Healthcare Improvement Scotland

SIGN

SIGN 152 • Cardiac arrhythmias in coronary heart disease

A national clinical guideline

September 2018

Evidence

KEY TO EVIDENCE STATEMENTS AND RECOMMENDATIONS

LEVELS OF EVIDENCE

1^{++}	High-quality meta-analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias
1^{+}	Well-conducted meta-analyses, systematic reviews, or RCTs with a low risk of bias
1^{-}	Meta-analyses, systematic reviews, or RCTs with a high risk of bias
2^{++}	High-quality systematic reviews of case-control or cohort studies High-quality case-control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal
2^{+}	Well-conducted case-control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal
2^{-}	Case-control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal
3	Non-analytic studies, eg case reports, case series
4	Expert opinion

RECOMMENDATIONS

Some recommendations can be made with more certainty than others. The wording used in the recommendations in this guideline denotes the certainty with which the recommendation is made (the 'strength' of the recommendation).

The 'strength' of a recommendation takes into account the quality (level) of the evidence. Although higher-quality evidence is more likely to be associated with strong recommendations than lower-quality evidence, a particular level of quality does not automatically lead to a particular strength of recommendation.

Other factors that are taken into account when forming recommendations include: relevance to the NHS in Scotland; applicability of published evidence to the target population; consistency of the body of evidence, and the balance of benefits and harms of the options.

R For '**strong**' recommendations on interventions that '**should**' be used, the guideline development group is confident that, for the vast majority of people, the intervention (or interventions) will do more good than harm. For '**strong**' recommendations on interventions that '**should not**' be used, the guideline development group is confident that, for the vast **majority** of people, the intervention (or interventions) will do more harm than good.

R For '**conditional**' recommendations on interventions that should be '**considered**', the guideline development group is confident that the intervention will do more good than harm for most patients. The choice of intervention is therefore more likely to vary depending on a person's values and preferences, and so the healthcare professional should spend more time discussing the options with the patient.

GOOD-PRACTICE POINTS

✓ Recommended best practice based on the clinical experience of the guideline development group.

NICE accredited
www.nice.org.uk/accreditation

NICE has accredited the process used by Scottish Intercollegiate Guidelines Network to produce clinical guidelines. The accreditation term is valid until 31 March 2020 and is applicable to guidance produced using the processes described in SIGN 50: a guideline developer's handbook, 2015 edition (www.sign.ac.uk/guidelines/fulltext/50/index.html). More information on accreditation can be viewed at www.nice.org.uk/accreditation

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Scottish Intercollegiate Guidelines Network

Cardiac arrhythmias in coronary heart disease

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Contents

1 Introduction

1.1 THE NEED FOR A GUIDELINE

Coronary heart disease (CHD) is a major challenge to the health of the nation, affecting an estimated 2.3 million people across the United Kingdom (UK).[1] CHD is the single biggest killer in Scotland and is responsible for 12% of all deaths,[2] or around 6,700 deaths each year.[1] Age-standardised death rates for CHD in Scotland are consistently among the highest seen across the UK.

Coronary heart disease is associated with many cardiac arrhythmias, with wide-ranging clinical consequences. Arrhythmias are common during acute coronary syndrome (ACS), with ventricular tachyarrhythmias being an important cause of cardiac arrest and sudden cardiac deaths (SCD) in this context. Patients with chronic CHD, particularly those with left ventricular dysfunction and heart failure are also at risk of ventricular arrhythmia and SCD in the longer term. An increasing number of patients with CHD are also affected by atrial fibrillation (AF) which is associated with significant morbidity as well as an increased risk of stroke and death, particularly in patients with other comorbid conditions such as heart failure.

Management of arrhythmias in CHD therefore requires a specialist approach which takes into account the management of important related conditions, principally ACS and heart failure. Since publication of this guideline in 2007, there have been major advances in catheter ablation and device-based therapies for arrhythmias, along with changes in pharmacological and device therapy for heart failure and interventional therapy for ACS. The SIGN guidelines for ACS[3] and heart failure[4] were updated in 2016 and this guideline has been updated to reflect evidence-based changes in management of arrhythmias in CHD. The SIGN guideline for cardiac rehabilitation includes recommendations for all patients with CHD.[5] Together these guidelines provide a framework for managing patients across the spectrum of coronary heart disease.

1.1.1 UPDATING THE EVIDENCE

This guideline updates SIGN 94: Cardiac arrhythmias in coronary heart disease, published in February 2007, to reflect the most recent evidence.

Where no new evidence was identified to support an update, text and recommendations are reproduced verbatim from SIGN 94. The original supporting evidence was not reappraised by the current guideline development group.

1.1.2 PATIENT PERSPECTIVE

Patients may have different perspectives on healthcare processes and outcomes from those of healthcare professionals. The involvement of patients in guideline development is therefore important to ensure that guidelines reflect their needs and concerns and address issues that matter to them.

Common issues raised by patient groups and through research include:

- patient involvement in treatment decisions
- attitudes and preferences to treatment
- quality of life issues
- self management
- psychosocial issues
- the role of arrhythmia specialist nurses in supporting patients and their carers.

1.2 REMIT OF THE GUIDELINE

1.2.1 OVERALL OBJECTIVES

This guideline provides evidence-based recommendations for the management of cardiac arrest and the arrhythmias associated with ACS, chronic CHD and cardiac surgery. It excludes arrhythmias not associated with CHD such as supraventricular tachycardias associated with accessory pathways or dual atrioventricular (AV) nodal physiology, arrhythmias caused by inherited ion channel disorders (eg long QT syndrome, Brugada syndrome) and arrhythmias associated with non-ischaemic cardiomyopathies. The evidence base in some areas (for example, management of cardiac arrest and atrial fibrillation) does not distinguish between patients whose arrhythmia has an ischaemic or non-ischaemic aetiology but wherever possible, the recommendations made are specific to CHD.

The rhythm management of AF is outlined in this guideline.

Recommendations on antithrombotic prophylaxis for atrial fibrillation are contained in SIGN guideline 129 on antithrombotic therapy.[6]

1.2.2 TARGET USERS OF THE GUIDELINE

This guideline will be of interest to healthcare professionals involved in the management of patients with cardiac arrhythmias including cardiac surgeons, cardiac nurse specialists cardiologists, clinical psychologists, general practitioners and other members of the primary healthcare team, paramedics and pharmacists, as well as patients, carers and voluntary organisations.

1.2.3 COMORBIDITIES TO CONSIDER WHEN MANAGING PATIENTS WITH ARRHYTHMIAS

The prevalence of multimorbidity increases with age and by age 65 the majority of the population has at least one comorbid condition. Among individuals with AF in Scotland, for example, 65% have three or more other health conditions.[7] Common comorbidities and coexisting health issues which have been considered when reviewing the evidence for this guideline are:

- chronic heart failure
- chronic kidney disease
- hypertension
- diabetes mellitus
- depression and anxiety.

1.2.4 SUMMARY OF UPDATES TO THE GUIDELINE, BY SECTION

1.1	The need for a guideline	Completely revised
1.2.2	Target users of the guideline	New
1.2.3	Comorbidities to consider when managing patients with arrhythmias	New
2	Key recommendations	New
3.3.1	Automated external defibrillators	Minor update
3.4.3	Therapeutic hypothermia	New
3.4.4	Bradycardia/sinoatrial dysfunction/heart block	Minor update
3.4.5	Polymorphic VT associated with QT prolongation	Updated
4.2	Conduction disturbances and bradycardia	Updated
4.3.1	Ventricular arrhythmias and ACS	Updated

4.3.2	Prevention of ventricular arrhythmias and sudden death	Updated
5.1	Atrial fibrillation	Updated
5.2.2	Implantable cardioverter defibrillator therapy in patients at risk of life-threatening arrhythmias (primary prevention)	Completely revised
5.2.4	Reducing inappropriate shocks associated with implantable cardioverter defibrillator therapy	New
5.2.6	Sustained monomorphic VT	New
5.2.7	Catheter ablation for recurrent ventricular arrhythmia/ electrical storm	New
6.4.1	Treatments for atrial fibrillation: Pharmacological therapies	Updated
6.4.3	Treatments for atrial fibrillation: Surgical ablation	New
7.2	Psychosocial assessment and screening	New
7.4	Psychosocial interventions	Updated
8	Provision of information	Updated
9	Implementing the guideline	Updated

1.3 STATEMENT OF INTENT

This guideline is not intended to be construed or to serve as a standard of care. Standards of care are determined on the basis of all clinical data available for an individual case and are subject to change as scientific knowledge and technology advance and patterns of care evolve. Adherence to guideline recommendations will not ensure a successful outcome in every case, nor should they be construed as including all proper methods of care or excluding other acceptable methods of care aimed at the same results.

The ultimate judgement must be made by the appropriate healthcare professional(s) responsible for clinical decisions regarding a particular clinical procedure or treatment plan. This judgement should only be arrived at through a process of shared decision making with the patient, covering the diagnostic and treatment choices available. It is advised, however, that significant departures from the national guideline or any local guidelines derived from it should be documented in the patient's medical records at the time the relevant decision is taken.

1.3.1 INFLUENCE OF FINANCIAL AND OTHER INTERESTS

It has been recognised that financial interests in, or close working relationships with, pharmaceutical companies may have an influence on the interpretation of evidence from clinical studies.

It is not possible to completely eliminate any possible bias from this source, nor even to quantify the degree of bias with any certainty. SIGN requires that all those involved in the work of guideline development should declare all financial interests, whether direct or indirect, annually for as long as they are actively working with the organisation. By being explicit about the influences to which contributors are subjected, SIGN acknowledges the risk of bias and makes it possible for guideline users or reviewers to assess for themselves how likely it is that the conclusions and guideline recommendations are based on a biased interpretation of the evidence.

Signed copies are retained by the SIGN Executive and a register of interests is available in the supporting material section for this guideline at **www.sign.ac.uk**

1.3.2 PRESCRIBING OF LICENSED MEDICINES OUTWITH THEIR MARKETING AUTHORISATION

Recommendations within this guideline are based on the best clinical evidence. Some recommendations may be for medicines prescribed outwith the marketing authorisation (MA) also known as product licence. This is known as 'off-label' use.

- Medicines may be prescribed off label in the following circumstances:
- for an indication not specified within the marketing authorisation
- for administration via a different route
- for administration of a different dose
- for a different patient population.

An unlicensed medicine is a medicine which does not have MA for medicinal use in humans.

Generally 'off-label' prescribing of medicines becomes necessary if the clinical need cannot be met by licensed medicines within the marketing authorisation. Such use should be supported by appropriate evidence and experience.[8]

"Prescribing medicines outside the conditions of their marketing authorisation alters (and probably increases) the prescribers' professional responsibility and potential liability."[8]

The General Medical Council (GMC) recommends that when prescribing a medicine 'off label', doctors should:

- be satisfied that such use would better serve the patient's needs than an authorised alternative (if one exists)
- be satisfied that there is sufficient evidence/experience of using the medicines to show its safety and efficacy, seeking the necessary information from appropriate sources
- record in the patient's clinical notes the medicine prescribed and, when not following common practice, the reasons for the choice
- take responsibility for prescribing the medicine and for overseeing the patient's care, including monitoring the effects of the medicine.

Non-medical prescribers should ensure that they are familiar with the legislative framework and their own professional prescribing standards.

Prior to any prescribing, the licensing status of a medication should be checked in the summary of product characteristics (www.medicines.org.uk). The prescriber must be competent, operate within the professional code of ethics of their statutory bodies and the prescribing practices of their employers.[9]

1.3.3 HEALTH TECHNOLOGY ASSESSMENT ADVICE FOR NHSSCOTLAND

Specialist teams within Healthcare Improvement Scotland issue a range of advice that focuses on the safe and effective use of medicines and technologies in NHSScotland.

The Scottish Medicines Consortium (SMC) provides advice to NHS boards and their Area Drug and Therapeutics Committees about the status of all newly licensed medicines and new indications for established products. NHSScotland should take account of this advice and ensure that medicines accepted for use are made available to meet clinical need where appropriate.

Until 1 October 2017, Healthcare Improvement Scotland reviewed Multiple Technology Appraisals (MTAs) produced by the National Institute for Health and Care Excellence (NICE) and provided advice about their applicability in NHSScotland. If Healthcare Improvement Scotland has advised that MTA guidance was applicable in Scotland, NHSScotland should take account of this and ensure that recommended medicines and treatment are made available to meet clinical need where appropriate.

NICE MTAs deemed valid for NHSScotland supersede extant SMC advice as they are generally underpinned by a larger and more recent evidence base.

SMC advice and NICE MTA guidance relevant to this guideline are summarised in section 9.4.

2 Key recommendations

The following recommendations were highlighted by the guideline development group as the key clinical recommendations that should be prioritised for implementation.

2.1 ARRHYTHMIAS ASSOCIATED WITH CARDIAC ARREST

R **Efforts to prevent sudden cardiac death should include:**

- **risk factor intervention in those individuals who are at high risk for coronary heart disease**
- **health promotion measures and encouragement of moderate-intensity physical activity in the general population.**

2.2 ARRHYTHMIAS ASSOCIATED WITH ACUTE CORONARY SYNDROME

R **All patients with ST-elevation acute coronary syndrome should undergo assessment of LV function for risk stratification at least six weeks following the acute event.**

2.3 ARRHYTHMIAS ASSOCIATED WITH CHRONIC CORONARY HEART DISEASE/LEFT VENTRICULAR DYSFUNCTION

R **Rate control is the recommended strategy for management of patients with well-tolerated atrial fibrillation.**

R **In patients with permanent AF or persistent AF following a rate-control strategy and a resting heart rate >110 bpm, appropriate rate-control therapy should be instituted with an initial target of resting heart rate <110 bpm.**

R **Implantable cardioverter defibrillators, cardiac resynchronisation therapy with defibrillator or cardiac resynchronisation therapy with pacing are recommended as treatment options for patients with heart failure with reduced ejection fraction, LVEF ≤35%.**

R **Patients with a primary-prevention ICD should have a single therapy zone programmed at a detection rate of 200 bpm.**

3 Arrhythmias associated with cardiac arrest

Management of cardiac arrest in the UK follows the Resuscitation Council (UK) guidelines.[10] These are based on the International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science with Treatment Recommendations (CoSTR).[11,12] Evidence presented in this section is based largely on the evidence evaluation worksheets from the CoSTR project which are referenced where appropriate.

3.1 PRIMARY PREVENTION OF SUDDEN CARDIAC DEATH

Coronary heart disease is the cause of SCD in approximately 70% of cases.[13] Sudden cardiac death occurs as a primary event in patients without previously recognised CHD, as well as in those with known CHD, and shares the same risk factors. These include diabetes mellitus, hypertension and left ventricular hypertrophy, hyperlipidaemia, dietary factors, excessive alcohol consumption, physical inactivity and smoking.[13] **4**

Asymptomatic individuals with multiple risk factors are at highest risk for primary SCD.[13] There is no RCT evidence that interventions in asymptomatic individuals prevent primary SCD. Clinical trials of lipid lowering and antihypertensive drugs in primary prevention of CHD have had insufficient statistical power to show reduction in SCD as a separate end point. A case-control study found that SCD was decreased in those whose leisure activity was gardening and/or walking for more than 60 minutes per week.[14] **4** **2+**

R **Efforts to prevent sudden cardiac death should include:**

- **risk factor intervention in those individuals who are at high risk for coronary heart disease**
- **health promotion measures and encouragement of moderate-intensity physical activity in the general population.**

See also SIGN guideline 149 on risk estimation and the prevention of cardiovascular disease.[15]

3.2 BYSTANDER CARDIOPULMONARY RESUSCITATION

Bystander cardiopulmonary resuscitation (CPR) is associated with increased survival in individuals who have out-of-hospital cardiac arrest. The likelihood of survival to hospital discharge approximately doubles when bystanders initiate CPR prior to the arrival of the emergency services.[16] Cardiopulmonary resuscitation training positively influences the willingness of laypeople to perform CPR.[17] **2+** **4**

R **The number of laypeople trained to initiate CPR in out-of-hospital cardiac arrest should be increased.**

Targeted training of laypeople selected by occupation, low training costs, or having high-risk household companions is substantially more cost effective than training unselected laypeople.[18]

R **Laypeople identified as having a high probability of witnessing a cardiac arrest should be offered CPR training.**

✓ All healthcare workers who have direct patient contact should have annual refresher training in cardiopulmonary resuscitation.

✓ CPR should be performed in accordance with the Resuscitation Council (UK) guidelines.

The delivery of CPR training programmes in schools is an effective way to promote widespread knowledge and retention of resuscitation skills.[19] **4**

R **CPR should be taught as part of the school curriculum.**

3.3 DEFIBRILLATION

Defibrillation is the definitive intervention in ventricular fibrillation (VF) or pulseless ventricular tachycardia (VT) and is the most important determinant of survival in cardiac arrest. Survival to hospital discharge is inversely related to the time interval between the onset of VF and the delivery of the first shock. A one minute delay in defibrillation is associated with a reduction in odds of survival of up to 21%.[20] However, in adult out-of-hospital cardiac arrest with ventricular fibrillation and response time greater than five minutes, a period of two minutes of CPR before attempting defibrillation may improve return of spontaneous circulation (ROSC) and survival to hospital discharge.[21] **2++ 4**

✓ Defibrillation should be administered in accordance with the Resuscitation Council (UK) guidelines.

R **Defibrillation in patients with VF or pulseless VT should be administered without delay for witnessed cardiac arrests and immediately following two minutes of CPR for unwitnessed out-of-hospital cardiac arrests.**

R **Prompt defibrillation should be available throughout all healthcare facilities.**

R **All healthcare workers trained in CPR should also be trained, equipped, authorised and encouraged to perform defibrillation.**

Defibrillators delivering biphasic waveforms require lower energy shocks to terminate VF than those delivering monophasic waveforms and result in less myocardial damage. Studies in patients do not show consistent differences between the type of waveform used during defibrillation and ROSC or survival to hospital discharge after cardiac arrest.[11] **4**

3.3.1 AUTOMATED EXTERNAL DEFIBRILLATORS

Automated external defibrillators (AEDs) are devices which guide first responders when assessing whether defibrillation is indicated to resuscitate a collapsed patient. Automated external defibrillators provide spoken instructions to the responder on when and how to deliver the defibrillation shock.

Use of AEDs by trained first responders dispatched by the emergency medical services has been shown to be clinically effective.[20-24] **1+ 2+ 4**

Use of AEDs by trained first responders is cost effective in urban areas where emergency medical service vehicle response times are minimised.[25,26]

R **Automated external defibrillators should be used by trained first responders, with their use integrated within the emergency medical services system.**

Use of AEDs in public areas (public access defibrillators) has been shown to be clinically effective in locations associated with a high probability of a cardiac arrest event.[11,21,27,28] **1+ 2+ 4**

R **Automated external defibrillators should be sited in locations which have a high probability of a cardiac arrest event.**

No evidence was identified on the clinical or cost effectiveness of AEDs in rural areas.

An RCT demonstrated that provision of a home AED did not improve survival following cardiac arrest when added to CPR training for relatives. The study was carried out in patients with previous myocardial infarction (MI) who did not require an implantable cardioverter defibrillator (ICD), based on left ventricular ejection fraction (LVEF) >35%, and in whom the SCD rate was <1% per year.[29] **1+**

3.4 ADJUNCTIVE THERAPIES IN THE PERI-ARREST PERIOD

3.4.1 REFRACTORY VT/VF

In patients with VT/VF, pressor agents are administered to increase coronary perfusion pressure and increase myocardial oxygen delivery. Despite the widespread use of adrenaline/epinephrine during resuscitation and several studies involving vasopressin, there is no placebo-controlled study that shows that the routine use of any vasopressor at any stage during cardiac arrest increases survival to hospital discharge.[30] **4**

In a meta-analysis, high-dose adrenaline/epinephrine (5–15 mg) produced higher ROSC but a trend towards lower survival to hospital discharge without neurological damage compared with standard dose (1 mg).[31] **1+**

Vasopressin acts on specific non-adrenergic receptors and theoretically may not produce the adverse increase in myocardial oxygen consumption seen with adrenaline/epinephrine. In a meta-analysis of the use of vasopressin in patients with cardiac arrest there was no advantage over adrenaline/epinephrine in terms of ROSC, survival to hospital admission or discharge from hospital.[32] **1+**

Amiodarone is effective in increasing ROSC and survival to hospital admission when given in patients with refractory VT/VF, but there is no evidence that it increases survival to discharge from hospital.[30] **4**

R **Intravenous adrenaline/epinephrine should be used for the management of patients with refractory VT/VF.**

R **Intravenous amiodarone should be considered for the management of patients with refractory VT/VF.**

✓ Adjuvant therapies should be administered in accordance with the Resuscitation Council (UK) guidelines.

3.4.2 ASYSTOLE AND PULSELESS ELECTRICAL ACTIVITY DURING CARDIAC ARREST

Asystole accounts for 20–40%, and pulseless electrical activity (PEA) for up to 10% of all cardiac arrests. Patients with cardiac arrests due to asystole or PEA occurring outside hospital have a poor outlook with a less than 4% survival to hospital discharge. Within hospital 10% of patients are resuscitated.[33] **2+**

Adrenaline/epinephrine is the pressor agent routinely used to increase coronary perfusion pressure in patients with cardiac arrest but there is no evidence that it improves survival. Its efficacy is impaired by the prevailing acidosis and hypoxia in cardiac arrest but there is no conclusive evidence that vasopressin is superior in the treatment of asystole or PEA.[11,32] **4** **1+**

R **Patients with cardiac arrest secondary to asystole or pulseless electrical activity should receive intravenous adrenaline/epinephrine.**

3.4.3 THERAPEUTIC HYPOTHERMIA

Targeted temperature management may reduce hypoxic brain injury in patients who suffer out-of-hospital cardiac arrest. Since the publication of two trials reporting reduced mortality and improved neurological outcomes in patients receiving mild therapeutic hypothermia in 2002, this intervention has been investigated more rigorously in larger cohorts. Studies can be divided broadly into those investigating prehospital and inhospital interventions. There has been considerable variation in the mode of delivery of temperature control and in the target temperatures intended and achieved, but most studies aim to lower body temperature to 32–35°C for a duration of 24 hours.

Fourteen systematic reviews or meta-analyses of mild therapeutic hypothermia were identified. Of these, two reviews were excluded due to the small number of studies included and because of possible publication bias; two were excluded due to inclusion of non-RCT evidence and one was excluded due to poor methodological quality. Due to the overlap in RCTs included in the remaining reviews, only two reviews were considered as evidence in this guideline: one meta-analysis of trials of prehospital cooling[34] and a Cochrane review of trials of inhospital and prehospital cooling.[35]

The meta-analysis included eight RCTs comparing cooling with no cooling in the prehospital setting. All studies had a high risk of bias and serious indirectness from variation in the populations recruited or timing of cooling in the patient pathway. Prehospital cooling had no significant effect on mortality at admission (relative risk (RR) 1.01, 95% confidence interval (CI) 0.98 to 1.04) or discharge (RR 1.05, 95% CI 0.92 to 1.19), and no effect on recovery of neurological function (RR 1.06, 95% CI 0.91 to 1.23). Prehospital therapeutic hypothermia was associated with a higher incidence of recurrent arrest compared with control groups (RR 1.23, 95% CI 1.02 to 1.48) but no difference in the rate of pulmonary oedema (RR 1.02, 95% CI 0.67 to 1.57).[34] **1+**

The Cochrane review incorporated five RCTs of inhospital therapeutic hypothermia in patients within six hours of cardiac arrest and a single RCT of prehospital therapeutic hypothermia. There was variation in the mean age (52–72 years), gender balance (19–39% female), setting and cardiac rhythms (asystole or pulseless electrical activity/VF/VF or non-perfusing VT) of the patients in each study. There was heterogeneity due to cooling methods used (haemofiltration in one study and different standard cooling methods in the remaining four trials) and in the control group used (no cooling versus targeted temperature control at 36°C).[35]

Although the pooled result comparing conventional cooling methods (surface cooling methods requiring cooling pads, ice packs, water immersion or intravascular cooling with cooling catheters or simply cold fluids) with no cooling showed a better neurological outcome for the conventional cooling group (RR 1.94, 95% CI 1.18 to 3.21) this finding was based on data from 437 patients in four small trials published between 2000 and 2002. The pooled result also indicated better survival to discharge among patients who received cooling (RR 1.35, 95% CI 1.10 to 1.65); this finding was based on data from 383 patients in three of these trials. These findings need to be interpreted cautiously because of the relatively short duration of cardiac arrest and heterogeneity of cooling methods used. **1++**

The largest single RCT of inhospital cooling, which was incorporated in the Cochrane review and included 939 patients, showed no effects on neurological outcome (RR 0.97, 95% CI 0.85 to 1.11) or survival (RR 0.97, 95% CI 0.86 to 1.10) for therapeutic hypothermia at 33°C compared with targeted temperature management at 36°C.[36] **1+**

It is important to state that there may be benefit from targeted temperature management in survivors of cardiac arrest but there is not conclusive evidence from the data examined that therapeutic hypothermia (typically target temperatures 32–35°C) confers survival benefit or neurological benefit when compared with physiological target temperature of 36°C in which a small degree of cooling, and avoidance of pyrexia, may confer benefit.

R **Therapeutic hypothermia should not routinely be administered to patients in the prehospital or inhospital setting after cardiac arrest.**

3.4.4 BRADYCARDIA/SINOATRIAL DYSFUNCTION/HEART BLOCK

Intravenous atropine improves heart rate and symptoms and signs in patients with symptomatic bradycardia in both the hospital and prehospital setting.[10,12] **4**

Second-line drugs for symptomatic bradycardia include adrenaline/epinephrine, dopamine, isoprenaline and aminophylline.[12] **4**

Glucagon is only likely to be useful in drug-induced bradycardias, for example beta-blocker and calcium-channel-blocker overdose.[10] **4**

The 2010 CoSTR consensus document includes recommendations for first-line treatment of symptomatic bradycardia with atropine and consideration of transcutaneous pacing when full-dose atropine fails, although the authors note that it may not be any more effective then second-line drug therapy.[12] The document reported an RCT comparing atropine, glycopyrrolate and transcutaneous pacing in 45 intraoperative patients which showed no significant differences in long-term outcomes. A further RCT compared dopamine with transcutaneous pacing in patients with bradycardia who had not responded to atropine. There was no difference in survival to discharge (70% *v* 69%). In 2014 the European Heart Rhythm Association, the Acute Cardiovascular Care Association and the European Association of Percutaneous Cardiovascular Interventions issued a joint position statement on cardiac arrhythmias in patients with ACS. This advised that "an external stimulator (transcutaneous) does not provide reliable ventricular stimulation and therefore should only be used, under strict haemodynamic and electrocardiographic monitoring, when no other option is available. As soon as possible, an alternative action should be undertaken (administration of chronotropic drugs or temporary or permanent pacing)."[37] 4

R **Atropine should be used in the treatment of patients with symptomatic bradycardia.**

R **When atropine is ineffective consider intravenous administration of further positively chronotropic agents before transvenous pacing is instituted.**

✓ Transcutaneous pacing should be followed as soon as possible by transvenous pacing unless the bradycardia has resolved.

3.4.5 POLYMORPHIC VT ASSOCIATED WITH QT PROLONGATION

Recurrent polymorphic VT (torsades de pointes) is usually associated with QT-interval prolongation, and can be secondary to hypokalaemia, hypomagnesaemia, bradycardia and combinations of drugs which prolong the QT interval.

Existing guidelines state that treatment is by withdrawal of QT-interval-prolonging drugs and administration of intravenous magnesium.[38] Sotalol is contraindicated in patients with torsades de pointes. Electrolyte abnormalities should also be corrected, in particular hypokalaemia. A number of guidelines have suggested repletion of potassium to a target concentration of 4–5 mmol/l,[39,40] however there is little evidence to support a concentration of >4.5 mmol/l, and a database study of 38,689 patients with acute MI showed the lowest risks of VF, cardiac arrest or death were when potassium concentrations were 3.5–4.5 mmol.[41] Once the arrhythmia has been corrected other treatment may be indicated to prevent relapse, such as overdrive suppression pacing.[10,12,42] 3 4

R **Patients with polymorphic VT should be treated with intravenous magnesium sulphate** (2 g over 10–15 minutes; 8 mmol, or 4 ml of 50% magnesium sulphate)**. QT-interval-prolonging drugs, if prescribed, should be withdrawn. If present, hypokalaemia should be corrected by potassium infusion.**

R **Overdrive suppression pacing should be considered to prevent relapse once the arrhythmia has been corrected.**

4 Arrhythmias associated with acute coronary syndrome

4.1 ATRIAL FIBRILLATION

In patients with ACS treated with thrombolytic therapy, new atrial fibrillation occurs in 7–10% of cases. The majority of these patients will be in sinus rhythm by the time of hospital discharge regardless of treatment strategy.[43]

In ACS, atrial fibrillation occurs more commonly in those who are older, have greater haemodynamic disturbance (eg higher Killip class) and have left ventricular (LV) dysfunction. Atrial fibrillation is an independent risk factor for mortality. Stroke rates are increased in patients with AF.[36]

Atrial fibrillation is covered in section 5.1.1. Recommendations on antithrombotic prophylaxis for atrial fibrillation are contained in the SIGN guideline on antithrombotic therapy.[6]

4.1.1 PROPHYLAXIS

Recurrence of AF is observed in around 20% of patients.[44] There is no evidence to support the use of prophylactic antiarrhythmic therapy in patients with ACS who have had AF but who have returned to sinus rhythm. Drugs which are used for their proven benefits on mortality, including beta blockers and angiotensin-converting enzyme (ACE) inhibitors, may also reduce the incidence of AF in patients with ACS.[45,46] **1+**

4.1.2 ANTIARRHYTHMIC DRUG THERAPY/CARDIOVERSION

There is limited evidence on the use of amiodarone in patients with AF following ACS, with one small randomised study which showed no difference in restoration of sinus rhythm compared to digoxin,[47] and observational studies which have shown no mortality benefit with amiodarone compared to no antiarrhythmic treatment.[43,48] **1+** **2+**

The safety and efficacy of class Ic drugs for the treatment of AF in ACS have not been studied in large-scale trials. Flecainide was associated with increased mortality in patients with frequent ventricular premature beats and LV dysfunction following ACS.[49] **1++**

Propafenone has not been studied in the context of ACS.

R **Class Ic antiarrhythmic drugs should not be used to treat AF in patients who have ACS.**

No good-quality studies on the effectiveness of synchronised direct current (DC) cardioversion in this patient population were identified.

Recommendations for treatment are based on existing guidelines and expert opinion.[50,51] These guidelines suggest that underlying causes and aggravating features should be corrected (eg heart failure, hypokalaemia and hypoxia). Further treatment measures then depend on the clinical condition of the patient with regard to haemodynamic instability (hypotension, heart failure) and ongoing ischaemia. **4**

R **Patients with AF and haemodynamic compromise should have urgent synchronised DC cardioversion or be considered for antiarrhythmic and rate-limiting therapy using:**

- **intravenous amiodarone**

or

- **digoxin, particularly in presence of severe LV systolic dysfunction with heart failure.**

R **Patients with AF with a rapid ventricular rate, without haemodynamic compromise but with continuing ischaemia should be treated with one of:**

- **intravenous beta blockade, in absence of contraindications**
- **intravenous verapamil where there are contraindications to beta blockade and there is no LV systolic dysfunction**
- **synchronised DC cardioversion.**

R **Patients with AF without haemodynamic compromise or ischaemia should be treated with rate-limiting therapy, preferably a beta blocker, and be considered for chemical cardioversion with amiodarone or DC cardioversion.**

✓ Where indicated, cardioversion should be performed under short-acting general anaesthesia or conscious sedation.

4.2 CONDUCTION DISTURBANCES AND BRADYCARDIA

No published randomised trials comparing different strategies of managing conduction disturbances after ACS were identified. All recommendations are based on previous consensus guidelines and expert opinion based on case series, including some prior to the routine use of reperfusion.[52]

Sinus bradycardia (<40 beats per minute (bpm)) occurs in around 28% of patients following ACS, either during or immediately after primary percutaneous coronary intervention (PCI).[37] Where sinus bradycardia is asymptomatic and haemodynamically well tolerated no action is required. Symptomatic bradycardia usually responds to atropine and the withdrawal of rate-slowing agents. High-grade AV block occurs in 5–10% of patients with ST-segment-elevation ACS, and at higher rates in patients with cardiogenic shock.[37] **4**

Temporary transvenous pacing is used for symptomatic or prognostically significant bradycardias. The requirement for temporary pacing is not in itself an indication for permanent pacing. Permanent pacemaker implantation can be deferred if the peri-infarction AV block is expected to resolve.[52] **4**

R **In patients with symptomatic bradycardia/conduction disturbance, concurrent therapies which predispose to bradycardia** (eg beta blockers, digoxin, verapamil) **should be discontinued.**

R **Isolated first-degree heart block does not require treatment. Mobitz type I second-degree heart block usually does not cause haemodynamic compromise and, as such, rarely requires treatment.**

R **Temporary transvenous pacing should be should be instituted in patients with high grade AV block without a stable escape rhythm who are unresponsive to positively chronotropic agents.**

R **Temporary transvenous pacing should be considered for patients with:**

- **sinus bradycardia** (heart rate <40 beats per minute) **associated with haemodynamic instability and unresponsive to atropine, other positively chronotropic agents** (unless contraindicated) **and withdrawal of any negatively chronotropic agents**
- **alternating left and right bundle branch block, new bifascicular or trifascicular block.**

R **Sequential AV pacing should be considered for patients with AV block, RV infarction and cardiogenic shock.**

R **Permanent pacing is indicated for patients with persistent** (>7 days post MI) **Mobitz type II second- or third-degree AV block.**

✓ All patients requiring a permanent pacemaker should be evaluated for an implantable cardioverter defibrillator and/or biventricular pacing.

✓ All patients with bundle branch block following MI should be evaluated for an implantable cardioverter defibrillator and/or cardiac resynchronisation therapy.

4.3 VENTRICULAR ARRHYTHMIAS

4.3.1 VENTRICULAR ARRHYTHMIAS AND ACS

Sustained ventricular arrhythmias, VT and/or VF, occur in up to 20% of patients with acute coronary syndrome. In hospitalised patients with ST-segment-elevation ACS, the most common sustained ventricular arrhythmia is primary VF, which occurs in 3–5% of patients within the first few hours following onset of infarction (75% of these within the first hour).[53,54]

Early (<48 hours) postinfarction primary VF is associated with increased inhospital mortality, but those who survive to hospital discharge have a similar outcome to patients without primary VF. Late VF (>48 hours) is less common (1–2%) and is associated with increased short- and long-term mortality.[55,56] Monomorphic VT (early or late) is associated with increased short-term mortality, to a lesser degree than VF, but is also associated with an increase in long-term mortality. Patients who have had both VT and VF have the worst short- and long-term mortality: in one study of patients with ST-segment-elevation acute coronary syndrome, 30 day mortality was 31% for patients with VF, 24% for patients with VT, 44% for patients with both and 6% for patients with neither.[57] The extent to which recurrent arrhythmia rather than heart failure or reinfarction contributes to the increased mortality in patients with VT and/or VF is not known. Secondary VF, in patients with heart failure or cardiogenic shock, is associated with high inhospital mortality (up to 50%).[58] **3**

No randomised studies of therapies to improve outcome after early VT/VF were identified.

The incidence of primary VF in ACS has not decreased in the last three decades, but there is evidence that modern medical management can reduce the subsequent mortality.[59] **3**

The indications for ICD implantation are discussed in section 5.2.2.

The incidence of VT/VF is less in patients with non-ST-segment-elevation ACS (about 2%; median time 78 hours) but is also associated with increased short- and long-term mortality.[57] **3**

R **Patients who have primary VF should be recognised as being at increased risk during their hospital stay, and therapy should be optimised.**

R **Patients who have VF or haemodynamically significant VT more than 48 hours after infarction should be considered for an implantable cardioverter defibrillator.**

The emergency treatment of sustained ventricular arrhythmias associated with ACS is discussed in sections 3.3 and 3.4.

4.3.2 PREVENTION OF VENTRICULAR ARRHYTHMIAS AND SUDDEN DEATH

Although there is a large volume of evidence about the benefits of drugs on survival following ACS, the primary outcome is usually total mortality, with sudden cardiac death as a secondary outcome or subanalysis.

The main evidence of benefit is for treatments which reduce total mortality, in part by reducing sudden death, in particular reperfusion, beta blockade, ACE inhibitors and statins.[3,45,50,60-62] Thrombolytic therapy may be associated with an early increased incidence of VF, but this is offset by the subsequent benefits of reperfusion, including reduction in sudden death.[13] Evidence from the PCI era shows a progressive reduction in sudden cardiac death rates following ACS.[63] A meta-analysis of early intravenous (IV) beta blockade combining evidence from the thrombolytic and PCI eras has demonstrated a reduction in ventricular arrhythmias, reinfarction and inhospital mortality.[64] The only RCT comparing IV beta blockade before reperfusion with oral administration after PCI suggested a reduction in infarct size and improvement in LVEF.[65] **1++**

Evidence and recommendations for the use of beta blockers in the initial management of patients with ACS are contained in section 4.6 of SIGN guideline 148.[3]

Antiarrhythmic drugs

Antiarrhythmic drugs (lidocaine, amiodarone) reduce arrhythmic death but with no, or minor, overall benefit on total mortality. Class Ic drugs have been shown to be associated with adverse outcomes following ACS.[50,66-68] **1++**

R **Routine use of antiarrhythmic drugs is not recommended following ACS.**

Omega-3 fatty acid supplements

The following text and recommendation is reproduced from SIGN 149: Risk estimation and the prevention of cardiovascular disease.[15]

There is no clear evidence that increased consumption of omega-3 fats, suggested as the protective element of oily fish consumption, reduces cardiovascular disease (CVD) when consumed as supplements. In a meta-analysis of RCTs examining the effects of omega-3 fatty acid for SCD prevention in patients with CVD, benefits were only observed in patients receiving suboptimal medical management. In patients treated according to guidelines, omega-3 fatty acids did not reduce the risk ratio of SCD (RR 0.96, 95% CI 0.84 to 1.10).[69] The impact of statins, aspirin, angiotensin converting enzyme (ACE) inhibitors and antiplatelet agents (reflecting current medical management) removed any benefit from the omega-3 fatty acid supplements. **1+**

In a meta-analysis of trials in adults with or at high risk of CVD, no clear effect from omega-3 fatty acids was reported on composite cardiovascular outcomes (RR 0.96, 95% CI 0.90 to 1.03), total mortality (RR 0.95, 95% CI 0.86 to 1.04), non-vascular mortality (RR 0.97, 95% CI 0.84 to 1.11), coronary events (RR 0.86, 95% CI, 0.67 to 1.11) or revascularisation (RR 0.95, 95% CI 0.89 to 1.00). There was also no evidence of benefit for cerebrovascular events (RR 1.03, 95% CI 0.92 to 1.16) or arrhythmia (RR 0.99, 95% CI 0.85 to 1.16). Omega-3 fatty acids did protect against vascular death (RR 0.86, 95% CI 0.75 to 0.99) but not sudden death (RR 1.00, 95% CI 0.75 to 1.33) which reflects the effects from omega-3 oils in those with CVD without current medical management. Adverse events were more common in those taking omega-3 fatty acids than placebo (RR 1.18, 95% CI 1.02 to 1.37), and were mainly gastrointestinal.[70] **1+**

Current dietary guidelines suggest consumption of two 140 g portions of fish per week, one of which should be an oily fish.[71] **4**

R **Omega-3 fatty acid supplements should not be offered for reduction of CVD risk.**

✓ As fish consumption may help to reduce intake of (saturated) fat from meat, and may have a role in reducing fatal CHD with low risk of adverse effects, individuals should be advised to follow Government dietary guidelines to consume two 140 g portions of fish per week, one of which should be an oily fish.

Aldosterone-receptor antagonists

Eplerenone, an aldosterone-receptor antagonist, showed a 21% relative risk reduction in sudden death and a 15% relative risk reduction in total mortality compared with placebo in a single study of patients with acute MI, LV dysfunction (LVEF ≤40%) and heart failure or diabetes mellitus. There was a small excess of serious hyperkalaemia (serum potassium >6.0 mmol/l) with eplerenone (5.5% *v* 3.9% with placebo).[72] **1+**

R **Patients who have suffered a recent myocardial infarction and have an LVEF ≤40% and either diabetes or clinical signs of heart failure should receive eplerenone unless contraindicated by the presence of renal impairment** (chronic kidney disease stage ≥4–5) **and/or elevated serum potassium concentration** (K^+ >5.0 mmol/l)**.**

4.3.3 ASSESSMENT OF RISK OF SUDDEN DEATH

Following ACS, sudden death is a continuing cause of mortality (7–10% at two years; up to 50% of total mortality), with the greatest risk being in the first 30 days (1.4% per month), declining during follow up (0.14% per month after two years).[13,50,52,73] The risk is associated with LV dysfunction, but sudden death can also occur in patients with preserved LV function following ACS. Left ventricular dysfunction is also a risk factor for non-sudden cardiac death.[67] **2-**

There have been many studies of variables that may identify patients at risk of sudden death following ACS. This risk may be related to the arrhythmia substrate (LV dysfunction; late potentials on signal-averaged electrocardiogram (ECG); inducibility at electrophysiology study; microvolt T-wave alternans), the occurrence of triggers (ventricular premature beats, non-sustained VT) and autonomic dysfunction (heart rate variability; baroreceptor sensitivity; heart rate turbulence). Such investigations have relatively low sensitivity (<50%), low positive predictive accuracy (<30%) but high negative predictive accuracy (>90%).[13,74] The predictive value can be improved by combining investigations but this is at the expense of sensitivity. Their predictive value has been reduced by the decrease in incidence of sudden death with modern management following ACS.[73,75,76] Many of these investigations are specialised and not widely available. **2+ 3**

There have only been a few studies in which these investigations have been used to guide therapy following ACS. The DINAMIT study of patients with reduced LV function and abnormal cardiac autonomic function following ACS (6–40 days) did not show benefit of ICD implantation.[77] Similarly, the Immediate Risk Stratification Improves Survival (IRIS) trial which included patients with reduced LV function and elevated heart rate and/or non-sustained VT did not show any benefit of ICD implantation early after ACS (5–31 days).[78] One study of early ICD implantation following ACS in patients with LVEF <40% and inducible VT suggested a low event rate in non-inducible patients but lack of randomisation meant that the effect of the strategy was not demonstrated.[79] **1+ 2+**

In the absence of proven benefit, the routine use of risk stratification tools beyond ejection fraction cannot be justified.

R **All patients with ST-elevation acute coronary syndrome should undergo assessment of LV function for risk stratification at least six weeks following the acute event.**

R **Non-invasive assessment of the risk of ventricular arrhythmias beyond LV function may be considered but is not routinely recommended.**

R **Invasive electrophysiological studies are not routinely recommended for patients after ACS.**

5 Arrhythmias associated with chronic coronary heart disease/left ventricular dysfunction

5.1 ATRIAL FIBRILLATION

5.1.1 INTRODUCTION

Atrial fibrillation is characterised by the absence of co-ordinated atrial electrical activity. This results in loss of co-ordinated atrial contraction and an irregular ventricular response mediated by atrioventricular nodal (AVN) conduction. For affected patients, this produces blood stasis in non-contractile atria and the subsequent risk of thromboembolic stroke and a variable symptom pattern of palpitation and breathlessness related to the irregular and often rapid ventricular rate.

Atrial fibrillation is a significant burden on health and is associated with a substantially increased risk of stroke and sudden death.[51,80] In 2015–2016, 96,367 individuals were included in the Quality and Outcomes Framework register (QOF) for atrial fibrillation in Scotland, which represents an estimated crude prevalence rate of 1.7%.[81] The prevalence of AF rises markedly with advancing age, and is around 6–8% in those aged 75–84 years.[82] The total burden of AF is set to rise as the population ages.

Although AF is a common complication of ischaemic heart disease, most of the studies of the management of AF have also encompassed patients with AF from other causes, including valvular heart disease and hypertension. The evidence base for treatment of patients with AF caused by ischaemic heart disease is complicated by the inclusion of patients with these other disease processes. In many cases subgroup analyses have identified that specific drugs may have different benefit/harm ratios depending on the presence of absence of structural heart disease. Evidence for treatment of AF due to any cause has been considered but, where possible, recommendations are derived from studies including populations or subgroups with CHD.

Factors associated with predisposition to atrial fibrillation include hypertension, left ventricular hypertrophy or dysfunction and heart failure. Several RCTs of beta-adrenoceptor antagonists or inhibitors of the renin-angiotensin-aldosterone system in patients with these conditions have reported reductions in the incidence of AF as a secondary end point, or in retrospective analysis.[45,83] Meta-analyses of the effects of ACE inhibitors or angiotensin receptor blockers have reported relative risk reductions of around 40% for the incidence of AF in patients with chronic heart failure, compared with a non-significant reduction of 27% in postinfarction studies.[83,84] Since treatment with beta-adrenoceptor antagonists and inhibitors of the renin-angiotensin-aldosterone system is already indicated for reduction in mortality in patients postinfarction or with chronic left ventricular dysfunction or heart failure, there is no need for a specific recommendation with respect to prevention of AF.[4]

Obesity and a sedentary lifestyle are important modifiable risk factors for atrial fibrillation. In one RCT, 150 overweight and obese patients with symptomatic atrial fibrillation were randomly assigned to an intensive weight management strategy (intervention group) or general lifestyle advice (control). The mean weight loss achieved in the intervention group was superior to that in the control group (14.3 kg *v* 3.6 kg, $p<0.01$), and this was associated with a reduction in atrial fibrillation symptom burden and severity, and also in beneficial cardiac remodelling.[85] **1+**

Non-randomised studies from the same investigators have reported that long-term sustained weight loss is associated with significant reduction of AF burden and maintenance of sinus rhythm.[86] In patients undergoing catheter ablation for atrial fibrillation, aggressive risk factor management improves the long-term success of AF ablation.[87] **3**

Recommendations on antithrombotic prophylaxis for atrial fibrillation are contained in SIGN guideline 129 on antithrombotic therapy.[6]

5.1.2 ANTIARRHYTHMIC DRUGS

Both amiodarone and sotalol are effective in preventing AF recurrence.[88-92] Evidence is limited by lack of specific reporting of coronary heart disease subgroups within trials. In a large (n=665) randomised, double-blinded trial, amiodarone and sotalol were superior to placebo in restoring sinus rhythm, and in preventing recurrence of AF. Amiodarone and sotalol were equally effective in restoring sinus rhythm, but amiodarone was superior to sotalol in preventing AF recurrence. A prespecified subgroup analysis of patients with ischaemic heart disease revealed no significant difference in efficacy between amiodarone and sotalol.[92] Amiodarone use may be associated with serious non-cardiac side effects including pneumonitis, thyroid disorders, liver dysfunction, photosensitivity and warfarin interaction.[93-95] These side effects are related to the dose and duration of exposure to the drug. Amiodarone has a long half-life and is associated with many drug interactions, including medicines frequently used in patients with CHD, such as atorvastatin, warfarin and digoxin (a complete listing can be found in the BNF).[8] Class Ic drugs (flecainide, propafenone) should not be used in patients with ischaemic heart disease.[49,51] Sotalol is contraindicated in patients with torsades de pointes *(see section 3.4.5)*.

1+
4

R **Amiodarone or sotalol treatment should be considered where prevention of atrial fibrillation recurrence is required on symptomatic grounds.**

✓
- Patients with arrhythmias successfully controlled on amiodarone should have the dose titrated down to the lowest effective level.
- Patients taking amiodarone should have thyroid and liver function measured at baseline and at six monthly intervals. A chest X-ray should be considered prior to initiating therapy.
- Patients with new or increasing cough or breathlessness during amiodarone therapy should be promptly referred for respiratory evaluation.
- Patients receiving amiodarone therapy should be provided with information on potential side effects.

Dronedarone is pharmacologically related to amiodarone, but does not contain iodine, and has a shorter half-life. A systematic review of eight RCTs involving patients with non-permanent AF (paroxysmal or persistent after cardioversion), reported that dronedarone increased the time to recurrence of AF compared with placebo (from 53 to 116 days), but with a high relapse rate (64%) in the first year.[96] This review included a single trial comparing its antiarrhythmic efficacy with that of amiodarone, but no direct comparison with other drugs was identified. A Cochrane Review of all antiarrhythmic drugs (AADs) for the maintenance of sinus rhythm following cardioversion from AF estimated the number needed to treat for one year, to avoid one recurrence of atrial fibrillation, was three with amiodarone, eight with sotalol, and nine with dronedarone.[97] Dronedarone does not cause the iodine-related organ toxicity that occurs with amiodarone, but is less effective and has been associated with increased mortality and heart failure across a wide spectrum of populations.[64] Adverse outcomes were found in patients with persistent AF or heart failure. Rarely, severe hepatotoxicity has been associated with dronedarone. Important drug interactions include dabigatran, digoxin and verapamil.

1++
1+

There is limited information about the use of dronedarone in patients with coronary artery disease as the percentage of such patients in the RCTs ranged from 20–30% in the studies of non-permanent AF (which showed benefit), to 41% in the study with permanent AF and 63% in the study of patients with heart failure (which both showed adverse outcomes).[98] The reported reduction in stroke and cardiovascular mortality with dronedarone in a study of patients with non-permanent AF was not confirmed by meta-analyses which include other studies.[64,97]

1++
1++
1-

A number of economic analyses were identified which suggested that dronedarone may be cost effective compared with other AADs or standard of care.[99-103] However, most of these studies are not generalisable to Scotland due to having been conducted outside of the UK, making assumptions on resource use which may not reflect Scottish practice, indexing costs to an earlier point in time (dating back to 2008) and discounting costs and benefits at different rates to UK practice. Furthermore, there is some uncertainty surrounding the clinical parameters used in some analyses, for example data relating to adverse events were based on assumptions, and general mortality is derived from the multinational ATHENA study involving patients at particularly high cardiovascular risk, which is likely to differ from standard Scottish mortality rates.

A NICE technology appraisal reports that dronedarone appears to be generally cost effective as a second-line treatment for people whose AF is not controlled by standard baseline therapy. It considered that a beneficial effect of dronedarone on all-cause mortality was not proven; however, it accepted that the risk of mortality with the other AADs was likely to be higher than with dronedarone.[104]

The SMC notes that dronedarone appears less effective than amiodarone in reducing atrial fibrillation recurrence but has the potential for improved tolerability compared to comparator medicines. The summary of product characteristics advises that "due to its safety profile, dronedarone should only be prescribed after alternative treatment options have been considered. Dronedarone should not be given to patients with left ventricular systolic dysfunction or to patients with current or previous episodes of heart failure" (www.medicines.org.uk/emc/product/497#INDICATIONS).

R **Dronedarone should be considered for prevention of atrial fibrillation recurrence in patients who are unable to tolerate, or who have failed to respond to amiodarone or sotalol and who do not have left ventricular systolic dysfunction or heart failure.**

✓
- Patients taking dronedarone should have liver function measured before treatment, after one week, after one month, then monthly for six months, at nine and 12 months and periodically thereafter.
- Patients taking dronedarone should have an ECG at least every six months to exclude permanent AF.
- Patients taking dronedarone should be evaluated for symptoms of heart failure, should be advised to report symptoms of heart failure and should be monitored for the development of left ventricular systolic dysfunction.

5.1.3 RATE VERSUS RHYTHM CONTROL

Management of atrial fibrillation may be by either rate control or rhythm control. Rate control is typically achieved using pharmacological therapies to limit AVN conduction and reduce ventricular rate, but in some patients AVN ablation and pacing may be required *(see section 5.1.5)*. Rhythm control can be achieved using a combination of AADs, DC cardioversion and left atrial catheter ablation. The evidence for catheter ablation for AF is considered in section 5.1.5. Evidence for the management of postoperative AF following cardiac surgery can be found in section 6.4.

In RCTs of patients with well-tolerated AF (predominantly persistent AF), rate control has been shown to be superior to pharmacological rhythm control in terms of morbidity and avoidance of hospitalisation. Where indicated, these studies included adjunctive non-pharmacological therapies (ie DC cardioversion supported by AADs in the rhythm control arm, and pacing with AV node ablation in the rate-control arm) but did not include left atrial catheter ablation for AF. There was no difference between the two strategies in the incidence of thromboembolism, incident heart failure, or mortality.[105-109] None of these studies specifically enrolled patients with CHD, and rates of CHD ranged from 23–44%. **1+** **1++**

The risks and benefits of rate versus rhythm control in patients with both AF and heart failure with a reduced ejection fraction have not been evaluated, and the conclusions from the above studies may not apply. Recommendations on heart failure management can be found in SIGN guideline 147.[4]

R **Rate control is the recommended strategy for management of patients with well-tolerated atrial fibrillation.**

✓ Patients with AF in combination with heart failure and a reduced ejection fraction should receive evidence-based therapy for heart failure and an individualised approach to AF management. In cases where AF is thought to be the primary cause of heart failure with a reduced ejection fraction, a rhythm-control strategy should be prioritised.

5.1.4 PHARMACOLOGICAL THERAPIES FOR RATE CONTROL

Although there have been few long-term studies, a systematic review of multiple small-scale trials over periods of up to four weeks demonstrated that beta blockers, calcium channel blockers (verapamil or diltiazem), digoxin and amiodarone are all capable of controlling ventricular rate in AF.[110] **1+**

There is no strong evidence to show superiority of any individual rate-control drug or class of drugs over another. The choice of agent usually depends on clinical factors including cardiac indications for specific drug groups, or contraindications.

In patients with persistent or permanent AF following a rate-control strategy, strict rate control (resting heart rate <80 bpm) was harder to achieve and not associated with clinical benefit when compared with a lenient strategy (resting heart rate <110 bpm).[111] Again, patients with CHD were not specifically enrolled and only 18% of this study population had CHD. Patients randomised to a lenient rate-control strategy took fewer tablets and had comparable quality of life (QoL).[112] The outcomes were similar in a prespecified subgroup of patients with heart failure, predominantly with preserved ejection fraction.[113]

Digoxin does not control rate effectively during exercise and should be used as first-line therapy only in people who are sedentary, or have overt heart failure.[110] **1+**

Commonly, a combination of drugs may be required to control ventricular rate in patients with atrial fibrillation.[111] Options include the addition of digoxin to either a beta blocker or a rate-limiting calcium channel blocker.[114,115] The combination of beta blocker plus verapamil can cause severe bradycardia or AV block and should be avoided.[116] **1+** **4**

R **In patients with permanent AF or persistent AF following a rate-control strategy and a resting heart rate >110 bpm, appropriate rate-control therapy should be instituted with an initial target of resting heart rate <110 bpm.**

R **Ventricular rate in AF should be controlled with beta blockers, rate-limiting calcium channel blockers** (verapamil or diltiazem)**, or digoxin and combination therapy may be required.**

R **Digoxin does not control rate effectively during exercise and should be used as first-line therapy only in people who are sedentary, or have overt heart failure.**

R **A combination of digoxin with either a beta blocker or diltiazem should be considered to control heart rate in patients with atrial fibrillation.**

✓ Patients with AF who remain severely symptomatic despite adequate rate control should be considered for rhythm control or for stricter rate control if their heart rate remains 80–110 bpm at rest.

✓ Thyrotoxicosis should be ruled out in patients with AF and a poorly-controlled ventricular rate.

5.1.5 NON-PHARMACOLOGICAL THERAPIES

Atrioventricular node ablation and permanent pacing

Atrioventricular node ablation and permanent pacing improve heart rate control, ejection fraction, symptomatic and functional status, and quality of life in patients with AF whose ventricular rate is uncontrolled on medical therapy.[117] Long-term right ventricular pacing may however be deleterious to left ventricular function.[118] Biventricular pacing may be preferable in patients with pre-existing left ventricular systolic dysfunction.[119]

2+
4
1+

✓ In patients with LV dysfunction being considered for pacing, any other indications for cardiac resynchronisation therapy with pacing (CRT-P) (ie presence of heart failure, QRS duration and morphology) and likely risks and benefits in the individual should be discussed prior to device implant.

Catheter ablation for atrial fibrillation

Since the observation that most episodes of paroxysmal AF are initiated by ectopic beats originating from one or more of the pulmonary veins,[120] considerable attention has focused on catheter ablation procedures, using either radiofrequency energy or cryotherapy, to isolate the pulmonary veins in order to prevent recurrences of atrial fibrillation.[121] The majority of the evidence for catheter ablation comes from studies which mandated electrical isolation of all the pulmonary veins, and the evidence for further ablation targets and further lesions is limited.[122]

Most studies report that catheter ablation can be successful in preventing recurrence of paroxysmal AF in 65–70% of patients at one year following the procedure (including a repeat procedure in approximately 30% compared with approximately 40–50% in those treated with AADs).[123-125] The risk of recurrent AF tends to be higher in patients with persistent AF and in patients with significant comorbidities. The patients studied are typically in the younger age groups of the overall population with AF and the majority have normal ejection fraction, minimal structural heart disease and no major comorbidities therefore the results may not be directly applicable to the wider population with CHD.

1++
1+

In general, RCTs comparing catheter ablation with AADs in patients with AF have been relatively small. A meta-analysis of 11 studies including 1,481 patients confirmed the reduction in recurrence of atrial tachyarrhythmia in patients treated with catheter ablation compared with AADs (28 *v* 65%; RR 0.40, 95% CI 0.31 to 0.52). This benefit was offset by an increase in major adverse events (RR 2.04, 95% CI 1.10 to 3.77, I^2=0%).[124] A second meta-analysis, which included many of the same studies (11 RCTs including 1,763 patients) also found that catheter ablation reduced AF recurrence (RR 0.47, 95% CI 0.38 to 0.58) and that it improved QoL (physical component summary: weighted mean difference (WMD), 2.23, 95% CI 0.24 to 4.21; mental component summary: WMD, 2.69, 95% CI 0.04 to 5.35). However, no statistically significant difference in all-cause mortality (RR 0.87, 95% CI 0.37 to 2.06) or stroke/transient ischaemic attack (RR 1.83, 95% CI 0.73 to 4.55) was seen.[125] No adequately-powered RCT assessing the impact of catheter ablation on mortality or stroke risk was identified.

1++
1+

Furthermore, the procedure itself carries a significant risk of complications, including cardiac tamponade, stroke, pulmonary vein stenosis, oesophageal injury (and, rarely, atrio-oesophageal fistula) and phrenic nerve injury.[123-125] Age is a risk factor for periprocedural complications. Ongoing and recently-completed studies may clarify whether or not catheter ablation might improve prognosis in selected patients with AF, but, at present, the aim is to reduce recurrences of AF and to improve symptoms.

1++
1+

The cost-effectiveness of ablation compared with AAD treatment alone is uncertain. A key cost-effectiveness driver is the assumption surrounding the maintenance of treatment benefit over time. Based on a lifetime horizon, catheter ablation may be cost effective (at a willingness to pay threshold of between £20,000 and £30,000), however, when the time horizon is truncated to less than five years, the incremental cost effectiveness ratio (ICER) increases above accepted UK thresholds. The analyses note that considerable uncertainty exists surrounding the maintenance of treatment benefit, specifically, long-term reduction in the risk of recurrent AF following ablation.[126,127]

A small number of studies has assessed whether catheter ablation is effective as first-line therapy for paroxysmal AF. A systematic review of three RCTs included a total of 491 patients, the majority of whom had paroxysmal AF, randomised to radiofrequency ablation or AAD treatment as first-line therapy for atrial fibrillation.[123-125] Those randomised to ablation experienced a significantly higher rate of freedom from recurrent AF (RR 0.63, 95% CI 0.44 to 0.92) along with more serious complications (one stroke-related death and seven cardiac tamponades in 238 patients randomised to ablation). As in many other AF studies, the patients were relatively young and the majority had no major comorbidity. Therefore, catheter ablation as a first-line approach might be considered in selected patients who are aware of the risks and benefits. **1++** **1+**

The role of catheter ablation for atrial fibrillation in patients with heart failure and reduced left ventricular ejection fraction has been evaluated in an RCT. The Catheter Ablation versus Standard Conventional Therapy in Patients with Left Ventricular Dysfunction and Atrial Fibrillation (CASTLE-AF) trial randomised 363 patients to either catheter ablation or medical therapy (rate or rhythm control). The median follow up was 37.8 months. The primary end point was a composite of death from any cause or hospitalisation for worsening heart failure. This primary end point occurred in 51 patients in the ablation group (28.5%) and 82 patients in the medical therapy group (44.6%; hazard ratio (HR) 0.62, 95% CI 0.43 to 0.87). There were fewer deaths in patients randomised to ablation therapy (24 *v* 46; HR 0.53, 95% CI 0.32 to 0.86). Subgroup analysis suggested that those with left ventricular ejection fractions in the range 25–35% were most likely to gain from ablation, compared with those with ejection fractions less than 25% (p value for interaction 0.01).[128] **1+**

R **Ablation and pacing should be considered for patients with AF who remain severely symptomatic or have LV dysfunction in association with poor rate control or intolerance to rate-control medication.**

R **Patients with highly symptomatic paroxysmal atrial fibrillation resistant to one or more antiarrhythmic drugs and little or no comorbidity should be referred to an arrhythmia specialist for consideration of ablation.**

R **Patients with symptomatic atrial fibrillation** (paroxysmal or persistent)**, symptomatic heart failure and left ventricular systolic dysfunction with a left ventricular ejection fraction of 25–35% should be referred to an arrhythmia specialist for consideration of ablation.**

R **Catheter ablation techniques for atrial fibrillation should focus on electrical isolation of the pulmonary veins.**

R **An early ablation strategy should be considered for highly symptomatic patients with little or no comorbidity.**

R **Any patient with highly symptomatic persistent atrial fibrillation should be referred to an arrhythmia specialist and ablation may be useful in selected cases.**

Catheter ablation for atrial flutter

Atrial flutter is an organised atrial tachycardia which is dependent on continuous conduction around an anatomical circuit within the atrium, producing an atrial rate of 250–350 bpm. Such circuits can be interrupted using lines of ablation lesions. The commonest form of atrial flutter utilises a circuit within the right atrium which includes the band of tissue between the inferior vena cava and the tricuspid valve (cavotricuspid isthmus-dependent flutter). When the electrical wave moves around the tricuspid annulus in an anticlockwise direction, this gives the appearance of 'typical' atrial flutter, which is characterised by a sharp sawtooth pattern in the inferior leads of the 12-lead ECG and short duration positively directed flutter waves in lead V1. A wave moving around the tricuspid annulus in a clockwise direction has a different ECG morphology, with undulating upright flutter waves in the inferior ECG leads. Both the typical (anticlockwise) and reverse (clockwise) types of atrial flutter are treatable by linear ablation lesions delivered between the tricuspid annulus and the inferior vena cava.

Other forms of atrial flutter also exist. Patients who have had right atrial surgery may be susceptible to a form of atrial flutter caused by re-entry around the surgical scar on the right atrium. Furthermore, some types of atrial flutter may be due to re-entry within the left atrium, and these tend to be commoner in patients who have had prior left atrial catheter ablation or left atrial surgery. The ECG patterns of these types of atrial flutter are variable, and in patients whose flutter morphology is not of the 'typical' form it might not be possible to determine from the 12-lead ECG whether it is right or left atrial in origin.

Catheter ablation as a treatment for the typical form of atrial flutter has been performed for over 20 years. However, a comprehensive Health Technology Assessment identified only two RCTs comparing the efficacy of catheter ablation and AAD therapy for atrial flutter, and few studies addressing the cost effectiveness of the procedure.[127] The first RCT of 61 patients with recurrent atrial flutter found a significant benefit favouring ablation over AADs in maintenance of sinus rhythm at 22 months (RR 2.2, 95% CI 1.33 to 3.63), with a very large effect favouring ablation with respect to freedom from atrial flutter (RR 14.03, 95% CI 3.67 to 53.71). A second RCT reported a more modest effect on freedom from atrial flutter favouring ablation in 104 older patients with a first episode of atrial flutter, randomised to ablation or cardioversion followed by amiodarone (RR 1.36, 95% CI 1.13 to 1.64). **1++**

Systematic reviews of non-randomised studies reporting on outcomes after flutter ablation have examined clinical effectiveness and safety. In a meta-analysis of 23 case series including 4,238 patients, freedom from atrial flutter at 12 months ranged from 85–92%, with a weighted mean of 88%.[127] In a further meta-analysis which included 1,323 patients acute procedural success was 91.7% (95% CI 88.4% to 94.9%) rising to 97.0% after a repeat procedure (95% CI 94.7% to 99.4%).[129] A meta-analysis of 158 studies comprising 10,719 patients reported a similar acute success rates (91.1%, 95% CI 89.5 to 92.4) which persisted over 14.3±0.4 months of follow up.[130] In contrast to AF ablation, complication rates for flutter ablation are relatively low with overall complication rates of 2–3% with AV block (0.5–1%), groin haematoma (1–2%) and pericardial effusion (0.5–1%) all reported.[127,129,130] **2++**

The available evidence supports the conclusion that catheter ablation of atrial flutter is safe and effective, which is reflected in expert opinion and guidelines.[51] **4**

Atrial flutter and atrial fibrillation are related rhythms with some shared risk factors, and a significant proportion of patients presenting with atrial flutter have a history of AF (42% of 7,328 patients) or will experience AF after ablation for atrial flutter (26.5% at 12–24 months, 95% CI 22.8 to 30.6%; 51.8% at >36 months, 95% CI 32.0 to 71.1).[130] The evidence suggests that thromboembolic risk in patients with atrial fibrillation and flutter is similar[131] and guidelines state that antithrombotic therapy should be prescribed as for AF.[51] **2- 4**

Since ablation of typical atrial flutter in the right atrium is a safe and highly effective procedure, it is often performed as a first-line intervention. However, if the atrial flutter is thought likely to be of left atrial origin, ablation would incur additional risks (similar to those of ablation for atrial fibrillation) and is likely to be more technically challenging. In such cases ablation might be considered as second-line treatment if the patient's symptoms are resistant to one or more antiarrhythmic drugs.

R **Patients who present with typical atrial flutter should be offered radiofrequency catheter ablation.**

✓ Patients presenting with atrial flutter are at high risk for AF in the medium term and decisions on antithrombotic therapy should take this into account.

✓ Atrial flutter with 1:1 conduction to the ventricles is a potentially life-threatening condition and patients should be discussed with an electrophysiologist for consideration of urgent inpatient catheter ablation.

5.2 VENTRICULAR ARRHYTHMIAS

5.2.1 REVASCULARISATION FOR SECONDARY PREVENTION OF VT/VF

Four small retrospective studies examined the effectiveness of revascularisation in improving survival and quality of life for patients with CHD who have had sustained VT or who have been resuscitated from VF.[132-135] Revascularisation (coronary artery bypass graft or percutaneous coronary intervention) reduced the subsequent development of ischaemic VT induced at electrophysiological study, sudden death and out-of-hospital collapse. **2+ 3**

R **Revascularisation should be considered in patients who have had sustained VT or VF.**

✓ Patients with previous sustained VT/VF should undergo assessment for inducible ischaemia by stress testing or myocardial perfusion imaging followed, if appropriate, by coronary arteriography and revascularisation. These patients should all be considered for implantable cardioverter defibrillator therapy.

5.2.2 IMPLANTABLE CARDIOVERTER DEFIBRILLATOR THERAPY IN PATIENTS AT RISK OF LIFE-THREATENING ARRHYTHMIAS (PRIMARY PREVENTION)

The following text, table and recommendations are reproduced from SIGN 147: Management of chronic heart failure.[4]

Heart failure with reduced ejection fraction (HF-REF) is a significant predictor of sudden cardiac death and prolonged QRS duration and the presence of left bundle branch block (LBBB) further increases this risk. There is evidence showing the benefits of treatment with an ICD, CRT-P or cardiac resynchronisation therapy with an implantable cardioverter defibrillator (CRT-D) compared with medical therapy. In patients with HF-REF and with prolonged QRS and LBBB, cardiac resynchronisation therapy, in addition to optimal medical therapy, improved exercise capacity and quality of life and reduced New York Heart Association (NYHA) class and hospitalisations for worsening heart failure,[136,137] and significantly reduced mortality in patients with reduced ejection fraction (HR 0.64, CI 0.48 to 0.85).[138] Most of the evidence for CRT applies to patients with HF who are in sinus rhythm. **1++ 1+**

An MTA considered the benefit of ICD and CRT in three populations of patients with heart failure at risk of sudden cardiac death from ventricular arrhythmia (13 trials comparing ICD and medical therapy, of which nine were primary-prevention and four were secondary-prevention trials); with HF-REF and cardiac dys-synchrony (four trials comparing CRT-P and medical therapy); and with HF-REF and cardiac dys-synchrony also at risk of sudden cardiac death from ventricular arrhythmia (nine trials comparing CRT-D versus ICDs).[139] Individual data from approximately 12,500 patients (covering 95% of enrolled patients from the identified studies) were utilised to inform the economic modelling. **1++**

Twenty subgroups of patients covering all combinations of NYHA class, QRS duration and presence of LBBB were examined. Incremental cost-effectiveness ratios for the devices were taken into consideration along with modifying factors such as the severity of the condition and the risk of harm. It was concluded that, based on current standard practice in the UK, severity of symptoms (NYHA class), duration of QRS by ECG and the presence or absence of LBBB are important clinical characteristics for identifying patients who are likely to benefit from CRT devices.[139] A meta-analysis demonstrated that the clinical benefit of CRT in patients with QRS durations between 120 and 140 milliseconds was smaller than those with a longer QRS duration, and it could have a potentially harmful effect in patients with a QRS duration of less than 126 milliseconds. In the absence of robust data for this particular patient group (QRS of 120–149 milliseconds) and the risk of harm, a more cautious approach to the use of CRT was suggested for these patients.[139] **1++**

Shocks from the devices are associated with poor psychological outcomes, although the reassurance patients experience from having the device may outweigh the anxiety over shocks. Implantation is also associated with adverse events and equipment malfunction. Improvements in the technology and implanter skills and experience may result in a decline in these adverse outcomes.[139] **1++**

Assessment of the cost effectiveness of either CRT-P or CRT-D in addition to optimal pharmacological therapy found the therapy to be considered cost effective with a £30,000 threshold.[139]

Treatment options with an ICD or CRT are shown in Table 1.

Table 1: Treatment options with an ICD or CRT for people with heart failure with an ejection fraction of 35% or less (according to NYHA class, QRS duration and presence of LBBB) (from NICE Technology Appraisal: Implantable cardioverter defibrillators and cardiac resynchronisation therapy for arrhythmias and heart failure).[139]

	NYHA class			
QRS interval (ms)	I	II	III	IV
<120	ICD if there is a high risk of sudden cardiac death			ICD and CRT not clinically indicated
120–149 (without LBBB)	ICD	ICD	ICD	CRT-P
120–149 (with LBBB)	ICD	CRT-D	CRT-P or CRT-D	CRT-P
≥150 (with or without LBBB)	CRT-D	CRT-D	CRT-P or CRT-D	CRT-P
ICD = implantable cardioverter defibrillator; CRT-D = cardiac resynchronisation therapy with an implantable cardioverter defibrillator; CRT-P = cardiac resynchronisation therapy with pacing				

R **Implantable cardioverter defibrillators, cardiac resynchronisation therapy with defibrillator or cardiac resynchronisation therapy with pacing are recommended as treatment options for patients with heart failure with reduced ejection fraction, LVEF ≤35%, as specified in Table 1.**

✓ Patients receiving cardiac resynchronisation therapy and/or an implantable cardioverter defibrillator should be offered pre- and postplacement counselling, including discussion of potential shocks from the device, and device deactivation.

5.2.3 IMPLANTABLE CARDIOVERTER DEFIBRILLATOR THERAPY IN PATIENTS SURVIVING LIFE-THREATENING ARRHYTHMIAS (SECONDARY PREVENTION)

Patients surviving VF or sustained symptomatic VT due to previous MI have improved survival following ICD implantation compared with amiodarone therapy.[140] In a meta-analysis of the key trials the majority of patients were in NYHA classes I–III.[140] Patients with LVEF ≤35% derived significantly more benefit from ICD therapy than those with better preserved left ventricular function. Patients with severe heart failure (eg NYHA class IV, with symptoms at rest) have been excluded from studies of ICDs, as such patients generally have poor prognosis due to progressive heart failure. **1+**

Table 2 summarises the entry criteria and results of the key trials.[141-143]

R **Patients surviving the following ventricular arrhythmias in the absence of acute ischaemia or treatable cause should be considered for ICD implantation:**

- **cardiac arrest** (VT or VF)
- **VT with syncope or haemodynamic compromise**
- **VT without syncope if LVEF ≤35%** (not NYHA IV)**.**

Table 2: Entry criteria and results of trials examining ICD effectiveness in secondary prevention of life-threatening arrhythmias

Trial entry criteria	AVID[141]	CIDS[142]	CASH[143*]
Resuscitated cardiac arrest (VT/VF)	Yes	Yes	Yes
VT with syncope	Yes	Yes	-
VT with presyncope or angina + LVEF ≤35%	-	Yes	-
VT with presyncope/angina or heart failure + LVEF ≤40%	Yes	-	-
Unmonitored syncope w/inducible VT	-	Yes	-
Results			
Mean follow up (months)	18	36	57
Control group mortality (%)	24	30	44
ICD group mortality (%)	16	25	36
RRR% (95% CI)	38 (19 to 53)	20 (-8 to 40)‡	17 (-33 to 48)‡
ARR (%)	8	5	8

* Comparison with amiodarone only
‡ Not statistically significant
RRR relative risk reduction
ARR absolute risk reduction

5.2.4 REDUCING INAPPROPRIATE SHOCKS ASSOCIATED WITH IMPLANTABLE CARDIOVERTER DEFIBRILLATOR THERAPY

Implantable cardioverter defibrillators can be programmed to deliver several types of treatment for different ventricular arrhythmias at different heart rates, and the programming can be customised for individual patients and altered during follow up if new arrhythmias develop. For example, if a patient receives a secondary-prevention ICD for symptomatic sustained ventricular tachycardia at a rate of 180 bpm, their ICD might be programmed to have a 'VT Zone' for detecting and treating arrhythmias at rates of 170–200 bpm. The detection time can be varied, because some patients might be prone to non-sustained arrhythmias which would terminate spontaneously within a few seconds. If the VT is sustained, it might initially be treated with one or more attempts at antitachycardia pacing (ATP), and in the majority of cases the ATP would be expected to terminate the VT painlessly. However, if ATP is unsuccessful, or if the arrhythmia accelerates, the patient would then receive one or more cardioversion shocks. The same patient's device would be programmed to also detect arrhythmias at a rate of over 200 bpm in the 'VF Zone', and any arrhythmia recognised at that rate would be treated as ventricular fibrillation, and the patient would receive one or more defibrillation shocks.

When functioning appropriately, ICDs deliver therapies which can prevent sudden cardiac death in patients with haemodynamically significant ventricular arrhythmias *(see sections 5.2.2 and 5.2.3)*. However, ICDs can also deliver therapies inappropriately for rhythms other than VT or VF, and unnecessarily for rhythms which will resolve without further intervention, leading to reduced quality of life for patients.[144-146] Traditionally, primary-prevention ICDs were set up similarly to secondary-prevention ICDs, with both a VT zone and VF zone programmed. Recent studies have investigated whether the programming of either a single VF-only therapy zone (>200 bpm) or a longer arrhythmia detection time can reduce inappropriate shock therapies without impacting on the time to restore normal rhythms.

A systematic review of three RCTs and one prospective, controlled, non-randomised study included 4,896 patients with either CHD or non-ischaemic dilated cardiomyopathy assigned to ICD therapy with longer or shorter arrhythmia detection times. There were variations in the ICD parameters used across studies, reflecting the use of different devices, but, in all cases, time to arrhythmia detection was longer in the long detection group than the control group. In the long detection group there were significant reductions in mortality (RR 0.77, 95% CI 0.62 to 0.96), and inappropriate shocks (RR 0.50, 95% CI 0.39 to 0.65), without significant increase in syncope (RR 1.23, 95% CI 0.84 to 1.79).[147] 1+

The Multicenter Automatic Defibrillator Implantation Trial-Reduce Inappropriate Therapy (MADIT-RIT) study (included in the systematic review described above) randomised 1,500 patients with a primary-prevention indication to one of three ICD programming configurations. The groups received either high-rate therapy (with a 2.5-second delay before the initiation of therapy at a heart rate of ≥200 bpm) or delayed therapy (with a 60-second delay at 170–199 bpm, a 12-second delay at 200–249 bpm, and a 2.5-second delay at ≥250 bpm) or conventional therapy (with a 2.5-second delay at 170–199 bpm and a 1.0-second delay at ≥200 bpm). The trial reported that high-rate and delayed therapy were associated with reductions in inappropriate therapy when compared with conventional programming (6% *v* 29% at 2.5 years). Mortality was significantly lower for high-rate therapy than conventional programming (HR 0.45, 95% CI 0.24 to 0.85) and not significantly different between delayed therapy and conventional therapy (HR 0.56, 95% CI 0.30 to 1.02). No increase in syncope or adverse events associated with delayed or high-rate therapy were identified in any of the studies.[148] 1+

R **Patients with a primary-prevention ICD should have a single therapy zone programmed at a detection rate of 200 bpm.**

✓ Consider extending detection intervals in patients with secondary-prevention ICDs.

5.2.5 ANTIARRHYTHMIC DRUG THERAPY

Class I antiarrhythmic drugs

Class I AADs used for treatment of premature ventricular beats or non-sustained VT in patients with previous MI show a strong trend towards increased risk of death.[13,149] 1++

R **Class I antiarrhythmic drugs should not be used for treatment of premature ventricular beats or non-sustained VT in patients with previous MI.**

Beta blockers

Routine use of beta blockers in patients following ACS reduces the risk of sudden death and all-cause mortality.[13] 1++

R **Long-term beta blockers are recommended for routine use in patients following ACS without contraindications.**

Amiodarone and sotalol

Amiodarone therapy in patients following ACS with impaired left ventricular function or frequent ventricular premature beats reduces the risk of sudden death, but does not significantly reduce all-cause mortality.[150,151] 1++

Amiodarone therapy in patients with LV dysfunction or heart failure without sustained ventricular arrhythmias reduces the risk of sudden death but does not significantly reduce all-cause mortality.[152,153] 1++

Sotalol therapy in unselected patients following ACS did not significantly reduce mortality.[154] 1+

R **Amiodarone therapy is not recommended for patients following ACS or patients with congestive heart failure who do not have sustained ventricular arrhythmias or atrial fibrillation.**

R **Sotalol therapy is not recommended for patients following ACS who do not have sustained ventricular arrhythmias or atrial fibrillation.**

In patients who have recovered from an episode of sustained VT (with or without cardiac arrest), amiodarone or sotalol therapy is more effective than electrophysiologically-guided class 1 antiarrhythmic therapy in preventing recurrent arrhythmic events and cardiac death.[13]

R **In patients who have recovered from an episode of sustained ventricular tachycardia** (with or without cardiac arrest) **who are not candidates for an ICD, amiodarone or sotalol should be considered.**

Calcium channel blockers

Calcium channel blocker therapy in post-MI patients does not reduce all-cause mortality.[13] **1++**

R **Calcium channel blocker therapy is not recommended for reduction in sudden death or all-cause mortality in patients following ACS.**

5.2.6 SUSTAINED MONOMORPHIC VT

For patients with sustained VT who are haemodynamically unstable, electrical cardioversion is the immediate treatment of choice.[155] **4**

No evidence has been found comparing the efficacy of electrical cardioversion versus AADs in patients with sustained VT.

One small RCT recruited 74 participants with wide QRS complex monomorphic tachycardias, of whom data could be analysed in 62. Intravenous procainamide was more effective than IV amiodarone in terminating wide complex tachycardia (22 of 33 participants, (67%) *v* 11 of 29 participants (38%), respectively; p=0.026). Intravenous procainamide was associated with fewer major cardiac adverse events (9% *v* 41%, odds ratio (OR) 0.1, 95% CI 0.03 to 0.6), the main one being severe hypotension, and total adverse events (24% *v* 48%, OR 0.34, 95% CI 0.12 to 1.00) in the acute study period (40 minutes from infusion initiation).[156] There were a number of uncertainties in the sample size calculation for this trial as the anticipated adverse event rates were 20% and 5% in the procainamide and amiodarone groups, respectively, requiring a sample of 302 patients to detect a difference of 15% in major adverse events between groups. After six years, only 74 patients had been recruited with a decline in inclusion rates noted over time. At this point, recruitment was stopped and consequently the study is underpowered. **1+**

The 2010 CoSTR guidance on advanced life support identified a small number of studies on the pharmacological management of wide complex tachycardias.[12] No studies were placebo controlled and all were of poor quality. In one small unblinded trial IV procainamide was more effective than IV lidocaine for termination of hemodynamically stable VT (12/15 *v* 3/14, p<0.01). When combining all VT occurrences, lidocaine was successful in 19% (6/31) and procainamide in 79% (38/48, p<0.001) of participants. The results are hampered by the lack of a true control group. Patients with severe congestive heart failure or acute myocardial infarction were excluded.

A double-blinded RCT reported that IV sotalol was more effective for termination of haemodynamically stable sustained VT as first-line drug compared with IV lidocaine (11/16 (69%) *v* 3/17 (18%)). Patients with acute MI were included and approximately half of the participants had LVEF <30%. Those with persistent VT 15 minutes after onset of administration of the first drug were crossed over to the other drug. Ventricular tachycardia was terminated in seven of the 14 patients who crossed from lidocaine to sotalol and in one of four who crossed from sotalol to lidocaine (p=0.04). None of the responders to sotalol (as first or second drug) experienced VT recurrence in the next 24 hours. In four patients VT terminated spontaneously within 25 minutes after the overall 30 minute study period. The second drug was sotalol in all these patients. **4**

Three case series (including 93 cases of sustained hemodynamically stable VT) reported outcomes associated with the use of amiodarone in a population mainly consisting of patients with coronary artery disease (66–85%) and with a mean LVEF of 31–34%. In the two studies which examined reversion rates at 20 minutes from the start of IV infusion, success rate was 20% (15/74 patients). In the two studies using the same loading dose

of 300 mg, the reversion rate at 60 minutes was 33% (20/60). The overall reported success rate in termination of VT for amiodarone was 31% (29/93). An additive effect of prior administration of multiple AADs cannot be excluded since amiodarone was not used as the first-line drug. Hypotension occurred in 14% (10/74) of participants, requiring electrical cardioversion due to haemodynamic deterioration in all but one case. **4**

Bearing in mind the limitations of retrospective case series with no controls or direct drug-to-drug comparison, altogether these three case series suggest that amiodarone may be less effective than procainamide or sotalol. However, procainamide may be pro-arrhythmic and should be used with caution in the setting of baseline QT prolongation.

Intravenous procainamide and sotalol are no longer available as licenced products in the UK.

Nifekalant has been developed in Japan and is in use there only. The studies on the use of this drug are promising but side effects such as QT prolongation and polymorphic VT have been reported.[12]

No studies have been sufficiently powered to provide mortality data or compare benefits and harms of AADs in a systematic manner, therefore recommendations are based on consensus guidelines.

R **Intravenous amiodarone should be considered in the management of patients with haemodynamically stable sustained monomorphic VT.**

✓ Intravenous drug therapy for ventricular tachycardia should ideally be given under expert guidance.

✓ If a first IV drug fails to restore sinus rhythm, electrical cardioversion or antitachycardia pacing should be considered.

5.2.7 CATHETER ABLATION FOR RECURRENT VENTRICULAR ARRHYTHMIA/ ELECTRICAL STORM

Ventricular arrhythmia (VA) storm is characterised by

- recurrent VA in a short time (≥3 separate episodes in 24 hours, each requiring termination by intervention)
- frequent defibrillator therapies (≥3 separate episodes separated by five minutes in 24 hours), or
- incessant VA (continuous VA recurring promptly despite intervention for termination over 12 hours).

There is a paucity of evidence to support catheter ablation for patients with VA and chronic CHD who suffer recurrent ventricular arrhythmias. Most published studies are case series or case reports and lack the methodological rigour of RCTs or larger observational studies.

In the largest systematic review of 38 case series, involving 447 patients undergoing invasive management, any inducible VA was successfully ablated in 72% of cases (95% CI 71% to 89%) and clinical VA was ablated in 91% of cases (95% CI 90% to 97%). The intervention was catheter ablation in 88% of participants. Procedure-related complications were low, with 10 (2%) patients having significant complications including three deaths, three strokes, three heart blocks and one cardiac tamponade. Importantly, 94% patients were free from VA storm on follow up, and arrhythmic sudden deaths were rare (4%). No data were reported on clinical outcomes.[157] **3**

R **Catheter ablation should be considered in patients with electrical storm, where maximal medical therapy and appropriate ICD reprogramming have failed to control the arrhythmia.**

6 Arrhythmias associated with coronary artery bypass graft surgery

6.1 INTRODUCTION

Atrial fibrillation is a common complication of coronary artery bypass graft (CABG) surgery, occurring in 17–53% patients.[158-166] In over 90% of patients, the condition is self limiting within four to six weeks of surgery.[167,168]

Although ventricular ectopics and runs of VT are frequent following CABG surgery, occurring in up to 36% of patients,[165] the incidence of VF or sustained VT is lower, ranging from 0.95%[169] to 3.1%,[170] although rates as high as 8.5% have been reported.[171]

Cardiac arrest as a result of VF/pulseless VT in the postoperative period has high inhospital mortality.[170,172] VT/VF often occurs in the early postoperative period when the patient is intensively monitored in a critical care area but may also occur more than a week postoperatively when the patient is not monitored.[165,170,172] Non-sustained VT following CABG surgery is a less specific marker of future ventricular arrhythmias than in the non-surgical setting.[169] The long-term prognosis of survivors of VF/VT arrest is similar to those who did not experience VF/ VT.[170,172]

A retrospective cohort of 14,720 patients undergoing cardiac surgery in the US reported postoperative ventricular arrhythmias in 1.7% of patients. Individuals with postoperative ventricular arrhythmias were older (63.5 *v* 61.6 years), had lower LVEF (43.7% *v* 51.3%), and had greater comorbidities.[173]

6.2 RISK FACTORS

Two systematic reviews with important methodological limitations, previous guidelines and two epidemiological studies identify age (a 20% increase in incidence for every 10 years over the age of 65) and previous AF as risk factors strongly associated with development of AF postoperatively.[51,174-176] **1⁻ 4**

Other preoperative factors have been indirectly associated with postoperative development of AF in trials of prophylactic interventions. These include male sex,[175] obesity,[177] hypertension,[178] chronic obstructive pulmonary disease (COPD),[179] digoxin use, peripheral arterial disease, valvular heart disease, left atrial enlargement, previous cardiac surgery, pericarditis, elevated postoperative adrenergic tone, concurrent valve surgery, atrial enlargement, poor LV function,[174] P wave dispersion and withdrawal of ACE inhibitors and beta blockers.[176] **3 1⁻ 4**

The major preoperative risk factor for postoperative VT and VF is low LVEF.[165] **2⁺**

R **In patients undergoing coronary artery bypass graft surgery, age, previous AF and left ventricular ejection fraction should be considered when assessing risk of postoperative arrhythmia.**

6.3 PROPHYLACTIC INTERVENTIONS

Although prophylaxis is effective in reducing the incidence of AF, the evidence is conflicting as to whether it decreases the incidence of stroke or mortality or shortens hospital stay.[162,164,166,180]

Even when such effects have been demonstrated, variation in study methodologies, including lack of definition of AF, adverse events not being primary outcomes, variation in definitions of end points, prolonged time period of studies during which beta blockers were widely introduced, and details of randomisation, concealment and attrition not being included limits the interpretation of these findings.[181,182]

Pharmacological treatment of AF is often quickly effective in restoring sinus rhythm or controlling heart rate.[51] Prophylaxis also reduces the incidence of ventricular arrhythmias but it does not reduce associated mortality.[164,181]

6.3.1 PHARMACOLOGICAL THERAPIES

Amiodarone/beta blockers

Amiodarone or beta blockers, including sotalol, reduce the incidence of AF following CABG surgery by a similar magnitude.[180-183] The potential relative risk reduction in incidence of AF with amiodarone is 46% and with beta blockers is 35%.[180] **1++**

R **Amiodarone may be used when prophylaxis for atrial fibrillation and ventricular arrhythmias is indicated following CABG surgery.**

R **Beta blockers including sotalol may be used when prophylaxis for atrial fibrillation is indicated following CABG surgery.**

✓ Preoperative beta blocker therapy should be reintroduced as soon as safe to do so after surgery.

Calcium channel blockers

Rate-limiting calcium channel blockers, for example verapamil and diltiazem, are effective in reducing the incidence of AF following surgery but dihydropyridines are ineffective.[184] **1++**

R **Verapamil and diltiazem may be used for prophylaxis of atrial fibrillation following CABG surgery.**

Digoxin

Digoxin does not reduce the incidence of AF following CABG surgery.[185] **1+**

R **Digoxin should not be used for prophylaxis of atrial fibrillation following CABG surgery.**

Glucose-insulin-potassium

One good-quality RCT[186] and one retrospective analysis[187] suggest that glucose-insulin-potassium regimens do not reduce the incidence of AF following cardiac surgery. An RCT with limitations around concealment of interventions showed some benefit.[188] **1++** **2-** **1-**

R **Glucose-insulin-potassium regimens should not be used for prophylaxis of atrial fibrillation following CABG surgery.**

n-3-polyunsaturated fatty acids

In one RCT, n-3-polyunsaturated fatty acids (PUFAs) (2 g/day) administered for five days preoperatively and postoperatively until the day of hospital discharge reduced the incidence of postoperative AF following elective CABG and reduced hospital stay.[167] This single study (n=160) provides insufficient evidence on which to base a recommendation. **1+**

6.3.2 MANIPULATION OF BLOOD ELECTROLYTES

Magnesium is effective in reducing the incidence of AF and ventricular arrhythmias after cardiac surgery.[158,162,164] Magnesium confers no additional reduction in AF when co-administered with sotalol.[189] **1++** **1+**

R **Magnesium may be used when prophylaxis for atrial fibrillation and ventricular arrhythmias is indicated following CABG surgery.**

One study has associated hypokalaemia or hypocalcaemia with the occurrence of VT following CABG surgery.[171] **2++**

No studies were identified that investigated whether correction of hypokalaemia or hypocalcaemia reduced the incidence of VT. However, correction of these deficits is accepted clinical practice.

✓ Blood levels of potassium and calcium should be measured frequently following CABG surgery and corrected if necessary.

6.3.3 ANAESTHESIA AND ANALGESIA

Whilst spinal anaesthesia does not reduce the incidence of AF, epidural analgesia results in a 48% reduction in the incidence of AF and tachycardia after CABG surgery.[190] Amiodarone is more effective than epidural analgesia and their combination confers no additional benefit.[191] **1+**

The choice of general anaesthetic agent (propofol, midazolam, sevoflurane, desflurane) does not influence the incidence of AF.[192] **1+**

There were conflicting results in two studies of the effects of non-steroidal anti-inflammatory drugs (NSAIDs). Ketorolac reduced the incidence of AF by 65% (relative risk reduction) compared with a control group whilst naproxen did not influence the incidence of AF.[193,194] **1+** **1++**

R **The choice of anaesthetic agent or technique and analgesia should be based on factors other than atrial fibrillation prophylaxis.**

6.3.4 SURGICAL TECHNIQUES

Off-pump surgery

Off-pump (without cardiopulmonary bypass) CABG surgery is associated with a reduction in the incidence of AF in elderly patients when compared with the use of cardiopulmonary bypass. The risks and benefits of off-pump CABG surgery remain controversial and the long-term outcomes remain unknown.[159,160,195,196] **2++** **1++** **1+**

R **The choice of whether or not to use cardiopulmonary bypass should be based on factors other than atrial fibrillation prophylaxis.**

Atrial pacing

Atrial pacing is associated with a 43% reduction in the incidence of AF following CABG surgery. Although use of pacing avoids the potential side effects of pharmacological measures it carries an extremely small risk of tamponade and death. There are potential infection problems if wires cannot be completely removed.[180,197] **1++**

R **Atrial pacing may be used for prophylaxis of AF in patients who have atrial pacing wires placed for other indications.**

Fat pad preservation

In one randomised study the preservation of the anterior epicardial fat pad between aorta and pulmonary artery when cross clamping during CABG reduced the incidence of postoperative AF when compared with fat pad dissection.[198] This small study (n=55) does not provide sufficient evidence on which to base a recommendation. **1+**

Bonded cardiopulmonary bypass circuits

A number of studies suggest that the use of heparin bonded circuits improves clinical outcomes in patients undergoing CABG.[199-202] Reduction in AF incidence is rarely a primary outcome and monitoring for AF is limited to 48 hours in some studies. It is unclear whether bonded cardiopulmonary bypass circuits are associated with a reduction in AF. **1+** **4**

R **Bonded cardiopulmonary bypass circuits should not be used on the basis of AF prophylaxis alone.**

Hypothermia

In a randomised study patients underwent mild (34° C) or moderate (28° C) hypothermic cardiopulmonary bypass. AF rates in each group were determined retrospectively by review of hospital records. There was a significantly higher incidence of AF in the moderate compared with the mild hypothermic group.[203] **1⁻**

6.3.5 DEFIBRILLATOR IMPLANTATION

In one study, prophylactic use of ICDs in patients at high risk for ventricular arrhythmias after CABG did not improve life expectancy in patients with a poor left ventricular ejection fraction.[204] **1⁺**

R **Defibrillators should not be routinely implanted in patients with a poor left ventricular ejection fraction at the time of coronary artery bypass graft surgery.**

6.4 TREATMENTS FOR ATRIAL FIBRILLATION

Postoperative AF following cardiothoracic surgery is the most common serious arrhythmia in the surgical setting, occurring in up to 40% of patients after coronary heart surgery.

Postoperative AF is associated with a greater risk of mortality and morbidity, with greater length of stay and rates of rehospitalisation.

6.4.1 PHARMACOLOGICAL THERAPIES

The NICE guideline on AF reported that in patients with postoperative AF, where various rhythm- and rate-control strategies have been compared, rhythm control results in greater cardioversion within one hour but not after 24 hours, shorter time for restoration of sinus rhythm, no difference in ventricular rate control, higher rates of therapeutic effectiveness and no difference in relapse rates.[205] **4**

R **In the immediate postoperative period, patients with persistent AF should be treated with a rhythm-control strategy.**

✓ Whatever pharmacological therapy is used for treatment of AF, the need for continuing treatment should be reviewed within six weeks of hospital discharge.

Anticoagulation

A systematic review identified no studies demonstrating effects of immediate anticoagulation on stroke risk in patients with AF following cardiac surgery.[206] The review identified one cohort study that provided some evidence that there is a risk of pericardial effusions with early anticoagulation.[207] **1⁺** **2⁻**

No evidence was identified about the clinical effectiveness, cost effectiveness or safety of treatment with the direct oral anticoagulants in patients experiencing atrial fibrillation after CABG.

✓ Anticoagulation should be considered on a case by case basis for patients with AF following CABG where it is anticipated that the AF is likely to persist.

6.4.2 DC CARDIOVERSION

Although one small study (n=48) found that DC cardioversion reduces the duration of AF there is no evidence that DC cardioversion reduces AF recurrence rate or the duration of hospital stay.[208] **1⁻**

The NICE guideline on AF reported that clinical experience and comparison of reversion rates between trials suggested benefit from DC cardioversion over pharmacological cardioversion for patients with AF of duration longer than 48 hours.[205] **4**

R

- **Patients with AF and haemodynamic compromise should have synchronised cardioversion.**
- **Patients with persistent AF should be considered for elective synchronised cardioversion.**

6.4.3 SURGICAL ABLATION

The development of open surgical procedures for the ablation of atrial fibrillation has led to their widespread application in patients undergoing cardiac operations, however, there is limited evidence regarding the efficacy and morbidities associated with surgical ablation in concomitant cardiac surgery.

A meta-analysis of 16 RCTs of ablation in patients with AF undergoing cardiac surgery included a range of types of ablative interventions (six studies used radiofrequency ablation, four studies used a Cox–maze surgical technique, three studies used cryoablation, five studies reported patients undergoing pulmonary vein isolation and two studies used microwave ablation).[209] The proportion of patients in sinus rhythm at discharge was significantly higher in the group receiving concomitant ablation compared with the cardiac surgery alone group (62.7% *v* 26.6%; OR 7.64, 95% CI 4.04 to 14.45; I^2=67%). The ablation group also had a significantly higher proportion of patients in sinus rhythm compared with surgery alone at the three month (62.5% *v* 29.8%; OR 4.79, 95% CI 2.79 to 8.23; I^2=56), six month (62.6% *v* 27.4%; OR 5.44, 95% CI 3.44 to 8.61; I^2=37%), and ≥12 month (66.7% *v* 26.1%; OR 6.72, 95% CI 4.88 to 9.25; I^2=0%) follow-up periods. There were no significant differences between surgical ablation versus no ablation in terms of all-cause mortality (8.7% *v* 7.6%; OR 1.05, 95% CI 0.66 to 1.68), 30-day all-cause mortality (5.3% *v* 3.8%; OR 1.23, 95% CI 0.65 to 2.39), pacemaker implantations (5.8% *v* 8.3%; OR 0.88, 95% CI 0.51 to 1.51) or neurological events (4.9% *v* 5.8%; OR 0.86, 95% CI 0.37 to 2.04). **1++**

One RCT randomised 260 patients with persistent AF who required mitral valve surgery to undergo either surgical ablation or no ablation during the mitral valve operation. Patients in the ablation group underwent further randomisation to pulmonary vein isolation or a biatrial maze procedure.[210] In keeping with the results of the meta-analysis, more patients in the ablation group than in the surgery alone group were free from AF at both six and 12 months (63.2% *v* 29.4%, p<0.001). One-year mortality was 6.8% in the ablation group and 8.7% in the surgery alone group (HR with ablation 0.76, 95% CI 0.32 to 1.84). There was no significant difference in the rate of freedom from AF between patients who underwent pulmonary vein isolation and those who underwent the biatrial maze procedure (61.0% and 66.0%, respectively; p=0.60). **1+**

Concern has been expressed that patients who appear to be free of AF at one year after surgical ablation may be considered cured of AF and have their anticoagulant medication discontinued. However, some patients may be at risk of subsequent recurrence of AF and might be at significant risk of thromboembolic complications.

Three studies were identified which investigated the cost effectiveness of surgical ablation concomitant to cardiac surgery. A Canadian study published in 2009 evaluated the cost effectiveness of ablation using a maze procedure at the time of mitral valve surgery compared with mitral valve surgery alone.[211] A cost-utility analysis estimated the costs and effects of each treatment arm over a 15-year time horizon. Based on the analysis, surgical ablation at the time of mitral valve surgery was considered to be cost effective resulting in an ICER of $4,446CAD, compared with mitral valve surgery alone (based on an incremental cost of $900 and an incremental quality-adjusted life year (QALY) gain of 0.20). A one-way sensitivity analysis indicated that results were sensitive to a variation in the time horizon. When this is decreased to five years, the ICER increases to $44,300CAD. A number of weaknesses were identified with the analysis including a lack of long-term follow-up data. The analysis assumes that the short-term clinical benefit associated with the intervention will be maintained over the duration of the time horizon, which is subject to considerable uncertainty and may not be appropriate. The primary concern surrounds the generalisability of results to a UK setting as resource use and costs were based on Canadian sources.

A UK study published in 2007 evaluated the cost effectiveness of high-intensity focused ultrasound-assisted surgical ablation, classic maze procedure and percutaneous ablation, all concomitant to cardiac surgery.[212] Surgical ablation was considered to be cost effective compared with no ablation, resulting in ICERs of £4,005, £7,448 and £6,660 for patients with permanent AF, persistent AF and paroxysmal AF, respectively. The maze procedure was the most cost effective of the techniques evaluated, with percutaneous ablation being least cost effective due to requiring a second procedure and rehospitalisation with the ensuing additional risks. However, all approaches were cost effective compared with no ablation.

A Dutch study published in 2011 examined the cost effectiveness of surgical ablation in patients with AF undergoing cardiac surgery, compared with cardiac surgery alone.[213] A cost analysis was conducted alongside an RCT and cost data were combined with QALYs in order to estimate the ICER. No economic model was attempted. The results were presented over one year. The base case results indicated that surgical ablation in patients with AF undergoing cardiac surgery was not cost effective, resulting in an ICER of €73,359 compared with surgery alone, based on an incremental cost of €4,425 and an incremental QALY gain of 0.06. Weaknesses were identified within the analysis. In addition to the short-term clinical data used within the analysis and the lack of economic modelling, the study was conducted from a societal perspective and includes indirect health care costs, ie paid work loss, domestic work loss and voluntary work loss. Furthermore, costs were indexed to 2004 and therefore may be considered outdated.

In summary, surgical ablation for atrial fibrillation may be cost effective in patients with AF who are undergoing a cardiac surgical procedure, however the evidence is conflicting and based on studies published between 2007 and 2012, which limits the current validity.

R **Patients who are referred for cardiac surgery and who have a history of atrial fibrillation** (paroxysmal or persistent) **should routinely be considered for surgical ablation as a concomitant procedure.**

R **Surgical ablation should involve electrical isolation of the pulmonary veins with or without other lesions.**

✓ The decision as to whether or not to perform concomitant AF ablation should be discussed with the patient prior to cardiac surgery.

✓ In patients who have undergone surgical ablation and are clinically free of atrial arrhythmias postoperatively, the decision on whether or not to discontinue antithrombotic therapy should take into account the patient's CHA_2DS_2-VASc score and the risk of stroke if the patient were to develop recurrent AF.

6.5 TREATMENTS FOR VENTRICULAR ARRHYTHMIAS

There is little evidence to guide treatment of ventricular arrhythmias associated with CABG surgery. Recommendations are based on published expert opinion.

Sternal reopening for internal massage, defibrillation or control of bleeding is most effective if carried out in critical care, less than 24 hours from surgery and if performed less than 10 minutes from arrest. It is of limited value when performed more than 24 hours after surgery or in the general ward.[214,215] Institution of cardiopulmonary bypass may be indicated in the early postoperative period to correct surgical bleeding or coronary artery graft occlusion and rest an exhausted myocardium.[215]

3
4

R

- **Patients with VF or pulseless VT should be defibrillated immediately.**
- **Intravenous adrenaline/epinephrine should be used for the management of patients with refractory VT/VF.**
- **Sternal reopening, internal heart massage and internal defibrillation should be considered in patients with refractory VT/VF.**
- **Intravenous amiodarone should be considered for the management of patients with refractory VT/VF.**

✓
- Cardiac tamponade following CABG surgery is a cause of cardiac arrest and should be considered as a differential diagnosis.
- Should other methods fail, sternal reopening should be performed promptly for cardiac arrest if the patient is in critical care and within 24 hours of surgery.
- The ability to institute cardiopulmonary bypass in the critical care area should be available in all units undertaking coronary artery bypass grafting surgery.

✓ Telemetric ECG monitoring of patients in the general ward allows early detection and treatment of patients in VT/VF.

✓ Patients suffering VT/VF >48 hours after CABG should be considered for ICD implantation.

6.6 PREOPERATIVE INFORMATION

No evidence was identified which related directly to the effectiveness of provision of information on arrhythmias post CABG. A well-conducted systematic review of a number of small, poor-quality studies did not identify any benefit for preoperative education in respect of medical outcomes for CABG.[216] Additionally, an RCT examining the impact of standardised preoperative education on recovery following coronary artery bypass surgery found no difference in length of stay, anxiety, pain, depression or well-being between control and intervention groups.[217] However, as described in SIGN guideline 148 on acute coronary syndrome and SIGN guideline 151 on the management of stable angina there is a range of factors relating to information/education needs of patients which should be considered by all health professionals in conjunction with appropriate educational and psychological strategies.[3,218] **1+ 4**

✓ Preoperative information/education, including that related to arrhythmias, should be tailored to individual patient's needs.

7 Psychosocial issues

7.1 INTRODUCTION

Psychosocial outcomes in patients with arrhythmias have mainly been examined as an adjunct to medical and mortality outcomes. Studies in this area often have methodological flaws and tend to focus on a limited range of quality of life issues: looking at physical or activity functioning rather than partner/family issues, memory difficulties and other psychosocial patient concerns.[219,220] **1+**

Psychological or emotional factors can influence and confound the incidence of cardiac arrhythmia.[221,222] Although anxiety and depressive disorders occur frequently in patients with CHD they are rarely identified or managed in the cardiology setting. Some patients may have had pre-existing mental health problems including depression. SIGN guideline 149 on risk estimation and the prevention of cardiovascular disease covers depression as a risk factor.[15] For other patients, cardiac ill health precipitates new anxieties, depression or cognitive dysfunction (including poor memory and concentration) affecting their ability to participate in treatment regimens and rehabilitation.[223,224] **1+ 2+ 4**

7.2 PSYCHOSOCIAL ASSESSMENT AND SCREENING

A systematic review of studies of mood problems following ICD implantation reported that prevalence of depressive disorders and anxiety disorders varied across studies (range 11–28% and 11–26%, respectively, three studies using validated diagnostic interviews, n=190).[225] The authors note that a prevalence rate around 20% is similar to rates reported in the larger evidence base describing patients following acute MI. Studies suggest that, without intervention, symptoms may persist when followed up at 3–12 months.[226,227]

In a randomly-selected population-based sample of 10,000 individuals aged 35 to 74 years drawn from a region within Germany, individuals with AF had a slightly higher burden of depressive symptoms than individuals without AF.[228] The association was more pronounced for the somatic symptom dimension of depression (OR 1.08, 95% CI 1.02 to 1.15) than for cognitive depressive symptoms (OR 1.05, 95% CI 0.98 to 1.11). Worse self-reported physical health status was also associated with AF (OR 0.54, 95% CI 0.41 to 0.70) as well as worse mental health status (OR 0.61, 95% CI 0.46 to 0.82). **3**

Physicians' and nurses' subjective judgements of patient anxiety are not as accurate as measurements of anxiety on validated scales. Further information on psychosocial interventions can be found in SIGN guideline 148 on acute coronary syndrome.[3] Standardised screening tools, such as the Hospital Anxiety and Depression Scale, Patient Health Questionnaire 9 (PHQ-9) and Generalized Anxiety Disorder 7 (GAD-7), are useful in psychological assessment with referral of more complex cases to psychological or other mental health services. Selective screening of cardiac patients for cognitive problems will aid patient care after cardiac arrest and in older people where the relationship between depression and cognitive impairment is complex.[223,224] **2+ 4**

SIGN 150 on cardiac rehabilitation recommends a matched-stepped-care model for delivering psychological therapies for patients with depression and a chronic physical health condition.[5] **4**

R **Patients with chronic cardiac arrhythmias and cardiac arrest should be screened for anxiety or depressive disorders with referral to specialist psychology services where appropriate.**

R **Selective cognitive screening should be available especially after a cardiac arrest and for older cardiac patients experiencing persistent memory or other cognitive difficulties.**

7.3 PSYCHOSOCIAL ISSUES FOR ICD RECIPIENTS

Fifteen to 60% of ICD recipients experience high levels of distress around the time of surgery, with anxiety and depression as the main emotional responses.[229] Although ICD implantation may relieve some of the fear of sudden death and is welcomed by most patients, it can impose new fears that can affect return to normal life roles or function. Specific ICD related fears include fear of shock, device malfunction or death. There may also be concerns around changes in body image.[220,230] **1+**

Lifestyle changes including reduced physical and sexual activity and enforced driving restrictions can also have a negative impact on quality of life.[220,230] **1+**

Psychosocial adjustment problems are more common in ICD recipients younger than the age of 50.[58,220,230] Functional status, coping style, family problems and inadequate social support are also associated with psychological adjustment.[230] Repeated shock experiences are associated with poor quality of life.[231] The phenomenon of phantom shocks may also contribute to maladjustment to ICD,[232,233] although evidence on the association of repeated shock experience with psychological problems is inconclusive.[230] Families and partners of the patient can experience similar fears and anxiety: there are several case reports of family members becoming overprotective and spouses exhibiting hypervigilant behaviours and reporting low marital satisfaction. There are no large-scale studies.[229] **1+ 3 4 2+**

A meta-analysis found no difference in psychological outcome between patients with ventricular arrhythmia treated with ICDs or medical therapy, or between patients before and after ICD implantation.[234] This highlights that poor psychosocial outcome in ICD recipients may also be associated with the underlying cardiac condition rather than a direct response to implantation of the ICD device and its therapy. **2+**

R **Psychosocial implications for people experiencing cardiac arrhythmias should be considered by all healthcare staff throughout assessment, treatment and care.**

✓ Psychosocial support for patients experiencing cardiac arrhythmias should not be restricted to recipients of ICDs.

7.4 PSYCHOSOCIAL INTERVENTIONS

Psychological interventions, as part of comprehensive cardiac rehabilitation programmes, can reduce anxiety and depression in patients with CHD.[229] There is no evidence of effect on total or cardiac mortality.[235] **2+**

One systematic review and two subsequent RCTs provide evidence of benefit from programmes incorporating cognitive behavioural therapy (CBT) in reducing anxiety and improving quality of life specifically in patients with ICDs.[230,236,237] A further cluster-randomised controlled trial assessed the clinical and cost effectiveness of a brief home-based cognitive behavioural rehabilitation programme (the ICD Plan) for patients undergoing implantation of an ICD. A greater reduction in the proportion with comorbid depression (-13.2% *v* -2.1%) and comorbid anxiety (-20.8% *v* -12.8%) was seen in the intervention group than in the control group six months after implantation. Differences in the number of ICD shocks for each group were not significant (p=0.53). The six-month per patient healthcare costs were £486 in the intervention group and £528 in the control group. The additional intervention cost per patient was £12.68. This was offset by the reduced healthcare costs, which were mainly due to a reduction in hospitalisations with the intervention (11% *v* 22%, p<0.01). The authors reported that the intervention had a 67% probability of being more cost effective than the control approach and generated an ICER of £1,429. **1+**

SIGN guideline 150 on cardiac rehabilitation includes the good practice point that CBT, as part of cardiac rehabilitation, should only be delivered by staff with accredited relevant competencies and approved clinical supervision.[5] **4**

As patients with ICDs have similar secondary-prevention, lifestyle change and educational needs as other CHD patients it would be appropriate to include them as part of existing cardiac rehabilitation services.[238] 4

R **Psychosocial interventions offered as part of a comprehensive rehabilitation programme should encompass a cognitive behavioural component.**

7.5 ANTIDEPRESSANT MEDICATIONS IN PATIENTS WITH CORONARY HEART DISEASE

Clinical depression is a risk factor for cardiovascular mortality including cardiac arrest.[190] Following ACS,15–20% of patients develop depression, which has been shown to be associated with increased mortality.[239] Tricyclic antidepressant drugs are associated with risk of cardiac arrhythmia and are considered to be contraindicated in those with ACS[240,241] *(see British National Formulary, BNF; www.bnf.org)*. Selective serotonin reuptake inhibitors have been shown to be safe and effective in patients with ACS in randomised controlled trials,[239] but have not been shown to improve prognosis.[242]

Caution should be exercised in prescription of drugs which may prolong the QT interval, particularly in older patients (aged 65 years or above). The risk of polymorphic VT may be significantly increased in the context of co-administration of multiple drugs with QT prolongation effects.[243] In patients with arrhythmias, selection of antidepressant or antipsychotic agents should be made with reference to their individual risk of QT-interval prolongation *(see, for example Credible-Meds® www.crediblemeds.org)*. 3

8 Provision of information

This section reflects the issues likely to be of most concern to patients and their carers. These points are provided for use by healthcare professionals when discussing arrhythmias with patients and carers and in guiding the production of locally-produced information materials.

8.1 PUBLICATIONS FROM SIGN

SIGN patient versions of guidelines are documents that 'translate' guideline recommendations and their rationales, originally developed for healthcare professionals, into a form that is more easily understood and used by patients and the public. They are intended to:

- help patients and carers understand what the latest evidence supports around diagnosis, treatment and self care
- empower patients to participate fully in decisions around management of their condition in discussion with healthcare professionals
- highlight for patients where there are areas of uncertainty.

A patient version of this guideline and the following guidelines on cardiac topics are available from the SIGN website www.sign.ac.uk:

- SIGN 147: Management of chronic heart failure
- SIGN 148: Acute coronary syndrome
- SIGN 149: Risk estimation and the prevention of cardiovascular disease
- SIGN 150: Cardiac rehabilitation
- SIGN 151: Management of stable angina.

8.2 SOURCES OF FURTHER INFORMATION

NHS inform

www.nhsinform.scot
Telephone: 0800 22 44 88 (8am–10pm)

NHS inform is the national health and care information service for Scotland. It includes a section on heart conditions with information and links to resources to support patients with heart disease.

www.nhsinform.scot/illnesses-and-conditions/heart-and-blood-vessels

There is also a section providing advice on healthy living for physical and mental wellbeing.

www.nhsinform.scot/healthy-living

Arrhythmia Alliance

www.heartrhythmalliance.org/aa/uk
Telephone: 01789 867 501
Email: info@heartrhythmalliance.org

Unit 6B, Essex House, Cromwell Business Park, Chipping Norton, OX7 5SR

The Arrhythmia Alliance is a coalition of charities, patient groups, patients, carers, medical groups and allied professionals working together to improve the diagnosis, treatment and quality of life for all those affected by arrhythmias.

British Heart Foundation

www.bhf.org.uk
Telephone: 0131 555 5891
Heart Helpline: 0300 330 3311
Email: bhfhi@bhf.org.uk

The Cube, 43a Leith Street, Edinburgh EH1 3AT

The British Heart Foundation (BHF) is a national heart charity and the largest independent funder of cardiovascular research in the UK. The BHF provides vital support, information and care for patients and their carers. It provides forums to listen to, engage and influence both patients and key stakeholders.

Chest Heart & Stroke Scotland

www.chss.org.uk
Telephone: 0131 225 6963
Advice Line Nurses: 0808 801 0899 (9.30am–4.00pm, Mon–Fri)
Email: admin@chss.org.uk

Third Floor, Rosebery House, 9 Haymarket Terrace, Edinburgh, EH12 5EZ

Chest Heart & Stroke Scotland is a health charity set up to improve the quality of life for people in Scotland affected by chest, heart and stroke illness, through medical research, influencing public policy, advice and information and support in the community. It helps to co-ordinate self-managed peer support groups throughout Scotland which provide a range of activities to support people affected by chest, heart and stroke illness.

CredibleMeds®

www.crediblemeds.org

CredibleMeds® is a website run by the Arizona Center for Education and Research on Therapeutics with a mission to foster the safe use of medicines. It maintains the CredibleMeds® website and the QTdrugs lists of drugs that have a risk of QT prolongation and cardiac arrhythmias under a contract with the US Food and Drug Administration Safe Use Initiative to support the safe use of medications.

8.3 CHECKLIST FOR PROVISION OF INFORMATION

This section gives examples of the information patients/carers may find helpful at the key stages of the patient journey. The checklist was designed by members of the guideline development group based on their experience and their understanding of the evidence base. The checklist is neither exhaustive nor exclusive.

- Offer reassurance to patients and their families, who may be anxious.
- Explain to patients and their families why they have been given medication after CPR/defibrillation.
- Inform patients and their families of tests and procedures that will be carried out to diagnose arrhythmias.
- Offer written information (for example, the SIGN patient booklets) to patients and their families.
- Discuss the need for ECG monitoring including a portable ECG.
- Explain the different types of abnormal heart rhythm.
- Discuss treatment options with patients and their families.
- Advise patients that AF can affect people who are fit and healthy.
- For patients who have had a cardiac arrest, explain to them and their families, the risk of having another one.
- Offer lifestyle advice.
- Advise patients about suitable exercise regimes.
- Discuss psychosocial issues, such as depression, anxiety, or stigma, with patients and their families.
- Discuss employment issues with patients and their families.
- Explain the need to attend annual pacemaker checks.

9 Implementing the guideline

This section provides advice on the resource implications associated with implementing the key clinical recommendations, and advice on audit as a tool to aid implementation.

9.1 IMPLEMENTATION STRATEGY

Implementation of national clinical guidelines is the responsibility of each NHS board and is an essential part of clinical governance. Mechanisms should be in place to review care provided against the guideline recommendations. The reasons for any differences should be assessed and addressed where appropriate. Local arrangements should then be made to implement the national guideline in individual hospitals, units and practices.

Implementation of this guideline will be encouraged and supported by SIGN.

9.2 RESOURCE IMPLICATIONS OF KEY RECOMMENDATIONS

No recommendations are considered likely to reach the £5 million threshold which warrants resource impact analysis.

9.3 AUDITING CURRENT PRACTICE

A first step in implementing a clinical practice guideline is to gain an understanding of current clinical practice. Audit tools designed around guideline recommendations can assist in this process. Audit tools should be comprehensive but not time consuming to use. Successful implementation and audit of guideline recommendations requires good communication between staff and multidisciplinary team working.

The guideline development group has identified the following as key points to audit to assist with the implementation of this guideline:

- the annual number of lay people trained to initiate CPR in out-of-hospital cardiac arrests
- the proportion of patients taking dronedarone who have a test of liver function before treatment, after one week, after one month, at monthly intervals for six months, at nine and 12 months and thereafter
- the proportion of patients with symptomatic bradycardia/conduction disturbance who are inappropriately continued on therapies which predispose to bradycardia (eg beta blockers, digoxin, verapamil)
- the proportion of patients with acute MI who have LV function assessed during the index admission
- the proportion of patients with typical atrial flutter who are offered radiofrequency catheter ablation
- the proportion of patients with a primary-prevention ICD experiencing repeated inappropriate shocks who have a single therapy zone programmed at a detection rate of 200 bpm and detection interval programmed to not less than 8 seconds
- the proportion of patients with chronic cardiac arrhythmias and cardiac arrest who are screened for anxiety or depressive disorders.

9.4 HEALTH TECHNOLOGY ASSESSMENT ADVICE FOR NHSSCOTLAND

In July 2012 the SMC advised that eplerenone (Inspra®) is accepted for use within NHSScotland in addition to standard optimal therapy, to reduce the risk of cardiovascular mortality and morbidity in adult patients with NYHA class II (chronic) heart failure and LVEF ≤30%.

In May 2005 the SMC advised that eplerenone (Inspra®) is accepted for use within NHSScotland in addition to standard therapy including beta blockers, to reduce the risk of cardiovascular mortality and morbidity between 3–14 days after MI in stable patients with left ventricular dysfunction (left ventricular ejection fraction 40%) and clinical evidence of heart failure.

In September 2010, the SMC advised that dronedarone (Multaq®) is accepted for restricted use within NHSScotland for the prevention of recurrence of AF in patients in whom beta blockers, class Ic drugs or amiodarone are contraindicated, ineffective or not tolerated. Treatment should be initiated on specialist advice only.

In June 2014, Healthcare Improvement Scotland advised that the recommendations in the NICE MTA on implantable cardioverter defibrillators and cardiac resynchronisation therapy for arrhythmias and heart failure[139] were as valid for Scotland as for England and Wales.

10 The evidence base

10.1 SYSTEMATIC LITERATURE REVIEW

The evidence base for this guideline was synthesised in accordance with SIGN methodology. A systematic review of the literature was carried out using an explicit search strategy devised by a SIGN Evidence and Information Scientist. Databases searched include Medline, Embase, and the Cochrane Library. The year range covered was 2010–2015. Internet searches were carried out on various websites including the US National Guidelines Clearinghouse. The main searches were supplemented by material identified by individual members of the development group. Each of the selected papers was evaluated by two Evidence and Information Scientists using standard SIGN methodological checklists before conclusions were considered as evidence by the guideline development group.

10.1.1 LITERATURE SEARCH FOR PATIENT ISSUES

At the start of the guideline development process, a SIGN Evidence and Information scientist conducted a literature search for qualitative and quantitative studies that addressed patient issues of relevance to management of patients with cardiac arrhythmias. Databases searched include Medline, Embase, Cinahl and PsycINFO, and the results were summarised by the SIGN Patient and Public Involvement Advisor and presented to the guideline development group.

10.1.2 LITERATURE SEARCH FOR COST-EFFECTIVENESS EVIDENCE

The guideline development group identified key questions with potential cost-effectiveness implications, based on the following criteria, where it was judged particularly important to gain an understanding of the additional costs and benefits of different treatment strategies:

- treatments which may have a significant resource impact
- opportunities for significant disinvestment or resource release
- the potential need for significant service redesign
- cost-effectiveness evidence could aid implementation of a recommendation.

A systematic literature search for economic evidence for these questions was carried out by a SIGN Evidence and Information Scientist in August 2015. Databases searched include Medline, Embase and NHS Economic Evaluation Database (NHS EED). Each of the selected papers was evaluated by a Health Economist, and considered for clinical relevance by guideline group members.

Interventions are considered to be cost effective if they fall below the commonly-accepted UK threshold of £20,000 per Quality-Adjusted Life Year.

10.2 RECOMMENDATIONS FOR RESEARCH

The guideline development group was not able to identify sufficient evidence to answer all of the key questions asked in this guideline *(see Annex 1)*. The following areas for further research have been identified:

- more sensitive measures of neurologic outcome following cardiac arrest. In particular, tests of episodic long-term memory are good indicators of subtle neurologic injury and may unmask as yet unknown effects of therapeutic hypothermia versus standard care.
- head-to-head trials of antiarrhythmic drugs to establish the relative benefits and harms in patients with CHD and haemodynamically stable ventricular tachycardia.
- trials of electrical versus pharmacological cardioversion to establish the relative benefits and harms in patients with CHD and haemodynamically stable ventricular tachycardia.
- trials to determine the impact of strict rate control in patients who remain highly symptomatic following lenient rate control.

- the safety and efficacy of lenient rate control in patients with heart failure and reduced ejection fraction.
- the efficacy of catheter ablation for long-term freedom from AF in patients with symptomatic paroxysmal atrial fibrillation (including those with cardiac comorbidities).
- the effect of programming longer detection intervals for the reduction in inappropriate shocks in patients with ICDs used for secondary prevention of cardiac arrhythmias.
- trials of the efficacy and safety of catheter ablation compared with medical therapy for the management of patients with VT storm.
- the clinical effectiveness, cost effectiveness and safety of treatment with the direct oral anticoagulants in patients experiencing AF after CABG.
- the indications for stopping anticoagulation following successful surgical ablation for AF.
- feasibility studies into performing concomitant surgical ablation with CABG in NHSScotland.

10.3 REVIEW AND UPDATING

This guideline was issued in 2018 and will be considered for review in three years. Any updates to the guideline in the interim period will be noted on the SIGN website: www.sign.ac.uk

Comments on new evidence that would update this guideline are welcome and should be sent to the SIGN Executive, Gyle Square, 1 South Gyle Crescent, Edinburgh, EH12 9EB (email: sign@sign.ac.uk).

11 Development of the guideline

11.1 INTRODUCTION

SIGN is a collaborative network of clinicians, other healthcare professionals and patient organisations and is part of Healthcare Improvement Scotland. SIGN guidelines are developed by multidisciplinary groups of practising healthcare professionals using a standard methodology based on a systematic review of the evidence. Further details about SIGN and the guideline development methodology are contained in 'SIGN 50: A Guideline Developer's Handbook', available at **www.sign.ac.uk**

This guideline was developed according to the 2015 edition of SIGN 50.

11.2 THE GUIDELINE DEVELOPMENT GROUP

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The membership of the guideline development group was confirmed following consultation with the member organisations of SIGN. All members of the guideline development group made declarations of interest. A register of interests is available in the supporting material section for this guideline at **www.sign.ac.uk**

Guideline development and literature review expertise, support and facilitation were provided by SIGN Executive and Healthcare Improvement Scotland staff. All members of the SIGN Executive make yearly declarations of interest. A register of interests is available on the contacts page of the SIGN website **www.sign.ac.uk**

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Aimie Little	*Administration Officer*
Gaynor Rattray	*Guideline Co-ordinator*
Domenico Romano	*Publications Designer*
Carolyn Sleith	*Evidence and Information Scientist*

11.3 THE STEERING GROUP

A Steering Group comprising the chairs of the six SIGN CHD guidelines and other invited experts was established to oversee the progress of the guideline development. This group met regularly throughout the development of the guidelines.

Professor Lewis Ritchie, OBE *(Chair)*	*Mackenzie Professor and Head of Department, Department of General Practice and Primary Care, University of Aberdeen*
Mr James Cant	*Director, British Heart Foundation Scotland*
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11.4 CONSULTATION AND PEER REVIEW

11.4.1 SPECIALIST REVIEWERS INVITED TO COMMENT ON THIS DRAFT

Dr Jonathan Affolter	*Specialist Registrar, Aberdeen Royal Infirmary*
Mrs Wendy Armitage	*Cardiac and User Development Manager, Chest, Heart & Stroke Scotland*
Dr Paul Broadhurst	*Consultant Cardiologist, Aberdeen Royal Infirmary*
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11.4.2 PUBLIC CONSULTATION

The draft guideline was also available on the SIGN website for a month to allow all interested parties to comment.

11.4.3 SIGN EDITORIAL GROUP

As a final quality control check, the guideline is reviewed by an editorial group comprising the relevant specialty representatives on SIGN Council to ensure that the specialist reviewers' comments have been addressed adequately and that any risk of bias in the guideline development process as a whole has been minimised. The editorial group for this guideline was as follows. All members of SIGN Council make yearly declarations of interest. A register of interests is available on the SIGN Council Membership page of the SIGN website **www.sign.ac.uk**

Dr Jenny Bennison	*Royal College of General Practitioners*
Dr Roberta James	*SIGN Programme Lead; Co-Editor*
Professor John Kinsella	*Chair of SIGN; Co-Editor*
Professor Gregory Lip	*Royal College of Physicians of Edinburgh*

Abbreviations

AAD	antiarrhythmic drug
ACE	angiotensin-converting enzyme
ACS	acute coronary syndrome
AED	automated external defibrillator
AF	atrial fibrillation
ARR	absolute risk reduction
ATHENA	A Placebo-Controlled, Double-Blind, Parallel Arm Trial to Assess the Efficacy of Dronedarone 400 mg bid for the Prevention of Cardiovascular Hospitalization or Death from Any Cause in Patients with Atrial Fibrillation/Atrial Flutter
ATP	antitachycardia pacing
AV	atrioventricular
AVID	Antiarrhythmics Versus Implantable Defibrillators
AVN	atrioventricular nodal
BHF	British Heart Foundation
BNF	British National Formulary
bpm	beats per minute
CABG	coronary artery bypass graft
CASH	Cardiac arrest study Hamburg
CASTLE-AF	Catheter Ablation versus Standard Conventional Therapy in Patients with Left Ventricular Dysfunction and Atrial Fibrillation trial
CBT	cognitive behavioural therapy
CHD	coronary heart disease
CI	confidence interval
CIDS	Canadian Implantable Defibrillator Study
COPD	chronic obstructive pulmonary disease
CoSTR	Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science with Treatment Recommendations
CPR	cardiopulmonary resuscitation
CRT	cardiac resynchronisation therapy
CRT-D	cardiac resynchronisation therapy with defibrillator
CRT-P	cardiac resynchronisation therapy with pacing
CVD	cardiovascular disease

DC	direct current
DINAMIT	Defibrillators IN Acute Myocardial Infarction Trial
ECG	electrocardiogram
GAD-7	Generalized Anxiety Disorder 7-item questionnaire
GMC	General Medical Council
HF-REF	heart failure with reduced ejection fraction
HR	hazard ratio
ICD	implantable cardioverter defibrillator
ICER	incremental cost effectiveness ratio
IRIS	Immediate Risk Stratification Improves Survival trial
IV	intravenous
LBBB	left bundle branch block
LV	left ventricular
LVEF	left ventricular ejection fraction
MA	marketing authorisation
MADIT-RIT	Multicenter Automatic Defibrillator Implantation trial - Reduce Inappropriate Therapy
MI	myocardial infarction
MTA	multiple technology assessment
NHS	National Health Service
NICE	National Institute for Health and Care Excellence
NSAID	non-steroidal anti-inflammatory drug
NYHA	New York Heart Association
OR	odds ratio
PCI	percutaneous coronary intervention
PEA	pulseless electrical activity
PHQ-9	Patient Health Questionnaire 9-item instrument
PUFAs	polyunsaturated fatty acids
QALY	quality-adjusted life year
QOF	Quality and Outcomes Framework
QoL	quality of life
QRS complex	The principal deflection in the electrocardiogram, representing ventricular depolarisation
QT interval	The time elapsing from the beginning of the QRS complex to the end of the T wave in an electrocardiogram, representing the total duration of electrical activity of the ventricles

RCT	randomised controlled trial
ROSC	return of spontaneous circulation
RR	relative risk
RRR	relative risk reduction
SCD	sudden cardiac death
SIGN	Scottish Intercollegiate Guidelines Network
SMC	Scottish Medicines Consortium
ST segment	portion of the electrocardiographic tracing that can indicate ischaemia
UK	United Kingdom
VA	ventricular arrhythmia
VF	ventricular fibrillation
VT	ventricular tachycardia
WMD	weighted mean difference

Annex 1

Key questions used to develop the guideline

This guideline is based on a series of structured key questions that define the target population, the intervention, diagnostic test, or exposure under investigation, the comparison(s) used and the outcomes used to measure efficacy, effectiveness, or risk. These questions form the basis of the systematic literature search.

Guideline section	Key question	
3.4.3	1.	In adults who have sustained a cardiac arrest does therapeutic hypothermia offer benefits over usual care? **Population:** adults who have sustained a cardiac arrest **Intervention:** therapeutic hypothermia (in both prehospital and hospital settings) **Comparators:** usual care **Outcomes:** • survival (all-cause mortality) • survival to hospital discharge • cognitive function • QoL
5.2.6	2.	What antiarrhythmic drugs are useful in treating patients with haemodynamically stable VT and CHD? **Population:** adults with sustained VT and CHD but no cardiac arrest **Intervention:** antiarrhythmic drugs (amiodarone, lidocaine, flecainide) **Comparators:** any drug therapy **Outcomes:** • survival (all-cause mortality) • restoration of sinus rhythm and cardiac output
5.1.2	3.	What are the clinical effectiveness, cost effectiveness and safety of dronedarone in patients with CHD and AF? **Population:** adults with CHD and AF **Intervention:** dronedarone **Comparators:** • placebo • other antiarrhythmic drugs **Outcomes:** • restoration of sinus rhythm and cardiac output • recurrence of AF • all-cause mortality • heart failure, • (pro)arrhythmia, • treatment-related harms • cost effectiveness

5.1.4	4.	What are the benefits and harms of strict versus lenient rate control in patients with atrial fibrillation? **Population:** adults with AF **Intervention:** strict rate control (<80 beats per minute) **Comparators:** lenient rate control (<100 beats per minute) **Outcomes:** • CV mortality • hospitalisation for heart failure/stroke • systemic embolism • bleeding • life-threatening arrhythmic events • QoL
5.1.5	5.	What are the clinical effectiveness, cost effectiveness and safety of catheter ablation for patients with atrial fibrillation? **Population:** adults with AF, including • persistent AF • paroxysmal AF **Intervention:** • ablation (radiofrequency ablation, cryoablation) • pulmonary vein isolation **Comparators:** pharmacological therapy **Outcomes:** • freedom from AF at one year • freedom from antiarrhythmic drugs • adverse events (stroke, cardiac tamponade, phrenic nerve paralysis, atrio-esophageal fistula, pulmonary vein stenosis) • QoL • cost effectiveness
5.1.5	6.	What are the clinical effectiveness, cost effectiveness and safety of ablation for patients with atrial flutter? **Population:** adults with atrial flutter (with or without atrial fibrillation) **Intervention:** ablation (radiofrequency ablation) **Comparators:** pharmacological therapy **Outcomes:** • freedom from atrial flutter at one year • freedom from AF at one year • freedom from antiarrhythmic drugs • adverse events (stroke, cardiac tamponade) • QoL • cost effectiveness

5.2.4	7.	What evidence is there that programming ICD/CRT-D devices leads to a reduction in inappropriate shocks and better patient outcomes? **Population:** adults with ICD or CRT-D devices **Intervention:** • devices programmed to reduce inappropriate shocks • "therapy reduction programming" **Comparators:** device default settings **Outcomes:** • all-cause mortality • reduction in ICD shocks • syncope • QoL
5.2.7	8.	What is the clinical effectiveness and safety of catheter ablation for VT/electrical storm? **Population:** adults with VT/electrical storm **Intervention:** catheter ablation **Comparators:** antiarrhythmic drugs **Outcomes:** • all-cause mortality • freedom from VT/electrical storm
6.4.1	9.	What are the clinical effectiveness, cost effectiveness and safety of treatment with direct oral anticoagulants in patients experiencing AF after coronary artery bypass graft surgery? **Population:** adults with AF after coronary artery bypass surgery **Intervention:** direct oral anticoagulants (dabigatran, rivaroxaban, apixaban, edoxaban) **Comparators:** warfarin **Outcomes:** • stroke • peripheral embolism • major and minor bleeding

6.4.3	10.	What is the clinical effectiveness, cost effectiveness and safety of surgical ablation for AF in patients who are undergoing cardiac surgical procedures? **Population:** adults with AF who are undergoing cardiac surgery **Intervention:** surgical ablation for AF (cryoablation, radiofrequency ablation, maze) plus cardiac surgery **Comparators:** cardiac surgery alone **Outcomes:** • freedom from AF at one year • freedom from antiarrhythmic drugs • adverse events (stroke, cardiac tamponade, phrenic nerve paralysis, atrio-esophageal fistula, pulmonary vein stenosis) • QoL • cost effectiveness
7.4	11.	In patients with arrhythmias do psychosocial interventions reduce the use of hospital resources/readmissions? **Population:** adults with arrhythmias **Intervention:** • psychological interventions (cognitive behavioural therapy, mindfulness) • psychosocial interventions **Comparators:** usual care without psychological or psychosocial interventions **Outcomes:** • hospitalisation • QoL

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