Complete Summary

GUIDELINE TITLE

Atrial fibrillation. National clinical guideline for management in primary and secondary care.

BIBLIOGRAPHIC SOURCE(S)

National Collaborating Centre for Chronic Conditions. Atrial fibrillation. National clinical guideline for management in primary and secondary care. London (UK): Royal College of Physicians; 2006. 173 p. [380 references]

GUIDELINE STATUS

This is the current release of the guideline.

** REGULATORY ALERT **

FDA WARNING/REGULATORY ALERT

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- February 28, 2008, Heparin Sodium Injection: The U.S. Food and Drug Administration (FDA) informed the public that Baxter Healthcare Corporation has voluntarily recalled all of their multi-dose and single-use vials of heparin sodium for injection and their heparin lock flush solutions. Alternate heparin manufacturers are expected to be able to increase heparin production sufficiently to supply the U.S. market. There have been reports of serious adverse events including allergic or hypersensitivity-type reactions, with symptoms of oral swelling, nausea, vomiting, sweating, shortness of breath, and cases of severe hypotension.
- August 16, 2007, Coumadin (Warfarin): Updates to the labeling for Coumadin to include pharmacogenomics information to explain that people's genetic makeup may influence how they respond to the drug.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Atrial fibrillation

GUIDELINE CATEGORY

Diagnosis
Evaluation
Management
Risk Assessment
Treatment

CLINICAL SPECIALTY

Cardiology
Emergency Medicine
Family Practice
Geriatrics
Hematology
Internal Medicine
Pharmacology
Pulmonary Medicine

INTENDED USERS

Health Care Providers
Hospitals
Nurses
Patients
Physicians
Public Health Departments

GUIDELINE OBJECTIVE(S)

To provide a user-friendly, clinical, evidence-based guideline for the National Health Service (NHS) in England and Wales that:

- Offers best clinical advice for atrial fibrillation (AF)
- Is based on best published evidence and expert consensus
- Takes into account patient choice and informed decision-making
- Defines the major components of NHS care provision for AF
- Indicates areas suitable for clinical audit

- Details areas of uncertainty or controversy requiring further research
- Provides a choice of guideline versions for differing audiences

TARGET POPULATION

Groups that are covered

The guideline will include people with:

- New onset or acute atrial fibrillation (AF)
- Chronic AF, including paroxysmal (recurrent), persistent and permanent/sustained AF
- Co-morbidities that impact upon AF
- Postoperative AF
- Atrial flutter that is indistinguishable from AF in terms of aim of treatment

Groups that are not covered

- People under age 18 years
- Congenital heart disease precipitating AF

INTERVENTIONS AND PRACTICES CONSIDERED

Diagnosis/Evaluation

1. Physical examination
    - Evaluation of presenting symptoms
    - Pulse palpitation
2. Electrocardiography
    - Standard electrocardiogram (ECG)
    - Ambulatory ECG
3. Echocardiography
    - Transthoracic
    - Transoesophageal

Treatment/Risk Assessment/Management

1. Cardioversion
    - Electrical
    - Pharmacological (flecainide, propafenone, amiodarone)
    - Electrical cardioversion with concomitant antiarrhythmic drugs (amiodarone or sotalol)
    - Transoesophageal echocardiography-guided cardioversion
2. Rhythm control for persistent atrial fibrillation (AF)
    - Beta-blockers
    - Amiodarone
    - Class Ic agents
    - Sotalol
3. Antithrombotic therapy for persistent AF
    - Warfarin
    - Heparin

4. Rate control for permanent AF
    - Beta-blockers
    - Calcium antagonists
    - Digoxin
5. Antithrombotic therapy for permanent AF
    - Warfarin
    - Aspirin
6. Rhythm control for paroxysmal AF
    - Avoidance of symptom precipitants
    - "Pill-in-the-pocket" strategy
    - Beta-blockers
    - Class Ic agents (such as flecainide or propafenone)
    - Sotalol
    - Amiodarone
7. Acute AF in haemodynamically unstable patients
    - Emergency electrical cardioversion
    - Intravenous amiodarone
    - Flecainide
    - Pharmacological rate-control strategy
    - Beta-blockers
    - Rate-limiting calcium antagonists
8. Antithrombotic therapy for acute-onset AF
    - Heparin
    - Oral anticoagulation
9. Prophylaxis for postoperative AF
    - Amiodarone
    - Beta-blockers
    - Sotalol
    - Rate-limiting calcium antagonists
10. Antithrombotic therapy in acute stroke patients
    - Management of uncontrolled hypertension
    - Imaging (computed tomography scan or magnetic resonance imaging)
    - Anticoagulation therapy (in the absence of haemorrhage)
11. Antithrombotic therapy following a stroke or trans ischaemic attack
    - Warfarin
12. Antithrombotic therapy for asymptomatic AF
    - Thromboprophylaxis
13. Assessment of bleeding risk for long-term anticoagulation
14. Assessment of risk factors for stroke and thromboembolism
15. Monitoring and referral
    - Anticoagulation self-monitoring
    - Follow-up post cardioversion
    - Referral for further specialist intervention

MAJOR OUTCOMES CONSIDERED

- Cardioversion success rate
- Recurrence of atrial fibrillation following successful cardioversion
- Incidence of stroke or thromboembolism
- Incidence of vascular death
- Efficacy of antiarrhythmic drugs
- Side effects of drugs

- Cost effectiveness

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Systematically Searching for the Evidence

The information scientist developed a search strategy for each question. Key words for the search were identified by the Guidance Development Group (GDG). In addition, the health economist searched for additional papers to inform detailed health economic work (e.g., modelling). Papers that were published or accepted for publication in peer-reviewed journals were considered as evidence by the GDG. Conference paper abstracts and non-English language papers were excluded from the searches.

Each clinical question dictated the appropriate study design that was prioritised in the search strategy but the strategy was not limited solely to these study types. The research fellow or health economist identified titles and abstracts from the search results that appeared to be relevant to the question. Exclusion lists were generated for each question together with the rationale for the exclusion. The exclusion lists were presented to the GDG. Full papers were obtained where relevant. See Appendix C of the original guideline document for literature search details.

Critically Appraising the Evidence

The research fellow or health economist, as appropriate, critically appraised the full papers. In general no formal contact was made with authors but there were ad hoc occasions when this was required in order to clarify specific details. Critical appraisal checklists were compiled for each full paper. One research fellow undertook the critical appraisal and data extraction. The evidence was considered carefully by the GDG for accuracy and completeness.

All procedures are fully compliant with:

- National Institute for Clinical Excellence (NICE) methodology as detailed in the Guideline development methods – information for National Collaborating Centres and guideline developers manual.
- National Collaborating Centre for Chronic Conditions (NCC-CC) quality assurance document and systematic review chart, available at www.rcplondon.ac.uk/college/ceeu/ncccc_index.htm

Incorporating Health Economic Evidence

There were constraints in the health economic resources and so the following approach was agreed for this guideline. Health economics was incorporated alongside the clinical questions.

- Searches in relevant databases were done by the information scientist using economic filters on the related clinical questions.
- No study design criteria were imposed a priori, i.e., the searches were not limited to randomised control trials (RCTs) or formal economic evaluations.
- Titles and abstracts identified in the economic searches were reviewed by the health economist and full papers were obtained once they met the inclusion/exclusion criteria.
- The full papers were critically appraised by the health economist and the relevant data were presented to the GDG.

Cost-effectiveness evidence from the UK was preferred, but all relevant evidence was considered, including non-UK studies.

The GDG identified areas for additional economic work. Five key areas were identified and three were given priority. The GDG agreed on the model structures. The health economist performed supplemental literature searches using key search terms in Medline and an Internet search engine to obtain additional information for modelling. None of the identified priority areas were modelled for various reasons (see Appendix A of the original guideline document for details).

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Levels of Evidence for Intervention Studies

1++ High quality meta-analysis (MA), systematic reviews (SR) of randomised controlled trials (RCTs), or RCTs with a very low risk of bias

1+ Well conducted MA, SR or RCTs, or RCTs with a low risk of bias

1- MA, SR of RCTs, or RCTs with a high risk of bias

2++ High quality SR of case-control or cohort studies.

High quality case-control or cohort studies with a very low risk of confounding, bias, or chance and a high probability that the relationship is causal

2+ Well conducted case-control or cohort studies with a low risk of confounding, bias, or chance and a moderate probability that the relationship is causal

2- Case-control or cohort studies with a high risk of confounding, bias, or chance and a significant risk that the relationship is not causal (Not used as a basis for making a recommendation)

3 Non-analytic studies (for example, case reports, case series)

4 Expert opinion, formal consensus

Levels of Evidence for Studies of the Accuracy of Diagnostic Tests

Ia Systematic review (with homogeneity)* of level-1 studies**

Ib Level-1 studies**

II Level-2 studies***

Systematic reviews of level-2 studies

III Level-3 studies****

Systematic reviews of level-3 studies

IV Consensus, expert committee reports or opinions and/or clinical experience without explicit critical appraisal; or based on physiology, bench research or 'first principles'

*Homogeneity means there are no or minor variations in the directions and degrees of results between individual studies that are included in the systematic review.

**Level-1 studies are studies:

- That use a blind comparison of the test with a validated reference standard (gold standard)
- In a sample of patients that reflects the population to whom the test would apply

***Level-2 studies are studies that have **only one** of the following:

- Narrow population (the sample does not reflect the population to whom the test would apply)
- Use a poor reference standard (defined as that where the 'test' is included in the 'reference', or where the "testing' affects the 'reference')
- The comparison between the test and reference standard is not blind
- Case-control studies

****Level-3 studies are studies that have **at least two or three** of the features listed for level-2 studies.

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Distilling and Synthesising the Evidence and Developing Recommendations

The evidence from each full paper was distilled into an evidence table and synthesised into evidence statements before being presented to the Guideline Development Group (GDG). This evidence was then reviewed by the GDG and used as a basis upon which to formulate recommendations.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Guidance Development Group (GDG)

The GDG met 14 times between July 2004 and December 2005 and comprised a multidisciplinary team of professionals, service users (people with atrial fibrillation [AF] or carers), and user organization representatives who were supported by the technical team.

Agreeing the Recommendations

The sign-off workshop employed formal consensus techniques to:

- Ensure that the recommendations reflected the evidence base
- Approve recommendations based on lesser evidence or extrapolations from other situations
- Reach consensus recommendations where the evidence was inadequate
- Debate areas of disagreement and finalise recommendations

The sign-off workshop also reached agreement on the following:

- Five priorities for implementation
- Five key research recommendations
- Algorithms

In prioritising key recommendations for implementation, the sign-off workshop also took into account the following criteria:

- High clinical impact
- High impact on reducing variation
- More efficient use of National Health Service (NHS) resources
- Allowing the patient to reach critical points in the care pathway more quickly

The audit criteria provide suggestions of areas for audit in line with the key recommendations for implementation.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Grading of Recommendations for Intervention Studies

Grade A:

- Level 1++ and directly applicable to the target population, or
- Level 1+ and directly applicable to the target population AND consistency of results
- Evidence from National Institute for Health and Clinical Excellence (NICE) technology appraisal

Grade B:

- Level 2 ++, directly applicable to the target population and demonstrating overall consistency of results, or
- Extrapolated evidence from studies rated as 1++ or 1+

Grade C:

- Level 2+, directly applicable to the target population and demonstrating overall consistency of results, or
- Extrapolated evidence from 2++

Grade D:

- Level 3 or 4, or
- Extrapolated from 2+, or
- Formal consensus

D (GPP):

A good practice point (GPP) is a recommendation for best practice based on the experience of the Guideline Development Group

Grading of Recommendations on Diagnostic Tests

Grade A (DS) Studies with level of evidence Ia or Ib

Grade B (DS) Studies with level of evidence II

Grade C (DS) Studies with level of evidence III

Grade D (DS) Studies with level of evidence IV

COST ANALYSIS

Details of the review of published cost analyses are provided in the original guideline document.

METHOD OF GUIDELINE VALIDATION

Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

The guideline was validated through two consultations.

1. The first draft of the guideline (The full guideline, National Institute for Clinical Excellence [NICE] guideline and Quick Reference Guide) were consulted with Stakeholders and comments were considered by the Guideline Development Group (GDG)
2. The final consultation draft of the Full guideline, the NICE guideline and the Information for the Public were submitted to stakeholders for final comments.

The final draft was submitted to the Guideline Review Panel for review prior to publication.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

The strength of recommendation grading [A–D (GPP)] and levels of evidence (1++–4) for interventional studies and strength of recommendation grading [A (DS)–D (DS)] and level of evidence (Ia–IV) for diagnostic studies are defined at the end of the "Major Recommendations" field.

Identification and Diagnosis

Presenting Symptoms/Pulse Palpitation

C - In patients presenting with any of the following:

- breathlessness/dyspnoea
- palpitations
- syncope/dizziness
- chest discomfort
- stroke/transischemic attack (TIA)

manual pulse palpation should be performed to assess for the presence of an irregular pulse that may indicate underlying atrial fibrillation (AF).

Electrocardiography

B (DS) - An electrocardiogram (ECG) should be performed in all patients, whether symptomatic or not, in whom AF is suspected because an irregular pulse has been detected.

Ambulatory ECG Recording

B (DS) - In patients with suspected paroxysmal AF undetected by standard ECG recording:

- a 24-hour ambulatory ECG monitor should be used in those with suspected asymptomatic episodes or symptomatic episodes less than 24 hours apart
- an event recorder ECG should be used in those with symptomatic episodes more than 24 hours apart

Echocardiography

Transthoracic echocardiography (TTE) should be performed in patients with AF:

- **D (GPP)** - for whom a baseline echocardiogram is important for long-term management, such as younger patients
- **C** - for whom a rhythm-control strategy that includes cardioversion (electrical or pharmacological) is being considered
- **D (GPP)** - in whom there is a high risk or a suspicion of underlying structural/functional heart disease (such as heart failure or heart murmur) that influences their subsequent management (for example, choice of antiarrhythmic drug)
- **C** - in whom refinement of clinical risk stratification for antithrombotic therapy is needed (see section below titled "Risk factors for Stroke and Thromboembolism")

D (GPP) - TTE should not be routinely performed solely for the purpose of further stroke risk stratification in patients with AF for whom the need to initiate anticoagulation therapy has already been agreed on appropriate clinical criteria (see section below titled "Risk factors for Stroke and Thromboembolism").

Transoesophageal echocardiography (TOE) should be performed in patients with AF:

- **D (GPP)** - when TTE demonstrates an abnormality (such as valvular heart disease) that warrants further specific assessment
- **D (GPP)** - in whom TTE is technically difficult and/or of questionable quality and where there is a need to exclude cardiac abnormalities
- **D (GPP)** - for whom TOE-guided cardioversion is being considered

Cardioversion

Electrical Versus Pharmacological Cardioversion

In patients with AF without haemodynamic instability for whom cardioversion is indicated:

- **D (GPP)** - the advantages and disadvantages of both pharmacological and electrical cardioversion should be discussed with patients before initiating treatment
- **B** - where AF onset was within 48 hours previously, either pharmacological or electrical cardioversion should be performed
- **D (GPP)** - for those with more prolonged AF (onset more than 48 hours previously) electrical cardioversion should be the preferred initial treatment option

Pharmacological Cardioversion

In patients with persistent AF, where the decision to perform pharmacological cardioversion using an intravenous antiarrhythmic agent has been made:

- **B** - in the absence of structural heart disease,* a Class 1c drug (such as flecainide or propafenone) should be the drug of choice
- **D (GPP)** - in the presence of structural heart disease,* amiodarone should be the drug of choice

*Coronary artery disease or left ventricular dysfunction

Electrical Cardioversion With Concomitant Antiarrhythmic Drugs

B - When patients with AF are to undergo elective electrical cardioversion and there is cause for heightened concern about successfully restoring sinus rhythm (such as previous failure to cardiovert or early recurrence of AF), concomitant amiodarone or sotalol* should be given for at least 4 weeks before the cardioversion.

*Sotalol to be progressively titrated from 80 mg twice daily up to 240 mg twice daily.

Transoesophageal Echocardiography-Guided Cardioversion

In patients with AF of greater than 48 hours duration, in whom elective cardioversion is indicated:

- **B** - both TOE-guided cardioversion and conventional cardioversion should be considered equally effective
- a TOE-guided cardioversion strategy should be considered:
    - **D (GPP)** - where experienced staff and appropriate facilities are available, and
    - **C** - where a minimal period of pre-cardioversion anticoagulation is indicated due to patient choice or bleeding risks

Treatment for Persistent AF

Rate Control Versus Rhythm Control

D (GPP) - As some patients with persistent AF will satisfy criteria for either an initial rate-control or rhythm-control strategy (for example, aged over 65 but also symptomatic):

- the indications for each option should not be regarded as mutually exclusive and the potential advantages and disadvantages of each strategy should be explained to patients before agreeing which to adopt
- any comorbidities that might indicate one approach rather than the other should be taken into account
- irrespective of whether a rate-control or a rhythm-control strategy is adopted in patients with persistent AF, appropriate antithrombotic therapy should be used

A rate-control strategy should be the preferred initial option in the following patients with persistent AF:

- **B** - over 65 years old
- **B** - with coronary artery disease
- **D (GPP)** - with contraindications to antiarrhythmic drugs
- **D (GPP)** - unsuitable for cardioversion*
- **B** - without congestive heart failure

A rhythm-control strategy should be the preferred initial option in the following patients with persistent AF:

- **D (GPP)** - those who are symptomatic
- **C** - younger patients
- **D (GPP)** - those presenting for the first time with lone AF
- **D (GPP)** - those with AF secondary to a treated/corrected precipitant
- **C** - those with congestive heart failure

*Patients unsuitable for cardioversion include those with:

- contraindications to anticoagulation
- structural heart disease (e.g., large left atrium >5.5 cm, mitral stenosis) that precludes long-term maintenance of sinus rhythm
- a long duration of AF (usually >12 months)
- a history of multiple failed attempts at cardioversion and/or relapses, even with concomitant use of antiarrhythmic drugs or non-pharmacological approaches
- an ongoing but reversible cause of atrial fibrillation (e.g., thyrotoxicosis)

Rhythm Control For Persistent AF

D (GPP) - An antiarrhythmic drug is not required to maintain sinus rhythm in patients with persistent AF in whom a precipitant (such as chest infection or fever) has been corrected and cardioversion has been performed successfully, providing there are no risk factors for recurrence.

In patients with persistent AF who require antiarrhythmic drugs to maintain sinus rhythm and who have structural heart disease*:

- **D (GPP)** - a standard beta-blocker should be the initial treatment option
- **A** - where a standard beta-blocker is ineffective, contraindicated or not tolerated amiodarone should be used

In patients with persistent AF who require antiarrhythmic drugs to maintain sinus rhythm and who do not have structural heart disease*:

- **D (GPP)** - a standard beta-blocker should be the initial treatment option
- where a standard beta-blocker is ineffective, contraindicated or not tolerated
    - **C** - a Class Ic agent or
    - **D (GPP)** - sotalol**

  should be given

B - where other drug classes are ineffective, contraindicated or not tolerated amiodarone should be administered.

*Coronary artery disease or left ventricular dysfunction.

**Progressively titrated from 80 mg twice daily up to 240 mg twice daily.

Antithrombotic Therapy For Persistent AF

C - Before cardioversion, patients should be maintained on therapeutic anticoagulation with warfarin (INR 2.5, range 2.0 to 3.0) for a minimum of 3 weeks.

D (GPP) - Following successful cardioversion, patients should remain on therapeutic anticoagulation with warfarin (INR 2.5, range 2.0 to 3.0) for a minimum of 4 weeks.

In patients with persistent AF where cardioversion cannot be postponed for 3 weeks:

- **D** - heparin should be given and the cardioversion performed, and
- **D (GPP)** - warfarin should then be given for a minimum of 4 weeks post cardioversion.

D (GPP) - Anticoagulation should be continued for the long term in patients with AF who have undergone cardioversion where there is a high risk or AF recurrence* or where it is recommended by the stroke risk stratification algorithm (see Figure 11.1 in the original guideline document).

D (GPP) - In patients with AF of confirmed duration of less than 48 hours undergoing cardioversion, anticoagulation following successful restoration of sinus rhythm is not required.

D (GPP) - Patients with atrial flutter should be given antithrombotic therapy in the same manner as those with AF.

*Factors indicating a high risk of AF recurrence include:

- a history of failed attempts at cardioversion
- structural heart disease (mitral valve disease, left ventricular dysfunction or an enlarged left atrium)
- a prolonged history of AF (greater than 12 months)
- previous recurrences of AF

Treatment For Permanent AF

Rate Control For Permanent AF

In patients with permanent AF, who need treatment for rate control:

- **A** - beta-blockers or rate-limiting calcium antagonists should be the preferred initial monotherapy in all patients.
- **D (GPP)** - digoxin should only be considered as monotherapy in predominately sedentary patients.

In patients with permanent AF where monotherapy is inadequate:

B - to control the heart rate only during normal activities, beta-blockers or rate-limiting calcium antagonists should be given with digoxin

B - to control the heart rate during both normal activities and exercise, rate-limiting calcium antagonists should be given with digoxin.

Antithrombotic Therapy For Permanent AF

D (GPP) - In patients with permanent AF a risk–benefit assessment should be performed and discussed with the patient to inform the decision whether or not to give antithrombotic therapy.

In patients with permanent AF where antithrombotic therapy is given to prevent strokes and/or thromboembolism (see section below titled "Risk factors for Stroke and Thromboembolism"):

A - adjusted-dose warfarin should be given as the most effective treatment

A - adjusted-dose warfarin should reach a target INR of 2.5 (range 2.0 to 3.0)

B - where warfarin is not appropriate, aspirin should be given at 75 to 300 mg/day

B - where warfarin is appropriate, aspirin should not be co-administered with warfarin purely as thromboprophylaxis, as it provides no additional benefit.

Treatment For Paroxysmal AF

Rhythm Control For Paroxysmal AF

D (GPP) - Where patients have infrequent paroxysms and few symptoms, or where symptoms are induced by known precipitants (such as alcohol, caffeine), a 'no drug treatment' strategy or a pill-in-the-pocket strategy should be considered and discussed with the patient.

D (GPP) - In patients with symptomatic paroxysms (with or without structural heart disease,* including coronary artery disease) a standard beta-blocker should be the initial treatment option.

In patients with paroxysmal AF and no structural heart disease:*

- where symptomatic suppression is not achieved with standard beta-blockers, either

    - **D (GPP)** - a Class Ic agent (such as flecainide or propafenone), or
    - **D (GPP)** - sotalol**

  should be given.

- where symptomatic suppression is not achieved with standard beta-blockers, Class Ic agents or sotalol, either
- **B** - amiodarone, or
- **A** - referral for non-pharmacological intervention (see section below titled "Referral") should be considered.

In patients with paroxysmal AF and coronary artery disease:

- **D (GPP)** - where standard beta-blockers do not achieve symptomatic suppression, sotalol should be given*
- where neither standard beta-blockers nor sotalol achieve symptomatic suppression, either
    - **B** - amiodarone, or
    - **A** - referral for non-pharmacological intervention (see section below titled "Referral")

  should be considered.

In patients with paroxysmal AF with poor left ventricular function:

- **D (GPP)** - where standard beta-blockers are given as part of the routine management strategy and adequately suppress paroxysms, no further treatment for paroxysms is needed
- where standard beta-blockers do not adequately suppress paroxysms, either
    - **B** - amiodarone or
    - **A** - referral for non-pharmacological intervention (see section below titled "Referral")

  should be considered.

D (GPP) - Patients on long-term medication for paroxysmal AF should be kept under review to assess the need for continued treatment and the development of any adverse effects.

*Coronary artery disease or left ventricular dysfunction.

**Progressively titrated from 80 mg twice daily up to 240 mg twice daily.

Treatment Strategy For Paroxysmal AF

C - In patients with paroxysmal AF, a pill-in-the-pocket strategy should be considered in those who:

- have no history of left ventricular dysfunction, or valvular or ischaemic heart disease; and
- have a history of infrequent symptomatic episodes of paroxysmal AF; and

- have a systolic blood pressure greater than 100 mm Hg and a resting heart rate above 70 bpm; and
- are able to understand how to, and when to, take the medication

Antithrombotic Therapy For Paroxysmal AF

B - Decisions on the need for antithrombotic therapy in patients with paroxysmal AF should not be based on the frequency or duration of paroxysms (symptomatic or asymptomatic) but on appropriate risk stratification, as for permanent AF (see section below titled "Risk Factors for Stroke and Thromboembolism").

Treatment For Acute-Onset AF

Acute AF in Haemodynamically Unstable Patients

D - In patients with a life-threatening deterioration in haemodynamic stability following the onset of AF, emergency electrical cardioversion should be performed, irrespective of the duration of the AF.

In patients with non life-threatening haemodynamic instability following the onset of AF:

- **D** - electrical cardioversion should be performed
- **D** - where there is a delay in organising electrical cardioversion, intravenous amiodarone should be used
- **D (GPP)** - in those with known Wolff–Parkinson–White syndrome:
    - flecainide may be used as an alternative for attempting pharmacological cardioversion
    - atrioventricular node-blocking agents (such as diltiazem, verapamil or digoxin) should not be used

D - In patients with known permanent AF where haemodynamic instability is caused mainly by a poorly controlled ventricular rate, a pharmacological rate-control strategy should be used.

Where urgent pharmacological rate-control is indicated, intravenous treatment should be with one of the following:

- **D** - beta-blockers or rate-limiting calcium antagonists
- **D** - amiodarone, where beta-blockers or calcium antagonists are contraindicated or ineffective

Antithrombotic Therapy For Acute-Onset AF

D (GPP) - In patients with acute AF who are receiving no, or subtherapeutic, anticoagulation therapy:

- in the absence of contraindications, heparin should be started at initial presentation
- heparin should be continued until a full assessment has been made and appropriate antithrombotic therapy has been started, based on risk

stratification (see section below titled "Risk factors for Stroke and Thromboembolism")

D (GPP) - In patients with a confirmed diagnosis of acute AF of recent onset (less than 48 hours since onset), oral anticoagulation should be used if:

- stable sinus rhythm is not successfully restored within the same 48-hour period following onset of acute AF, or
- there are factors indicating a high risk of AF recurrence,* or
- it is recommended by the stroke risk stratification algorithm (see Figure 11.1 in the original guideline document)

D (GPP) - In patients with acute AF where there is uncertainty over the precise time since onset, oral anticoagulation should be used, as for persistent AF (see section above titled "Rhythm Control for Persistent AF").

D (GPP) - In cases of acute AF where the patient is haemodynamically unstable, any emergency intervention should be performed as soon as possible and the initiation of anticoagulation should not delay any emergency intervention.

*Factors indicating a high risk of AF recurrence include:

- a history of failed attempts at cardioversion
- structural heart disease (mitral valve disease, left ventricular dysfunction or an enlarged left atrium)
- a prolonged history of AF (greater than 12 months)
- previous recurrences of AF

Postoperative AF

Drug Prophylaxis For Postoperative AF

D (GPP) - In the prophylaxis and management of postoperative AF, the appropriate use of antithrombotic therapy and correction of identifiable precipitants (such as electrolyte imbalance or hypoxia) is recommended.

In patients undergoing cardiothoracic surgery:

- the risk of postoperative AF should be reduced by the administration of one of the following:
    - **A** - amiodarone
    - **A** - a beta-blocker
    - **A**- sotalol
    - **B** - a rate-limiting calcium antagonist
- **B** - digoxin should not be used.

A - In patients undergoing cardiac surgery on pre-existing beta-blocker therapy, this treatment should be continued unless contraindications develop (such as postoperative bradycardia or hypotension).

Treatment for Postoperative AF

C - Unless contraindicated, a rhythm-control strategy should be the initial management option for the treatment of postoperative AF following cardiothoracic surgery.

D (GPP) - Unless contraindicated, postoperative AF following non-cardiothoracic surgery should be managed as for acute-onset AF with any other precipitant.

Antithrombotic Therapy

Initiating Antithrombotic Therapy

D (GPP) - In patients with newly diagnosed AF for whom antithrombotic therapy is indicated (see section below titled "Risk Factors for Stroke and Thromboembolism"), such treatment should be initiated with minimal delay after the appropriate management of comorbidities.

Antithrombotic Therapy in Acute Stroke Patients*

*NICE is developing a clinical guideline on the diagnosis and management of stroke (publication is expected for 2008).

D (GPP) - In all patients with AF who have had an acute stroke, any uncontrolled hypertension should be appropriately managed before antithrombotic therapy is started.

D (GPP) - In patients with AF and an acute stroke:

- imaging (CT scan or MRI) should be performed to exclude cerebral haemorrhage
- in the absence of haemorrhage, anticoagulation therapy should begin after 2 weeks
- in the presence of haemorrhage, anticoagulation therapy should not be given
- in the presence of a large cerebral infarction, the initiation of anticoagulation therapy should be delayed

D (GPP) - In patients with AF and an acute TIA:

- imaging (CT scan or MRI) should be performed to exclude recent cerebral infarction or haemorrhage
- in the absence of cerebral infarction or haemorrhage, anticoagulation therapy should begin as soon as possible

Antithrombotic Therapy Following a Stroke or TIA

In patients with AF who are either post-stroke, or have had a TIA:

- **A** - warfarin should be administered as the most effective thromboprophylactic agent
- **D (GPP)** - aspirin or dipyridamole should not be administered as thromboprophylactic agents unless indicated for the treatment of comorbidities or vascular disease.

D (GPP) - Treatment of post-stroke or post-TIA patients with warfarin should only begin after treatment of relevant comorbidities (such as hypertension) and assessment of the risk–benefit ratio.

Antithrombotic Therapy For Asymptomatic AF

D (GPP) - Patients with asymptomatic AF should receive thromboprophylaxis as for symptomatic AF (refer to sections above for persistent AF, permanent AF and paroxysmal AF).

Risks of Long-Term Anticoagulation

D (GPP) - Both the antithrombotic benefits and the potential bleeding risks of long-term anticoagulation should be explained to and discussed with the patient.

The assessment of bleeding risk should be part of the clinical assessment of patients before starting anticoagulation therapy. Particular attention should be paid to patients who:

- **D** - are over 75 years of age
- **C** - are taking antiplatelet drugs (such as aspirin or clopidogrel) or non-steroidal anti-inflammatory drugs
- **C** - are on multiple other drug treatments (polypharmacy)
- **C** - have uncontrolled hypertension
- **C** - have a history of bleeding (for example, peptic ulcer or cerebral haemorrhage)
- **D (GPP)** - have a history of poorly controlled anticoagulation therapy

Risk Factors For Stroke And Thromboembolism

C - The stroke risk stratification algorithm (section 11.7 of the original guideline document) should be used in patients with AF to assess their risk of stroke and thromboembolism, and appropriate thromboprophylaxis given.

D (GPP) - Risk stratification should be reconsidered whenever individual risk factors are reviewed.

Monitoring and Referral

Anticoagulation Self-Monitoring

C - In patients with AF who require long-term anticoagulation, self-monitoring should be considered if preferred by the patient and the following criteria are met:

- the patient is both physically and cognitively able to perform the self-monitoring test, or in those cases where the patient is not physically or cognitively able to perform self-monitoring, a designated carer is able to do so
- an adequate supportive educational programme is in place to train patients and/or carers
- the patient's ability to self-manage is regularly reviewed

- the equipment for self-monitoring is regularly checked via a quality control programme

Follow-Up Post Cardioversion

D - Following successful cardioversion of AF routine follow-up to assess the maintenance of sinus rhythm should take place at 1 month and 6 months.

D - At the 1-month follow-up the frequency of subsequent reviews should be tailored to the individual patient taking into account comorbidities and concomitant drug therapies.

D (GPP) - At each review the clinician should take the opportunity to re-assess the need for, and the risks and benefits of, continued anticoagulation.

D - At 6 months, if patients remain in sinus rhythm and have no other need for hospital follow-up, they should be discharged from secondary care with an appropriate management plan agreed with their GP.

D (GPP) - Patients should be advised to seek medical attention if symptoms recur.

D (GPP) - Any patient found at follow-up to have relapsed into AF should be fully re-evaluated for a rate-control or rhythm-control strategy (see section above titled "Antithrombotic Therapy for Persistent AF").

Referral

Referral for further specialist intervention (for example, pulmonary vein isolation, pacemaker therapy, arrhythmia surgery, AVJ catheter ablation or use of atrial defibrillators) should be considered in the following patients:

B - those in whom pharmacological therapy has failed

B - those with lone AF

C - those with ECG evidence of an underlying electrophysiological disorder (e.g., Wolff–Parkinson–White syndrome).

D (GPP) - The reasons for referral for specialist intervention should be explained and discussed with the patient.

Definitions:

Levels of Evidence for Intervention Studies

1++ High quality meta-analysis (MA), systematic reviews (SR) of randomised controlled trials (RCTs), or RCTs with a very low risk of bias

1+ Well conducted MA, SR or RCTs, or RCTs with a low risk of bias

1- MA, SR of RCTs, or RCTs with a high risk of bias

2++ High quality SR of case-control or cohort studies.

High quality case-control or cohort studies with a very low risk of confounding, bias, or chance and a high probability that the relationship is causal

2+ Well conducted case-control or cohort studies with a low risk of confounding, bias, or chance and a moderate probability that the relationship is causal

2- Case-control or cohort studies with a high risk of confounding, bias, or chance and a significant risk that the relationship is not causal (Not used as a basis for making a recommendation)

3 Non-analytic studies (for example, case reports, case series)

4 Expert opinion, formal consensus

Levels of Evidence for Studies of the Accuracy of Diagnostic Tests

Ia Systematic review (with homogeneity)* of level-1 studies**

Ib Level-1 studies**

II Level-2 studies***

Systematic reviews of level-2 studies

III Level-3 studies****

Systematic reviews of level-3 studies

IV Consensus, expert committee reports or opinions and/or clinical experience without explicit critical appraisal; or based on physiology, bench research or 'first principles'

*Homogeneity means there are no or minor variations in the directions and degrees of results between individual studies that are included in the systematic review.

**Level-1 studies are studies:

- that use a blind comparison of the test with a validated reference standard (gold standard)
- in a sample of patients that reflects the population to whom the test would apply

***Level-2 studies are studies that have **only one** of the following:

- narrow population (the sample does not reflect the population to whom the test would apply)
- use a poor reference standard (defined as that where the 'test' is included in the 'reference', or where the "testing' affects the 'reference')
- the comparison between the test and reference standard is not blind
- case-control studies

****Level-3 studies are studies that have **at least two or three** of the features listed for level-2 studies.

Grading of Recommendations for Intervention Studies

Grade A:

- Level 1++ and directly applicable to the target population, or
- Level 1+ and directly applicable to the target population AND consistency of results
- Evidence from National Institute for Health and Clinical Excellence (NICE) technology appraisal

Grade B:

- Level 2 ++, directly applicable to the target population and demonstrating overall consistency of results, or
- Extrapolated evidence from studies rated as 1++ or 1+

Grade C:

- Level 2+, directly applicable to the target population and demonstrating overall consistency of results, or
- Extrapolated evidence from 2++

Grade D:

- Level 3 or 4, or
- Extrapolated from 2+, or
- Formal consensus

D (GPP):

A good practice point (GPP) is a recommendation for best practice based on the experience of the Guideline Development Group

Grading of Recommendations on Diagnostic Tests

Grade A (DS) Studies with level of evidence Ia or Ib

Grade B (DS) Studies with level of evidence II

Grade C (DS) Studies with level of evidence III

Grade D (DS) Studies with level of evidence IV

CLINICAL ALGORITHM(S)

The following clinical algorithms are provided in the original guideline document:

- Atrial fibrillation (AF) care pathway
- Treatment strategy decision tree
- Cardioversion with transoesophageal echocardiography(TOE)-guided strategy
- Cardioversion treatment algorithm
- Rhythm-control treatment algorithm for persistent AF
- Rate-control treatment algorithm for permanent AF
- Rhythm-control treatment algorithm for paroxysmal AF
- Haemodynamically unstable AF treatment algorithm
- Stroke risk stratification algorithm

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for each recommendation (see "Major Recommendations").

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate treatment of atrial fibrillation to restore sinus rhythm and reduce the risk of morbidity and mortality

POTENTIAL HARMS

Side effects of therapy

CONTRAINDICATIONS

CONTRAINDICATIONS

- Due to concerns regarding contraindications of Class Ic agents in patients with left ventricular dysfunction, amiodarone was regarded as the drug of choice in these patients with symptomatic paroxysms despite initial beta-blocker therapy
- Treatment with atrioventricular (AV) node blockers (e.g., adenosine, digoxin, verapamil, diltiazem) will unmask or exacerbate a rapid atrial fibrillation (AF) due to a Wolff–Parkinson–White (WPW) syndrome and are therefore contraindicated in such patients.
- In patients undergoing cardiac surgery on pre-existing beta-blocker therapy, this treatment should be continued unless contraindications develop (such as postoperative bradycardia or hypotension)
- Obvious bleeding factors, such as recent bleeding peptic ulcer or intracranial bleeding, are contraindications to anticoagulation.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- The purpose of this guideline is to support clinical judgement, not to replace it. This means the treating clinician should:
    - Take into consideration any contraindications in deciding whether or not to administer any treatment recommended by this guideline
    - Consider the appropriateness of any recommended treatment for a particular patient in terms of the patient's relevant clinical and non-clinical characteristics
- Wherever possible, before administering or changing any treatment the treating clinician should follow good practice in terms of:
    - Discussing with the patient why the treatment is being offered and what health outcomes are anticipated
    - Highlighting any possible adverse events or side effects that have been associated with the treatment
    - Obtaining explicit consent for the treatment
- For those recommendations involving pharmacological treatment, the most recent edition of the *British National Formulary* (www.bnf.org.uk) should be followed for the determination of:
    - Indications
    - Drug dosage
    - Method and route of administration
    - Contraindications
    - Supervision and monitoring
    - Product characteristics

  Exceptions to the above are cases where guidance is provided within the recommendation itself.

- The guideline will normally only make drug recommendations that fall within licensed indications. If a drug is recommended outside of its licensed indication this will be made clear in the guideline (see Appendix D of the original guideline document).

Disclaimer

- Healthcare providers need to use clinical judgement, knowledge and expertise when deciding whether it is appropriate to apply guidelines. The recommendations cited here are a guide and may not be appropriate for use in all situations. The decision to adopt any of the recommendations cited here must be made by the practitioner in light of individual patient circumstances, the wishes of the patient, clinical expertise and resources.
- The National Collaborating Centre for Chronic Conditions (NCC-CC) disclaims any responsibility for damages arising out of the use or non-use of these guidelines and the literature used in support of these guidelines.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

Implementation in the National Health Service (NHS)

The Healthcare Commission assesses the performance of NHS organisations in meeting core and developmental standards set by the Department of Health in 'Standards for better health' issued in July 2004. Implementation of clinical guidelines forms part of the developmental standard D2. Core standard C5 says that national agreed guidance should be taken into account when NHS organisations are planning and delivering care.

National Institute for Clinical Excellence (NICE) has developed tools to help organisations implement this guidance (listed below). These are also available on our website (www.nice.org.uk/CG036).

- Slides highlighting key messages for local discussion
- Costing tools
    - Costing report to estimate the national savings and costs associated with implementation.
    - Costing template to estimate the local costs and savings involved
- Implementation advice on how to put the guidance into practice and national initiatives which support this locally.
- Audit criteria to monitor local practice (see Appendix D of "Atrial fibrillation: The management of atrial fibrillation", Clinical guideline; no. 36 [Accessing information in "Availability of Companion Documents" field of this summary]).

IMPLEMENTATION TOOLS

Audit Criteria/Indicators
Clinical Algorithm
Patient Resources
Quick Reference Guides/Physician Guides
Resources
Slide Presentation

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

National Collaborating Centre for Chronic Conditions. Atrial fibrillation. National clinical guideline for management in primary and secondary care. London (UK): Royal College of Physicians; 2006. 173 p. [380 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2006

GUIDELINE DEVELOPER(S)

National Collaborating Centre for Chronic Conditions - National Government Agency [Non-U.S.]

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National Institute for Health and Clinical Excellence (NICE)

GUIDELINE COMMITTEE

Guideline Development Group

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Members of the Guidance Development Group (GDG) declared any interests in accordance with the National Institute for Clinical Excellence (NICE) technical manual. A register is available from the National Collaborating Centre for Chronic Conditions (NCC-CC) for inspection upon request (ncc-cc@rcplondon.ac.uk).

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) format from the National Institute for Health and Clinical Excellence (NICE) Web site.

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- Atrial fibrillation. The management of atrial fibrillation. London (UK): National Institute for Health and Clinical Excellence; 2006 Jun. 47 p. (Clinical guideline; no. 36). Electronic copies: Available in Portable Document Format (PDF) from the National Institute for Health and Clinical Excellence (NICE) Web site.
- Atrial fibrillation. The management of atrial fibrillation. Quick reference guide. London (UK): National Institute for Health and Clinical Excellence; 2006 Jun. 19 p. (Clinical guideline; no. 36). Electronic copies: Available in Portable Document Format (PDF) from the National Institute for Health and Clinical Excellence (NICE) Web site.
- Implementation advice. Atrial fibrillation. London (UK): National Institute for Health and Clinical Excellence; 2006 Jun. 19 p. (Clinical guideline; no. 36). Electronic copies: Available in Portable Document Format (PDF) from the National Institute for Health and Clinical Excellence (NICE) Web site.
- Atrial fibrillation: the management of atrial fibrillation. Costing report. Implementing NICE guidance in England. London (UK): National Institute for Health and Clinical Excellence; 2006 Jul. 39 p. (Clinical guideline; no. 36).

Electronic copies: Available in Portable Document Format (PDF) from the National Institute for Health and Clinical Excellence (NICE) Web site.

- Costing template. Atrial fibrillation: the management of atrial fibrillation. London (UK): National Institute for Health and Clinical Excellence; 2006 Jul. various p. (Clinical guideline; no. 36). Electronic copies: Available in Portable Document Format (PDF) from the National Institute for Health and Clinical Excellence (NICE) Web site.
- Atrial fibrillation. Presenter slides. London (UK): National Institute for Health and Clinical Excellence; 2006 Jun. 34 p. (Clinical guideline; no. 36). Electronic copies: Available in Portable Document Format (PDF) from the National Institute for Health and Clinical Excellence (NICE) Web site.
- Guidelines manual 2006. London (UK): National Institute for Health and Clinical Excellence; 2006 Feb. Electronic copies: Available in Portable Document Format (PDF) from the National Institute for Health and Clinical Excellence (NICE) Web site.

Print copies: Available from the National Health Service (NHS) Response Line 0870 1555 455. ref: N1054. 11 Strand, London, WC2N 5HR.

PATIENT RESOURCES

The following is available:

- Atrial fibrillation. Understanding NICE guidance. Information for people who use NHS services. National Institute for Clinical Excellence (NICE), 2006 Jun. 15 p. Available in Portable Document Format (PDF) from the National Institute for Health and Clinical Excellence (NICE) Web site.

Print copies: Available from the National Health Service (NHS) Response Line 0870 1555 455, ref: N1055. 11 Strand, London, WC2N 5HR.

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC STATUS

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