JAMA | Original Investigation

Effect of a Home-Based Wearable Continuous ECG Monitoring Patch on Detection of Undiagnosed Atrial Fibrillation
The mSToPS Randomized Clinical Trial

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IMPORTANCE Opportunistic screening for atrial fibrillation (AF) is recommended, and improved methods of early identification could allow for the initiation of appropriate therapies to prevent the adverse health outcomes associated with AF.

OBJECTIVE To determine the effect of a self-applied wearable electrocardiogram (ECG) patch in detecting AF and the clinical consequences associated with such a detection strategy.

DESIGN, SETTING, AND PARTICIPANTS A direct-to-participant randomized clinical trial and prospective matched observational cohort study were conducted among members of a large national health plan. Recruitment began November 17, 2015, and was completed on October 4, 2016, and 1-year claims-based follow-up concluded in January 2018. For the clinical trial, 2659 individuals were randomized to active home-based monitoring to start immediately or delayed by 4 months. For the observational study, 2 deidentified age-, sex- and CHA_2DS_2-VASc–matched controls were selected for each actively monitored individual.

INTERVENTIONS The actively monitored cohort wore a self-applied continuous ECG monitoring patch at home during routine activities for up to 4 weeks, initiated either immediately after enrolling (n = 1364) or delayed for 4 months after enrollment (n = 1291).

MAIN OUTCOMES AND MEASURES The primary end point was the incidence of a new diagnosis of AF at 4 months among those randomized to immediate monitoring vs delayed monitoring. A secondary end point was new AF diagnosis at 1 year in the combined actively monitored groups vs matched observational controls. Other outcomes included new prescriptions for anticoagulants and health care utilization (outpatient cardiology visits, primary care visits, or AF-related emergency department visits and hospitalizations) at 1 year.

RESULTS The randomized groups included 2659 participants (mean [SD] age, 72.4 [7.3] years; 38.6% women), of whom 1738 (65.4%) completed active monitoring. The observational study comprised 5214 (mean [SD] age, 73.7 [7.0] years; 40.5% women; median CHA_2DS_2-VASc score, 3.0), including 1738 actively monitored individuals from the randomized trial and 3476 matched controls. In the randomized study, new AF was identified by 4 months in 3.9% (53/1366) of the immediate group vs 0.9% (12/1293) in the delayed group (absolute difference, 3.0% [95% CI, 1.8%-4.1%]). At 1 year, AF was newly diagnosed in 109 monitored (6.7 per 100 person-years) and 81 unmonitored (2.6 per 100 person-years; difference, 4.1 [95% CI, 3.9-4.2]) individuals. Active monitoring was associated with increased initiation of anticoagulants (5.7 vs 3.7 per 100 person-years; difference, 2.0 [95% CI, 1.9-2.2]), outpatient cardiology visits (33.5 vs 26.0 per 100 person-years; difference, 7.5 [95% CI, 7.2-7.9), and primary care visits (83.5 vs 82.6 per 100 person-years; difference, 0.9 [95% CI, 0.4-1.5]). There was no difference in AF-related emergency department visits and hospitalizations (1.3 vs 1.4 per 100 person-years; difference, 0.1 [95% CI, −0.1 to 0]).

CONCLUSIONS AND RELEVANCE Among individuals at high risk for AF, immediate monitoring with a home-based wearable ECG sensor patch, compared with delayed monitoring, resulted in a higher rate of AF diagnosis after 4 months. Monitored individuals, compared with nonmonitored controls, had higher rates of AF diagnosis, greater initiation of anticoagulants, but also increased health care resource utilization at 1 year.

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Atrial fibrillation (AF) is the most common sustained arrhythmia, with a lifetime risk of 37% after age 55 years.[1] When identified clinically, AF increases the risk of stroke 5-fold and accounts for almost one-third of all strokes.[2-4] For approximately 20% of individuals who experience a stroke due to AF, the occurrence of AF was not diagnosed until the time of their stroke or shortly afterward.[5] However, if AF is recognized, therapeutic anticoagulation can lead to an absolute risk reduction in all strokes of 2.7% per year for primary and 8.4% per year for secondary prevention, as well as a 0.5% per year absolute risk reduction in mortality.[6] Accordingly, guidelines of multiple professional societies recommend screening for AF, although primarily via opportunistic pulse palpation or electrocardiogram (ECG) rhythm strip during routine medical visits.[7,8]

The recent validation of several new digital technologies for diagnosing AF has enabled the potential for innovative screening strategies. In parallel, the ubiquity of the Internet and smartphones can support remote clinical trial participation, eliminating many of the common impediments to research enrollment and participation.[9] It is now possible to identify specific individuals for potential enrollment using large information resources, obtain informed consent remotely, and monitor and collect longitudinal clinical data from each enrollee.[10]

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Animated Summary Video: Effect of a Wearable ECG Patch on Detection of Atrial Fibrillation

Leveraging these advances, a randomized, pragmatic, direct-to-participant, digitally enabled trial carried out within a large US health plan organization was conducted to explore the value of screening for undiagnosed AF through the use of a wearable continuous ECG monitoring patch.

Key Points

Question Can a home-based self-applied wearable electrocardiogram (ECG) patch improve the diagnosis of atrial fibrillation (AF) relative to routine care?

Findings In this randomized clinical trial of 2659 individuals at increased risk for AF, immediate monitoring using a self-applied ECG patch, compared with delaying ECG monitoring for 4 months, led to a significantly higher rate of AF diagnosis at 4 months (3.9% vs 0.9%).

Meaning Among individuals at increased risk for AF, use of a home-based self-applied ECG patch facilitated AF diagnosis; further research is needed regarding clinical implications.

Methods

Study Design and Oversight

The mHealth Screening to Prevent Strokes (mSToPS) Trial, including the randomized and observational cohort studies, was approved by the Scripps Office for the Protection of Research Subjects. Participants in the randomized, actively monitored cohort provided written informed consent digitally. Individuals making up the matched observational cohort met all eligibility criteria but had not been invited to participate in the trial. The claims data of this cohort were collected and analyzed as routine for the health plan organization. Protected health information for the observational cohort was not disclosed.

The trial was an investigator-initiated, randomized, pragmatic, siteless clinical trial involving a large health insurance plan's members throughout the United States. Details of the trial design have been previously published (the full trial protocol and statistical analysis plan are in Supplement 1 and Supplement 2).[11] Eligible individuals were invited by email or direct mail and directed to a web-based informational website if interested in learning more about the study. This site contained detailed information about the study and directed those potentially interested in participating through several high-level screening questions (eg, confirming health plan membership and no recent AF diagnosis or placement of a pacemaker).

Those still eligible were then led through a self-navigating, modular digital consent process requiring comprehension confirmation for each section completed. All individuals who signed the consent and were reconfirmed as eligible health plan members underwent active monitoring and were randomized to either immediate monitoring or delayed monitoring (initiated 4 months after enrollment date). The primary end point was the difference in new AF diagnoses between these 2 groups at 4 months, prior to any active monitoring in the delayed group. In the follow-on, prospective observational study to evaluate the clinical consequences associated with ECG screening, the 2 randomized groups were combined into 1 actively monitored cohort and their results at 1 year after enrollment were compared with a matched observational cohort.

Outcomes data from claims were collected by Healthagen Outcomes, and for ECG patch results, by Scripps Translational Science Institute. Analysis of the combined data was carried out by Healthagen and Scripps Translational Science Institute.

Participant Population

The study population was derived from the Aetna Fully Insured Commercial and Medicare Advantage populations. Inclusion criteria for invitation were developed to include as broad a population as possible that might have an increased likelihood of having undiagnosed AF (eTable 1 in Supplement 3). Eligibility for the study included age of 75 years or older, or a male older than age 55 years or female older than 65 years with 1 or more comorbidities listed in eTable 1 in Supplement 3. Individuals were excluded from the study primarily if they had any current or prior diagnosis of AF, atrial flutter, or atrial tachycardia; were already prescribed anticoagulation therapy; or had an implantable pacemaker, defibrillator, or both.

For the routine care, observational cohort, 2 matched controls were selected for each of the actively monitored participants from the pool of individuals in the original eligible population who had not been invited to enroll. Matching was based on sex, exact age, and exact CHA_2DS_2-VASc (congestive heart

failure, hypertension, age ≥75 years [doubled], diabetes, stroke/transient ischemic attack/thromboembolism [doubled], vascular disease [prior myocardial infarction, peripheral artery disease, or aortic plaque], age 65-75 years, sex category [female]) score at the time of the actively monitored participant's date of enrollment. Due to variable enrollment dates, eligibility of the observational cohort was also reassessed prior to establishing a match.

Study Procedures

ECG screening was carried out using the iRhythm Zio^{XT}, a Food and Drug Administration-approved, single-use, water-resistant, 14-day, ambulatory ECG monitoring skin adhesive patch that monitors and retains in memory the wearer's continuous ECG for up to 2 weeks. After enrollment, participants were randomized by computer-generated random number to receive their patch either within 2 weeks (immediate group) or 4 months later (delayed group) along with instructions for self-application. Participants were asked to wear the patch and then to mail it back to the patch developer via a prepaid mail package. All participants were asked to wear 2 different patches for a period of up to 2 weeks for each patch, each 3 months apart to evaluate the additional potential benefit of more than 2 weeks of monitoring.

After participants returned the patch, the rhythm data stored in the device were analyzed using a Food and Drug Administration-approved algorithm. The results then underwent technical review for report generation and quality assurance after which the report was uploaded to a secure website for independent review by the study's principal investigator. All possible ECG diagnoses of AF were adjudicated, blinded to any diagnosis, by the Clinical Events Adjudication Committee.

All ECG patch results were returned to participants at the completion of monitoring. If any potentially actionable results were identified, including a finding of AF, any sustained tachyarrhythmia, or prolonged pause, the participant was contacted by telephone per protocol. After discussion of the findings, the report was sent to the participants and, if they agreed, also was sent to their physician.

Study End Points

The primary end point in the randomized clinical trial was the incidence of newly diagnosed AF (as defined by ≥30 seconds of AF or flutter detected by device or a new clinical diagnosis recorded in claims data) at the end of the 4-month monitoring period in the immediate monitoring group compared with the delayed monitoring group, in both the intent-to-treat and per-protocol populations (eFigure 1 in Supplement 3). A diagnosis by claims data required a single entry of an *International Classification of Diseases, Ninth Revision (ICD-9)* code of 427.3, 427.31, or 427.32, or an *International Statistical Classification of Diseases and Related Health Problems, Tenth Revision (ICD-10)* code of I48.0, I48.1, I48.2, I48.3, I48.4, I48.91, or I48.92.

Intention-to-treat analysis for the randomized clinical trial included all participants who enrolled in the study according to their randomly assigned group (immediate monitoring or delayed monitoring). The per-protocol cohort was defined by the subset of the overall cohort who wore an ECG sensor patch with at least 30 minutes of analyzable data. In the randomized trial, follow-up time for individuals in the immediate monitoring group began the day of enrollment and ended at 4 months following that date or the time of completion of monitoring with their final patch, whichever was longest. For study participants in the delayed group, follow-up began the date of enrollment and ended 4 months after that date.

For this 1-year outcome analysis, due to membership attrition, the end point was the incidence rate per 100 person-years of a new diagnosis of AF in the per-protocol cohort and their matched controls, using the same definition of AF as was used in the randomized study.

To evaluate the clinical consequences associated with screening, additional prespecified end points determined via claims data included the initiation of AF-related therapies including anticoagulants, antiarrhythmic agents, cardioversions, ablation procedures, or hospitalizations and emergency department visits with a primary diagnosis of AF. As general measures of health care utilization, we evaluated outpatient visits to primary care or cardiology, plus emergency department visits and hospitalizations for any cause. We also included pacemaker or defibrillator implantation, although this outcome was not prespecified. Incremental cost differences associated with active monitoring are planned at 3 years and not included in this report.

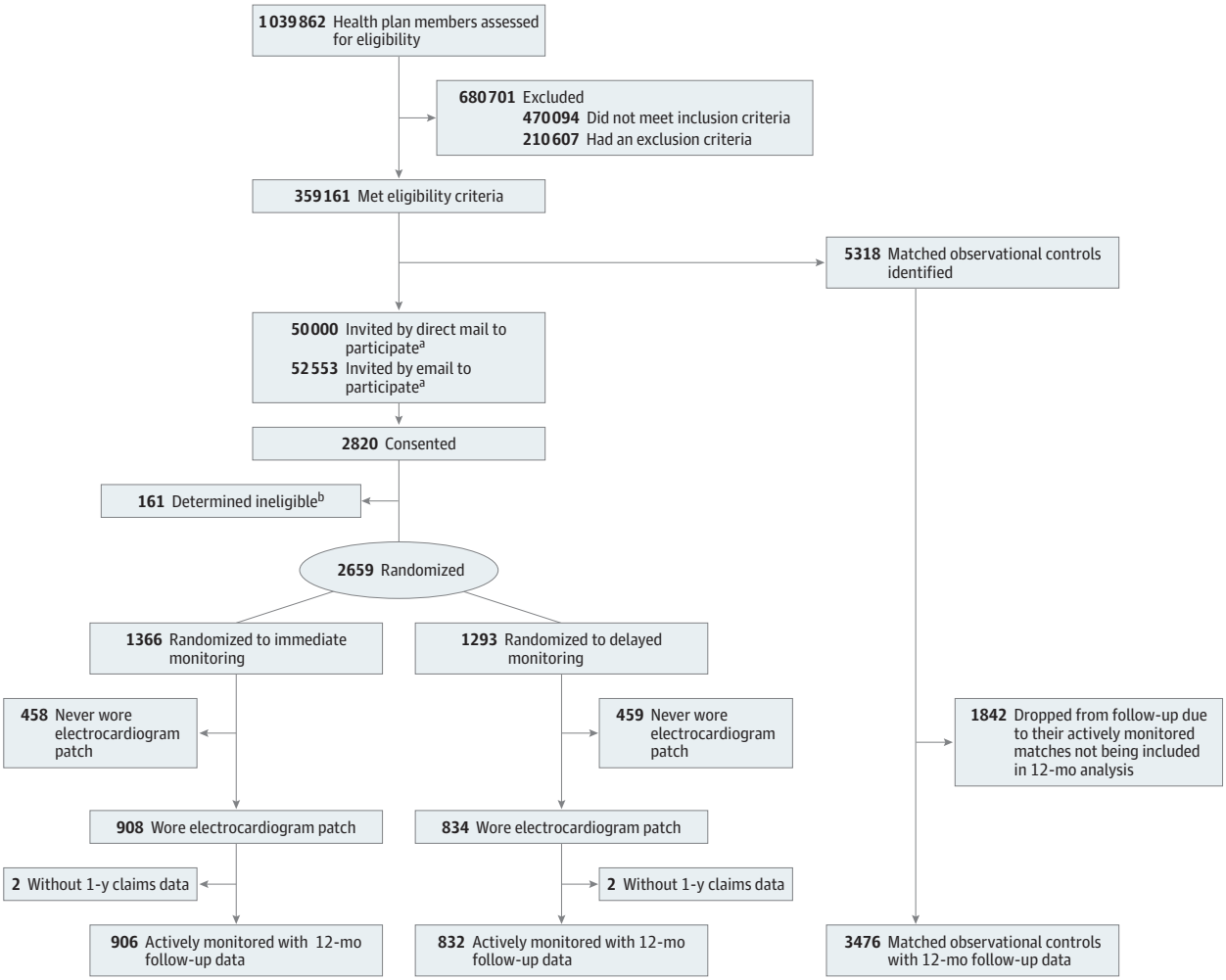
The start date for determination of outcomes from the health plan database for both monitored participants and their matched controls was the date of enrollment of the participant. The end date was 12 months by exact day from the start date.

Statistical Analysis

A target sample size of 2000 study participants for the monitored cohort matched to controls at a 1:2 ratio was based on health plan data of diagnosed AF. This led to conservative estimates for the 3-year study of an incidence of AF[11] of 10% in both cohorts and an expected combined stroke event[12] rate of 12% in the control cohort and 5% in the monitored cohort, yielding 81% power to detect a difference in time to event between the cohorts by log rank test.[11] This was anticipated to achieve more than 99% power for the 4-month end point to find a difference in the expected AF rate of 5%. This was based on data from studies with implantable cardiac monitors with short-term AF detection rates of approximately 10% in a higher-risk population than the current study, among those randomized to immediate monitoring vs 0.5% in the delayed monitoring group with a 2-sided alpha of .05.[13,14]

For patch-based outcome data in the monitored cohort, missing data could occur by either not wearing the patch or by patch failure to record (which was minimal because total analyzable time was 97.8% of total wear time). Individuals in the monitored cohort who did not wear a patch were assumed not to have AF unless identified via claims data as having AF. All nonsensor patch outcome and covariate data were obtained from the claims database, which was assumed to be complete after allowing for a lag in recording of claims of up to 3 months. All randomized participants were included in the intention-to-treat analysis for the 4-month outcome. Due to health plan membership attrition over longer-term follow-up,

Figure 1. Participant Flow Diagram



[a] Information on why plan members chose not to participate is not available.

[b] The 161 ineligible participants includes 77 who were not health plan members or disenrolled before approval; 61 members who no longer met inclusion/exclusion criteria; and 23 with incomplete informed consent.

participants were censored at the time of plan disenrollment. In addition, 4 study participants who wore a patch but withdrew from long-term follow-up with claims data were excluded from the 1-year analysis.

Baseline and follow-up characteristics of actively monitored participants and controls, as well as the subset of those diagnosed as having AF, were compared using *t* tests for continuous variables and χ^2 or Fisher exact test for categorical variables. For the outcome of incident AF occurring within 4 months (randomized clinical trial), the proportions with a new diagnosis of AF were compared. For 12-month outcomes (observational cohort), the number of individuals with newly diagnosed AF in number per person-time of follow-up in the monitored cohort (denominator) was compared with that of the unmonitored observational cohort using Poisson regression to yield an incidence rate ratio.

Multivariable analysis of the primary outcome was also performed using Poisson regression models including baseline demographic (age and sex) and clinical (CHA_2DS_2-VASc score and comorbidities) covariates. As a sensitivity analysis, other claims-based definitions of a diagnosis of AF were explored that included 2 separate *ICD-9* or *ICD-10* AF diagnostic codes, rather than a single entry, and the Health Profile Database algorithm.[15,16] All statistical tests were 2-sided with a significance threshold of $P < .05$. (For the secondary outcomes, the potential for type I error due to multiple comparisons was not accounted for; thus, these outcomes should be interpreted as exploratory.) The statistical software used was SAS Enterprise Guide version 6.1 (SAS Institute Inc).

Results

Study Participants

Of 359 161 individuals who met eligibility criteria, 52 553 had previously self-identified as preferring email vs direct mail for communications and constituted the primary population for enrollment outreach. An additional 50 000 individuals

Table 1. Baseline Characteristics of the Immediate and Delayed Randomized Groups

Characteristic	No. (%)	
	Immediate Monitoring Group (n = 1366)	Delayed Monitoring Group (n = 1293)
Age, mean (SD), y	73.5 (7.4)	73.1 (7.2)
Female	521 (38.1)	505 (39.1)
CHA_2DS_2-VASc score, median (Q1-Q3)[a]	3 (2-4)	3 (2-4)
Qualified by age ≥75 y only	680 (49.8)	606 (46.9)
Qualified as female with age >65 y plus comorbidity	212 (15.5)	237 (18.3)
Qualified as male with age >55 y plus comorbidity	474 (34.7)	450 (34.8)
Comorbidities		
Stroke	187 (13.7)	182 (14.1)
Heart failure	69 (5.1)	59 (4.6)
Hypertension	1053 (77.1)	993 (76.8)
Diabetes	529 (38.7)	472 (36.5)
Sleep apnea	341 (25.0)	374 (28.9)
Prior myocardial infarction	75 (5.5)	72 (5.6)
Chronic obstructive pulmonary disease	129 (9.4)	112 (8.7)
Obesity[b]	236 (17.3)	238 (18.4)
Chronic renal failure	148 (10.8)	124 (9.6)

Abbreviation: CHA_2DS_2-VASc, congestive heart failure, hypertension, age ≥75 years (doubled), diabetes, stroke/transient ischemic attack/thromboembolism (doubled), vascular disease (prior myocardial infarction, peripheral artery disease, or aortic plaque), age 65-75 years, sex category (female).

[a] CHA_2DS_2-VASc score is a clinical prediction score for estimating the risk of stroke in individuals with nonrheumatic atrial fibrillation. An individual's score can range from 0-9, with a high score associated with higher risk. Components include congestive heart failure (1 point); hypertension (1 point); age ≥75 years (2 points); diabetes (1 point); prior stroke or transient ischemic attack (2 points); vascular disease (1 point); age 65-74 years (1 point); and sex category (female; 1 point).

[b] Obesity is defined through the Health Profile Database using a combination of data types including a documented body mass index of 30 or greater and/or an obesity-related diagnosis or procedure (eg, bariatric surgery).

preferring direct mail were also included to enable a 1-time baseline comparison between the 2 methods of outreach. A total of 52 553 health plan members were sent an email invitation to participate. A total of 41 836 of those individuals received that email and 17 373 (41.5%) opened it. Of these, 2280 (13.1%) were enrolled in the study. Of the 50 000 who were sent an invitation by direct mail, 379 were enrolled (0.76%), providing a total of 2659 enrolled individuals who were randomized to either immediate or delayed monitoring (**Figure 1**). Individuals who chose to enroll were, in general, slightly younger, more often male, and had fewer comorbidities than those who did not (eTable 2 in Supplement 3). Baseline characteristics were similar between the immediate and delayed monitoring groups except for the immediate group having fewer individuals with sleep apnea (**Table 1**).

Of the 2659 enrolled individuals, 34.5% (n = 917) did not wear a patch (characteristics of those who did and did not wear a patch are in eTable 3 in Supplement 3), and an additional 4 individuals lacked claims data follow-up at 1 year, leaving 1738 actively monitored individuals and 3476 matched controls to be included in the 1-year observational study (Figure 1). Over 12 months of follow-up, 11.4% of the monitored cohort disenrolled from the health plan; 1.0% prior to the 4-month end point, then at a mean rate of 1.3% per month for the following 8 months.

Baseline characteristics of the actively monitored and observational control cohorts are compared in **Table 2**. Imbalances in some baseline characteristics were found, with a higher percentage of prior stroke and sleep apnea among the actively monitored, and more chronic obstructive pulmonary disease and prior myocardial infarction in controls.

The mean (SD) wear time per ECG patch was 11.7 (4.1) days, with 97.8% analyzable ECG data. A total of 481 individuals wore one patch, and 1257 wore both ECG patches, providing a median total monitoring time of 593.3 hours (interquartile range [IQR], 327.8-662.2 hours) per monitored participant.

Primary End Point

In the intention-to-treat analysis of the randomized clinical trial, the incidence of new AF cases was 3.9% (53/1366) in the immediate monitoring group vs 0.9% (12/1293) in the delayed monitoring group (absolute difference, 3.0% [95% CI, 1.8%-4.1%]). Similar results were found in the per-protocol analysis including only those individuals who wore a monitoring patch (5.1% [46/906] vs 0.6% [5/832]; absolute difference, 4.5% [95% CI, 3.0%-6.1%]). Using different claims databased diagnoses for AF also did not significantly change the results (eTable 4 in Supplement 3).

Secondary End Points

In the observational study, over 12 months of follow-up, 190 new cases of AF were detected, 109 of 1738 (6.7 per 100 person-years) in the actively monitored cohort and 81 of 3476 (2.6 per 100 person-years) among observational controls (absolute difference, 4.1 [95% CI, 3.9-4.2]) (**Figure 2**).

In the actively monitored cohort, 65 individuals were first found to have AF by ECG patch (43 with first patch and 22 only with the second patch). In this cohort, 44 individuals received a clinical diagnosis of AF either prior to monitoring (n = 12) or after monitoring was completed without any findings of AF during monitoring (n = 32).

Sensitivity Analysis

Sensitivity analyses using different claims-based definitions of AF did not significantly change the results (eTable 5 in Supplement 3) nor did adjusting for baseline differences between cohorts (eTable 6 in Supplement 3).

Characteristics of AF

Twelve of 69 participants (17.4%) who had AF while wearing a patch (including those clinically diagnosed as having AF prior to wearing the patch) recalled, when prompted, having some symptoms potentially associated with AF. Most symptoms were mild and did not lead to a clinical evaluation, although 2 individuals did have symptoms while wearing the patch that led to them seeking care and a clinical diagnosis of new AF that aligned with the timing of the ECG-based diagnosis.

When AF was diagnosed by ECG patch, 3 study participants were found to have continuous AF throughout the

Table 2. Baseline Characteristics of Actively Monitored Individuals and Their Matched Observational Controls

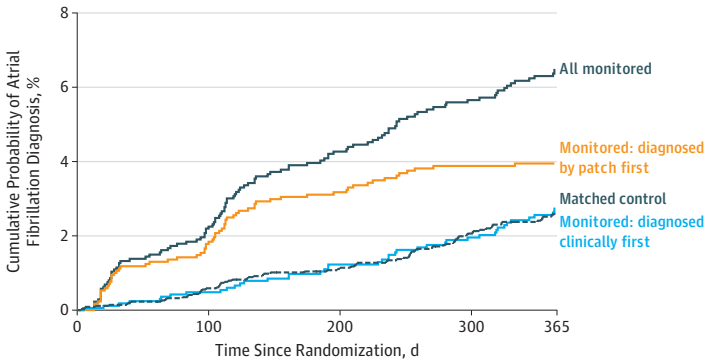
Characteristic	No. (%)		Difference (95% CI)
	Actively Monitored (n = 1738)	Matched Controls (n = 3476)	
Age, mean (SD), y	73.7 (7.0)	73.7 (7.0)	Matched
Female	704 (40.5)	1408 (40.5)	Matched
CHA_2DS_2-VASc score, median (Q1-Q3)[a]	3.0 (2-4)	3.0 (2-4)	Matched
Comorbidities			
Stroke	220 (12.7)	336 (9.7)	3.0 (1.2 to 4.8)
Heart failure	87 (5.0)	210 (6.0)	−1.0 (−2.3 to 0.3)
Hypertension	1307 (75.2)	2635 (75.8)	−0.6 (−3.1 to 1.9)
Diabetes	606 (34.9)	1216 (35.0)	−0.1 (−2.9 to 2.6)
Sleep apnea	462 (26.6)	718 (20.7)	5.9 (3.5 to 8.4)
Prior myocardial infarction	91 (5.2)	238 (6.9)	−1.6 (−3.0 to −0.3)
Chronic obstructive pulmonary disease	138 (7.9)	348 (10.0)	−2.1 (3.7 to −0.5)
Obesity[b]	289 (16.6)	608 (17.5)	−0.9 (−3.0 to 1.3)
Chronic renal failure	186 (10.7)	310 (8.9)	1.8 (0.1 to 3.5)

Abbreviation: CHA_2DS_2-VASc, congestive heart failure, hypertension, age ≥75 years (doubled), diabetes, stroke/transient ischemic attack/thromboembolism (doubled), vascular disease (prior myocardial infarction, peripheral artery disease, or aortic plaque), age 65-75 years, sex category (female).

[a] CHA_2DS_2-VASc score is a clinical prediction score for estimating the risk of stroke in individuals with nonrheumatic atrial fibrillation. An individual's score can range from 0-9, with a high score associated with higher risk. Components include congestive heart failure (1 point); hypertension (1 point); age ≥75 years (2 points); diabetes (1 point); prior stroke or transient ischemic attack (2 points); vascular disease (1 point); age 65-74 years (1 point); and sex category (female; 1 point).

[b] Obesity is defined through the Health Profile Database using a combination of data types including a documented body mass index of 30 or greater and/or an obesity-related diagnosis or procedure (eg, bariatric surgery).

Figure 2. Cumulative Rate of First Diagnosis of Atrial Fibrillation in the Actively Monitored and Observational Cohorts



No. at risk

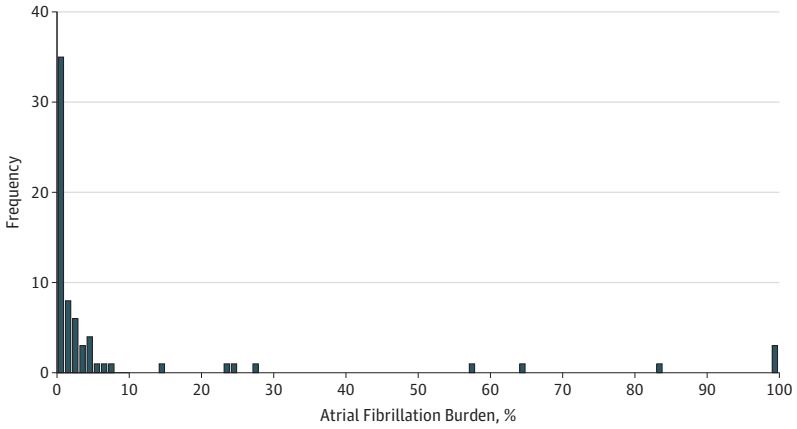
All monitored	1738	1681	1555	1469	1446
Monitored: diagnosed by patch first	1738	1681	1555	1469	1446
Monitored: diagnosed clinically first	1738	1681	1555	1469	1446
Matched control	3476	3348	3028	2832	2762

The initial rapid increase in atrial fibrillation diagnoses seen in the diagnosed by patch group is due to those in that group who were randomized to the patch immediately. The second region of rapid rise in this curve, starting around 120 days, is primarily due to those in the delayed patch group. The immediate and delayed groups initiated monitoring at a median of 13 days and 102 days, respectively. Patch diagnosis of atrial fibrillation is defined as 30 seconds or more of atrial fibrillation or flutter detected by device. Clinical diagnosis defined as a single entry of an *International Classification of Diseases, Ninth Revision* code of 427.3, 427.31, or 427.32, or an *International Statistical Classification of Diseases and Related Health Problems, Tenth Revision* code of I48.0, I48.1, I48.2, I48.3, I48.4, I48.91, or I48.92.

duration of monitoring. All others had self-limited periods of AF, with a mean of 9.8 episodes per monitoring period. The median duration of an individual's longest duration of AF was 185.5 minutes (IQR, 30.1-606.0 minutes). The longest individual episode of AF was less than 5 minutes in 7.2%, 5 minutes to 6 hours in 55.0%, 6 to 24 hours in 24.6%, and more than 24 hours in 13.0%. The median burden of AF (percentage of monitored time in AF) was 0.9% (IQR, <1.0%-4.0%) (**Figure 3**). Nineteen of the 65 individuals (29.2%) first found to have AF by ECG monitoring only had AF on their second patch. The median duration of time after either ECG patch placement until first detection of AF was 2.0 days (IQR, 1.0-5.0 days) (**Figure 4**).

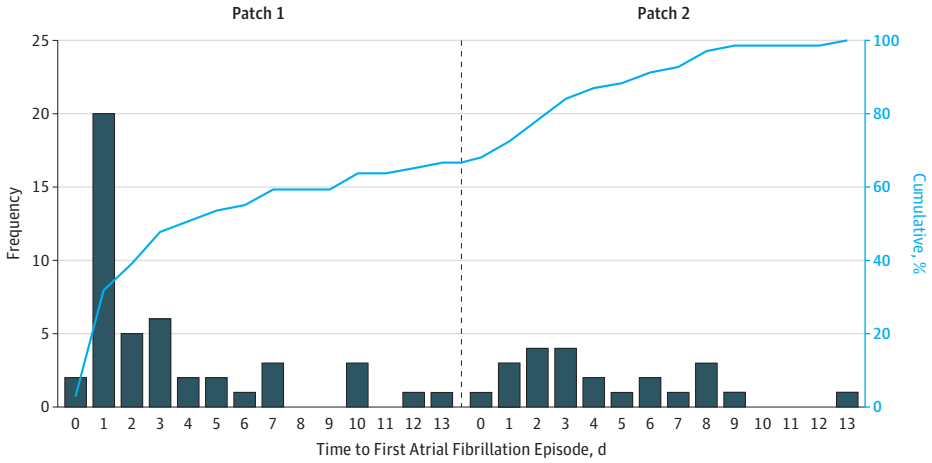
Clinical characteristics of individuals found to have AF are shown in **Table 3**. Clinically diagnosed individuals were significantly more likely to have chronic renal failure and less likely to have sleep apnea than those diagnosed by ECG. The association between baseline CHA_2DS_2-VASc score and a new AF diagnosis based on cohort is shown in eFigure 2 in

Figure 3. Distribution of Individual Percentage of Total Atrial Fibrillation Burden During Monitoring



Atrial fibrillation burden indicates percentage of total monitoring time in atrial fibrillation. A total of 69 participants had patch-detected atrial fibrillation. The median monitoring time was 26.5 days (interquartile range, 16.5-27.6 days).

Figure 4. Days of Electrocardiogram Patch Wear Until a First Diagnosis of Atrial Fibrillation (AF) on the First or Second Patch and the Cumulative Wear Time Until Diagnosis



Patch 2 indicates patients who had AF on patch 2 only. Of the 1738 monitored participants, 1669 had no AF detected by patch. Of the 69 monitored participants with AF detected by patch, 21 had AF detected on patch 1 only, 6 of whom wore only 1 patch; 23 had AF detected on patch 2 only; and 25 had AF detected on both patches.

Supplement 3. Age (per additional 10 years), heart failure, and chronic obstructive pulmonary disease were associated with increased incidence of new AF, while female sex was associated with decreased incidence (eTable 6 in Supplement 3).

Clinical Consequences

Active monitoring was associated with a higher rate of initiation of anticoagulant therapy in general (5.7 vs 3.7 per 100 person-years; absolute difference, 2.0 [95% CI, 1.9-2.2]), as well as specifically for AF (2.4 vs 1.3 per 100 person-years; absolute difference, 1.1 [95% CI, 1.0-1.2]) (**Table 4**). Of other AF-related interventions, active monitoring was also associated with an increase in initiation of antiarrhythmic medication and ablation or cardioversion procedures, but not hospitalizations or emergency department visits for AF. Active monitoring was also associated with greater use of health care resources, especially with an increase in individuals with outpatient cardiology visits. Although not prespecified, pacemaker or defibrillator placements were also higher in the monitored cohort (Table 4).

Adverse Events and Other Findings

Forty individuals reported skin irritation associated with wearing the ECG patch, leading to 32 people discontinuing their patch early, 2 of whom sought medical attention and received topical therapy.

A total of 70 participants were found to have potentially actionable arrhythmias other than AF. Twenty-four individuals had nonsustained ventricular tachycardia of more than 5 beats' duration and a cardiomyopathy diagnosis, 22 had prolonged or symptomatic supraventricular tachycardia, 25 had a significant pause or high-degree atrioventricular block, and 1 person had very frequent ectopy (27% of QRS complexes).

Discussion

Among individuals at high risk for AF, immediate monitoring with a home-based wearable ECG sensor patch, compared with delayed monitoring, resulted in a higher rate of AF diagnosis after 4 months. Monitored individuals, compared

Table 3. Baseline Clinical Characteristics of Individuals With and Without a New Diagnosis of AF at 1 Year, and Whether First Diagnosed by ECG Patch or Clinically, in the Actively Monitored Cohort Only

	Characteristics at 1 y			Method of Diagnosis		
	No. (%)			No. (%)		
Characteristic	No AF (n = 1629)	New Diagnosis of AF (n = 109)	Difference (95% CI)	AF First Diagnosed Clinically (n = 44)	AF First Diagnosed by ECG Patch (n = 65)	Difference (95% CI)
Age, mean (SD), y	73.5 (7.0)	76.7 (7.1)	−3.2 (−4.6 to −1.8)	77.3 (7.8)	76.3 (6.7)	0.9 (−1.9 to 3.8)
Female	668 (41.0)	36 (33.0)	8.0 (−1.2 to 17.1)	13 (29.6)	23 (35.4)	−5.8 (−23.6 to 12.0)
CHA_2DS_2-VASc score, median (Q1-Q3)	3 (2-4)	3 (2-4)	−0.1 (−0.3 to 0.2)[a]	3 (2-4)	3 (2-4)	0.1 (−0.4 to 0.6)[a]
Comorbidities						
Stroke	205 (12.6)	15 (13.8)	−1.2 (−7.8 to 5.5)	7 (15.9)	8 (12.3)	3.6 (−9.8 to 17.0)
Heart failure	77 (4.7)	10 (9.2)	−4.5 (−10.0 to 1.1)	6 (13.6)	4 (6.2)	7.5 (−4.2 to 19.2)
Hypertension	1227 (75.3)	80 (73.4)	1.9 (−6.6 to 10.5)	32 (72.7)	48 (73.9)	−1.1 (−18.1 to 15.8)
Diabetes	587 (36.0)	19 (17.4)	18.6 (11.1 to 26.1)	8 (18.2)	11 (16.9)	1.3 (−13.3 to 15.9)
Sleep apnea	440 (27.0)	22 (20.2)	6.8 (−1.0 to 14.7)	5 (11.4)	17 (26.2)	−14.8 (−29.0 to −0.6)
Prior myocardial infarction	87 (5.3)	4 (3.7)	1.7 (−2.0 to 5.4)	1 (2.3)	3 (4.6)	−2.3 (−9.1 to 4.4)
Chronic obstructive pulmonary disease	126 (7.7)	12 (11.0)	−3.3 (−9.3 to 2.7)	5 (11.4)	7 (10.8)	0.6 (−11.4 to 12.6)
Obesity[b]	276 (16.9)	13 (11.9)	5.0 (−1.3 to 11.4)	5 (11.4)	8 (12.3)	−0.9 (−11.4 to 13.3)
Chronic renal failure	175 (10.7)	11 (10.1)	0.7 (−5.2 to 6.5)	8 (18.2)	3 (4.6)	13.6 (1.1 to 26.1)

Abbreviations: AF, atrial fibrillation; CHA_2DS_2-VASc, congestive heart failure, hypertension, age ≥75 years (doubled), diabetes, stroke/transient ischemic attack/thromboembolism (doubled), vascular disease (prior myocardial infarction, peripheral artery disease, or aortic plaque), age 65-75 years, sex category (female); ECG, electrocardiogram.

[a] Difference in means.

[b] Obesity is defined through the Health Profile Database using a combination of data types including a documented body mass index of 30 or greater and/or an obesity-related diagnosis or procedure (eg, bariatric surgery).

Table 4. Clinical Utilization Over 1 Year in Those Actively Monitored and Their Matched Observational Controls

	Actively Monitored Group (n = 1738)	Matched Control Group (n = 3476)	Difference (95% CI)
AF-related therapeutic interventions, No./100 person-years)			
Pharmacy fill for an anticoagulant	5.7	3.7	2.0 (1.9 to 2.2)
Pharmacy fill for an anticoagulant for individuals with AF	2.4	1.3	1.1 (1.0 to 1.2)
Pharmacy fill for an antiarrhythmic medication	0.8	0.3	0.5 (0.4 to 0.5)
Cardioversion procedures	0.24	0.19	0.05 (0.03 to 0.08)
Cardiac ablation	0.3	0.1	0.2 (0.18 to 0.24)
ED visit or inpatient stays with an AF diagnosis	1.3	1.4	0.1 (−0.1 to 0)
Clinical use (No./100 person-years)			
Placement of a pacemaker or defibrillator	0.79	0	0.79 (0.75 to 0.84)
Any cause ED visit or inpatient stays	22.5	23.7	−1.2 (−1.5 to −0.9)
Participants with at least 1 all-cause outpatient office visit to a primary care clinician	83.5	82.6	0.9 (0.4 to 1.5)
Participants with at least 1 all-cause outpatient office visit to a cardiologist	33.5	26.0	7.5 (7.2 to 7.9)
Participants with at least 1 all-cause outpatient office visit to a cardiologist or primary care clinician	89.2	88.1	1.1 (0.5 to 1.7)
Clinical use (No./person-year)			
Primary care visits	2.78	2.84	−0.07 (−0.17 to 0.03)
Cardiology visits	0.67	0.48	0.19 (0.15 to 0.24)
Cardiology or primary care visits	3.45	3.32	0.12 (0.01 to 0.23)

Abbreviations: AF, atrial fibrillation; ED, emergency department.

with nonmonitored controls, had higher rates of AF diagnosis, greater initiation of anticoagulants, but also increased health care resource utilization at 1 year.

Most individuals who had AF diagnosed by ECG patch had a relatively low burden of paroxysmal AF; only a small percentage of incident cases (3/65 [4.6%]) were found to have persistent AF. These results suggest that spot checking for AF, whether by a random pulse check for irregularity or obtaining a brief ECG, would likely miss most individuals with undiagnosed AF. Prior studies of ECG screening for AF in unselected older adults using a single 30-second ECG have found rates of incident AF of 1% to 1.5%.[17,18] Longer-term screening with brief, recurring ECG checks

for 2 weeks or 12 months have found new AF rates of 3% to 4%.[19,20] However, several recent trials of implantable cardiac monitors have identified new AF in 22% to 40% of individuals, with monitoring up to 30 months.[13,14,21]

Resource utilization following ECG screening for AF has not previously been well described. Beyond informing participants of their findings, and supplying those results to their physicians when requested, no further actions were dictated by the study. A higher rate of initiation of anticoagulant therapies in the overall active monitoring cohort was found, as well as specifically for a diagnosis of AF. Monitoring was associated with a higher rate of outpatient physician visits, especially cardiology visits, and small but significant increased rates of pacemaker placement and antiarrhythmic medication initiation.

The study population was selected based on relatively broad inclusion criteria to better explore whether undiagnosed AF may be more common in populations that differ from those that are at increased risk for clinically diagnosed AF. For example, individuals with underlying heart failure, one of the most important risk factors for AF, may be much more likely to become rapidly symptomatic and therefore manifest clinically almost immediately.[22] In this study, there was no difference in the clinical characteristics of those individuals diagnosed by ECG patch as those diagnosed clinically, with age and heart failure most strongly associated with a new AF diagnosis. Future screening programs will benefit from being able to target those at highest risk for undiagnosed AF. The addition of genetic risk factors will allow for even greater refinement.[1,23]

It is possible that individuals with asymptomatic AF diagnosed only by ECG represent a different population than those whose AF manifests clinically. Therefore, to optimize future screening programs, the significance of short episodes of AF, especially when asymptomatic, will require greater clarity. A new diagnosis of AF would never be considered a normal finding and, even when asymptomatic, is strongly associated with the development of clinical AF.[24] Early recognition could encourage the implementation of strategies to prevent progression, such as treatments of sleep apnea or morbid obesity. However, currently, the primary clinical question for screen-detected AF revolves around the risks and benefits for the initiation of anticoagulants. AF duration influences stroke risk because individuals with paroxysmal AF have a lower stroke risk than those with persistent and permanent forms of AF.[25,26]

Most recent data evaluating the clinical outcomes associated with screening for AF come from studies of cardiac implantable devices, with some data suggesting only populations with episodes of longer than 24 hours of atrial high-rate events are at increased risk of stroke, but other analyses of all available data support the lack of a threshold duration with a lower relative risk of stroke.[27,28] It is likely that other individual characteristics, such as age, comorbidities, and overall AF burden, influence stroke risk beyond just the longest duration of AF episodes, which mandates greater individualization of targeted screening.[29,30] This is especially important because the diagnosis of AF can impair quality of life well beyond symptom burden or disease severity.[31,32]

The methods used in the current study demonstrate how digital technologies can enable the re-imagining of clinical research to be more inclusive and participant-centric. The unique design of the study offers both benefits and limitations. By conducting this study within a health insurance system, only individuals meeting all inclusion criteria could be invited to participate. In addition, clinically meaningful outcomes could be passively tracked. Digital outreach and participant-centered monitoring with a wearable sensor, even in this population with a mean age of approximately 74 years, allowed for siteless, nationwide enrollment and the inclusion of individuals who otherwise would likely have no access to clinical trials. It is possible that these innovations may lower study costs while potentially enabling the findings to be implemented for the care of patients without delay.

Limitations

The study has several limitations. First, only a limited number of eligible individuals invited successfully enrolled (2655/102 553 [2.6%]). Second, a substantial number (38%) of those who were initially interested in participating changed their minds and never wore a patch. Combining these 2 limitations, only 1.7% of the invited population was successfully monitored. Third, health plan membership is fluid, with the potential to change annually for individuals, therefore, longer-term claims-based follow-up is not guaranteed. Furthermore, in this study, more than 10% of randomized individuals were no longer health plan members at 12 months. Fourth, because actively monitored individuals were invited to a study of heart rhythm screening, unlike the observational cohort, it is possible that the monitored cohort could have been prompted to more aggressively seek clinical evaluation even premonitoring. The fact that there was no difference in the rate of clinical AF diagnosis in the delayed group premonitoring vs matched observational controls (0.60% vs 0.54%) suggests this was not the case. Fifth, clinical outcome data were not included in this analysis but will be reported when the planned 3-year follow-up is complete.

Conclusions

Among individuals at high risk for AF, immediate monitoring with a home-based wearable ECG sensor patch, compared with delayed monitoring, resulted in a higher rate of AF diagnosis after 4 months. Monitored individuals, compared with nonmonitored controls, had higher rates of AF diagnosis, greater initiation of anticoagulants, but also increased health care resource utilization at 1 year.

ARTICLE INFORMATION

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Author Contributions: Drs Steinhubl and Waalen had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.
Concept and design: Steinhubl, Waalen, Mehta, Ebner, Carter, Baca-Motes, Felicione, Sarich, Topol.
Acquisition, analysis, or interpretation of data: Waalen, Edwards, Ariniello, Mehta, Ebner, Baca-Motes, Topol.
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