Remote Screening for Asymptomatic Atrial Fibrillation: the AMALFI Randomized Clinical Trial

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Key Points

Question: What is the long-term effect on AF diagnosis of screening older individuals at moderate-to-high stroke risk using a single 14-day, patch-based continuous ambulatory ECG monitor?

Findings: In this randomized siteless clinical trial that included 5040 individuals in primary care, AF was diagnosed by 2.5 years after randomization in 172 individuals (6.8%) in the intervention group vs 136 (5.4%) in the control group, a significant difference.

Meaning: A mail-based AF screening program led to a modest long-term increase in AF diagnosis.

Abstract

Importance

Screening for atrial fibrillation (AF) might reduce stroke if it increases long-term AF detection and anticoagulation use compared to usual care.

Objective

To investigate the long-term efficacy of AF screening in older individuals at moderate-to-high stroke risk using 14-day patch-based continuous ambulatory ECG monitoring.

Design, Setting, and Participants

Parallel group unblinded siteless randomized controlled trial recruiting from 27 UK primary care practices from 2nd May 2019 to 28th February 2022. All eligible individuals aged ≥65 years with CHA_2DS_2VASc score ≥3 (men) or ≥4 (women) with no previous AF/atrial flutter were identified via automated electronic health record searches. Of 22044 individuals invited, 5040 (22.9%) were randomized. Last follow-up was on 29th August 2024.

Intervention

Participants were randomized to receive and return an ECG patch monitor by postal mail (intervention, n=2520) or to usual care (control, n=2520).

Main Outcome and Measure

Intention-to-treat analysis of the proportion of participants with AF recorded in primary care records within 2.5 years post-randomization. Exploratory outcomes included exposure to oral anticoagulation and stroke.

Results

Participants' mean age was 78 years (SD 6), 47% were female, and median CHA_2DS_2VASc score was 4 (IQR 3-5). 2126 participants (84.4%) wore and returned the patch. AF was detected by patch in 89 participants (4.2%), 55% of whom had an AF burden <10%. After 2.5 years, a post-randomization record of AF was present in 172 individuals (6.8%) in the intervention group vs 136 (5.4%) in the control group (ratio of proportions 1.26, 95% CI 1.02-1.57, p=0.03), with consistent results in pre-specified sub-groups. Mean exposure to oral anticoagulation by 2.5 years was 1.63 months (95% CI 1.50-1.76) in the intervention group and 1.14 months (95% CI 1.01-1.26) in the control group (difference 0.50 months, 95% CI 0.24-0.75, p<0.001). Stroke occurred in 69 participants (2.7%) in the intervention group and 64 (2.5%) in the control group (rate ratio 1.08, 95% CI 0.76-1.53).

Conclusions and Relevance

Mail-based AF screening with an ECG patch in older patients at moderate-to-high stroke risk led to a modest long-term increase in AF diagnosis at 2.5 years.

Trial Registration

ISCRTN Identifier: 15544176

Introduction

Atrial fibrillation (AF) is associated with increased risk of stroke, heart failure, and premature death.[1] Cardioembolic strokes presumed to be related to AF account for up to one-third of ischemic strokes,[2] and oral anticoagulation in high-risk individuals with AF reduces stroke risk by about two-thirds and all-cause mortality by a quarter.[3] AF can be asymptomatic and/or occur intermittently, and hence may not be clinically evident, but this does not affect either stroke risk or the efficacy of, or indication for, anticoagulation in AF.[4-7]

Screening has been proposed as a way to increase early AF detection and prevent cardioembolic strokes with anticoagulation.[8,9] US recommendations state that there is insufficient evidence to support population-based ECG screening,[10] whilst European guidelines give a class IIA recommendation for screening using a prolonged non-invasive ECG-based approach in high-risk individuals.[7] Importantly, any impact of AF screening on clinical outcomes depends on achieving a greater sustained increase in AF detection and anticoagulation use than that resulting from usual care alone, highlighting the importance of long-term studies to generate the evidence needed to justify establishing formal screening programs[11].

The Active Monitoring for AtriaL FIbrillation (AMALFI) trial tested whether remote screening for asymptomatic AF, using a single non-invasive long-term (14-day) continuous monitoring ECG patch in older individuals at moderate-to-high risk of stroke, led to a greater rate of AF diagnosis at 2.5 years after randomization compared with usual care. Effects on anticoagulation use and stroke were exploratory outcomes.

Methods

Study design

AMALFI is an investigator-initiated, parallel group, unblinded, randomized controlled trial which recruited individuals from 27 primary care practices in the United Kingdom. AMALFI is an entirely remote trial, with no physical study sites or in-person visits. The trial design and protocol (Supplement 1) have been published[12]. The protocol and subsequent modifications were approved by the University of Oxford (trial sponsor), the London Bromley Research Ethics Committee (19/LO/0220), and the Health Research Authority (IRAS234837). AMALFI is registered in ISCRTN (15544176). CONSORT reporting guidelines were followed.

Participants

Individuals aged ≥65 years with CHA_2DS_2VASc score ≥3 (men) or ≥4 (women) were eligible. The key exclusion criterion was a previous diagnosis of AF or atrial flutter. Participants with qualifying risk factors were identified via automated electronic health record searches performed in participating primary care practices, as described previously[12]. Participants provided written informed consent. Data on race and ethnicity were extracted from primary care records prior to and up to 2.5 years post randomization, because they influence AF epidemiology[13]. Where discrepancies occurred, the category listed most frequently was assigned. Where no informative primary care records were available, race and ethnicity were sourced from secondary care records and classified in an identical manner. Full details on the coding of race and ethnicity and other patient characteristics have been published previously.[12]

Randomization

Participants were randomized 1:1 between intervention (patch) and control (usual care) groups. A minimization algorithm was used to ensure adequate

balance between groups with regards to important features associated with the presence of AF and stroke, namely age, sex, and residual CHA_2DS_2VASc score. There was no masking and participants, their general practitioners (GPs), and the trial team were aware of study group allocation. However, access to tabular results of study outcomes by randomized allocation was not available to the research team, chief investigators, trial statisticians, or GPs, prior to finalizing the statistical analysis plan (Supplement 2) and conducting the main trial analyses.

Procedures

AMALFI tested a remote screening strategy using a non-invasive single lead ECG patch for long-term (14-day) continuous ambulatory cardiac monitoring (Zio XT, iRhythm Technologies, San Francisco, CA, USA), hereafter referred to as "patch" or "ECG monitor".

Participants allocated to the intervention group were sent the patch by mail and asked to self-apply it. Instructions were included with the patch and a short video was available on the study website, as was further assistance via telephone or email. Those randomized to the control group received a letter confirming their allocation and were not required to undertake any further action. The trial design and all participant-facing materials were reviewed by a patient panel prior to recruitment starting, to ensure that the information was comprehensive and intelligible.

Automated alert systems were in place for patch findings of AF and other clinically actionable arrhythmias, which were communicated to GPs immediately by secure email. Results letters were also sent to GPs detailing the presence or absence of AF, along with duration, heart rate, and burden. GPs managed findings at their discretion as part of clinical care; no guidance on management of AF or other arrhythmias was provided by AMALFI, besides referencing relevant guidelines.[7,14]

Further details regarding the patch and its analysis are available in the eMethods (Supplement 3).

Outcomes

The primary outcome was the proportion of participants with the presence of AF in primary care records within 2.5 years post-randomization, which was analyzed using an intention-to-treat approach. Secondary outcome assessments involved intention-to-treat comparisons of the primary outcome by subgroups of age (<80 and ≥80 years) and, separately, sex. Sensitivity analyses of the primary and secondary outcomes were performed using AF diagnoses captured in either primary care or secondary care records. Exploratory outcomes included randomized assessments of time to AF detection within 2.5 years after randomization, time spent with a known AF diagnosis up to 2.5 years from randomization, and anticoagulation exposure within 2.5 years after randomization. Other exploratory long-term assessments included randomized comparisons of numbers and proportions of stroke and death (all-cause and cardiovascular) in both groups. Full details are available in the Statistical Analysis Plan (Supplement 2).

For detailed description of the definition and derivation of baseline characteristics and outcomes, including race and ethnicity, see eMethods (Supplement 3) and the AMALFI protocol paper[12].

Statistical analysis

The sample size for AMALFI was initially specified as 2500 but later increased to 5000 (before any unblinded data were reviewed) both to increase the power of the trial overall, and to provide sufficient power to analyze the primary outcome for subgroups of age and, separately, sex. Based on an estimated AF detection rate over 2.5 years from randomization of 4.4% in the patch group and 1.75% in

the usual care group (ratio 2.5), it was estimated that a sample size of 5000 would provide >90% power at 2-tailed p<0.01 and that this level of power and significance would be maintained for a smaller 2-fold, rather than 2.5-fold, difference in proportions. There would be approximately 90% power at 2-tailed p<0.05 to analyse the primary outcome for subgroups of age at randomization (with a cut-off of 80 years) and, separately, sex.

The chi-square test was used to conduct intention-to-treat comparisons of the primary outcome. The same method was employed in age and, separately, sex subgroups; these are reported with a chi-square test for heterogeneity of the results between the two subgroups. Individuals with no record of AF during this time frame who died, were withdrawn, or lost to follow-up from the primary care records before 2.5 years from randomization were included with those with no record of AF. Analogous methods were used to conduct intention-to-treat comparisons of the sensitivity analyses of the primary and secondary outcomes (with AF diagnoses captured in either primary or secondary care records), and of the exploratory outcome of proportion of participants with a record of oral anticoagulation (captured in nationwide community pharmacy dispensing records) within 2.5 years after randomization.

Log-rank methods were used to conduct intention-to-treat comparisons of the exploratory outcome of time to first post-randomization record of AF in the primary care record, censoring at the earliest of death, withdrawal, loss to follow-up in the primary care record, and 2.5 years. Log-rank test p-values are presented with rate ratios used to quantify differences between groups. Rate ratios were obtained from the log rank observed minus expected number of events (O-E) and its variance (V), and calculated as exp(O-E/V). Time from urgent patch report to first primary care record of AF was analyzed using the same method. Exploratory outcomes of time to first post-randomization record of oral anticoagulation, stroke, and death were also analyzed using log-rank methods,

but were not censored at loss to follow-up in the primary care record as outcomes were based wholly (oral anticoagulation and death) or in part (stroke) on secondary care records or nationwide community pharmacy dispensing records. As calendar month and year but no exact dates were available in the dispensing records, results of the oral anticoagulation comparison are presented in months rather than days from randomization. Oral anticoagulation prescriptions during the month of randomization contribute to baseline rates and not post-randomization records as it is not possible to determine which are truly post-randomization.

A permutation test[15] was used to compare mean time spent with a diagnosis of AF in all those randomized to patch compared to all those randomized to usual care, with time spent with a diagnosis of AF defined as the number of days from first post-randomization AF record in the primary care data to 2.5 years, or date of death or withdrawal (if earlier). Those with no diagnosis of AF by this time point contributed zero time with AF and those who were lost to follow-up from the primary care record before 2.5 years were assumed to have the same future days with AF as the average of those remaining without AF in that treatment arm at the time the person was lost to follow-up.

A permutation test was used to compare total exposure to oral anticoagulation by randomized treatment allocation.

A two-tailed p value <0.05 was considered to indicate statistical significance for the primary outcome. Allowance for multiple hypothesis testing is made in the interpretation of the secondary, sensitivity and exploratory outcomes, but without formal adjustment to the p values. Consequently, the reported 95% confidence intervals should not be used to infer definitive treatment effects with regards to these outcomes.

Analyses and plotting used SAS version 9.4 and R version 4.5.0 in RStudio version 2025.05.0 (Build 496).

More information is available in the Statistical Analysis Plan (Supplement 2).

Results

From May 2019 to February 2022, 22044 individuals were invited, of whom 5040 (22.9%) were randomly assigned to intervention (n=2520) or control (n=2520; Figure 1).

Complete primary care follow-up information was available in 2408 participants (95.6%) in the patch group and 2410 (95.6%) in the control group; the main reason for incomplete primary care follow-up was the participant moving to a non-participating GP practice during the trial (Figure 1). Complete secondary care data were available for 2514 participants (99.8%) in the patch group and 2512 (99.7%) in the control group.

At randomization, AMALFI participants had mean age 78 years (SD 6), 2360 (47%) were female, 4528 (90%) had hypertension, 963 (19%) had a prior stroke or TIA, and median CHA_2DS_2VASc score was 4 (IQR 3-5; Table 1). A small number of individuals (n=68, 1.3%) had a recorded CHA_2DS_2VASc score <3, likely due to methodological changes to data coding in primary care after the eligibility check. A small proportion (7%) were taking oral anticoagulation prior to randomization, most likely for treatment or prevention of pulmonary embolism or deep vein thrombosis, as 12% of trial participants had a history of a prior thromboembolism. Further characteristics of the study population are provided in Table 1. 2126 intervention individuals (84.4%) wore and returned the patch; in this group, median analyzable ECG duration was 14 days (IQR 13-14; eTable 1 in Supplement 3). Baseline characteristics by adherence to the patch are reported in eTable 2; adherence was higher in individuals with lower CHA_2DS_2VASc score and no heart failure.

A post-randomization primary care record of AF was present at 2.5 years in 172 individuals (6.83%, 95% confidence interval [CI] 5.84-7.81%) in the intervention group vs 136 (5.40%, 95% CI 4.51-6.28%) in the control group (ratio of

proportions 1.26, 95% CI 1.02-1.57, p=0.03; Figure 2). The results were consistent in pre-specified age and sex subgroups, with no significant evidence of heterogeneity (Figure 2). Log rank analysis of time to first post-randomization AF indicated that the arrhythmia was detected more frequently and earlier in the intervention group than in the control group, with a rate ratio of 1.29 (95% CI 1.03-1.61; p=0.03; Figure 3). In those with post-randomization AF recorded in primary care, diagnosis was at a median of 103 days (IQR 43-539) in the intervention group vs 530 days (IQR 276-688) in the control group. However, the rate of AF clinical diagnosis in the control group was numerically much higher than had been expected (5.6% observed vs 1.75% predicted at 2.5 years, Figure 3), resulting in a smaller than expected difference between groups. The mean number of days spent with a diagnosis of AF up to 2.5 years after randomization was 41 (95% CI 37-45) in all those randomized to the intervention group vs 21 (95% CI 17-25) in the control group (difference 20 days [95% CI 13-28], p<0.001). Sensitivity analyses of the primary outcome overall and by subgroups using AF diagnoses captured in either primary or secondary care records showed similar findings (eFigure 1).

In the intervention group, ECG monitoring detected AF in 89 individuals (3.53% of those randomized to the patch; 4.19% of those who wore and returned the patch). A further 13 individuals in this group were noted to have atrial flutter on the patch (eTable 3). Amongst the 89 individuals with patch-detected AF, the arrhythmia was detected on the first day of monitoring in 51 (57%; eFigure 2A). Patch-detected AF burden was bimodally distributed, with 29 (33%) AF cases having 100% burden, and 49 (55%) having an AF burden <10% (eFigure 2B). The longest AF episode was ≥24 hours in 37 participants (42%), ≥6 hours and <24 hours in 18 (20%), ≥6 minutes and <6 hours in 26 (29%) and ≥30 seconds and <6 minutes in 8 (9%; eFigures 2C, 2D). The distributions of maximum and minimum heart rate during AF episodes in patch-detected AF are shown in eFigures 2E and 2F. 83 (93%) of those with patch-detected AF had a post-

randomization record of AF in the primary care record, 78 within 3 months of the GP being informed. Median time to reporting was 14 days (95% CI 9-26 days; eFigure 3).

A total of 23 individuals were found to have complete or high-grade AV block or Mobitz II AV block (full list of patch findings in eTable 3). Patch findings in the 102 participants in the intervention group who had either AF and/or atrial flutter detected on their patch are shown in eFigure 4.

Oral anticoagulation was prescribed to 364 (14.4%) intervention vs 322 (12.8%) control group individuals up to 2.5 years after randomization (relative risk 1.13, 95% CI 0.98-1.30, p=0.08). Log rank analysis gave a rate ratio of 1.15 (95% CI 0.99-1.34; p=0.07) when comparing intervention versus control (Figure 4A). Mean exposure to oral anticoagulation by 2.5 years after randomization was 1.63 months (95% CI 1.50-1.76) in all those randomized to intervention vs 1.14 months (95% CI 1.01-1.26) in the control group (difference 0.50 months, 95% CI 0.24-0.75, p<0.001).

By 2.5 years, 103 participants (4.1%) in the intervention group and 126 (5.0%) in the control group had died. Stroke occurred in 69 participants (2.7%) in the intervention group and 64 (2.5%) in the control group (event rate ratio 1.08 [95% CI 0.76-1.53]; Figure 4B).

Discussion

AMALFI shows that a remote strategy for AF screening with a 14-day ambulatory ECG monitor in older patients at moderate-to-high stroke risk recruited from UK primary care leads to a modest increase in AF diagnosis and anticoagulation exposure. Whilst AMALFI met its primary endpoint, several aspects of the results merit further discussion.

Opportunistic AF screening is recommended by some clinical guidelines.[7] However, several large randomized trials have failed to show an increase in AF detection with opportunistic screening using handheld ECG devices compared to usual care.[16-18] Wearable devices can detect pulse irregularity, but their accuracy for AF diagnosis is probably too low for systematic population-based screening.[19] Meanwhile, the STROKESTOP, LOOP, STROKESTOP II, and GUARD-AF randomized trials have provided data on the potential impact of systematic or prolonged ECG-based AF screening on stroke and other clinical events, but none has convincingly demonstrated clinical benefit.[20-23] Taken together, these results highlight ongoing uncertainty regarding whether AF screening has proven benefits, the optimal screening method, and who to screen.

AMALFI aimed to investigate the feasibility and efficacy of a completely remote strategy of screening for AF using 14-day patch-based continuous ambulatory ECG monitoring delivered and returned by mail. This approach was taken with a view to streamlining delivery, including individuals who may be less likely to access care, and minimizing costs in any future national screening program, whilst simultaneously making the study readily accessible to participants. AMALFI specifically targeted recruitment of an older population at moderate-to-high stroke risk, as this population have both an increased likelihood of asymptomatic AF[24] and a thrombotic risk that would warrant consideration of anticoagulation if AF were detected. Furthermore, it is also possible that detection of AF in these individuals might be a marker of occult heart failure or

high vascular risk and could lead to initiation of appropriate evidence-based therapies (beyond anticoagulation) that might independently improve prognosis. AMALFI focused on AF diagnosis, as the impact of AF screening on clinical outcomes depends on achieving a higher rate of AF detection (and anticoagulation use) over time than would have occurred with usual care.

We found that the rate of AF diagnosis in the control group in AMALFI, and the proportion of individuals in the intervention group whose clinical AF diagnosis was unrelated to the patch, were both substantially higher than had been predicted ahead of the trial. Consequently, the difference in the proportion of patients with an AF diagnosis in each group at 2.5 years was much closer than expected. Whilst a degree of narrowing between the groups over time in a one-time screening trial is almost inevitable, it highlights potential improvements in AF detection in usual care, and the importance of the robust design of AMALFI, where long-term outcome ascertainment is undertaken equally across randomized groups.

Patch-detected AF burden in AMALFI showed a bimodal distribution. There was a high proportion of both persistent AF and AF detected on the first day of monitoring, but over half of patch-detected AF had a burden below 10%. There is increasing uncertainty regarding the net clinical benefit of oral anticoagulation for the prevention of cardioembolic events in individuals with low AF burden, driven by the results of two recent randomized trials of oral anticoagulation in individuals with sub-clinical AF detected by an implantable cardiac device. NOAH-AFNET[25] and ARTESIA[26] together suggested that the net clinical benefit of oral anticoagulation in individuals with a history of low-burden device-detected AF is borderline, because the ~35% relative reduction in stroke or systemic embolism was offset by a 30-35% relative increase in major bleeding. Of note, the stroke rate in these patients was 0.9-1.2% per person per year, much lower than in equivalent patients with clinically-detected AF.[27]

AMALFI had several important strengths. It was conducted entirely remotely with no patient visits, and participants were identified via an automated search of electronic records, minimizing cost and burden on practice staff and participants. The remote recruitment strategy could have allowed recruitment of a more comorbid study population than in trials where participants are required to attend a dedicated clinic visit. Similarly, outcome data were obtained electronically from routine primary care and national health records, ensuring unbiased and high rates of ascertainment of the primary, secondary, and exploratory outcomes. There were high rates of response to study invitation and adherence to the intervention, notable in the context of a remote study where participants had to self-apply the patch and return it by mail. Finally, potentially prognostically relevant incidental findings such as advanced heart block, long pauses, and sustained ventricular tachycardia that were detected in multiple individuals were fed back urgently to GPs; this invites speculation that appropriate and prompt treatment of these conditions may have contributed to the numerically lower rate of cardiovascular death seen in the patch group, but this tentative hypothesis needs to be tested prospectively.

Limitations

Firstly, participants in both groups may have changed their behavior in relation to detection of AF due to the influence of participating in AMALFI and associated increased awareness regarding AF. Secondly, the duration and burden of diagnosed AF in the control group is unknown, but it is reasonable to assume that AF diagnosed in the absence of systematic screening is more likely to be longer-lasting and symptomatic than patch-detected AF. If this were the case, it could have implications for the relative stroke risk, and hence the net clinical benefit of oral anticoagulation, in each group. Our exploratory analyses have shown no trends in the rate of stroke between groups within 2.5 years from randomization, but AMALFI was not powered for clinical outcomes. Finally,

AMALFI was conducted within a national health system that is universally accessible and free at the point of care; as such, our findings on the medium-term efficacy of an AF screening program may not be transferable to other settings.

Conclusions

AMALFI shows that AF screening with a self-applied 14-day patch-based ambulatory ECG monitor can be undertaken remotely in older patients at moderate-to-high stroke risk. At 2.5 years post-randomization this strategy led to a modest increase in AF diagnosis and anticoagulation exposure. Over half of patch-detected AF had a burden below 10%. Together, these findings suggest that AF screening in this setting may have limited impact on stroke events at 2.5 years.

Data sharing

See Supplement 4.

Acknowledgements

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Figure Legends

Figure 1: Trial profile. ECG = electrocardiogram; GP = general practitioner.

Figure 2: Proportions, absolute differences and ratios of proportions of participants with a primary care record of atrial fibrillation (AF) between randomization and 2.5 years by randomized group, overall and in age and sex subgroups. Ratios of proportions in subgroups are plotted as squares with the size of each square proportional to the amount of statistical information available. The primary outcome of ratio of proportions overall is represented by a diamond. The horizontal lines and the width of the diamond represent 95% confidence intervals (not adjusted for multiplicity), and the dashed vertical line indicates the overall ratio of proportions for the effect of patch on AF. Squares or a diamond to the right of the solid vertical line indicate a higher proportion of AF with the patch, but the comparison is only significant (at $p<0.05$) if the horizontal line, or diamond, does not overlap with the solid vertical line.

Figure 3: Kaplan Meier plot of time from randomization to first primary care record of atrial fibrillation (AF) by randomized allocation. The number of participants at risk at the start of each half year period is shown in the patch group as compared with the control group. Solid lines indicate the observed curves whereas dotted line are used for the corresponding original estimates of the curves (see supplement 1, section 8 for assumptions underlying the estimates of screen-detected AF and yearly rates of AF detected via usual care). The data are shown with an expanded scale to highlight the differences, with the y-axis extending from zero to ten percent.

Figure 4: Exploratory outcomes of (A) Oral anticoagulation and (B) Death and stroke. Panel A shows a Kaplan Meier plot of the time from randomization to first record of oral anticoagulation by randomized allocation. The number of participants at risk at the start of each 6 month period is shown in the patch group as compared with the control group. The data in the panel are shown with an expanded scale to highlight the differences, with the y-axis extending from zero to twenty percent. Panel B shows rate ratios from time to event analyses, where events occurred between randomization and 2.5 years in the secondary care record (death and stroke outcomes) or primary care records (stroke outcomes only). Presumed ischemic strokes include unspecified types of strokes with the assumption that the majority of these will be of ischemic origin. Rate ratios are plotted as squares with the size of each square proportional to the amount of statistical information available. “Any death” and “any stroke” are represented by diamonds. The horizontal lines and the width of the diamonds represent 95% confidence intervals (not adjusted for multiplicity). Squares or diamonds to the right of the solid vertical line indicate a higher rate of events in the patch group (i.e. favors the usual care group), but the comparison is only significant (at $p<0.05$) if the horizontal line, or diamond, does not overlap with the solid vertical line.

Table 1: Baseline characteristics of the randomized population.

	Randomized allocation	
	Patch (N = 2520)	**Usual care (N = 2520)**
Age at randomization (years)		
<75	683 (27.1%)	683 (27.1%)
≥75, <80	1032 (41.0%)	1061 (42.1%)
≥80	805 (31.9%)	776 (30.8%)
Sex		
Males	1340 (53.2%)	1340 (53.2%)
Females	1180 (46.8%)	1180 (46.8%)
Race and ethnicity		
Asian	27 (1.1%)	29 (1.2%)
Black	2 (0.1%)	9 (0.4%)
White	2045 (81.2%)	2056 (81.6%)
Other[a]	21 (0.8%)	22 (0.9%)
Missing	425 (16.9%)	404 (16.0%)
Body mass index (kg/m^2)		
<25	488 (19.4%)	516 (20.5%)
25 to <30	751 (29.8%)	788 (31.3%)
≥30	571 (22.7%)	572 (22.7%)
Missing	710 (28.2%)	644 (25.6%)
CHA_2DS_2VASc score		
<3	33 (1.3%)	35 (1.4%)
3	685 (27.2%)	674 (26.7%)
4	983 (39.0%)	976 (38.7%)
≥5	819 (32.5%)	835 (33.1%)
Prior diagnoses at randomization		
Hypertension	2255 (89.5%)	2273 (90.2%)
Diabetes	713 (28.3%)	719 (28.5%)
Stroke or TIA	485 (19.2%)	478 (19.0%)
Chronic kidney disease (stage ≥3)	438 (17.4%)	463 (18.4%)
Thromboembolism	271 (10.8%)	319 (12.7%)
Myocardial infarction	269 (10.7%)	255 (10.1%)
Heart failure	244 (9.7%)	259 (10.3%)
Peripheral arterial disease	214 (8.5%)	206 (8.2%)

	Randomized allocation	
	Patch (N = 2520)	**Usual care (N = 2520)**
Medication prior to randomization		
Statin	1739 (69.0%)	1737 (68.9%)
RAAS inhibition	1599 (63.5%)	1545 (61.3%)
Proton-pump inhibitors or H2-antagonists	1265 (50.2%)	1276 (50.6%)
Calcium-channel blockers	1200 (47.6%)	1289 (51.2%)
Diuretics	713 (28.3%)	709 (28.1%)
Aspirin or dipyridamole	705 (28.0%)	674 (26.7%)
Beta-blockers	619 (24.6%)	586 (23.3%)
P2Y12 inhibition	363 (14.4%)	320 (12.7%)
Oral anticoagulation	174 (6.9%)	168 (6.7%)
Direct oral anticoagulant	128 (5.1%)	148 (5.9%)
Vitamin K antagonist	59 (2.3%)	32 (1.3%)
Insulin	117 (4.6%)	113 (4.5%)

1

IQR = Interquartile range, SD = standard deviation, RAAS =Renin Angiotensin Aldosterone System. [a]Other category includes multiracial ethnicities (n=22) and 'any other ethnicity' (code S) recorded in secondary care (n=21).

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