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Risk of stroke and oral anticoagulant use in atrial fibrillation:

a cross-sectional survey

Abstract

Background
Oral anticoagulants substantially reduce the risk of stroke in atrial fibrillation but are underutilised in current practice.

Aim
To measure the distribution of stroke risk in patients with atrial fibrillation (using the $CHADS_2$ and CHA_2DS_2-VASc scores) and changes in oral anticoagulant use during 2007–2010.

Design and setting
Longitudinal series of cross-sectional survey in 583 UK practices linked to the QResearch® database providing 99 351 anonymised electronic records from people with atrial fibrillation.

Method
The proportion of patients in each $CHADS_2$ and CHA_2DS_2-VASc risk band in 2010 was calculated; for each of the years 2007–2010, the proportions with risk scores ≥2 that were using anticoagulants or antiplatelet agents were estimated. The proportions identified at high risk were re-estimated using alternative definitions of hypertension based on coded data. Finally, the prevalence of comorbid conditions in treated and untreated high-risk ($CHADS_2$ ≥2) groups was derived.

Results
The proportion at high risk of stroke in 2010 was 56.9% according to the $CHADS_2$ ≥2 threshold, and 84.5% according to CHA_2DS_2-VASc ≥2 threshold. The proportions of these groups receiving anticoagulants were 53.0% and 50.7% respectively and increased during 2007–2010. The means of identifying the population of individuals with hypertension significantly influenced the estimated proportion at high risk. Comorbid conditions associated with avoidance of anticoagulants included history of falls, use of nonsteroidal anti-inflammatory drugs, and dementia.

Conclusion
Oral anticoagulant use in atrial fibrillation has increased in UK practice since 2007, but remains suboptimal. Improved coding of hypertension is required to support systematic identification of individuals at high risk of stroke and could be assisted by practice-based software.

Keywords
anticoagulants; atrial fibrillation; electronic health records; primary health care; stroke.

INTRODUCTION

Atrial fibrillation (AF) is the commonest disorder of heart rhythm and an important risk factor for thromboembolic stroke.[1] An individual's risk of stroke can be estimated using risk-stratification schemes that have been validated in various studies.[2–5] In Europe, the $CHADS_2$ and CHA_2DS_2-VASc scores are recommended (Box 1).[6] CHA_2DS_2-VASc is significantly more inclusive of common stroke risk factors, while $CHADS_2$ is simpler, easier to remember, and was proposed over 10 years ago, so has tended to be used more extensively in clinical practice. However, the limitations of the $CHADS_2$ score have been highlighted recently.[7,8] The CHA_2DS_2-VASc score is more effective at identifying the 'truly low-risk' population where (in patients with a CHA_2DS_2-VASc score = 0) no thromboprophylaxis is needed.[9] For the higher-risk groups, oral anticoagulation significantly reduces the risk of stroke and mortality.[10]

Decisions over anticoagulation need to be tailored to the individual. However, suboptimal use and uptake in AF is a global phenomenon.[11–13] Opportunities are thereby missed to impact significantly on an important cause of cardiovascular morbidity and mortality.

Surveys of stroke risk in AF based on UK primary care data have been published previously.[14–16] The authors were interested not only in the patterns of risk and levels of anticoagulant use, but also in the ability of primary care data to support risk estimation. A software tool (GRASP-AF — Guidance on Risk Assessment and Stroke Prevention in Atrial Fibrillation) has been developed for UK general practices,[17] which produces lists of high-risk but untreated individuals. The success of this approach depends on the data quality of the source systems, including the disease registers.

Specifically, the hypertension register is problematic. Clinicians may not always enter a hypertension code if the person is already on another disease register that has a blood pressure target. To do so may duplicate the processes of recall. For those with AF, exclusion of a patient with hypertension from the hypertension register runs the risk of underestimating stroke risk and of failing to identify the need for anticoagulation. While administrative registers may be useful for estimating the prevalence of hypertension at population level,[18,19] their adequacy for supporting estimation of stroke risk has not been confirmed.

This study used the QResearch® database to determine the distribution of $CHADS_2$ and CHA_2DS_2-VASc scores and changes in prescribing of oral anticoagulant and antiplatelet agents during the years 2007–

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How this fits in

Suboptimal use of oral anticoagulants in patients with atrial fibrillation is a missed opportunity to impact on an important cause of thromboembolic stroke. Systematic identification of those at high stroke risk requires consistent recording of risk factors during routine care. About one in seven will currently be missed if inclusion in the hypertension register is used to determine hypertensive status, highlighting the need for improved recording of hypertension in this group. A number of barriers must be overcome to optimise the safe and effective use of anticoagulants for stroke prevention in patients with atrial fibrillation.

2010, following publication of a National Institute for Health and Clinical Excellence (NICE) guideline on AF.[20] This was the prevailing guideline for the period of the study. The impact on numbers identified of alternative definitions of hypertension was investigated. The study also measured the differences between treated and untreated populations in the prevalence of a range of prespecified comorbidity codes potentially relevant to anticoagulant prescribing.

METHOD

Source of data

The QResearch database contains anonymous electronic data from over 600 UK practices. Records in this database from people with a diagnosis of AF were identified. Individual records were excluded if the person had been registered for less than 12 months, or was a temporary resident. No other exclusion criteria were applied, and all available eligible records were included in the study. QResearch has been validated using other nationally published sources, as broadly representative of the UK population.[21]

Statistical methods

Analyses were carried out using STATA (version 11) and SAS (version 9.2). The χ^2 test was used to measure differences in proportions and to calculate *P*-values for significance.

Cross-sectional surveys

For each identified record, a stroke risk score was carried out using the $CHADS_2$ and CHA_2DS_2-VASc algorithms. For each risk band, the proportion currently treated with anticoagulants or antiplatelet drugs was derived, based on the presence of a prescription for the drug in the record in the last 6 months. This cross-sectional survey was repeated for each of the years 2007 to 2010. The main outcomes of the study used the most recent (2010) cross-section.

Influence of different definitions of hypertension

The cross-sectional surveys required a coded diagnosis of hypertension for the risk score, and a range of Read Codes were used, similar to those supporting the Quality and Outcomes Framework (QOF).[22] These are all 'child' codes of the G2 Read Code group. More inclusive means of identifying the population of individuals with hypertension (Box 2) were then used, based on use of antihypertensive medication and blood pressure values. The most recent cross-sectional survey (for 2010) was repeated using these alternative definitions, to measure the impact on the numbers identified.

Comorbidity codes associated with lack of use of anticoagulation

The prevalence of a range of comorbidity codes was examined in the treated and untreated high-risk populations recommended anticoagulation; χ^2 tests were used to measure the significance of differences in prevalence.

RESULTS

The sample included 583 UK practices, and 99 351 patient records. Of these, 59 804 were available for the main cross-section of 1 October 2010; the remainder had died, left the practice, or were in a practice whose most recent data upload was before 1 October 2010. Table 1 gives the patient

Box 1. $CHADS_2$ and CHA_2DS_2-VASc risk scores

Unless indicated otherwise, 1 point is allocated to each risk factor

$CHADS_2$ (maximum 6 points)

C	Congestive heart failure
H	Hypertension
A	Age >75 years
D	Diabetes
S	Stroke, transient ischaemic attack (TIA), or other thromboembolism history (2 points)

CHA_2DS_2–VASc (maximum 9 points)

C	Congestive heart failure
H	Hypertension
A	Age >75 years (2 points)
D	Diabetes
S	Stroke, TIA, or other thromboembolism history (2 points)
V	Vascular disease (coronary artery or peripheral vascular disease)
A	Age 65–74 years
Sc	Sex category (female 1 point, male 0 points)

People with a $CHADS_2$ score of 2 or higher are recommended anticoagulation unless contraindicated. Those with $CHADS_2$ score less than 2 can be assessed using CHA_2DS_2-VASc. Those with CHA_2DS_2-VASc =0 require no thromboprophylactic therapy.

Box 2. Definitions of hypertension based on primary care data (details available from the authors)

Definition A: Requires a specific G2 Read code for hypertension, as in the Quality and Outcomes Framework (QOF)

Definition B: As for A, but includes also those with no specific hypertension code, but using an antihypertensive agent

Definition C: As for B, but excludes those with no hypertension code that have another possible reason for using an antihypertensive agent (for example, coronary heart disease if taking a calcium channel blocker, heart failure if taking an angiotensin-converting enzyme inhibitor)

Definition D: As for C, but includes also those with evidence for hypertension based on recorded blood pressure values (mean of the last three measurements if available ≥150 mmHg systolic or ≥90 mmHg diastolic, even for another possible reason) or those not on treatment for hypertension but with blood pressure ≥160 mmHg systolic or ≥100 mmHg diastolic

For the main cross-sectional surveys 2007–2010, definition A was used.

characteristics for the 2010 cross-section. The median age in 2010 was 80.0 years with interquartile range 71.0 to 87.0 years. The median age at AF diagnosis was 73.0 years.

Table 2 shows the distribution of risk for the main survey of 2010 and the proportions treated with anticoagulants, antiplatelet agents, or both. An estimated 56.9% of people with AF had a $CHADS_2$ score ≥2, and 84.5% had a CHA_2DS_2-VASc score ≥2. Only 53.0% and 50.7% of these groups respectively were using oral anticoagulants, with the majority of the remainder receiving an antiplatelet agent.

Table 1. Characteristics of the population with atrial fibrillation (AF)

	Total population with AF, *n* = 99 351	
	Median	**Interquartile range**
Age, years		
At AF diagnosis	73.0	64.0 to 81.0
In 2010 (of 69 762 registered in 2010)	80.0	71.0 to 87.0
Registration history, months		
Prior to AF diagnosis	146.3	31.1 to 283.3
Total	222.8	111.3 to 355.7
	Count	**% of *n***
Age group at AF diagnosis, years		
<50	6721	6.8
50–64	19 696	19.8
65–74	27 769	28.0
≥75	45 165	45.5
Age group in 2010, years		
<50	3096	3.1
50–64	10 629	10.7
65–74	19 215	19.3
≥75	66 411	66.8
Sex		
Male	52 527	52.9
Female	46 824	47.1
Current status of patient		
Died	20 729	20.9
Left practice	9205	9.3
Currently registered	69 417	69.9

Table 3 and Figure 1 report the changes in numbers identified and proportions treated for the years 2007–2010. The proportion with $CHADS_2$ score ≥2 remained stable and use of anticoagulants in this group increased from 49.7% in 2007 to 53.0% in 2010 (P<0.001).

Table 4 gives the numbers identified in each risk band, according to the alternative definitions of hypertension A–D for the 2010 cross-section only. Definition A requires a G2 Read Code for hypertension and is the basis for the estimated 56.9% of AF patients with $CHADS_2$ ≥2 in 2010. This figure rises to 67.2% using definition B (which also includes people with no G2 code but taking an antihypertensive drug). When those with a possible alternative reason to be taking the drug, such as heart failure or angina (definition C), are removed, the proportion is 65.9%. Adding to this, people who do not have a coded diagnosis of hypertension but do have evidence of raised blood pressure (definition D), the figure is 66.1%.

Table 5 gives the prevalence of relevant comorbidity codes in the treated and untreated populations for those recommended anticoagulants according to the $CHADS_2$ ≥2 threshold, and the significance estimates for the differences. The difference is significant for most comorbidity codes, but those particularly relevant for clinical practice include a history of falls, peptic ulceration, and other upper gastrointestinal (GI) tract disorders; use of drugs for dyspepsia; and use of nonsteroidal anti-inflammatory drugs. These may be associated with avoidance of oral anticoagulation therapy.

DISCUSSION

Summary

Only 53.0% of patients in the study at high risk of stroke were using oral anticoagulants. This proportion increased only slightly in the years 2007–2010. At the same time, higher than expected usage was found in the low-risk groups: 32.1% of people with $CHADS_2$ = 0 and 23.0% with CHA_2DS_2VASc = 0. While anticoagulation may be appropriate for some of these individuals (for example, those with valvular disease), this suggests that use of these algorithms has still to become established. $CHADS_2$ was first proposed over a decade ago, while CHA_2DS_2-VASc was introduced much more recently.

The estimated high-risk population increases when more inclusive definitions of hypertension are used. The authors considered the safest to be 'C', which increases the proportion identified from

Table 2. Distribution of stroke risk for the 2010 cross-sectional survey (*n* = 59 804) by use of anticoagulants and antiplatelet agents

Risk band	Proportion of AF population identified (%)	Proportion of the risk band using anticoagulants (%)	Proportion receiving an antiplatelet agent (%)	Proportion receiving neither (%)
$CHADS_2$				
0	16.8	32.1	30.1	41.7
1	26.3	46.0	40.2	18.9
2	28.5	50.8	41.7	13.1
3	15.2	56.1	40.7	10.3
4	9.6	54.5	45.0	8.4
5	3.2	54.4	43.7	8.8
6	0.5	52.6	47.0	9.3
≥2	56.9	53.0	42.2	11.3
CHA_2DS_2-VASc				
0	6.1	23.0	18.5	61.2
1	9.4	36.4	31.7	35.6
2	14.6	47.2	37.6	20.2
3	20.5	50.6	40.0	14.8
4	21.3	50.3	42.9	12.5
5	14.7	52.9	43.7	10.5
6	8.7	53.2	46.2	8.5
7	3.7	51.7	47.4	8.4
8	1.0	53.8	45.6	8.3
9	0.2	47.6	55.3	7.8
≥2	84.5	50.7	42.0	13.4

Table 3. Trends in prescribing of anticoagulants in those with $CHADS_2$ ≥2 and CHA_2DS_2-VASc ≥2, 2007–2010[a]

	2007	2008	2009	2010
Size of sample with atrial fibrillation	62 146	64 524	63 533	59 804
Number identified with $CHADS_2$ ≥2	34 827	36 394	35 948	34 041
Percentage with $CHADS_2$ ≥2	56.0	56.4	56.6	56.9
Proportion, %				
Anticoagulant	49.7	50.3	51.2	53.0
Antiplatelet	43.9	43.8	43.4	42.2
Both	6.0	6.3	6.5	6.5
Neither	12.4	12.1	11.9	11.3
Number identified with CHA_2DS_2VASc ≥2	52 668	54 526	53 781	50 547
Percentage with CHA_2DS_2-VASc ≥2	84.7	84.5	84.7	84.5
Proportion, %				
Anticoagulant	48.0	48.7	49.3	50.7
Antiplatelet	42.9	43.2	42.9	42.0
Both	5.7	6.0	6.2	6.1
Neither	14.7	14.1	13.9	13.4

[a]*Changes in the proportions treated with anticoagulants were all significant at the P<0.01 level.*

56.9% to 65.9%. The additional inclusion of those with raised blood pressure levels (definition D) may be unreliable, particularly given the recent emphasis on home, rather than office-based measurements for diagnosis.[23] About one in seven people at high risk of stroke ($CHADS_2$ ≥2) will have their risk estimated as $CHADS_2$ = 1 and therefore not be recognised as requiring anticoagulant therapy by this decision rule if the presence of a code for hypertension (G2) is required to confirm hypertensive status. Improved coding of hypertension in primary care could readily be assisted by practice-based software.

Certain comorbidity codes were found to be more prevalent in the records of untreated compared with treated people in the $CHADS_2$ ≥2 population. This analysis is observational and needs to be interpreted

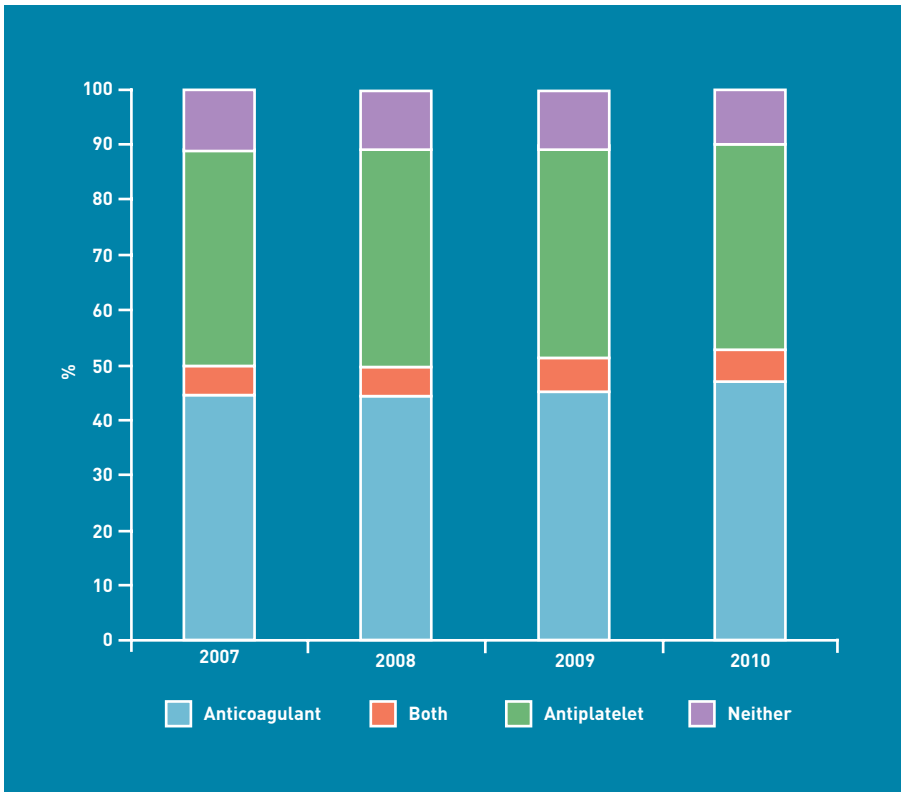

Figure 1. Trends in prescribing of anticoagulants in those with $CHADS_2 \geq 2$, 2007-2010.

with caution. The increased recording of adverse reactions to anticoagulants in the treated population may reflect the fact that such recording only occurs in people exposed to treatment and that this does not always require withdrawal of the drug. Similarly, the recording of a bleeding tendency may be noted as a result of treatment and is more common in the treated population. Alcohol overuse and chronic liver disease do not, perhaps surprisingly, appear to be barriers to anticoagulation, but other findings confirmed previously suspected obstacles, including a history of falls. Each person needs to be assessed individually, as some are at much higher risk from this than others, but the risk from falls (compared to the benefits of anticoagulation) may be overestimated by clinicians managing people with AF and at risk of stroke.[24] Drugs for dyspepsia are used more commonly in untreated individuals, who are also more likely to have a record of peptic ulcer or other upper GI disorders. Whether this history is a sufficient basis for avoidance is again an individual matter, and may depend on how recently the upper GI pathology occurred. The present survey also suggests avoidance of anticoagulants in people using nonsteroidal anti-inflammatory drugs, which interact with warfarin but are not an absolute contraindication in most cases. Those with dementia may be less able to concur with treatment and monitoring, and less able to consent to treatment, so in some cases avoidance in such people may be appropriate. Stroke is more often disabling than fatal, and individuals vary widely in their anticipated quality of life utility associated both with stroke and with antithrombotic therapies.[25,26]

Use of anticoagulants in the $CHADS_2$ and CHA_2DS_2-VASc risk groups above the level of 2 tends to level off rather than increase with stroke risk (Table 2). This may imply that comorbidity itself offsets rather than increases the tendency to prescribe. Those at highest risk of thromboembolism are also at highest risk of bleeding complications, a fact that may influence clinicians. Haemorrhages related to warfarin are a significant problem and may be more common in 'real-world' practice[27] than under the more careful monitoring arrangements of randomised trials.[28] Despite this, the risk–benefit ratio is particularly in favour of anticoagulant therapy in the higher-risk groups,[29] provided it is carefully monitored.

Table 4. Influence of alternative definitions of hypertension on the numbers identified as requiring anticoagulation for the latest survey, 2010[a]

	Number identified and proportion of total AF population in 2010 (n = 59 804)			
	$CHADS_2 \geq 2$		CHA_2DS_2-VASc ≥ 2	
Definition	*n*	%	*n*	%
A	34 041	56.9	50 547	84.5
B	40 178	67.2	53 110	88.8
C	39 417	65.9	53 022	88.7
D	39 544	66.1	53 066	88.7

[a]*Differences in the proportions identified were all significant at the P<0.01 level. AF = atrial fibrillation.*

Strengths and limitations

This is a large survey of a representative population of people with AF diagnosed and managed in both primary and secondary care settings. It includes people with all forms of AF, including both paroxysmal as well as chronic AF. The study may have not detected some individuals receiving anticoagulant prescriptions in secondary care. The National Patient Safety Agency has emphasised the importance of good communication between different bodies sharing responsibility for prescribing potentially interacting medication,[30] and this has increased the use of codes in primary care to maintain awareness of anticoagulant therapy prescribed elsewhere. Identifying people taking both

Table 5. Prevalence of comorbidity codes in the anticoagulant treated and untreated populations of those in whom anticoagulation is recommended by $CHADS_2$ ≥2, (*n* = 34 041)

	Prevalence of the comorbidity code in the population in which anticoagulation is recommended according to $CHADS_2$ ≥2 (%)			
	Overall, *n* = 34 041	Treated group, *n* = 18 042	Untreated group, *n* = 15 999	*P*-value
Haemorrhagic stroke or intracranial haemorrhage	2.0	1.2	3.0	<0.001
Post-traumatic intracranial haemorrhage	0.2	0.1	0.4	<0.001
Allergy to warfarin/other anticoagulants	1.8	2.4	1.2	<0.001
History of GI tract bleeding	5.4	4.3	6.6	<0.001
Uncontrolled blood pressure[a]	80.0	79.2	80.9	<0.001
Bleeding tendency	2.5	2.7	2.3	0.013
History of other bleeding	13.6	15.2	11.8	<0.001
History of bruising	2.2	2.2	2.2	0.80
Falls	4.7	3.2	6.3	<0.001
Other significant injury	37.2	34.7	39.9	<0.001
Peptic ulceration and other upper GIT disorders	30.9	28.9	33.1	<0.001
GIT malignancy — at any time	2.8	2.3	3.4	<0.001
GIT malignancy — 1 October 2005 or later	1.5	1.2	1.8	<0.001
Other malignancy — at any time	17.0	16.2	17.9	<0.001
Other malignancy — 1 October 2005 or later	10.9	10.5	11.4	0.006
Liver dysfunction/disease	5.2	5.3	5.1	0.53
Chronic kidney disease	2.0	2.0	2.1	0.81
Anaemia	13.7	11.9	15.9	<0.001
Alcohol abuse[b]	11.0	11.8	10.1	<0.001
Epilepsy	2.1	1.9	2.2	0.033
Terminal illness	0.2	0.2	0.3	0.042
Dementia	1.1	0.6	1.7	<0.001
Drugs used for dyspepsia	40.7	34.9	47.3	<0.001
Anti-inflammatory drugs	27.8	23.6	32.5	<0.001

GIT = gastrointestinal tract. [a]Specific definition available from the authors. [b]Codes available from the authors.

anticoagulants and antiplatelet agents is difficult in surveys of this kind, because a person changing from one treatment to the other may have evidence of both in their recent record and this proportion may be slightly overestimated. The prevalence of falls in the population with AF is higher than reported in this study because a limited code set was used to identify them. A limited set of 'chronic kidney disease' codes was chosen in order to identify those with more significant forms of renal disease.

Comparison with existing literature

The findings of this study support other studies reporting suboptimal uptake of oral anticoagulants in AF.[11] The figure for the proportion of individuals with $CHADS_2$ ≥2 treated with oral anticoagulants (53%) is very similar to that derived from a Canadian study published in 2011.[13] This study has confirmed the lower usage in people with a history of falls, and those with dementia, previously reported in 2008.[15]

Implications for practice and research

There is still huge potential for reducing the stroke risk of the population with AF by identifying people in primary care requiring anticoagulant treatment. Routinely collected data are able to support this process but consistent coding of hypertension is important. Several factors may have contributed to the minor improvements demonstrated in this study. The NICE guideline of 2006 may have raised awareness of the benefits of this treatment.[20] The BAFTA (Birmingham Atrial

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Ethics committee

QResearch studies are ethically approved by Trent MREC 03/04/021.

Provenance

Freely submitted; externally peer reviewed.

Competing interests

Paul Cload was an employee of GE Healthcare during this project. Candace Gunnarsson had financial support from GE Healthcare for the study. There are no other competing interests.

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Fibrillation Treatment of the Aged) trial was published in 2007 and was reassuring over the risks/benefits of warfarin in older people with AF.[31] A further factor was the introduction in 2006 of AF registers as part of the UK QOF, involving payments based on the proportion of people with AF treated with either anticoagulants or antiplatelet agents (irrespective of stroke risk level). From April 2012, the targets include the proportion of those with identified $CHADS_2$ score ≥2 who are receiving anticoagulant therapy.[32]

However, it is increasingly recognised that some patients with a $CHADS_2$ score of 0–1 are at significant risk and would benefit from anticoagulation. Among those with $CHADS_2$ = 0, the stroke/thromboembolism risk can vary between 0.84%/year (if the CHA_2DS_2-VASc score = 0) to 3.2%/year (if the CHA_2DS_2-VASc score = 3).[33] Thus, a $CHADS_2$ score of 0–1 is not necessarily 'low risk' and only the CHA_2DS_2-VASc score can identify the truly low-risk group. The $CHADS_2$ ≥2 threshold for determining anticoagulant uptake under the QOF is therefore an audit standard and not a definition of best practice.

A recent consensus statement from the Royal College of Physicians of Edinburgh (RCPE) supports this conclusion, arguing for anticoagulation in all but the truly low-risk groups.[34] According to the present survey results and their threshold, this would mean that around 91.6% of people with AF should be considered for this treatment. Strokes related to AF are associated with higher case fatality and more profound disability in survivors than non-AF related strokes,[35] but could be minimised by this approach. As recommended in the European Society for Cardiology guidelines,[6] risk scores have evolved to become more useful for identifying those at low risk (not requiring treatment) than those at high risk.[36] The RCPE also recommends that, as aspirin is ineffective as thromboprophylaxis in AF, it should not be used for this reason alone. These developments have simplified decision-making policy and are likely to change practice significantly towards anticoagulation. Newer oral anticoagulants may potentially improve uptake still further. Future studies need to explore the remaining barriers, including the qualitative issues influencing patient-centred decision making over anticoagulation.

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