

COMMENTS RECEIVED FROM EXTERNAL REFEREES AND OTHERS

SIGN 152: Cardiac arrhythmias in coronary heart disease

All reviewers submitted declarations of interests which were viewed prior to the addressing of comments.

Invited reviewers			Type of response and declared interests
AMC	Dr Anna Maria Choy	Senior Clinical Lecturer and Hon Consultant, Ninewells Hospital and Medical School, Dundee	Individual response. Nothing declared
AR	Dr Alan Robertson	Consultant Cardiologist, NHS Tayside, Dundee	Individual response. <i>Remuneration from consultancy or other fee paid work – Physician panel, Abbott speaker fee, Novartis.</i>
JA	Dr Jonathan Affolter	Cardiologist, Aberdeen Royal Infirmary, Aberdeen	Individual response. Nothing declared
KS	Dr Karen Smith	Nurse Consultant Cardiology, NHS Tayside, Dundee	Individual response. Nothing declared
MO	Dr Morag Osborne	Consultant Clinical Psychologist, NHS GGC	Individual response. Nothing declared
PB	Dr Paul Broadhurst	Consultant Cardiologist, Aberdeen Royal Infirmary, Aberdeen.	Individual response. Nothing declared
PS	Dr Paul Syme	Honorary Senior Lecturer, University of Edinburgh, Edinburgh	Individual response. <i>Remuneration from consultancy or other fee paid work – Have acted as an advisor for several companies Boehringer Ingelheim, Pfizer, Daiichi Sankyo. Of no relevance to this guideline.</i>
PSo	Ms Pernille Sorensen	Senior Cardiology Pharmacist, NHS Lecturer, Queen Elizabeth University Hospital/University of Strathclyde, Glasgow.	Individual response.
Open consultation			Type of response and declared interests
BCS		Comments submitted by Professor Nicholas John Linker, Consultant Cardiologist & Honorary Secretary, British Cardiovascular Society	Group response. <i>Nature and purpose of group – Professional organisation representing cardiologists and related</i>

			<p>allied health professionals.</p> <p><i>How might the statements and recommendations in the draft SIGN guideline impact on your organisation's functions/status/productivity?</i> – Draft recommendations in this SIGN guideline will have no discernible impact on the function or productivity of our organisation.</p>
CHS		<p>Comments submitted by Jill Adams, Specialist Services Manager, Chest, Heart and Stroke Scotland.</p>	<p>Group response.</p> <p><i>Nature and purpose of group</i> – Third sector organisation providing support to patients.</p> <p><i>How might the statements and recommendations in the draft SIGN guideline impact on your organisation's functions/status/productivity?</i> – Our organisation appreciates the guidance offered by this draft but recognises the need for further evidence, particularly in regard of psychological support.</p>
Med		<p>Comments submitted by Mark Chapman, Director, Health Economics, Medtronic Ltd</p>	<p>Group response.</p> <p><i>Nature and purpose of group</i> – Medical device manufacturer.</p> <p><i>How might the statements and recommendations in the draft SIGN guideline impact on your organisation's functions/status/productivity?</i> – The draft guidance would support the current and continued use of the products for example ICD/CRD-D/P and Cardiac Ablation technologies within our product portfolio.</p>
NC	Dr Nick Cruden	<p>Consultant Cardiologist, Royal Infirmary of Edinburgh, Edinburgh</p>	<p>Individual response.</p>

			<p><i>Remuneration from employment</i> – Consultant Cardiologist, NHS Lothian.</p> <p><i>Remuneration from consultancy</i> – Please see declaration held on file by SIGN (Stable Angina guideline development group (GDG)).</p>
RCPE		Comments submitted by Tom Mackay, Vice President, Royal College of Physicians, Edinburgh.	<p>Group response.</p> <p><i>Nature and purpose of group</i> – Medical Royal College.</p> <p><i>How might the statements and recommendations in the draft SIGN guideline impact on your organisation's functions/status/productivity?</i> - Draft recommendations in this SIGN guideline will have no discernible impact on the function or productivity of our organisation.</p>
RCST		Comments submitted by Margot Russell, Director, NMAHP practice development, Resuscitation and Clinical skills team, NHS Lanarkshire	<p>Group response.</p> <p><i>Nature and purpose of group</i> – Training provider and policy support.</p> <p><i>How might the statements and recommendations in the draft SIGN guideline impact on your organisation's functions/status/productivity?</i> – Overall there will be benefit from the draft SIGN recommendation, however, there will need to be a degree of organisational change to support the recommendations. Some of the recommendations also require greater clarity of definitions to prevent ambiguity.</p>

Section	Comments received	Development group response	Editorial response
General			
	AMC	A well organised comprehensive overview. The preamble is important in defining the scope and remit.	Thank you
	AR	On p48 (11.4.1 SPECIALIST REVIEWERS INVITED TO COMMENT ON THIS DRAFT) would you please ensure my title is updated? It should now read: Dr Alan Robertson Consultant Cardiologist, Ninewells Hospital, Dundee	Thank you. We have corrected this.
	JA	The survey should not be exclusive on what we can comment on..... i.e. "only factually incorrect will be considered" This can perpetuate old models and modes of thinking and clinical approach and should be subject to challenge at every opportunity to ensure contemporary clinical practice is reflected in your text.	Consultation is sought only on new draft additions to a published guideline. If current recommendations are affected by new evidence or changes in practice, clinicians may provide feedback to SIGN at any time using the "small change request" forms on the SIGN website.
	KS	No additional comments.	Noted
	NC	Well done to GDG for an excellent and comprehensive guideline. Easy to follow and intuitive. Probably not for this version but future version may want to review the title / remit. Title is "cardiac arrhythmias" but not doesn't cover all cardiac arrhythmias partly due to overlap with CHF and partly due to focus on IHD.	Thank you. The title was truncated in error. It has been reverted to the original title "Cardiac arrhythmias in coronary heart disease".
	PB	There is quite a lot about arrhythmias and cardiac surgery. One surgeon was involved in the guideline development group and no cardiac surgeon was asked to peer review the draft.	No surgical reviewers were nominated following requests to RCS or RCPSG. The guideline group was unable to nominate a surgical reviewer. The surgeon on the group has liaised with further cardiac surgery colleagues.
	PS	Authoritative guide. Needs patient version.	Thank you. A patient version is in development.
	PSo	Thanks for the draft version of the new SIGN. It is easy to read and find	Thank you.

		what you are looking for.		
	RCPE	The College is generally supportive of this draft guideline; however we note that in the section on Atrial Fibrillation (AF), there is only one sentence with regard to antithrombotic therapy management, referring to another guideline. Stroke prevention is the cornerstone of AF management (perhaps the most important, given that strokes in AF have major mortality/morbidity) and therefore we suggest more emphasis on the importance of appropriate thromboprophylaxis should be made.	Thank you. Antithrombotic therapy is considered in greater detail in SIGN 129 where an entire chapter is dedicated to the management of atrial fibrillation.	
Section 1				
1.1	AMC	Succinct, no issues	Thank you	
	AR	I wonder if the title of the guideline needs to be made clearer, in that it is only dealing with arrhythmia in the context of CHD? This only becomes apparent when reading the introduction.	Thank you. The title was truncated in error. It has been reverted to the original title "Cardiac arrhythmias in coronary heart disease".	
	JA	Nothing to change	Noted	
	KS	Good introduction. I think however this omits highlighting the role of the multi professional team within the specialist approach. 'Since the original publication of this guideline in 2007, there have been major advances in catheter ablation and device-based therapies for arrhythmias, changes in pharmacological and device therapy for heart failure and interventional therapy' in addition to these elements stated there have been development within specialist arrhythmia nurses roles who can provide support for arrhythmia patients including psychological support for ICD patients furthermore BHF have supported the testing of specialist services to provide support through integrated care models offering nurse led clinics, education and support to streamline care pathways and reduce waiting times and support recovery see https://www.bhf.org.uk/publications/healthcare-and-innovations/integrated-care_siric for ACS.	The areas updated in this version of the guideline reflect original key questions where new evidence was identified to support revision of recommendations. SIGN is aware that other aspects of the management of a condition may also have changed, but this is outwith the remit of this update.	
	PS	Important area of medicine with clear need for this guideline	Thank you	
	PSo	No comments – all areas covered.	Noted	
	RCST	Clearly articulated	Thank you	

1.1.1	AMC	Although the list of new inclusions and updates is listed in this section, it would be useful to have the sections that are new or updated highlighted in the text when going out for consultation, review. It makes it clearer to the reviewer/ reader where the work has focused. Not essential but it would be helpful.	Thank you for this suggestion. There is a balance to be made between flagging new information and not highlighting certain content as more important. All recommendations in the draft guideline are judged to be current, irrespective of when they were developed, however we are only able to consider feedback on newly developed content. Previously developed content is assumed to be robust, by virtue of passing through SIGN methodology, including peer review and consultation. If current recommendations are affected by new evidence or changes in practice, clinicians may provide feedback to SIGN at any time using the "small change request" forms on the SIGN website.	
	JA	Nothing to change	Noted	
	KS	Seems logical approach	Thank you	
	PS	No issues	Noted	
	RCST	Clearly articulated	Thank you	
1.1.2	AMC	An important and timely inclusion	Thank you	
	JA	Nothing to change	Noted	
	KS	Concerns raised by patient groups and through research include: a list. The last bullet point implies the role of specialist nurses is a concern. Should this not be a statement about the potential role of these nurses in supporting pts and their carers.	Thank you. Agreed. This has been revised	
	PS	Important	Thank you	
	RCST	Clearly articulated	Thank you	
1.2	AMC	Comprehensive. this is good to defined clearly early on in the document	Thank you	
	AR	See comment on 1.1. It does seem a slightly false dichotomy to make however I appreciate inclusion of the other areas would make for a much bigger guideline and is perhaps	Thank you. The title was truncated in error. It has been reverted to the original title "Cardiac arrhythmias in coronary	

		impractical within the resources allocated.	heart disease” which reflects the remit of the original guideline.	
	JA	Nothing to change	Noted	
	PS	Focus on arrhythmias linked to ACS, chronic CVD and cardiac surgery.	Noted	
	RCST	No issue	Noted	
1.2.1	AMC	No issues	Noted	
	JA	Nothing to change	Noted	
	KS	No additional comments	Noted	
	PS	Rhythm management of AF in association with IHD	Noted	
	RCST	No issue	Noted	
1.2.2	AMC	Inclusive, good	Thank you	
	JA	Nothing to change	Noted	
	KS	Should this not also include GPs and primary health care teams, what about paramedics? and SAS?	Thank you. These professions have been added.	
	PS	Authoritative guideline suitable for specialists in the field. Patients and carers will find a lot of this guideline too complex. A simple patient friendly version is required with this target audience in mind.	Thank you. A patient version is in development.	
	PSo	No comments – the principal potential users covered.	Thank you	
	RCST	No issues	Noted	
1.2.3	AMC	While is good to see that important comorbidities are included, should CKD also be included? CKD is very prevalent in patients with CAD and arrhythmias and is a major consideration in terms of therapies as well as prognosis.	Thank you. Agreed. This has been added, although the ACC guideline for AF lists CKD as the eighth most common comorbidity in patients with AF. CKD was taken into consideration for the recommendation on aldosterone receptor antagonists in section 4.3.2	
	JA	Nothing to change	Noted	
	KS	No additional comments	Noted	
	PSo	No comments – the main comorbidities highlighted.	Thank you	
	RCST	No issues. Comments for section 1.3 missing on form.	Section 1.3 is a standard section included in every SIGN guideline. It is not eligible for consultation.	

Section 2				
NO COMMENTS RECEIVED				
Section 3				
3.1	AMC	No issues	Noted	
	JA	Nothing to change	Noted	
	PS	Important but not reappraised.	Noted	
3.2	AMC	No issues	Noted	
	AR	Very important topic, glad to see this included - the recommendation re inclusion in the school curriculum is absolutely key and I hope is one of the major messages in the media briefings when this guideline is published.	Thank you	
	CHS	3.2 and 3.3 bystander CPR & Defibrillation should consider the impact of rehabilitation and aftercare for those affected by out of hospital cardiac arrest (OHCA). Although there is limited evidence in this area, bystanders, patients and healthcare workers should be supported following the event, as stated in the OHCA Strategy for Scotland 2015, Scottish Government, page 30	Thank you. SIGN 150 provides recommendations on cardiac rehabilitation for all patients with CHD. The OHCA strategy suggests ambitions for 2020 in survivors of cardiac arrest based on a focus group and literature search. No methodology was published about the process used to conduct these and these do not represent evidence for inclusion in a SIGN guideline.	
	JA	Nothing to change	Noted	
	PS	This is an important area which was not reappraised. Defibrillators are now being instated in most public buildings. Training the public to resuscitate in accordance with the resuscitation council guideline seems a very tall order. Work needs to be done to identify and simplify the process	Disagree. The GDG believes that the Resuscitation Council guidelines are straightforward. The Adult Basic Life support algorithm has five steps.	
	RCST	In this section – does this apply only to adults or does this cover adults and children?	The guideline remit does not distinguish between adults and children experiencing cardiac arrhythmias although the majority of evidence will be in adult populations only. While the GDG is aware of differences in the delivery of resuscitation to adults and children, these do not influence the	

		Also, clarification is required regarding healthcare professionals annual refresher – is this suggesting an annual practical skills session or will e-learning modules suffice?	recommendations contained in the guideline. This is an issue for NHS organisations, and was not considered in the key questions for this guideline.	
3.3	AMC	No issues	Noted	
	JA	Nothing to change	Noted	
	KS	<p><i>“Defibrillators delivering biphasic waveforms require lower energy shocks to terminate VF than those delivering monophasic waveforms and result in less myocardial damage.</i></p> <p><i>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.”</i></p> <p>? relevance of this text given that in OHCA you only have equipment available and no choice of what to use. May not be clear whether its mono or biphasic anyway.</p>	Noted. This is general information about the function of arrhythmias rather than an issue affecting on the point defibrillation. It also informs future purchases of new defibrillators.	
	PS	Prompt defibrillation	Noted	
	PSo	No comments - accurate	Thank you	
3.3.1	AMC	The RCT mentioned in the last paragraph, ref 31, was the study population comparable to Scotland? If not, this qualification should be included if this trial is to be included.	Yes. 14.6% of the patients were recruited in the UK.	
	AR	I'm surprised cost of equipment is ranked so highly - the relevant references (29 & 30) are now 15 years old so I wonder if this needs updated. A quick online search shows ones available at £699+VAT which does not seem too large a cost. Agree training is a cost, but this should also be something covered whenever CPR is being taught.	Agreed. This paragraph has been removed.	
	JA	Nothing to change	Noted	
	PS	Work needs to be done to encourage members of the public to become first responders	Noted	
3.4.1	JA	Nothing to change	Noted	
	PSo	No comments – still valid	Noted. Thank you	
3.4.2	JA	Nothing to change	Noted	

<p>3.4.3</p>	<p>AMC</p>	<p>Inconsistent Terminology: The use of the terms 'systematic review' and 'meta-analysis' seem to be used interchangeably, but this use is inaccurate: the former answers a defined research question by collecting and summarising all empirical evidence that fits prespecified eligibility criteria, while the latter is the use of statistical methods to summarise the results of these studies.</p> <p>Also, the varied used of both terms 'therapeutic hypothermia' and 'conventional cooling' is confusing, is it the same thing or are they different procedures? If the latter case, than a brief description in the first paragraph outlining the main differences in cooling techniques and target temperatures should be considered.</p> <p>The last paragraph is very confusing, especially the last sentence about the single RCT. Was this RCT part of the Cochrane review being discussed? Was the point of it being mentioned the fact that was the only one that showed no benefit or was it different because of the target temperature?</p> <p>If the Cochrane evidence was in favour but the SR was not, what was the overriding evidence that decided in favour of the recommendation against cooling? Some clarify as to the discussion/decision and conclusion underpinning this final recommendation is needed.</p>	<p>The terms systematic review and meta-analysis are not used interchangeably and are used appropriately. The titles of references 36 (Huang review) and 37 (Cochrane review) use the terms correctly and these are reflected in the body text of this section.</p> <p>Agreed. This is complicated by different studies using different definitions, however, we have added a description of therapeutic hypothermia to the first paragraph and a definition of conventional cooling (taken from the Cochrane review) to paragraph 5.</p> <p>Agreed. The haemofiltration trial was included in the Cochrane review but has been given unwarranted emphasis in the final paragraph and has now been removed.</p> <p>The Huang systematic review and meta-analysis examined 8 prehospital trials (2,379 participants) compared with six in the Cochrane review (1,412 participants), and the conclusions differ because two up-to date trials are excluded from Cochrane. Huang concludes that there is no difference in either mortality or neurologic outcome with therapeutic hypothermia. The Cochrane review does not refer to the Huang meta-analysis whereas it does refer to three other reviews.</p> <p>However, no individual contemporary large-scale study demonstrates mortality benefit, and few</p>	
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			show improvement in any neurological parameter, to the point we consider a level of evidence on which to base a recommendation to use therapeutic hypothermia.	
	AR	Does this section need to differentiate between actively undertaking therapeutic hypothermia for all patients vs its use in patients that otherwise have reduced GCS and are requiring ITU support?	There is no evidence from individual studies to support different advice for management of patients with different GCS levels. All studies in the meta-analysis refer to patients with low GCS.	
	JA	Nothing to change	Noted	
	KS	Seems reasonable given the limited and inconsistent evidence	Noted. Thank you	
	NC	p10 3.4.3 Therapeutic hypothermia. I agree current data would suggest targeted temperature control (36C) is the optimal strategy but for me this is not clear from text. The results of the Cochrane review are emphasised, suggesting a better neurological and survival outcome with in hospital hypothermia but the recommendation is that this should not be routinely administered.	Thank you. Agreed. We have clarified the support for the recommendation (see response to AMC comment above).	
	PB	The conclusion that therapeutic hypothermia should not be routinely administered in this setting does not seem to be borne out by the statements made in the last paragraph of 3.4.3	Thank you. Agreed. We have clarified the support for the recommendation (see response to AMC comment above).	
	PS	Important negative result	Noted	
	PSo	No comments - agree in interpretation and recommendation	Noted. Thank you	
3.4.4	AMC	Should there be some comment on the choice of second chronotropic agent after atropine, particularly in the setting of types of CAD; ACS versus chronic CAD, CHF etc. In practical terms , should isoprenaline be used in preference to adrenaline, when should dopamine be used etc.	This topic was not included as a key question, therefore we cannot recommend a specific second-line agent. However, the GDG is not aware of evidence to support a clear recommendation in this area. Specialist advice should be sought.	
	JA	Nothing to change	Noted	
	KS	Reflective of UK Resusc. Council considerations in this situation	Noted	
	PS	The lack of adequate training for	Agreed. This is not the	

		junior staff with regard to temporary pacing is an issue requiring further work	remit of this guideline.	
3.4.5	AMC	<p>Risk factors for QT prolongation and TdP should also include extreme bradycardia, especially longstanding CHB in the elderly. As well as withdrawal of suspect QT-prolonging medications, management should also include an assessment of potentially aggravating drug-drug interactions, and new impaired renal function causing reduced renal excretion and resultant increased drug levels of the offending drug, prime example being sotalol.</p> <p>AHA guidelines (<i>Circulation</i>. 2010;121:1047-1060) recommend not just Mg infusion regardless of the serum Mg level, but also repletion of K to the upper limit of normal (<i>J Am Coll Cardiol</i>. 2006; 48: e247–e346).</p>	<p>Agreed. We have added “bradycardia and combinations of drugs which prolong the QT interval”.</p> <p>Agreed. We have added a comment to consider repletion of K and cited evidence to suggest that a concentration of 3.5–4.5 mmol/l is associated with lowest risk of VF, cardiac arrest or death.</p>	
	AR	Sensible idea to highlight potential benefit of overdrive pacing to prevent relapse	Noted. Thank you	
	JA	<p>Should mention temporary atrial pacing for helping reduce QT interval if possible and the combination of A pace and beta blockade.</p> <p>Polymorphic VT is so frequently seen in the context of ischaemia, if QT is normal, that angio should be considered.</p>	<p>Evidence and a recommendation for “overdrive pacing” is included. The GDG notes that temporary atrial pacing is often poorly performed in many hospitals. This section was not updated in the current review so the issues raised here have not been investigated and no significant changes will be made. However, the recommendation and text have been reworded to “overdrive suppression pacing” which more accurately describes the procedure.</p>	
	KS	Offers clear guidance.	Thank you	
	PSo	Within NHSGGC we have tried to standardize the protocols for high risk cardiac drugs - magnesium sulphate included. The use of magnesium sulphate in polymorphic VT remains unlicensed which I think most of us can live with. We went for 8 mmol (2 gram) magnesium sulphate over 15 minutes. Most literature recommend	Agreed. This has been changed to “10–15 minutes”	

		between 10–15 minutes mainly based on current practice.		
Section 4				
4.1	AMC	The line: 'the majority (70–100%) ...' are these percentages meaningful when it is already stated 'the majority'?	Agreed. (70–100%) figure has been removed.	
	PS	No issues for this section.	Noted	
	RCPE	The College is generally supportive of this draft guideline; however we note that in the section on Atrial Fibrillation (AF), there is only one sentence with regard to antithrombotic therapy management, referring to another guideline. Stroke prevention is the cornerstone of AF management (perhaps the most important, given that strokes in AF have major mortality/morbidity) and therefore we suggest more emphasis on the importance of appropriate thromboprophylaxis should be made.	Thank you. Antithrombotic therapy is considered in greater detail in SIGN 129 where an entire chapter is dedicated to the management of atrial fibrillation.	
4.1.2	AMC	Recommend caution when using amiodarone with Digoxin. Amiodarone doubles digoxin concentrations and therefore digoxin doses must be halved before initiating amiodarone. Unfortunately, there have been cases due to inadvertent use of Amiodarone infusions to acutely control HR to a patient already on digoxin leading to digoxin induced VT and VF. 4.1.2 Last good practice point, 'CV under conscious sedation', this should be performed by some-one trained and with competency in conscious sedation.	Noted. The guideline does not recommend use of these drugs together. The recommendation is for either amiodarone or digoxin. Agreed, however the GDG believes this to be implicit in the wording, especially given the option of general anaesthesia. No change required.	
	JA	May be worth explaining that AF alone that causes the haemodynamic compromise can be considered for DCCV rather than any situation that might have AF associated with another non cardiac situation that lies behind the reduced BP, the example that would not merit DCCV would be sepsis with low BP and coincidental AF.	Noted. However, the remit of this section is arrhythmias associated with ACS. We have stated that underlying causes must be corrected, so no further changes required.	
4.2	AR	No mention of isoprenaline as a temporising agent bridging to PPM rather than risk temporary pacing wire; although mentioned in passing in recommendation by way of 'positively chronotropic agents' there is nothing in the discussion text.	The recommendation includes "positively chronotropic agents" which includes isoprenaline. No change required.	

	JA	It should be made clear that data frequently shows that even stopping AV nodal blocking drugs will frequently not change the need for device therapy.	Agreed, if high degree AV block. However, this is a section on Acute Coronary Syndrome, not an exhaustive textbook on every aspect of bradycardia. This specific question was not included in the key questions for the current update, therefore no evidence has been identified.	
	KS	The following recommendation omits the role of atropine in symptomatic patients. This should be included for consistency 'in patients with symptomatic bradycardia/conduction disturbance, concurrent therapies which predispose to bradycardia (eg beta blockers, digoxin, verapamil) should be discontinued'	Disagree. The recommendation includes atropine "Temporary transvenous pacing....."	
	KS	Seems clear.	Thank you	
	PSo	Don't know if worth including the less obvious rate-limiting drugs e.g. eyedrops should the patient not receive any other rate-limiting drugs.	Noted. The guideline already states "beta blockers". It is not necessary to specify the formulation. No change required.	
4.3.1	AMC	Recommendation 2 is not very clear. The recommendation 'should be considered for a Lifevest ' needs a statement for how long or till a defined endpoint.ie a permanent intervention e.g. Transvenous ICD or subcutaneous? Inconsistent terminology. MI is used throughout , but in paragraph 6, non-St segment elevation ACS is used, instead of MI.	Thank you. We have removed the word "wearable". This is a secondary prevention population. Agreed. References to MI have been replaced with ACS in this section.	
4.3.3	JA	It might help to clarify that post infarct a repeat echo/MUGA/MRI in 4–6 weeks' time after institution of full or reasonable medical therapy will allow better appreciation of EF% and better define need for ICD. The repeat echo should really be essential to ensure those needing an ICD do not miss the opportunity to be offered one.	Agreed. This recommendation was retained from the previous version of the guideline and the evidence has not been re-appraised. Therefore we are not aware of any evidence for the six week period, which we assume is pragmatic, however after discussion the GDG felt that increasing the detail in the recommendation would be likely to lead to improved monitoring and we have revised the wording to "All	

		Where such imaging shows 36–40% EF then we should advise EPS to see if monomorphic VT can be induced to justify ICD offer.	patients with ST-elevation ACS should undergo assessment of LV function for risk stratification at least six weeks following the acute event.” The GDG is not aware that this is routinely performed and is not consistent with current UK guidelines. However, see section 5 on arrhythmias in chronic CAD (and also SIGN 147 on heart failure).	
	PS	Assessment of LVF is an issue due to difficulty in obtaining echocardiograms	Noted.	
Section 5				
5.1.1	AR	Perhaps there should be a pointer to this much fuller explanation of AF in the previous section where it is mentioned?	Noted. Earlier section was limited to AF in ACS, so this fuller description is more relevant here. A cross reference has been added to section 4.1.	
	BCS	There is good recent data, including randomised controlled trials, looking at the effects of lifestyle changes on AF management. These highlight the benefits of weight loss and exercise in reducing AF burden. I think it is important that something is added to the document in relation to this. I am sure Derek Connolly can provide more information.	Thank you. Agreed – however, these issues were not included in the key questions at the time of this update. We have added two paragraphs on this subject.	
	PS	Importance of AF	Noted	
	RCPE	The College is generally supportive of this draft guideline; however we note that in the section on Atrial Fibrillation (AF), there is only one sentence with regard to antithrombotic therapy management, referring to another guideline. Stroke prevention is the cornerstone of AF management (perhaps the most important, given that strokes in AF have major mortality/morbidity) and therefore we suggest more emphasis on the importance of appropriate thromboprophylaxis should be made.	Thank you. Antithrombotic therapy is considered in greater detail in SIGN 129 where an entire chapter is dedicated to the management of atrial fibrillation.	
5.1.2	AMC	An often unappreciated amiodarone side effect is neuropathy, usually never asked about when reviewing patients for amiodarone toxicity. Amiodarone has many drug interaction, not just with warfarin. The	Agreed. We have removed the statement about warfarin and replace with “Amiodarone has a long half-life and is associated with many drug	

		<p>current sentence gives the impression that this is the only important drug interaction (see earlier comment about digoxin interaction).</p> <p>Dronedronone: Emphasis is made of the meta-analysis by Chatterjee in 2012 showing a trend for increased all cause and CVS mortality and HF with dronedarone across a wide spectrum of population, there was heterogeneity in the treatment effects (adverse outcomes but also reduced hospitalisation for AF) which may have been related to the very heterogeneous patients in the meta-analysis. In fact this was subsequently shown by another meta-analysis (<i>Europace. 2014 Aug;16(8):1117-24</i>) where this heterogeneity of outcome depended on baseline patient clinical criteria. These analysis showed that patients with permanent AF were at most risk of CVS mortality and HF hospitalisation, and in those with non-permanent AF, there was benefit in terms of CVS hospitalisation. Indeed, the FDA approval for dronedarone is within these narrow confines of patient's criteria (PAF patients in SR or in AF planned for CV, with CVS risk factors, to reduce risk of CVS hospitalisation. A more recent systematic review (referenced in para 3, page 18 9, ref 94) found sotalol but not dronedarone to be associated with increased all-cause mortality.</p>	<p>interactions, including medicines frequently used in patients with CHD, such as atorvastatin, warfarin and digoxin (see BNF for a complete listing)".</p> <p>Thank you. The GDG has considered this evidence and the recommendation is consistent with these points. No change required.</p>	
	AR	<p>Appropriate mention of the risks of amiodarone but why no mention of risk of QT prolongation and Torsades with sotalol here?</p>	<p>Agreed – the warning about contraindication for sotalol in Torsades de pointes and a cross reference to 3.4.5 have been added.</p>	
	NC	<p>p18. 5.1.2 The text suggests that class 1a AAD are not to be used for treatment of AF in patients with IHD as increased mortality in trials.</p> <p>Is the evidence strong enough to make this a recommendation? A similar recommendation is made later in guideline with class 1 agents for ventricular arrhythmia.</p>	<p>Yes. The evidence is robust and we note similar recommendations in the ESC and NICE guidelines.</p>	
	PB	<p>The good practice statement that 'Patients taking amiodarone should.... have baseline set of lung function</p>	<p>Agreed. The SPC of amiodarone states that "Consideration should be</p>	

		tests including DLCO is not current practice at least in Aberdeen or anywhere else I have worked. This was after discussion with our chest physicians. Use of such inconvenient, expensive tests should be justified with some data.	given to a carry out a chest X-ray before starting therapy.” Clinical experience suggests that lung function tests are only required if toxicity suspected. We have removed the reference to lung function testing and replaced with chest X-ray.	
	PS	Importance of amiodarone then dronedarone	Noted	
	PSo	No comments Not in the scope of SIGN but would it be worth that a group of pharmacists developed a standard information leaflet for amiodarone to ensure all patients across Scotland receive the same information?	Noted. Comment passed to Scottish Patient Safety Programme – Medicines team and Royal Pharmaceutical Society representative on SIGN Council.	
5.1.3	PB	The benefits of rhythm control with catheter ablation over medical therapy especially in the heart failure population has recently been supported by the publication of the CASTLE-AF study. This should be acknowledged and stated.	Thank you. We have reviewed and added a paragraph (para 7) to the section on catheter ablation for atrial fibrillation (5.1.5) to describe CASTLE-AF. A new recommendation has also been added.	
	PS	Importance of rate control not new	Noted	
5.1.4	JA	Strict rate control rather than lenient should be first line if there is a possibility of the AF rate actually causing the deterioration in LV function.	Noted. This may be true – but this has not been rigorously assessed in clinical trials.	
	PB	Good practice point in poorly controlled AF is to ensure the patient is euthyroid. The good practice point that is stated is unclear in its meaning.	While the GDG believes that this GPP is straightforward and clear, we have added a further GPP <i>“Thyrotoxicosis should be ruled out in patients with AF and poorly controlled ventricular rate.”</i>	
	PS	Importance of lenient rate control vs strict control important recommendation	Noted. Thank you	
5.1.5	AR	I think CASTLE-AF merits a mention here - I appreciate it won't have been out when the guidelines were being developed but seems worthy of a mention. Sensible recommendations when it comes to catheter ablation. Sensible section re cross-over between flutter/fibrillation and need to	Thank you. We have reviewed and added a paragraph (para 7) to the section on catheter ablation for atrial fibrillation to describe CASTLE-AF. A new recommendation has also been added.	

		keep that in mind when looking at anticoagulation.		
JA		<p>Highlight the fact that late referral for AF ablation is more likely than not to affect success rates as one has to avoid conversion to persistent AF so as to preserve better ablation success rates when the patient with PAF is offered an ablation.</p> <p>Once on a rhythm control drug for symptomatic PAF close FU may be needed to ensure prompt ablation offer is available.</p> <p>No mention is made of modifiable risks, while all know about TFT there are more common and effective risks to be modified, namely BMI>27 (applicable to all stages of AF treatment), HT management, OSA, most AF treatments will be futile if untreated OSA is not diagnosed and addressed. These measures may be highly successful.</p>	<p>Probably true, and backed up by observational studies – we’ve already mentioned the “ablation as first-line Rx” studies – no further change is needed.</p> <p>As in guidelines, ablation is a treatment for symptoms. No amendment needed to guidelines.</p> <p>Agreed, two paragraphs on weight management have been added to section 5.1.1.</p>	
NC		<p>p22. 5.1.5. Presumably all patients undergoing AF ablation (not just early strategy) should understand the risks. Can't think of a situation where one would undertake this if they didn't. From the data presented risk of a serious procedural complication in patients undergoing ablation as a first line treatment for AF is approaching 1 in 25.</p> <p>Is the evidence of benefit strong enough to justify this as a recommendation?</p>	<p>Agreed. On balance we prefer to remove “who understand the risks of this procedure” to the current recommendation rather than add them to all. The provision of full information about the risks and benefits of any intervention is implicit in the consideration of any appropriate therapy.</p> <p>The evidence is strong enough to support a conditional recommendation to consider the use of this intervention.</p>	
PB		<p>Might be worth mentioning the emerging role of His bundle pacing in this situation. In the section on catheter ablation for atrial flutter, the last sentence in the first paragraph is technically incorrect, this centres around the use of the term 'typical' atrial flutter. This might suggest that atypical atrial flutter is not cavotricuspid isthmus (CTI) dependent but from an electrophysiological perspective</p>	<p>The GDG notes that His bundle pacing has not (yet) been subject to RCTs.</p> <p>Atypical flutter can include clockwise RA flutter but may also include other mechanisms. We have added further clarification</p>	

		typical and atypical refers to the direction the flutter passes through the isthmus (counterclockwise or clockwise).	of the difference between typical and other forms of flutter.	
	PS	Catheter ablation if patients are more symptomatic. This includes LVF. This is more common in older patients but risk of this procedure is greater in the elderly. Will there be an age cut off?	Thank you. The evidence for the size of benefit and risk stratified by age have not been evaluated, however we have emphasised the issue in the sentence " <i>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</i> ". Decisions around ablation will be made jointly by patient and HCPs on an individual basis taking all relevant factors into account (including age).	
5.2.2	JA	RBBB may be included in the NICE guideline and it has very poor evidence for use of CRT despite a wide QRS, in fact CRT may cause harm in RBBB. Would it be possible to tidy up NICE advice on this as RBBB is not a routine CRT indication and increasingly LBBB and greater QRS width are key predictors?	This section describes the NICE MTA but does not discuss RBBB. Table 1 shows indications for ICD or CRT using NYHA class, QRS interval and presence of LBBB as criteria. No action required.	
	KS	re "...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." this should not be restricted to patient also their families as there are many concerns and misconception about such therapies within families	Noted, however some patients may not consent to this information being shared with family.	
5.2.3	Med	Acknowledging the evidence in this section was not reappraised, in light of the NICE TA 314 and the significant Individual patient network analysis that informed the recommendations, which is included in the draft SIGN update, p23 5.2.2. The cost effectiveness statement contained in the paragraph on the bottom of page	Agreed. Paragraph has been removed.	

		25 is now factually incorrect and we respectfully ask that this be removed or amended with reference to the contemporary evidence and data.		
5.2.7	AR	Agree with inclusion of catheter ablation option.	Noted. Thank you	
	JA	Brief mention should be made of adjuncts to ablation in storm and a brief expansion of the optimised medical therapy, ie sedation, optimised HF therapy, exclusion of ischaemia, GA or rarely thoracic epidural.	All these therapies are mentioned in the quoted meta-analysis but each has not been subject to rigorous evaluation. This is a highly specialised field. No change required.	
	PB	It might be worth stating that catheter ablation should be considered in patients with symptomatic electrical storm - occasional patients have frequent VT, often treated by ATP and who are unaware of the episodes or the ICD intervention. Little evidence to support routine invasive ablation in this situation.	Noted, however this is of relevance only to the very small number of ablationists in Scotland. No change required.	
Section 6				
6.2	KS	There has been a significant increase in emphasis on the importance of risk and lifestyle factors on the outcomes associated with AF eg QoL this was a very prominent topic in recent ESC heart rhythm meetings and features highly in the nice and ECS guidelines of AF management	Noted. These are general comments and addressed by additions to previous sections.	
6.4.1	AMC	Comment regarding AAD? Amiodarone versus sotalol?	This structure was retained from the previous guideline, however is confusing, so we have moved the first and third bullet points in the recommendation to section 6.4.2, leaving the relevant second bullet point within this section on pharmacological therapy. We have also added a description of the NICE guideline's review of the cardioversion evidence to support the moved recommendations, as the original recommendation was based on guideline evidence in 2007.	
6.4.3	AR	First recommendation is missing bold for "(paroxysmal or persistent)".	This is consistent with SIGN style.	
	JA	Should surgical AF ablation be subject	Studies are inconsistent in	

		to proof they have isolated the antral area... this should be an accepted endpoint rather than just apply ablation...?	the extent to which they define methods. This is highly specialised. No change required.	
6.5	JA	For VT and VF surrounding recent CABG you have not mentioned consideration of re imaging of grafts.	This section has not been revised, and the references have not been re-evaluated in this update.	
6.5.1	AR	Was surprised to see this needing a sub-section to itself, but presumably must still be an area of debate within cardiac surgery? I can't think of any external non-surgical defibrillators in recent years that have been monophasic!	Noted. We have removed this section as no longer relevant.	
Section 7				
7.1	KS	There has been significant investment if specialist nursing roles in these areas eg BHF service development funding to address psychological and lifestyle issues through an integrated approach to care	Thank you. Noted	
	MO	This section is clear and informative.	Thank you	
7.2.1	KS	<i>Patients with chronic cardiac arrhythmias and cardiac arrest should be screened for anxiety or depressive disorders with referral to specialist psychology services where appropriate</i> although I agree with this there is a level of psychological support which can be provided before the need for specialist psychology intervention, this can be provided through integrated services, specialist nurses in arrhythmia and rehabilitation service. Again link to the NICE and ESC guidelines about the role of these nurse and integrated services is omitted	We are unable to identify any arrhythmia-specific evidence in HRA, NICE or ESC around psychological care, stepped care or an integrated multidisciplinary approach. We have added a link to SIGN 150 - " <i>SIGN 150: cardiac rehabilitation recommends a matched-stepped-care model for delivering psychological therapies for patients with depression and a chronic physical health condition.</i> "	
	MO	Good section	Thank you	
	PS	Important screening post cardiac arrest	Thank you	
7.3	KS	I think this is an area of need which should not be underestimated for patients and carers - there are a number of qualitative studies in this area	Noted. Thank you	
	MO	Good Section. Paragraph 3 – psychosocial adjustment difficulties more common	Thank you. A word was omitted from	

		in ICD recipients younger THAN age ... - I'm assuming it's meant to say 'younger IN age'.	this sentence in the draft. It has now been restored and reads "Psychosocial adjustment problems are more common in ICD recipients younger than age 50."	
7.4	CHS	As per the OHCA Strategy for Scotland we anecdotally know people are struggling psychologically, particularly following an OHCA. While we recognise the benefits of CBT as a key component of psychological support we would also advocate to highlight the benefits of Peer Support. There is a growing body of evidence to support this and it is the experience of CHSS that peer support is a key factor for engagement and sustained change.	Thank you. We have emphasised this issue in the Provision of Information Section (section 8) listing for CHSS. We did not look at the evidence base for peer support and this is not included in SIGN 150.	
	JA	Why is there no mention in this section on the role of arrhythmia nurses? They are a valuable resource and most patients benefit from their presence greatly.	Thank you. This was not part of our remit. Not all health boards in Scotland have funding for specialist arrhythmia nurses.	
	KS	This section touches on CR and its role in arrhythmias. This should link into the Cochrane review of Exercise-based cardiac rehabilitation for adults with atrial fibrillation - published in Issue 2, 2017. Recognising however exercise is not the only component - dispelling misconception providing education and psychological support are all part of an integrated service and high on the HRA, NICE and ESC agendas	This Cochrane review 2017 notes that the exercise approach led to no clinically relevant impact on QOL but may increase exercise capacity. We are unable to identify any arrhythmia-specific evidence in HRA, NICE or ESC around psychological care, stepped care or an integrated multidisciplinary approach. We have linked to SIGN 150 " <i>SIGN 150: cardiac rehabilitation recommends a matched-stepped-care model for delivering psychological therapies for patients with depression and a chronic physical health condition.</i> "	
	MO	Good section	Thank you.	
	PS	Important intervention but shortage of psychologists	Noted. Thank you.	
7.5	AMC	A comment on caution if patients are on concomitant medications that prolong QT, particularly anti-arrhythmic drugs, because of risk of	Thank you. A comment about risk of coprescribing of drugs which may prolong the QT interval	

		polymorphic VT. A very information website re QT prolonging medications could be referenced. www.crediblemeds.org	has been added to section 7.5 and the CredibleMeds website has been included in the Provision of Information section.	
Section 8				
General	PS	No issues	Noted	
8.1	PS	Important to have patients friendly guideline.	Noted. Thank you	
8.2	AMC	www.crediblemeds.org	Thank you. This has been added to the Provision of Information section.	
	PS	No issues	Noted	
8.3	PS	Adequate	Noted. Thank you	
Section 9				
9.1	PS	No issues	Noted	
9.3	PS	Important areas for audit	Noted. Thank you	
Section 10				
10.1	KS	Clear process	Noted. Thank you	
	PS	No issues	Noted	
10.1.1	KS	Description of process clear however I think there is some important literature which has been omitted in this part	Section 10 does not include literature.	
	PS	No issues, standard practice.	Noted	
10.1.2	KS	Clear process	Noted. Thank you	
	PS	No issues	Noted	
10.2	KS	Again omits any potential greater exploration of psychological effects of arrhythmias and their management implementation and evaluation of arrhythmia specialist nursing services	Thank you. One key question was allocated to psychosocial interventions. The implementation and evaluation of arrhythmia specialist nursing services was outwith the remit of this update.	
	PS	Research on hypothermia seems appropriate. the difficulty will be identifying neuro criteria	Noted. Thank you	
10.3	AR	SIGN email address should be clickable link (as were the ones in earlier section for charities)	Thank you. This has been corrected.	
	KS	Should be consider in the recommendations in nice and esc now re lifestyle factors, integrated care and rehabilitation	We do not understand this comment.	
	PS	No issues	Noted	

Annex 1				
	KS	<p>In patients with arrhythmias do psychosocial interventions reduce the use of hospital resources/readmissions?</p> <p>Should not all be about reducing readmission but about what's important to patients eg self-efficacy, self-management, less anxiety and depression and improved quality of life.</p>	<p>Thank you. The GDG decided that there was no reason to doubt that psychosocial interventions were as effective in reducing anxiety and depression as they are in the general population. The question therefore focuses on specific cardiac and service delivery outcomes.</p>	
Annex 2				
	AMC	<p>Class III should state potassium channel blockers.</p> <p>Inconsistencies: it is mentioned that sotalol has also class II actions, but amiodarone also has class I, II and IV actions, but this is not mentioned.</p> <p>Perhaps consider describing the electrophysiological effect which may be more informative eg Class I, slows conduction (prolongs PR, QRS), class II; slows heart rate and AVN conduction, class III; prolongs repolarization (prolongs QT)</p> <p>Class IV: slows sinus rate and AVN conduction.</p>	<p>After discussion, the guideline development group has agreed that the Vaughan Williams classification is now rather general and may not provide helpful information. The NYHA classification refers to heart failure and is included in the introduction to SIGN 147. Therefore we have removed annexes 2 and 3.</p>	
	KS	Clear	Noted. Thank you	