Atrial fibrillation (AF) is a major risk factor for thromboembolic stroke. Oral anticoagulants (OACs) reduce stroke risk in AF by 60% to 70%, but their uptake is suboptimal. Risk factors for stroke are generally well recorded in UK primary care electronic health records, providing an opportunity for automated risk assessment. We developed a software tool AURAS-AF (Automated Risk Assessment for Stroke in Atrial Fibrillation) designed to identify such individuals during routine care through a cluster-randomized trial.

**Methods** — Screen reminders appeared each time the electronic health records of an eligible patient was accessed until a decision had been taken over OAC treatment. Where OAC was not started, clinicians were prompted to indicate a reason. Control practices continued usual care. The primary outcome was the proportion of eligible individuals receiving OAC at 6 months. Secondary outcomes included rates of cardiovascular events and reports of adverse effects of the software on clinical decision-making.

**Results** — Forty-seven practices were randomized. The mean proportion–prescribed OAC at 6 months was 66.3% (SD=9.3) in the intervention arm and 63.9% (9.5) in the control arm (adjusted difference 1.21% [95% confidence interval −0.72 to 3.13]). Incidence of recorded transient ischemic attack was higher in the intervention practices (median 10.0 versus 2.3 per 1000 patients with atrial fibrillation; \( P=0.027 \)), but at 12 months, we found a lower incidence of both all cause stroke (\( P=0.06 \)) and hemorrhage (\( P=0.054 \)). No adverse effects of the software were reported.

**Conclusions** — No significant change in OAC prescribing occurred. A greater rate of diagnosis of transient ischemic attack (possibly because of improved detection or overdiagnosis) was associated with a reduction (of borderline significance) in stroke and hemorrhage over 12 months.

**Clinical Trial Registration** — URL: [http://www.isrctn.com](http://www.isrctn.com). Unique Identifier: ISRCTN55722437.

**Key Words:** anticoagulants ■ atrial fibrillation ■ electronic health records ■ reminder systems ■ stroke
2. If a patient identified as eligible for but not using OAC was seen at the practice by a clinician, a screen reminder message would appear.

The tool was designed to challenge clinicians to justify treatment decisions at the point of care when the patient would be present. There was no requirement imposed by the trial to adhere to guidelines or follow any specific treatment pathway.

Control Practices
Practices allocated to the control arm continued to provide usual care to AF patients, including the requirements of the Quality and Outcomes Framework funding system.

Outcome Measures

Primary Outcome
The primary outcome was the proportion of patients eligible for OAC who were currently prescribed an OAC at the end of the 6-month intervention period.

Secondary Outcomes
(1) Proportion with CHADS<sub>2</sub> score ≥2 currently prescribed OAC at 6 months; (2) Practices were asked to report instances of inappropriate clinical or prescribing decisions related to anticoagulation in patients with AF; Incidences of (3) thromboembolic stroke, transient ischemic attack, or systemic (arterial) thromboembolism; (4) hemorrhagic stroke and other hemorrhagic events; Incidence rates for the following events were added on the advice of the Data Monitoring Committee: (5) thromboembolic stroke; (6) transient ischemic attack; (7) systemic thromboembolism; (8) hemorrhagic stroke; (9) other hemorrhagic events; (10) unspecified stroke events; (11) all-cause stroke (thromboembolic, hemorrhagic, or unspecified).

All outcomes were measured at 6 months and repeated at 12 months (6 months after the end of the intervention period).

Audit of Cardiovascular Events
Each thromboembolic or hemorrhagic event occurring during the intervention period was investigated to identify whether it might have resulted from use of the software, for instance, through inappropriate prescribing decisions.

Allocation
Practices were randomized with an allocation ratio of 1:1 and minimized on practice list size, and proportion of eligible patients with AF prescribed OACs at baseline.
Data Collection

Anonymized outcome data from the practices were extracted via a virtual private network linked to Oxford University. This source includes all electronically coded information, including diagnoses and medication.

Sample Size

We estimated that a sample of 46 practices would be needed for 95% power to detect a relative difference of 25% in the primary outcome with 5% significance.6

Statistical Analysis

Statistical analyses were undertaken using SPSS version 22 and Stata 13 on an intention to treat basis. Cluster summary measures were analyzed using a weighted linear regression model, with the minimization variables fitted as covariates. If assumptions of linear regression were violated, a Mann–Whitney U test was applied.

Results

We approached 570 potentially eligible practices; 70 expressed interest, and 47 were randomized (Figure). One withdrew during the first 3 months of the trial, leaving 46 in the intention-to-treat sample. These provided a combined patient population of 359,937 with 6429 patients with AF at baseline (February 20, 2014), of which 5339 (83%) were eligible for OAC, and of these, 3340 (62.6%) were already treated. The population characteristics were similar in each arm (Table 1).

Primary Outcome

The mean proportion (SD) of eligible patients prescribed OAC at 6 months was 66.3% (9.25) in the intervention arm and 63.9% (9.46) in the control arm. The adjusted mean difference (95% confidence interval) was 1.21% (--0.72 to 3.13); P=0.213.

Secondary Outcomes

The proportion in the subgroup with a CHADS3 score ≥2 prescribed anticoagulants at the end of the study was not significantly different between trial arms. There were no reports of inappropriate clinical or prescribing decisions or cardiovascular events triggered by use of the software. Practice-based searches supporting the cardiovascular event audit confirmed the validity of the remote data extraction.

Table 2 gives the incidence of cardiovascular events during the 6- and 12-month time periods after randomization. The increased rate of thromboembolic events in the intervention arm is because of a higher rate of transient ischemic attack diagnosis, with no increase in thromboembolic stroke or unspecified stroke. In fact, there is a reduction of borderline significance in strokes of all types (P=0.06) and of hemorrhage (P=0.054) at 12 months.

Discussion

Strengths and Limitations

This was a pragmatic randomized trial involving a diverse range of practices across a wide geographical area using a modern, web-based electronic health record platform.

Table 1. Baseline Characteristics of Practice Populations by Trial Arm

<table>
<thead>
<tr>
<th>Baseline Characteristics</th>
<th>Control</th>
<th>Intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median (IQR) Unless Indicated</td>
<td></td>
<td></td>
</tr>
<tr>
<td>List size</td>
<td>7039 (4724–10,832)</td>
<td>6803 (4071–11,368)</td>
</tr>
<tr>
<td>Prevalence of AF per 100 patients</td>
<td>1.71 (1.11–2.20)</td>
<td>1.92 (1.77–2.21)</td>
</tr>
<tr>
<td>Proportion of AF patients who are female</td>
<td>44.6% (40.9–50.0)</td>
<td>46.3% (42.4–50.0)</td>
</tr>
<tr>
<td>Proportion of AF patients under 80 y</td>
<td>56.5% (51.0–62.3)</td>
<td>56.9% (51.6–59.8)</td>
</tr>
<tr>
<td>Proportion eligible for OAC and prescribed OAC at baseline*</td>
<td>61.9% (9.89)</td>
<td>63.5% (8.85)</td>
</tr>
</tbody>
</table>

AF indicates atrial fibrillation; IQR, interquartile range; and OAC, oral anticoagulant.

*Mean (SD).

Table 2. Incidence of Cardiovascular Events in AF Patients Over 6 and 12 Month

<table>
<thead>
<tr>
<th>Events</th>
<th>Incidence (Patients With At Least 1 Event per 1000 AF Patients)</th>
<th>PValue*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Control (N=23)</td>
<td>Intervention (N=23)</td>
</tr>
<tr>
<td>Thromboembolic stroke, TIA, or other major thromboembolism</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6 mo</td>
<td>0 (0–7.75)</td>
<td>10.3 (0–16.3)</td>
</tr>
<tr>
<td>12 mo</td>
<td>12.6 (0–22.3)</td>
<td>14.5 (4.2–26.1)</td>
</tr>
<tr>
<td>Hemorrhage (including hemorrhagic stroke)†</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6 mo</td>
<td>26.5 (15.0)‡</td>
<td>21.0 (14.7)‡</td>
</tr>
<tr>
<td>12 mo</td>
<td>50.3 (33.4–57.3)</td>
<td>34.7 (27.4–43.6)</td>
</tr>
<tr>
<td>All cause stroke†</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6 mo</td>
<td>8.5 (0–17.7)</td>
<td>7.9 (0–13.4)</td>
</tr>
<tr>
<td>12 mo</td>
<td>24.8 (19.3–28.9)</td>
<td>15 (9.1–28.3)</td>
</tr>
<tr>
<td>Transient ischemic attack</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6 mo</td>
<td>0 (0–0)</td>
<td>6.4 (0–12.2)</td>
</tr>
<tr>
<td>12 mo</td>
<td>2.3 (0–9.0)</td>
<td>10.0 (4.2–18.2)</td>
</tr>
<tr>
<td>Thromboembolic stroke</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6 mo</td>
<td>0 (0–0)</td>
<td>0 (0–4.1)</td>
</tr>
<tr>
<td>12 mo</td>
<td>0 (0–12.8)</td>
<td>0 (0–5.0)</td>
</tr>
<tr>
<td>Hemorrhagic stroke†</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6 mo</td>
<td>0 (0.0)‡</td>
<td>0 (0.0)‡</td>
</tr>
<tr>
<td>12 mo</td>
<td>0 (0–0.96)</td>
<td>0 (0–3.14)</td>
</tr>
<tr>
<td>Unspecified stroke</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6 mo</td>
<td>5.2 (0–16.4)</td>
<td>3.2 (0–9.4)</td>
</tr>
<tr>
<td>12 mo</td>
<td>17.0 (11.4)‡</td>
<td>13.3 (11.0)‡</td>
</tr>
</tbody>
</table>

AF indicates atrial fibrillation; and TIA, transient ischemic attack.

*Mann–Whitney U test.
†N=22 in the control arm for hemorrhagic event searches (see Figure). The other searches were unaffected.
‡Mean (SD).
§P value obtained from weighted linear regression.
Comparison to Other Studies
The findings concur with other studies demonstrating small or modest impacts of reminder interventions on clinician behavior.\(^9\)

Interpretation
Since the trial was conceived, there has been a refocusing of the identification problem away from those eligible for OAC and toward the minority who do not require it,\(^10\) making stroke risk assessment less important compared with other more difficult barriers. Decisions over anticoagulation may take longer to make than our 6-month intervention period. A longer follow-up might also be required to confirm the improvements in stroke and hemorrhage rates suggested by our data.

Conclusions
Use of the software was associated with no significant change in prescribing, but improved stroke and hemorrhage rates (of borderline significance) at 12 months.

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Disclosures
None.

References
Automated Software System to Promote Anticoagulation and Reduce Stroke Risk: Cluster-Randomized Controlled Trial


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