ORIGINAL ARTICLE

Guideline-related barriers to optimal prescription of oral anticoagulants in primary care

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ABSTRACT

Guidelines provide recommendations for antithrombotic treatment to prevent stroke in people with atrial fibrillation, but oral anticoagulant prescriptions in Dutch primary care are often discordant with these recommendations. Suboptimal guideline features (i.e. format and content) have been suggested as a potential explanatory factor for this type of discordance. Therefore, we systematically appraised features of the Dutch general practitioners' (NHG) atrial fibrillation guideline to identify guideline-related barriers that may hamper its use in practice. We appraised the guideline's methodological rigour and transparency using the Appraisal of Guidelines, Research and Evaluation (AGREE) II tool. Additionally, we used the Guideline Implementability Appraisal (GLIA) tool to assess the key recommendations on oral anticoagulant prescription. The editorial independence of the guideline group scored highly (88%); scores for other aspects of the guideline's methodological quality were acceptable, ranging from 53% for stakeholder involvement to 67% for clarity of presentation. At the recommendation level, the main implementation obstacles were lack of explicit statements on the quality of underlying evidence, lack of clarity around the strength of recommendations, and the use of ambiguous terms which may hamper operationalisation in electronic systems. Based on our findings we suggest extending stakeholder involvement in the guideline development process, standardising the layout and language of key recommendations, providing monitoring criteria, and preparing electronic implementation parallel with guideline development. We expect this to contribute to optimising the NHG atrial fibrillation guideline, facilitating its implementation in practice, and ultimately to improving antithrombotic treatment and stroke prevention in people with atrial fibrillation.

KEYWORDS

Atrial fibrillation, anti-thrombotic treatment, cardiology/standards, practice guidelines as topic, primary stroke prevention

INTRODUCTION

Prevalence of atrial fibrillation (AF), a common arrhythmia, has increased over the last 30 years.[1] In 2006 its prevalence ranged from 0.7% (age group 55-59) to 17.8% (age group > 85). AF increases the risk and severity of stroke.[2,3] Antithrombotic therapy with oral anticoagulation (OAC) decreases this stroke risk, but at the same time increases the risk of major bleeding.[2] National and international clinical practice guidelines on AF management provide guidance on how to weigh these risks against expected benefits, and include recommendations on antithrombotic treatment.[3,4] Yet, antithrombotic treatment is often not in line with these recommendations.[5,6] For example, a study in the Netherlands estimated that less than 50% of AF patients received treatment according to national guidelines.[6]

Various types of barriers may thwart physicians in following guidelines in clinical practice, such as lack of familiarity with the guideline's content, lack of skills or resources to change current practice or patients not reconciling with guideline recommendations.[7] Suboptimal

guideline features (i.e. format and content) may also hamper implementation.[7,8] Lugtenberg et al. reported this as one of the barriers that hindered general practitioners (GPs) in following the Dutch College of General Practitioners (NHG) AF guideline.[9]

Improving these features may positively affect guideline use.[8,10,11] Therefore, this study systematically appraised the format and content of the NHG AF guideline[4] to identify suboptimal features that may hamper its use in Dutch primary care. We focused on the guideline section related to prescription of OACs for stroke prevention in AF patients. The results of this appraisal may contribute to improving features of future AF guideline versions, as well as to developing tools and strategies for AF guideline implementation.

MATERIAL AND METHODS

The NHG AF guideline

The NHG aims to promote evidence-based primary care by bridging the gap between theory and practice. With 12,000 members,[12] they cover around 80% of all Dutch GPs[13] and nurse practitioners.[14] The NHG has developed over 100 guidelines covering the diagnosis and treatment of acute and chronic conditions, with ten guidelines related to cardiovascular diseases. In the current study, we reviewed the 2013-updated version of the NHG guideline on diagnosis and treatment of patients with atrial fibrillation.[4] It consists of 34 pages of background information on AF, recommendations for practice, endnotes and references. We focused on three key recommendations: (I) Eligibility criteria for OACs; (II) Which type of OAC to prescribe: coumarin derivatives versus new OACs (NOACs); and (III) Type and dosage of coumarin derivatives. The recommendations are displayed in *table 1*.

Table 1. *Key recommendations on oral anticoagulants prescription included in the NHG AF guideline*

Recommendation 1 [R1] – Eligibility criteria for OACs
The following recommendations apply to patients aged 65 years and older with atrial fibrillation; younger patients are eligible for assessment by a cardiologist:
- Recommend oral anticoagulants to all women aged 65 and older and all men 75 years and older (i.e. for patients with a CHA2DS2-Vasc score of 2 or higher)
- Discuss with male patients aged 65 to 75 years without cardiovascular comorbidities (CHA2DS2-Vasc score of 1) that the benefits of antithrombotic medication (prevention of thromboembolism) are outweighed by the disadvantages (risk of side effects, such as bleeding) and for that reason antithrombotic medication is not indicated
- Recommend aspirin when a contraindication for oral anticoagulants is present. See table with most important contraindications for antithrombotic medication

Recommendation 2 [R2] – Which type of OAC to prescribe: coumarin derivatives versus NOACs
When an indication for oral anticoagulants is present, coumarin derivatives are preferred. Consider NOACs only if all of the following conditions are met:
  - Age below 80 (arbitrary)
  - Relatively little comorbidity
  - Normal kidney function (GFR> 50 ml / min)
  - High medication adherence
- Absolute contraindications for NOACs are:
  - Patients with a mechanical artificial heart valve
  - Patients with a (currently rare) rheumatic mitral stenosis

Recommendation 3 [R3] – type and dosage of coumarin derivatives
Choice of coumarin derivative is partly determined by agreement with the local thrombosis service. In the Netherlands, short-acting acenocoumarol 1 mg and long-acting phenprocoumon 3 mg are available
- In general, the thrombosis services recommend taking the tablets once daily in the evening
- When starting a coumarin derivative, a loading dose is given for the first days according to the table with loading doses of coumarin derivatives for different patient populations
- Self-monitoring of INR may be considered for patients who find regular monitoring by the local thrombosis service burdensome
- Coumarin derivative dosing by a thrombosis service should aim for an INR between 2.0 and 3.0

AF = atrial fibrillation; CHA2DS2-Vasc score = score calculating stroke risk in AF patients; GFR = glomerular filtration rate; INR = international normalised ratio; NHG = Nederlands Huisartsgenootschap; NOACs = new oral anticoagulants; OAC = oral anticoagulant; R = recommendation.

Systematic appraisal of guideline features

To systematically appraise the features of the NHG AF guideline, we used the Appraisal of Guidelines, Research and Evaluation (AGREE) II tool[15] and the GuideLine Implementability Appraisal (GLIA) tool.[16] Both tools are publicly available, and have previously been used for guideline appraisals.[17-19]

The AGREE II tool focuses on assessing the methodological rigour and transparency with which a guideline has been developed. It contains 23 items grouped in six domains (*table 2*, first column). Each item reflects a statement that refers to the guideline as a whole (e.g., 'Key recommendations are easily identifiable'), and is scored on a seven-point Likert scale, ranging from 1 (strongly disagree) to 7 (strongly agree).[15]

To identify obstacles to implementation of the guideline's key recommendations on OAC prescription (*table 1*), we completed GLIA appraisals. GLIA consists of 21 items in eight dimensions that – in contrast to AGREE II — are scored at the level of individual recommendations (*table 3*, first column). Each item is formulated as a question (e.g., 'Is justification for the recommendation stated explicitly?') with response categories 'yes', 'no', 'not applicable', and 'unsure'. We did not assess GLIA's global dimension that appraises the guideline in its entirety and largely overlaps with the AGREE appraisal.

Data collection and analysis

Following the AGREE II and GLIA manuals,[20,21] our appraisal panel consisted of four experts, representing a mix of clinical and methodological guideline expertise: one general practitioner (WL), one expert on antithrombotic treatment and stroke prevention in AF patients (DA), and two experts on guideline development and implementation (AB, SV). Panel members first individually performed the appraisals, using the online AGREE (www.agreetrust.org) and GLIA (eGLIA; http://nutmeg.med.yale.edu/glia) tools. They also provided additional information in free text fields to explain their scores. The appraisal process was primarily informed by the guideline document itself, but when necessary, extra information was collected from: i) the NHG website; ii) the booklet on NHG guideline development procedures;[22] and iii) a structured interview with two members of the NHG AF guideline development group. The appraisal coordinator (AB) then summarised the results as input for a group discussion based on which panel members could alter their scores when they considered this appropriate (e.g., to correct for available data that were overlooked during the initial appraisal). We discussed every item for which scores differed by more than one point, and every item for which the NHG development group members provided additional information.

AGREE II domain scores were calculated by summing up the individual appraisers' scores for each item within a domain (i.e., obtained score), and then standardising this as a percentage of the possible maximum score for that domain,[20] as follows:

$$\text{Domain score in \%} = \frac{\text{(obtained score – minimum possible score)}}{\text{(maximum possible score – minimum possible score)}}$$

As a result of the consensus procedure for GLIA scores, features were categorised as optimal ('Y' in *table 3*) or suboptimal ('N' in *table 3*). Per recommendation, we calculated the percentage of suboptimal features as follows:

$$\text{Percentage of suboptimal features} = \frac{\text{\# suboptimal features of recommendation}}{\text{total \# GLIA features – not applicable features}}$$

RESULTS

AGREE II appraisal of overall guideline features

Appendix 1 presents the individual appraisers' scores before and after group discussion. The group discussion resulted in 24 out of 92 (26%) scores being changed. The main reasons for appraisers to change their scores were: correction for available data that were overlooked during the initial appraisal (8 of 24 changes; 33%); a change of opinion following clarification of other appraisers' opinion (7 of 24; 29%); correction for additional information provided by the NHG guideline development group members (6 of 24; 25%). After the group discussion, standard deviations of item scores ranged between 0 and 1.6, with the majority (75%) being 1 or lower.

Table 2 presents the final item and domain scores assigned during the AGREE appraisal of the guideline. Domain scores ranged from 52.8% for 'Stakeholder involvement' to 87.5% for 'Editorial independence'.

GLIA appraisal of key recommendation features

Table 3 displays suboptimal features at the recommendation level, which may hinder the guideline's implementation and applicability in practice. The percentage of suboptimal features for the three key recommendations on OAC prescription (R1-3) ranged from 24% to 45%. The panel considered the domains 'Effect on process of care' and 'Measurability' optimal across all recommendations.

We found that all recommendations suffered from suboptimal decidability due to ambiguous or unclear

Table 2. *AGREE II scores of the NHG AF guideline section on prescription of oral anticoagulants*

AGREE II domains, domain scores[a], and items	Item scores (SD)[b]	Illustration of suboptimal features per domain
SCOPE AND PURPOSE (63.9%)		
Overall objective of the guideline is specifically described	4.8 (1.5)	Although some health questions are included as subheadings, the guideline does not provide an easy-to-access overview of all questions covered It is unclear whether children are included in the guideline's target population
Health questions covered by the guideline are specifically described	4.0 (1.4)	
Target patient population of the guideline is specifically described	5.8 (1.0)	
STAKEHOLDER INVOLVEMENT (52.8%)		
All relevant professional groups were included in the guideline development group	4.0 (0.8)	The guideline development group did not include cardiologists, pharmacists, neurologists, or representatives of anticoagulation clinics The national patient association was asked for external review, but it is unclear if and how their suggestions were addressed in the final guideline document
Views and preferences of the target patient population were sought	2.8 (0.5)	
Target users of the guideline are clearly defined	5.8 (1.0)	
RIGOUR OF DEVELOPMENT (63.0%)		
Systematic methods were used to search for evidence	4.8 (1.0)	Although the guideline group did apply selection criteria, these were not made explicit before evidence selection[d], and not available within the guideline document For some studies, the group performed a quality appraisal, but without applying a formal tool Furthermore, recommendations lack a summary of the quality of underlying evidence that is easy to find and interpret for guideline users It is unclear how evidence was translated into recommendations, and there is no description of how the guideline group solved any disagreements arising during recommendation formulation The Netherlands Society of Cardiology did not externally review the guideline prior to publication, but most other relevant stakeholder groups did
Criteria for selecting the evidence are clearly described	2.5 (1.3)	
Strengths and limitations of the body of evidence are clearly described[c]	3.0 (1.6)	
Methods for formulating recommendations are clearly described	2.5 (1.0)	
Health benefits, side effects, and risks were considered	6.5 (0.6)	
There is an explicit link between recommendations and supporting evidence	5.5 (1.0)	
The guideline was externally reviewed by experts prior to publication	6.5 (0.6)	
Procedure for updating the guideline is provided	7.0 (0.0)	
CLARITY OF PRESENTATION (66.7%)		
Recommendations are specific and unambiguous[e]	5.5 (1.0)	Key recommendations are not easily identifiable because they do not have one specific layout or font; some, but not all are (partly) captured in boxes. Further, some text boxes hold other types of information, such as a description of guideline development procedures, or a summary of what has changed since the previous version of the guideline
Different disease management options are clearly presented	6.0 (0.8)	
Key recommendations are easily identifiable	3.5 (0.6)	
APPLICABILITY (57.3%)		
Facilitators and barriers to application of the guideline are described	4.0 (0.8)	The guideline describes several barriers and facilitators. However, most are not clearly labelled as a such, and they are scattered throughout the text instead of grouped or summarised in one section The criteria for monitoring the dose of coumarin derivatives are clearly described, but less so for other OAC types. The guideline does not provide any criteria to audit adherence or monitor impact at the GP practice level
Guideline provides advice and tools for applying recommendations in practice	4.8 (1.5)	
Potential resource implications of applying recommendations were considered	6.0 (0.0)	
The guideline presents monitoring and/or auditing criteria	3.0 (0.8)	
EDITORIAL INDEPENDENCE (87.5%)		
Views of funding body did not influence the guideline content	6.0 (0.8)	[no substantial suboptimal features with regard to the guideline's editorial independence]
Competing interests of authors were recorded and addressed	6.5 (0.6)	

AF = atrial fibrillation; GP = general practitioner; GRADE = Grading of Recommendations Assessment, Development and Evaluation; NHG = Nederlands Huisartsgenootschap; OAC = oral anticoagulant; SD = standard deviation. [a]Domain scores range between 0 and 100% and were calculated by summing up the individual appraiser's scores for each item within a domain, and then standardising this as a percentage of the possible maximum score for that domain. [b]Average item scores of four appraisers. Item scores can range between 1 and 7, with lower scores indicating less optimal features. [c]Overlaps with GLIA item 'Is quality of evidence that supports each recommendation stated explicitly?' [d]Based on data collected during structured interviews with guideline development group members. [e]Overlaps with GLIA 'Executability' and 'Decidability' domains; see *table 3*.

Table 3. *GLIA scores of the three NHG recommendations on prescription of oral anticoagulants*[a]

GLIA domains and items ↓	Scores per recommendation			Illustration of suboptimal features[b]
	R1	R2	R3	
EXECUTABILITY				
Is the recommended action stated specifically and unambiguously?	Y	N	Y	[*R2*] GPs might not execute the action '…consider NOACs…' consistently [*R2*] Type and dose of NOACs are not specified
Is sufficient detail provided to perform the recommended action?	Y	N	Y	
DECIDABILITY				
Can one consistently determine whether each condition in the recommendation was satisfied?	N	N	N	Examples of conditions that may not be consistently applied by most GPs: [*R1 – referenced table*] Contraindications, such as 'severe disturbance of liver function'; [*R2*] 'High medication adherence'; [*R3 – referenced table*] 'Relative contraindications' to treatment with warfarin and phenprocoumon
Are all reasonable combinations of conditions addressed?	Y	Y	Y	
Is the logical relationship between conditions clear?	Y	Y	Y	
VALIDITY				
Is justification for the recommendation stated explicitly?	N	Y	Y	[*R1*] Justification is stated in end notes, but not referenced as such in the recommendation For none of the recommendations, evidence quality was systematically appraised or stated
Is quality of evidence that supports each recommendation stated explicitly?[c]	N	N	N	
FLEXIBILITY				
Is the strength of each recommendation stated explicitly?	N	N	N	For all recommendations the strength is unclear due to a lack of standardised terminology or labels
Are patient characteristics specified that permit individualisation?	Y	Y	Y	
Are practice characteristics specified that permit modification?	n.a.	n.a.	Y	
EFFECT ON PROCESS OF CARE				
Can the recommendation be executed without substantial disruption in current workflow?	Y	Y	Y	n.a.
Can the recommendation be pilot tested without substantial resource commitment?	Y	Y	Y	
MEASURABILITY				
Can adherence to this recommendation be measured?	Y	Y	Y	n.a.
Can outcomes of this recommendation be measured?	Y	Y	Y	
NOVELTY & INNOVATION				
Can the recommendation be performed without acquisition of new knowledge/skills?	Y	N	Y	[*R2*] GPs need to gain knowledge on the recommended use and (side) effects of NOACs [*R2*] NOAC prescription is discouraged, while patients may expect access to the latest drugs, or explicit room for shared decision making
Is the recommendation consistent with attitudes/beliefs of the intended audience?	Y	Y	Y	
Is the recommendation consistent with patient expectations?	Y	N	Y	
COMPUTABILITY				
Are all patient data available for electronic implementation of the recommendation?	N	N	N	All recommendations have some conditions for which data are unavailable (e.g., artificial heart valve, arrangements between patient and anticoagulation clinic), or that lack specificity (see Decidability items) [*R1*] The action in statement c ('Discuss with…') may not be specific enough to allow electronic implementation
Are the recommendation's conditions defined specifically enough for electronic implementation?	N	N	N	
Is each recommended action defined specifically enough for electronic implementation?	N	Y	Y	
Is it clear by what means a recommended action can be executed in an electronic setting?	Y	Y	Y	
Number (%) of suboptimal features per recommendation	7 (35)	9 (45)	5 (24)	

GLIA = guideline implementability appraisal; GPs = general practitioners; N = suboptimal feature/GLIA score 'No'; NHG = Nederlands Huisartsgenootschap; NOACs = new oral anticoagulants; R = recommendation; Y = optimal feature/GLIA score 'Yes'; n.a. = not applicable. [a]See *table 1* for a description of each of the three key recommendations. [b]This column contains examples to illustrate why recommendation features were considered suboptimal; each example is preceded by the number of the key recommendation – for example, [*R1*] – it refers to. [c]This item overlaps with AGREE II item 'Strengths and limitations of the body of the evidence are clearly described'.

conditions for when to apply a recommendation. For example, not all GPs may agree on what could be considered 'high' (R2) levels of medication adherence, or 'relative contraindications' for prescribing (R3 - referenced table). This, together with the lack of detail on how to prescribe NOACs (i.e., suboptimal executability of R2), led the panel to score many of the computability features as problematic. This reflects the panel's expectation that operationalising the recommendations in an electronic information system may be difficult.

The strength of recommendations, and thus the degree to which they applied to all patients, was often unclear, resulting in a suboptimal flexibility score. This stemmed from a lack of standardisation of how recommendations were formulated. Terminology ranged from *'absolute contraindications* of NOACs *are*...' (R2) to 'Coumarin derivative dosing [...] *should* aim' (R3), and from '*Recommend* oral anticoagulants ...' (R1) to '... *consider* NOACs *only*...' (R2). In some cases, actions were only suggested indirectly: '...coumarin derivatives are preferred' (R2); '...a loading dose is given for the first days' (R3).

DISCUSSION

In this study we systematically appraised features of the NHG AF guideline to identify guideline-related barriers that may hamper optimal prescription of oral anticoagulants in Dutch primary care. The editorial independence of the guideline development group scored highly; scores for all other aspects of the guideline's methodological quality were acceptable. At the recommendation level, the main implementation obstacles were the lack of explicit statements on the quality of the underlying evidence, lack of clarity around the strength of recommendations, and suboptimal computability hampering operationalisation of recommendations in electronic systems.

The scores for the NHG AF guideline were high in comparison with those assigned in other, similar guideline appraisal studies. For example, the systematic review of guideline appraisal studies by Alonso-Coello et al.[23] summarised the methodological quality of 626 guidelines, and reported mean AGREE II scores that were lower for all six domains. The study by Sabharwal et al.[17] appraised 101 cardiac clinical practice guidelines. Compared with the NHG AF guideline, they found higher mean scores for the 'Scope and Purpose' domain (64% and 85%, respectively) and for 'Clarity of Presentation' (67% versus 82%), but lower scores for the four remaining domains.

Suggestions to improve the NHG AF guideline

1. Extend stakeholder involvement in the guideline development process

The AGREE II domain 'Stakeholder involvement' obtained the lowest score of all domains (53%). This was partly due to the lack of representation of a wide range of stakeholders in the guideline development group, which consisted of general practitioners and an epidemiologist. Other relevant disciplines, such as neurologists and representatives of anticoagulation clinics, were consulted at the external review stage. Yet, AGREE II and other accepted guideline standards advocate multidisciplinary development groups because they tend to generate more balanced views than single-speciality groups.[24,25] Inviting representatives of other disciplines as members of the NHG guideline development group would be one way to increase multidisciplinary involvement. An alternative approach may be to consult the current panel of external reviewers earlier on in the process, for example when setting the guideline scope, selecting or rating the evidence, or when formulating the recommendations.

The low 'Stakeholder involvement' score also stemmed from the apparent limited extent to which patient experiences and expectations informed the NHG AF guideline. The national patient organisation was invited for external review, but it was unclear if and how their suggestions were addressed. Similar to the approaches for increased stakeholder involvement described above, patient involvement may be facilitated by having patient representation in the guideline development group, or by formal patient consultation at earlier stages of guideline development.[26] Alternatively, a literature review or patient interviews could inform a guideline section summarising patient views on and experiences with antithrombotic treatment for stroke prevention.

2. Standardise layout and language of key recommendations

Although the key recommendations are clearly presented in the online summary of the guideline (https://www.nhg.org/standaarden/samenvatting/atriumfibrilleren), they remain hidden in the full text version. Using a specific font, framing them in a box, or (if possible) presenting them as a flowchart would support distinguishing key recommendations from other types of information in the guideline. Additionally, applying standardised language may help guideline users to recognise recommendations as such, whilst aligning interpretations of whether recommendations should be considered relevant for all patients. The Grading of Recommendations, Assessment, Development and Evaluation (GRADE) framework[27] proposes standardised guideline language: recommendations can be either strong (level '1') or weak (level '2'), which translate into the phrases 'we recommend' or 'we suggest', respectively. Adopting GRADE as part of the guideline development methodology also ensures systematic assessment of the quality of the underlying evidence, with the letters 'A' (indicating high quality) to

'D' (very low quality) explicitly communicating evidence quality at the recommendation level. For future versions of the AF guideline, the NHG's updated procedure booklet (published January 2015) includes guidance on how to use the GRADE framework for assessing and summarising quality of the underlying evidence.

3. Suggest criteria for monitoring the guideline's use in practice
Facilitating local or regional monitoring of the guideline's use in practice requires clearly defined criteria derived from the guideline's key recommendations. For the NHG AF guideline, examples of criteria may be 'the percentage of female patients who are prescribed oral anticoagulants and are aged 65 years or older', or 'the percentage of patients on coumarin derivatives with an INR between 2.0 and 3.0'. Suggesting monitoring criteria as part of the guideline would provide a suitable starting point for developing audit and feedback, which Dutch GPs considered an encouraging strategy to improve guideline adherence.[28]

4. Prepare electronic implementation in parallel with the guideline development process
Recent studies have focused on providing GPs with clinical decision support systems (CDSS) to improve primary care stroke prevention in AF patients.[29-31] These systems use decision rules to evaluate the current treatment of the patient and, if necessary, recommend the GP to modify it. Creating these decision rules involves translating guidelines into a format that is interpretable by a computer. The GLIA dimensions 'Decidability' and 'Computability' relate to obstacles for electronic implementation, i.e. translating guideline recommendations into actionable, computable decision rules. In the current study, the NHG AF guideline scored poorly for these dimensions, indicating presence of ambiguous terms. Although this guideline was included in CDSSs for Dutch GPs,[26,29] the suboptimal computability hampered interpretation and translation of individual guideline statements into electronic decision rules. Especially the lack of clear definitions for certain contraindications and the unavailability of structured data to identify contraindications in electronic health records required input from an expert group of clinicians to fully convert the guideline into unambiguous decision rules.[26] Based on this finding we suggest involving a CDSS specialist when formulating recommendations for future updates of the NHG AF guideline. By preparing electronic implementation in parallel with the guideline development process, vague and inconsistent recommendations can be identified and resolved before publication.[30] This may not only improve overall implementability of the guideline in practice, but also facilitate the development of effective CDSS interventions.

In conclusion, this study provides pointers for optimising future versions of the NHG AF guideline. Future research should investigate whether applying these suggestions indeed positively affects implementation of the guideline in primary care, which in turn may improve the adequacy of antithrombotic treatment and stroke prevention in patients with atrial fibrillation.

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Appendix 1. *Individual appraisers' scores for AGREE II appraisal after group discussion; scores prior to group discussion are given in round brackets if they differed from scores after the discussion*

Appraiser					**Obtained domain score**
Domain and items	**1**	**2**	**3**	**4**	
SCOPE AND PURPOSE					
Overall objective of the guideline is specifically described	6	6	3	4	58
Health questions covered by the guideline are specifically described	4	3	3	6	
Target patient population of the guideline is specifically described	5	5	6	7	
STAKEHOLDER INVOLVEMENT					
All relevant professional groups were included in the guideline development group	3	5	4 (6)	4 (6)	50
Views and preferences of the target patient population were sought	2	3 (5)	3 (5)	3 (5)	
Target users of the guideline are clearly defined	6	7	5	5	
RIGOUR OF DEVELOPMENT					
Systematic methods were used to search for evidence	5 (2)	6	4 (1)	4	153
Criteria for selecting the evidence are clearly described	1	3	4 (5)	2	
Strengths and limitations of the body of evidence are clearly described	3	5 (7)	3	1	
Methods for formulating recommendations are clearly described	1	3	3 (5)	3 (6)	
Health benefits, side effects, and risks have been considered	7	7	6	6 (5)	
There is an explicit link between recommendations and supporting evidence	5	5	5	7	
The guideline was externally reviewed by experts prior to publication	6	7	7	6	
Procedure for updating the guideline is provided	7 (2)	7	7 (1)	7 (3)	
CLARITY OF PRESENTATION					
Recommendations are specific and unambiguous	5	5	5	7	60
Different disease management options are clearly presented	6	5	6	7	
Key recommendations are easily identifiable	3	4	4 (7)	3 (7)	
APPLICABILITY					
Facilitators and barriers to application of the guideline are described	5	4 (2)	4 (3)	3	71
Guideline provides advice and tools for applying recommendations in practice	4	6	3	6	
Potential resource implications of applying recommendations have been considered	6	6	6 (1)	6	
The guideline presents monitoring and/or auditing criteria	3	3	2 (1)	4 (6)	
EDITORIAL INDEPENDENCE					
Views of funding body have not influenced the guideline content	6 (1)	7	6	5	50
Competing interests of authors have been recorded and addressed	6 (4)	7	7	6	