	^f Subgroup findings from 1 of the studies (SAFE trial) ¹⁵ suggested that screening may not increase detection among female participants; no subgroup findings were reported by the other 4 studies, all of which included female participants; thus, this finding is uncertain.				
	^g The study by Phillippen et al was not included when considering strength of evidence; that study compared a 72-hour Holter monitor with an insertable cardiac monitor that was left in place for a median of 588 days; the Holter monitor was placed approximately 1 month after the insertable monitor was placed, and it is uncertain whether AF events occurring after Holter monitoring period were prevalent cases or new onset.				
	^h Consistent for oscillometric BP with automated AF detection algorithm, with exception of 1 study ²⁹ for which sensitivity was reported as 0.30 for 1 brand of oscillometric monitor and for which a study author disclosed				
			conflict of interest. The evidence for single-lead ECG was less consistent, resulting in a low strength of evidence for that strategy.		
			ⁱ Moderate for oscillometric BP with automated AF detection and general practitioner ECG interpretation and 6-lead ECG; low for single-lead ECG with automated AF detection. Sensitivity influenced by reference standard used; continuous ECG reference standards are more likely to detect paroxysmal AF, resulting in lower sensitivity for 1-time or intermittent index tests.		
			^j Number of participants included a subset of 1940 of the 14 802 participants in the SAFE study, although study reporting relating to anxiety outcomes was unclear.		
			^k Includes 1738 participants who were also part of the mSTOP RCT (immediate and delayed monitoring groups combined). ³³		
			^l The detection of clinically actionable non-AF arrhythmias could be considered a benefit if it results in treatment or intervention that prevents an untoward outcome. However, it could be a harm if additional treatment or procedures (and related side effects or adverse events) were provided for an arrhythmia that might never have caused symptoms or issues. Similarly, the initiation of treatments or subsequent procedures could be considered a benefit or harm depending on the health consequences of such actions.		
			^m Findings were only statistically significantly higher in the cohort study, except for use of oral anticoagulants, which was also significantly higher in the RCT (RR, 4.4 [95% CI, 1.5-12.8]).		
			ⁿ The 4 direct oral coagulants were apixaban, dabigatran, edoxaban, and rivaroxaban.		
			^o The network meta-analysis also found no statistically significant differences for the 4 direct oral coagulants in comparison with one another: Compared with vitamin K antagonists, 3 of the direct oral coagulants (apixaban, dabigatran, and edoxaban) were associated with a lower risk of bleeding (range of ORs, 0.64 [95% CI, 0.46-0.90] to 0.85 [95% CI, 0.65-1.11]), but the difference was only statistically significant for edoxaban (OR, 0.64 [95% CI, 0.46-0.90]). For rivaroxaban compared with vitamin K antagonists, the odds of major bleeding was 1.03 (95% CI, 0.68-1.57).		
			^p Given the event rate in control group (\approx 1%), a properly powered trial to detect a 60% increase in major bleeding (RR, 1.6) would require 11 838 participants (2-tailed $\alpha = .05$, power = 0.8).		
			^q Although findings were imprecise and quality was fair, the strength of evidence was graded as moderate considering evidence on dose response (with higher international normalized ratios increasing bleeding risk) and evidence on treatment of conditions other than AF that shows consistent evidence of bleeding risk.		

Conclusions

Although screening can detect more cases of previously unknown AF, evidence regarding effects on health outcomes is limited.

Anticoagulation was associated with lower risk of first stroke and mortality but with increased risk of major bleeding, although estimates for this harm are imprecise; no trials assessed benefits and harms of anticoagulation among screen-detected populations.

ARTICLE INFORMATION

Accepted for Publication: November 17, 2021.

Author Contributions: Dr Kahwati had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Concept and design: Kahwati, Asher, Keen, Jonas. **Acquisition, analysis, or interpretation of data:** All authors.

Drafting of the manuscript: Kahwati, Asher, Keen, Ali, Jonas.

Critical revision of the manuscript for important intellectual content: All authors.

Statistical analysis: Kahwati, Keen.

Obtained funding: Kahwati, Jonas.

Administrative, technical, or material support: Kahwati, Asher, Ali, Schwimmer, Jonas.

Supervision: Kahwati, Asher, Jonas.

Conflict of Interest Disclosures: None reported.

Funding/Support: This project was funded under contract HHS-290-2015-00011-1, Task Order 15, from the Agency for Healthcare Research and Quality (AHRQ), US Department of Health and Human Services, to support the US Preventive Services Task Force (USPSTF). Dr Kadro was supported by the National Center for Complementary and Integrative Health National Research Service Award (NRSA) Institutional Research Training Program (T32) at University of North Carolina, grants 5T32AT003378-13 and 5T32AT003378-14.

Role of the Funder/Sponsor: Investigators worked with USPSTF members and AHRQ staff to develop the scope, analytic framework, and key questions for this review. AHRQ had no role in study selection, quality assessment, or synthesis. AHRQ staff provided project oversight, reviewed the report to ensure that the analysis met methodological standards, and distributed the draft for peer review. Otherwise, AHRQ had no role in the conduct of the study; collection, management, analysis, and interpretation of the data; and preparation, review, or approval of the manuscript findings. The opinions expressed in this document are those of the authors and do not represent the official position of AHRQ or the US Department of Health and Human Services.

Additional Contributions: We thank the following individuals for their contributions to this project: Howard Tracer, MD, Tina Fan, MD, MPH, and Tracy Wolff, MD, MPH (AHRQ); current and former members of the USPSTF who contributed to topic deliberations; and Christiane Voisin, MSL, Carol Woodell, BSPH, Sharon Barrell, MA, and Loraine Monroe (RTI International-University of North Carolina Evidence-based Practice Center). USPSTF members, peer reviewers, and federal partner reviewers did not receive financial compensation for their contributions.

Additional Information: A draft version of the full evidence report underwent external peer review from 5 content experts (Larisa Tereshchenko, MD, PhD, Oregon Health & Science University; Emma

Svennberg, MD, PhD, Karolinska Institute; Marco Perez, MD, Stanford University; Alvaro Alonso, MD, PhD, Emory University; and Michael LeFevre, MD, MSPH, University of Missouri) and 4 individuals from 2 federal partner reviewers (Centers for Disease Control and Prevention, National Institutes of Health). Comments from reviewers were presented to the USPSTF during its deliberation of the evidence and were considered in preparing the final evidence review.

Editorial Disclaimer: This evidence report is presented as a document in support of the accompanying USPSTF Recommendation Statement. It did not undergo additional peer review after submission to *JAMA*.

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