

National Institute for Health and Care Excellence
Atrial Fibrillation
Guideline Consultation Table
15/01/14-26/02/14
MASTER

ID	Type	Stakeholder	Order No	Document	Page No	Line No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
8	SH	ABPI SAFI (Stroke Prevention in Atrial Fibrillation Initiative)	1	FULL	General	General	<p>About ABPI SAFI The Association of the British Pharmaceutical Industry (ABPI) Stroke in Atrial Fibrillation Initiative (SAFI) was created in 2012 to improve patient access to the Novel Oral Anticoagulants (NOACs) for the prevention of non-valvular AF-related stroke. ABPI SAFI has five members, all research-driven pharmaceutical companies that have developed and are marketing a NOAC or plan to launch in the near future. Our members are Bayer Healthcare; Boehringer Ingelheim; Bristol-Myers Squibb; Daiichi Sankyo and Pfizer.</p> <p>ABPI SAFI welcomes this draft updated NICE guideline on Atrial Fibrillation and the opportunity to comment on it. The inclusion of the NOACs in the update is welcome as they represent a major advance in treatment of patients with Atrial-Fibrillation-related stroke. Some of the pharmaceutical companies involved in ABPI SAFI will also take the opportunity to comment</p>	Thank you for your comment.

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							<p>individually through separate submissions. Management of Atrial Fibrillation (AF) is currently sub-optimal. AF is a major risk factor for stroke leading to a five-fold increase in risk (Wolf PA, Abbott RD, Kannel WB. Atrial fibrillation as an independent risk factor for stroke: the Framingham study. <i>Stroke</i> 1991; 22: 983–88) For this reason alone, optimal management of this serious condition is crucial to the outcome of patients, the UK health economy and wider society as a whole.</p> <p>The poor standard of current NHS management of AF has recently been reflected in the draft report for the National Screening Committee http://www.screening.nhs.uk/atrialfibrillation reviewing screening for Atrial Fibrillation for people aged 65 and over authored by Dr Martin Allaby, Consultant in Public Health, Solutions for Public Health. This report reviewed the introduction of screening against the UK National Screening Committee criteria for viability, effectiveness and appropriateness. In his conclusions Dr Allaby conceded that whilst “a national screening programme for atrial fibrillation in people aged 65 and over would produce more benefit than harm at a population level, and be cost-effective” currently “NHS management of AF that is detected through routine clinical practice is known to be frequently</p>	

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							poor, both because patients who should receive anticoagulants do not receive anticoagulants, and because treatment with warfarin is often problematic." He continued to conclude that for this reason "it would be unethical to introduce a screening programme without being confident that screen-detected patients would be well managed." This is a very sad reflection on the current state of NHS AF management.	
277	SH	All Party Parliamentary Group on Atrial Fibrillation	1	FULL	General	General	The All-Party Parliamentary Group on Atrial Fibrillation (APGAF) welcomes the publication of the draft guideline on AF. APGAF is chaired by Glyn Davies MP and the secretariat is provided by the AF Association. The purpose of the group is to raise awareness of the issues affecting patients with AF, and to work to ensure the diagnosis, care , treatment and management and research of AF is a priority for the NHS.	Thank you for your comment.
128	SH	Arrhythmia Alliance, The Heart Rhythm Charity	16	FULL	General	General	A-A would like to thank the Committee for producing a comprehensive set of documents which makes clear the considerations, priorities and NICE approved therapies and treatments for optimal management of AF in England, Wales and Northern Ireland.	Thank you for your comment.
179	S	British	1	FU	Ge	Ge	The British Heart Foundation (BHF) is the nation's	Thank you for your comment.

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	H	Heart Foundation		LL	neral	neral	<p>leading heart charity. We are working to achieve our vision of a world in which people do not die prematurely or suffer from cardiovascular disease. In the fight for every heartbeat we fund ground breaking medical research, provide support and care to people living with cardiovascular disease and advocate for change.</p> <p>The BHF is committed to helping to detect undiagnosed atrial fibrillation. This includes raising public awareness of how a simple pulse check can help to identify an irregular heart rhythm. GPs can then assess the patient and, if confirmed as atrial fibrillation, this can be effectively managed.</p> <p>In order to ensure that as many people as possible who have atrial fibrillation (AF) are diagnosed and treated, alongside supporting the addition of pulse checks in NHS health checks we also support opportunistic pulse checks when people potentially at risk are in contact with the health service. Pilots offering pulse checks for patients attending flu clinics and integrating pulse checks into chronic disease management templates have demonstrated that this is an effective and cost effective way to ensure that people living with undetected AF are identified.</p>	

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							<p>We therefore warmly welcome the proposed guidance on AF which will build on the Quality and Outcomes Framework which has helped to incentivise detection and treatment of people living with AF.</p> <p>If you have any queries regarding this response please contact Joseph Clift, Policy Manager, cliftj@bhf.org.uk</p>	
251	SH	British Hypertension Society	1	FULL	General	General	The BHS welcomes a fresh look at AF. The available document is certainly comprehensive at 311 pages. The ESC Guideline on AF is 61 pages long which seemed sufficient in 2011. Our response will concentrate on the algorithms.	Thank you for your comment.
256	SH	British Hypertension Society	6	FULL	General	General	Recommend specific comment about low CHADS-VASC risk over 10 years.	Thank you for your comment. An important aspect of the new guideline relating to this patient group is that following an initial decision that the risks at the commencement of the 10 year period referred to do not warrant anticoagulation, the patient will remain under annual review and, should the risks increase, as they will inevitably with time in any case, the decision can be reconsidered.
257	SH	British Hypertension Society	7	FULL	General	General	Recommend specific comment about NOACS v Warfarin, in the light of the 2013 meta-analysis.	Thank you for your comment. NICE already has guidance (technology appraisal) in this area and it was

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		ion Society			al	al		not appropriate to review individual NOACs within this guideline. The technology appraisals have been fully incorporated in this guideline.
90	SH	Department of Health	1	FULL	General	General	<p>Thank you for the opportunity to comment on the draft for the above clinical guideline.</p> <p>I wish to confirm that the Department of Health has no substantive comments to make, regarding this consultation</p>	Thank you for your comment.
150	SH	MEDTRONIC LIMITED	5	FULL	General	General	<p>Medtronic presents new evidence which was not available at the time of the scoping exercise for the updated guidance and so we would like the GDG to consider including a new section on the use of enhanced pacing modalities for patients with bradycardia in order to slow the progression of AF in this patient group and suggest an additional section be added as "The use of Enhanced Pacing Modalities for patients with Bradycardia who are at risk of AF"</p> <p>New Evidence presented at the American Heart Association's Scientific Sessions in November 2013 shows that Medtronic Pacemakers with enhanced pacing features have the ability to slow down the progression of AF in patients with Bradycardia. The results of the MINERVA (MINimize Right Ventricular pacing to prevent Atrial fibrillation and heart failure) study found that Medtronic pacemakers with atrial antitachycardia pacing</p>	Thank you for your comment. The GDG did not prioritise a question on modalities of pacing. We will consider this evidence when we update the guideline.

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							<p>(Reactive ATP(TM)), managed ventricular pacing (MVP®) and atrial intervention features were able to significantly decrease the incidence of mortality, cardiovascular hospitalizations or permanent AF at two years compared to pacemakers without these features. The effects of these features were most evident by a significant delay in the progression of atrial tachyarrhythmias to permanent AF, with a 61 percent relative risk reduction at two years.</p> <p>The study's primary objective was to evaluate whether the combination of these features reduces the composite incidence of mortality, cardiovascular hospitalizations or permanent AF at two years compared to standard pacing. Enrolled patients had standard indications for dual-chamber pacing and prior atrial tachyarrhythmias and were without complete heart block or permanent AF. The study found that DDDRP (dual chamber pacing with rate response and antitachycardia pacing) +MVP patients experienced a 26 percent reduced incidence (p=0.04) of the composite endpoint compared to standard paced patients. The effects of DDDRP+MVP were primarily driven by the 61 percent relative risk reduction in the progression to permanent AF (p=0.004).</p> <p>Delays in AF progression were noted by significant</p>	

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							<p>reductions with DDDRP+MVP in the risk of AF episodes lasting longer than one day and persistent AF episodes. Impact to expensive health care utilizations was also observed by a 52 percent relative reduction in AF-related hospitalizations and emergency room visits ($p < 0.0001$).</p> <p>Giuseppe Boriani, M.D., Institute of Cardiology at the University of Bologna, Bologna, Italy, lead author and presenter of the MINERVA study at the meeting said "This is the first study to show that using these enhanced pacing features in combination not only delays the AF disease progression, but also has an impact on health care utilization. Based on this compelling evidence, an update of society guidelines should be considered."</p>	
151	SH	MEDTRONIC LIMITED	6	FULL	General	General	<p>Medtronic presents new evidence which was not available at the time of the scoping exercise for the updated guidance and so we would like the GDG to consider including a new section on the value of "Device Detected AF and risk for stroke". In the study by Boriani et al European Heart Journal 10.1093/eurheartj/eh491 2013 "an analysis of < 10,000 patients from the SOS AF Project (Stroke prevention On Strategies based on Atrial Fibrillation information from Implanted Devices) the study</p>	Thank you for your comment. This was beyond the scope of the guideline.

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							<i>assessed the association between maximum daily AF burden and risk of stroke. Cardiac implanted electronic devices (CIED) enhance detection of AF, providing a comprehensive measure of AF burden. During a medium follow up of 24 months, 43% of 10,016 patients experienced at least 1 day of at least 5 minutes of AF burden and for them the medium time to maximum AF burden was sixth months. A Cox regression analyses adjusted for the CHADS2 score and the anticoagulants baseline demonstrated that AF burden was an independent predictor of ischemic stroke. Among the thresholds of ischemic burden that was evaluated 1 hour was associated with the highest Hazard ration (HR) for ischemic stroke i.e. 2.11 (95% CI 1.22-3.64, p value 0.008). Conclusion: Device detected AF burden is associated with increased risk of ischemic stroke in a relatively unselected population of CIED's patients. This finding may add to the basis for timely and clinically appropriate decision-making on anticoagulation treatment."</i>	
1	SH	Merck Sharp & Dohme	1	FULL	General	General	MSD appreciates the opportunity to comment on the draft Atrial Fibrillation clinical guideline. I can confirm that MSD have no comments.	Thank you for your comment.
193	SH	Resuscitation Council	1	FULL	General	General	Thank you for giving the Resuscitation Council (UK) the opportunity to provider stakeholder feedback on these documents. This is attached. We	Thank you for your comment. We have corrected the English and punctuations.

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		(UK)					<p>congratulate the GDG on producing a carefully considered set of clinical guidelines and hope that our comments are helpful and constructive.</p> <p>As we have mentioned in our feedback, the documents require a good deal of careful editing and formatting to correct very large numbers of errors of punctuation and use of English, which risk distracting some readers and detracting from the credibility of the guidance.</p>	
40	SH	Royal College General Practitioners	30	FULL	47	All Algorithms	Font size too small to read even with glasses	Thank you for your comment. We have simplified the algorithms, and enlarged the font size.
67	SH	Royal College General Practitioners	56	FULL	115		Then para below says that gender effect small and CHADSVASc 1 is low risk. Need to also consider the treatment options and would these low risk men be allowed a NOAC under NICE TA or condemned to warfarin??	Thank you for your comment. You are correct, there is a very small sub group of patients with a CHA ₂ DS ₂ -vasc score of 1, who would be risk stratified for anticoagulation, but would not fulfil the criteria for a NOAC in the individual technology appraisals. It is a small population and for those men who do not have a risk factor that would meet NOAC licensing requirements, the guideline recommends the consideration of treatment options (which may include warfarin or no treatment) through discussion with a healthcare professional.

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72	SH	Royal College General Practitioners	61	FULL	General		<p>The key points for primary care and commissioning will be advice about ECHO and referral which I think need to be clear. My belief is that it should also be clear which patients can have an up front choice about a NOAC. If we are offering anti coagulation to people at lower risk who would not have been included in the trials and are following TA advice that only people who would have been in the trial can be offered a NOAC unless control is poor then we are offering warfarin to young people over a long period of time with little trial evidence for risk and benefit.</p> <p>GP need to be very clear who can be offered a choice or not.</p> <p>The flow charts need to be very clear because they will develop into patient pathways and become working documents for most non specialists</p>	Thank you for your comment. The recommendations from the technology appraisals were not updated as part of the current guideline update, as described in the section on guideline update on page 11 of the full guideline.
180	SH	Royal College of Nursing	1	FULL	General	General	<p>This is to inform you that there are no comments to submit on behalf of the Royal College of Nursing to inform on the above draft guideline consultation.</p> <p>Thank you for the opportunity to participate.</p>	Thank you for your feedback

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48	SH	Royal College General Practitioners	38	FULL	50	2	Perform a TIMELY ECG	Thank you for your comment. Recommendation 2 within the Identification and diagnosis chapter was not updated as part of the current guideline update, as described in the section on guideline update on page 11 of the full guideline.
49	SH	Royal College General Practitioners	39	FULL	50	8	Again ? 24hr any good for suspected asymptomatic, presumably in people who have had a stroke	Thank you for your comment. Recommendation 3 on Identification and diagnosis was not updated as part of the current guideline update, as described in the section on guideline update on page 11 of the full guideline.
55	SH	Royal College General Practitioners	45	FULL	53	Line 18	Identify modifiable factors such as postural hypotension and social factors	Thank you for your comment. Assessing the cause of falls was not an objective of this guideline and therefore we did not look for evidence on this. Although we agree it would be an important part of clinical practice.
56	SH	Royal College General Practitioners	46	FULL	53	Line 20	Continuously monitor TTR as integral part of INR monitoring process	Thank you for your comment. The guideline recommends that TTR should be calculated at each anticoagulation clinic visit and in this sense monitoring is continuous.
45	SH	Royal College General Practitioners	35	FULL	49	21	Would this also include the need for antiarrhythmic agents as per recent ESC European survey	Thank you for your comment. We would regard it implicit in the recommendation that to discuss the risks and benefits would include a reduced need for antiarrhythmic drugs. We have added this to the linking evidence to recommendation in section 17.4.
52	S	Royal	4	FU	51	21	? Evidence 40 year old hypertensive with	Thank you for this comment. As you imply, this

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	H	College General Practitioners	2	LL			paroxysmal AF?	patient is at low (but not zero) risk. The literature regarding paroxysmal AF suggests that this is not lower risk than persistent or permanent. Hypertension will count as one risk factor. The guideline addresses this patient in a "Consider anticoagulation" category – so it would be anticipated that the low (but not zero) risk would be discussed with the patient and that he together with his doctor would reach an informed decision, reflecting the patient's preferences, on whether or not to commence anticoagulation.
46	SH	Royal College General Practitioners	36	FULL	49	22	? also to add to discuss the need for anticoagulation	Thank you for your comment. This was not a question which was prioritised by the stakeholders or GDG, so the evidence has not been looked at, and a recommendation cannot be made. However the GDG debated your point and a paragraph has been added to the LETR in section 17.4.
53	SH	Royal College General Practitioners	43	FULL	51	25	Prefer not tolerated as all contraindications same except allergy	Thank you for your comment. The draft guideline recommendation 14 pertaining to dual antiplatelet was removed, following stakeholder comments and extensive discussion with the GDG.
58	SH	Royal College General Practitioners	48	FULL	54	25	? mention what is defined as rate control for those who will only read they key points	Thank you for your comment. The GDG have added a definition of rate control to the LETR section 14.2.4 at the end of the 'trade-off between clinical benefits and harms' box.
60	SH	Royal College	50	FULL	55	25	? renal impairment ? eGFR < what level	Thank you for your comment. We do not think we can give a specific answer other than that caution should

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		General Practitioners						apply to patients with any degree of renal impairment.
43	SH	Royal College General Practitioners	33	FULL	48	34	To include CKD eGFR <30	Thank you for this comment. It is absolutely correct that abnormal renal function contributes to the HAS-BLED score. However, the bulleted list referred to here is a list of modifiable risk factors. It did not seem to the GDG that renal impairment would be likely to be modifiable from the viewpoint of correcting bleeding risk – they were of the view that any modifiable renal impairment would in any case already have been corrected.
50	SH	Royal College General Practitioners	40	FULL	50	36	To include stroke risk assessment	Thank you. We have amended the wording of the first bullet point to read 'stroke awareness and measures to prevent stroke' which is inclusive of stroke risk assessment.
61	SH	Royal College General Practitioners	51	FULL	55	30 and 56 line 9	Is Dronaderone first lien rather than amiodarone??	Thank you for your comment. It was beyond the scope of the review to consider amiodarone in comparison with dronaderone, other than to state the contraindications and cautions in their use. The Medicines and Prescribing team at NICE are developing a patient decision tool to support the implementation of this guideline.
159	SH	NHS Trafford CCG	4	FULL	19	14	There appears to be a high number of expert panel members with many declared conflicts of interest	Thank you for your comment. GDG full member declarations were considered in accordance with NICE's declaration of interest policy. Those with a relevant conflict of interest withdrew from the

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								recommendation debate. Invited experts did not participate in writing the recommendations. .
112	SH	Arrhythmia Alliance, The Heart Rhythm Charity	1	FULL	23	23	A-A is pleased that the categories of review and the review questions are inclusive and appropriately linked to the significant patient outcomes.	Thank you for your comment.
247	SH	Bristol-Myers Squibb and Pfizer	10	FULL	30	2.4	<p>Section 2.4 outlines a research recommendation to evaluate whether patients whose anticoagulation is poor, or is predicted to be poor, with warfarin would benefit from changing to a NOAC. This section goes on to say that the threshold of TTR at which a NOAC might offer benefit is unclear.</p> <p>A recent sub-analysis of the pivotal trial evaluating apixaban compared with warfarin in stroke prevention in AF (ARISTOTLE) examined treatment effects in relation to predictions of time in therapeutic range (TTR) on warfarin. This study found that the efficacy and safety benefit associated with apixaban was similar across the ranges of predicted TTR quartiles, whether that was predicted on the basis of the centre average TTR or the individual TTR.</p> <p>This TTR sub-analysis (Wallentin 2013) coupled with the sub-analysis looking at VKA-experienced</p>	<p>Thank you for this comment. We would agree that there are differences between the individual NOAC trials in relation to subgroup analysis related to quality of anticoagulant control in the warfarin group. Although it might have seemed reasonable to anticipate that the benefits of NOACs in comparison with vitamin K antagonists would have been greater in patients with poor anticoagulant control, the evidence from the NOAC trials is not consistent on this aspect. We would suggest that this lack of consistency makes a trial along the lines we have suggested even more appropriate. This guideline and indeed the previous individual NOAC STAs have made the recommendation that patients with poor anticoagulant control on vitamin K antagonists should be changed to a NOAC. However, there is no evidence to confirm that this approach would be effective. If, for example, poor INR control reflected poor compliance, the individual would be unlikely to be any better off on a NOAC. It therefore seems reasonable to us to point</p>

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							<p>patients (Garcia 2013) demonstrates that apixaban is associated with similar results in patients previously treated with warfarin and in patients who achieve both a high or low average TTR with warfarin treatment.</p> <p>As such, we suggest that further research is not necessarily required.</p>	<p>out the lack of evidence in this area and to suggest that these guideline recommendations should be trialled.</p>
252	SH	British Hypertension Society	2	FULL	43	Algorithm 1	<p>The BHS agrees with anticoagulation for men of CHADS-VASC ≥ 1, or women ≥ 2. Our view is that patients with lower CHADS-VASC scores have a lower risk of stroke, but this risk is not zero. We note that Olesen's 2012 study of the Danish population is not referenced. Although not a trial, the epidemiological evidence in this paper shows that a CHADS-VASC 0 score still has a one year risk of stroke of 0.5-1.0%. Or a ten year risk of about 10% (Taillandier et al, JCE 2012). NICE now recommends statins for a ten year CHD risk $>10\%$, so NICE AF should be more specific about anticoagulation where similarly, stroke risk is 10% over 10 years. A non-fatal MI is sometimes an inconvenience, but a non-fatal stroke can be a catastrophe.</p> <p>Ruff 2013 Lancet is not referenced. This important meta-analysis shows the NOACs to be superior to</p>	<p>Thank you for your comment. We acknowledge your point. However at $CHA_2DS_2VASc=0$ (male or female) the risk is so low, even to general population levels, and evidence suggests this low level of thromboembolic event risk does not outweigh the risk or costs of stroke prevention treatment. The economic model took a lifetime horizon, and therefore took into account a longer time horizon in its evaluation.</p> <p>Ruff et al Lancet 2013 E-pub is not referenced, as it appears after the evidence cut-off date and would have been excluded as it compares NOACs to warfarin, and this comparison was outside the scope of the guideline.</p>

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							<p>Warfarin, in stroke prevention and in safety and in mortality outcomes. This is a crucial area of guidance and the BHS believes NICE should be specific about these drugs.</p> <p>Ruff CT, et al. Comparison of the efficacy and safety of new oral anticoagulants with warfarin in patients with atrial fibrillation: a meta-analysis of randomised trials Lancet, Early Online Publication, 4 December 2013 doi:10.1016/S0140-6736(13)62343-0</p>	
11	SH	ABPI SAFI (Stroke Prevention in Atrial Fibrillation Initiative)	4	FULL	44		<p>We believe that patient values and preferences should be more explicitly mentioned at the point at which the decision is made to prescribe an oral anticoagulant. Furthermore, we suggest that the guideline should include a recommendation for anticoagulation treatment to be initiated within the shortest clinically appropriate window and that the absence of the requirement for regular anti-coagulation monitoring should be considered as part of that decision.</p>	<p>Thank you for your comments.</p> <p>The GDG did not look at the evidence in relation to time and the differing regimes for initiation of warfarin or NOACs, and therefore no recommendations could be made on this. However, the GDG have agreed a new recommendation to discuss the options of anticoagulation with the person with AF.</p>
136	SH	AntiCoagulation Europe	1	FULL	44	general	<p>The Algorithm 1 appears to direct VKA(warfarin) as treatment option for stroke prevention when there are three new oral anticoagulants which are now</p>	<p>Thank you for your comment. The algorithm has been edited.</p>

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							<p>available for stroke prevention too and there is no reference to these in this illustration Quality of control is limited to VKA monitoring and time in therapeutic range – and this</p> <p>could be misleading and impact on the choices of anticoagulants currently recommended for AF and stroke prevention. Guidelines for Dabigatran, Rivaroxaban and Apixaban all state ‘ that the decisions to start any of these treatments should be made after an informed decision has taken place’ and therefore we would suggest that the algorithm is reconfigured to include reference to all anticoagulation treatments currently available for this indication.</p>	
183	SH	Boehringer Ingelheim	3	FULL	44		<p>Algorithm is at odds with full guideline:</p> <ul style="list-style-type: none"> • NOACs are positioned below anticoagulation with warfarin and only ‘if poor anticoagulation control cannot be improved’. This is at odds with the NOAC technology appraisals (e.g. TA 249) which position the NOACs at the same level as warfarin. • NOACs are positioned on the ‘NO’ side of the ‘anticoagulation offered’, incorrectly implying that NOACs are not anticoagulants. This has the potential to cause considerable 	Thank you for your comment. The algorithm has been edited.

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							confusion to users of the algorithm.	
7	SH	Nottingham University Hospitals NHS Trust	1	FULL	44	Algorithm	There is no discussion about patient choice. Also, it appears that NOACs are second line (to warfarin). European Society of Cardiology guidelines (2013) suggest that NOAC is preferred to VKA (warfarin). Need to take this into account as all NOACs (at all tested doses) are superior to warfarin in terms of intracerebral bleed (which is the most catastrophic consequence of anticoagulation) and Dabigatran (from thromboembolism prevention perspective) and apixaban (from reducing Intracerebral haemorrhage) are superior to VKA (warfarin)	Thank you, the GDG have agreed a new recommendation about patient choice. The algorithm has been edited appropriately.
37	SH	Royal College General Practitioners	27	FULL	44	Algorithm 1 Stroke Prevention	Box 1 ? also after ablation NOAC box should be on the left hand side as follows AC offered however not clear if this suggests VKA first line or NOAC first line with box in this position?? Do we give the patient an informed choice of all the NICE approved options?	Thank you for your comment. The algorithm has been edited, and the GDG have agreed a new recommendation about patient choice.
265	SH	Bayer Healthcare	2	Full	44	1	There appears to be an inconsistency between the text in the 'NICE', and the stroke prevention algorithm in the 'Full' versions of the draft clinical guideline. This causes confusion as to the true	Thank you for your comment. The algorithm has been edited.

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							<p>intent of the recommendation.</p> <p>The 'NICE' version of the guideline clearly states in section 1.5 - Interventions to prevent stroke (p16):</p> <p>"Anticoagulation</p> <p>Anticoagulation may be with apixaban, dabigatran etexilate, rivaroxaban or a vitamin K antagonist.</p> <p>1.5.1 Offer anticoagulation to people with a CHA₂DS₂-VASc score of 2 or above, taking bleeding risk into account. [new 2014]</p> <p>1.5.2 Consider anticoagulation for men with a CHA₂DS₂-VASc score of 1, and take bleeding risk into account. [new 2014]"</p> <p>The recommendations from the technology appraisals for the three novel oral anticoagulants (NOACs) have also been included verbatim in line with the review decision for these appraisals from April 2013.</p> <p>However, the stroke prevention algorithm in the full guideline appears to suggest that if the decision "<i>anticoagulation offered</i>" is no – then a novel oral anticoagulant (NOAC) could be "<i>offered in accordance with the NICE STAs</i>".</p> <p>(<i>Diagram sent separately</i>)</p> <p>This appears to not only incorrectly imply that the</p>	

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							<p>NOACs are not 'anticoagulants' but also that they are only recommended where vitamin K antagonists (VKAs) are not 'offered', which is not in line with the recommendations from the technology appraisals for these interventions.</p> <p>We are also concerned that there could be patient safety implications if it is not appreciated that NOACs are anticoagulants.</p> <p>We believe that this box belongs on the left-hand side of the algorithm along with VKAs, and it should be made clear that all interventions are options.</p>	
266	SH	Bayer Healthcare	3	Full	44	1	<p>In addition to the above comment regarding the location of the <i>"NOAC offered in accordance with the NICE STAs"</i> box in the stroke prevention algorithm, we also note that the box itself does not actually appear to form an integrated part of the algorithm.</p> <p>As the recommendations from the NOAC technology appraisals have been 'incorporated' into the clinical guideline, so too should they be fully 'incorporated' into the algorithm, so that all NICE recommendations, whether derived from the technology appraisal process or the clinical guideline development process, and how they integrate, can be clearly seen in an unambiguous manner. Any uncertainty could lead to confusion</p>	Thank you for your comment. The algorithm has been edited.

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							<p>and may hinder uptake of NICE recommendations, of which the offer of anticoagulation to people with a CHA₂DS₂-VASc score of 2 or above (taking bleeding risk into account) is a key priority for implementation.</p> <p>We believe that a more accurate representation of the NICE recommendations could be illustrated as shown (Diagram sent separately)</p>	
267	SH	Bayer Healthcare	4	Full	44	1	<p>The current algorithm also implies that left atrial appendage occlusion (LAAO) could be considered if poor anticoagulation control cannot be improved with VKAs, however it should be made clear that it is recommended that LAAO should not be offered “as an alternative to anticoagulation unless anticoagulation is contraindicated or not tolerated” (recommendation 31). This means that NOACs should be considered before LAAO if poor anticoagulation control cannot be improved with VKAs as depicted in the alternative proposed algorithm:</p> <p>(Diagram sent separately)</p>	Thank you for your comment. The algorithm has been edited.
268	SH	Bayer Healthcare	5	Full	44	1	<p>Recommendations 29 and 30 (from the full guideline) related to ‘review’ of interventions to prevent stroke are included in this algorithm, but recommendation 28: <i>“For people with atrial fibrillation who are not taking an anticoagulant,</i></p>	Thank you for your comment. Algorithm 1 has been simplified and has one box pertaining to the important element of review. The GDG felt that it was important to simplify the algorithms rather than add more recommendations.

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							<p><i>review stroke risk when they reach age 65 or if they develop any of the following at any age:</i></p> <ul style="list-style-type: none"> <i>diabetes</i> <i>heart failure</i> <i>peripheral arterial disease</i> <i>coronary heart disease</i> <i>stroke, transient ischaemic attack or systemic thromboembolism</i> <p>is not currently included. We suggest that this important recommendation should also be incorporated into the algorithm as depicted below: (Diagram sent separately)</p>	
241	SH	Bristol-Myers Squibb and Pfizer	4	FULL	44	Algorithm 1	<p>Algorithm 1 on Stroke Prevention does not appear to reflect the written recommendations in Section 1.5 of the NICE guideline. We are concerned that this diagram could be misinterpreted.</p> <p>The only treatment option that appears after the 'yes' arm of the 'anticoagulation offered' diamond leads into 'anticoagulation control for VKAs.' Meanwhile the NOACs appear in a box on their own next to the word 'no.' This could leave the reader with the wrong impression that, if anticoagulation is offered, NOACs are not</p>	Thank you for your comment. NICE already has guidance (technology appraisal) in the area and it was not appropriate to review individual NOACs within this guideline. The technology appraisals have been fully incorporated into the guideline.

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							<p>recommended and only VKA therapy should be considered.</p> <p>We suggest that, in line with recommendation 1.5 of the full guideline, the algorithm should state: <i>Offer anticoagulation to people with a CHA2DS2-VASc score of 2 or above, taking bleeding risk into account. Anticoagulation may be with apixaban, dabigatran etexilate, rivaroxaban or a vitamin K antagonist.</i> It should be made clear that the NOACs are positioned alongside VKA therapy as a first-line option.</p> <p>There is evidence to support a first-line recommendation for apixaban. A sub-analysis of patients treated with apixaban found no significant differences between VKA-naïve and VKA-experienced patients in the primary efficacy and safety outcomes of stroke/systemic embolism and major bleeding (Garcia et al., 2013).</p>	
242	SH	Bristol-Myers Squibb and Pfizer	5	FULL NICE	44 19	Algorithm 1 1.5. 12	<p>Algorithm 1 further differs from Section 1.5 of the NICE guideline with regards to the recommendations for patients for whom poor anticoagulation control cannot be improved (i.e. second-line therapy).</p> <p>The NICE guideline states that 'alternative stroke</p>	Thank you for your comment. The algorithm has been edited.

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							<p>prevention strategies' should be considered for patients with poor VKA control [1.5.12]. The Algorithm also states this, but goes on to suggest that 'alternative stroke prevention strategies' for people unable to achieve control with VKA therapy may comprise of NOACs or LAAO.</p> <p>Clarification should be made that NOACs may be an 'alternative stroke prevention strategy' in patients for whom poor anticoagulation control cannot be improved in the NICE version of the guideline, as it is in the algorithm.</p>	
279	SH	All Party Parliamentary Group on Atrial Fibrillation	3	FULL	44	4.1.2 Algorithm 1	<p>APGAF welcomes the commitment to "not offer aspirin monotherapy solely for stroke prevention to people with Atrial Fibrillation" and "only consider dual antiplatelet therapy with aspirin and clopidogrel for stroke prevention if anticoagulation is contraindicated or not tolerated and the person has a CHA2DS2-VASc score of 2 or above"</p> <p>This is an important and welcome development. Whilst aspirin has only been associated with a stroke risk reduction of only 19 percent, compared to 64 percent for oral anticoagulation, GRASP-AF data shows that 35 percent of AF patients are still being prescribed aspirin. This can be largely attributed to indicators within the Quality and</p>	<p>After comments from other stakeholders, the recommendation referring to the use of aspirin and clopidogrel has been removed from the final guidance. This was because there was concern firstly that after removal of aspirin from the guidance, patients might inappropriately be channelled towards the aspirin / clopidogrel combination and secondly that there would be very few patients in whom all forms of anticoagulation were contraindicated who would not also have a contraindication to aspirin / clopidogrel. The removal of the recommendation does not preclude the use of the combination and indeed its use is still discussed in the LETR.</p> <p>NICE already has guidance (technology appraisal) in</p>

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							Outcomes Framework (QOF) which encourage the use of aspirin and its cheaper cost in comparison to anticoagulants. In order to provide additional clarity about the ineffectiveness of aspirin, it would be helpful if the guideline provided a full comparison with various forms of anticoagulation including NOACS and Warfarin.	the area and it was not appropriate to review a full comparison of NOACs within this guideline. The technology appraisals have been fully incorporated in to the guideline.
278	SH	All Party Parliamentary Group on Atrial Fibrillation	2	FULL	44	4.1.2 Algorithm 1	<p>In order to ensure that AF related stroke is prevented, it is important that any guidance provides clarity as to best practice in this area. However, we are concerned that this algorithm does not provide this certainty and either does not include the required information or is mistaken and confused in many of its assumptions.</p> <p>1) The full guidance identifies the need to provide information for patients, however this is not included within the algorithm. Currently, the process starts with a CHADS VASc and HAS-BLED assessment, however best practice dictates that the next step should be to provide further patient information and discuss available treatment options. Including this within the Algorithm would ensure consistency with NICE CG138 which recommends that patients are supported by clinicians to understand therapy options and benefits alongside the</p>	<p>Thank you for your comments. The algorithm has been altered, and addresses your concerns in points 1 to 4. In regards to point 5 we have updated the stroke prevention algorithm so it does not have this recommendation stated twice.</p> <p>We agree that the NICE interventional procedure guidance 349 recommended that the procedure can be used provided that normal arrangements are in place for clinical governance, consent and audit. This enabled the GDG to make the recommendation that LAAO can be considered if anticoagulation is contraindicated or not tolerated. We do not believe that our recommendation contradicts the NICE interventional guidance (IPG) 349, rather it provides further guidance as to whom it may be most appropriate to offer LAAO based expert opinion of the current clinical and economic evidence base.</p>

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							<p>risks and possible side effects.</p> <p>2) There is a lack of clarity as to what should happen if a patient is not offered anti coagulation. The algorithm seems to suggest that a patient should then be prescribes a Novel Oral Anti-Coagulant (NOAC) however this approach appears confused. It appears to wrongly suggest that NOACs are not a form of anticoagulation or that they are inferior to warfarin. This approach is not backed up by clinical evidence and it is important that the algorithm seems to suggest that NOACs should be considered a second line choice to warfarin. This is incorrect, as dabigatran, apixaban and rivaroxaban have all been subjected to full NICE guidance (TA 248,256 and 275) and none were places as a second line therapy behind warfarin.</p> <p>3) APGAF is unsure why the algorithm places the options for consideration of NOACs or LAAO alongside the "Quality of Anticoagulation Control" box. This seems to wrongly suggest that both options will only be available if there is poor anticoagulation control.</p> <p>4) Placing the "quality of anticoagulation control" box in its current position suggests</p>	<p>The Interventional procedure guidance included one RCT (PROTECT-AF trial) that was included in the guideline review (Holmes 2009). This clinical guideline also had the 2.3 year followed up for this trial (Reddy 2013). The recommendation was also based on findings of an economic evaluation (published after the IPG) that found great uncertainty that the intervention was cost effective. A strong recommendation in favour of routine use of LAAO for all population groups would require evidence indicating a high likelihood that the intervention is cost effective. To note the IPG guidance did not look at different populations of AF within their recommendation.</p> <p>This issue was discussed once again by the GDG following your comments. The GDG remain of the opinion that the treatment is appropriate for patients in whom anticoagulation is contraindicated or not tolerated, and that until longer term follow-up is available, its use should be restricted to this group.</p>

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							<p>that a Vitamin K antagonist is considered the first line choice. It is important that this is amended, as it neither represents clinical best practice nor is consistent with existing NICE guidance.</p> <p>5) The algorithm twice states: “ Do not offer left atrial appendage occlusion (LAAO) as an alternative to anticoagulation unless anticoagulation is contraindicated or not tolerated.” However, this statement contradicts NICE interventional Guidance 349 which states that the condition can be offered routinely as a treatment option for people with non- valvular atrial fibrillation if the patient understands and agrees to the treatment. It is important that further clarity is provided, and that NICE makes clear its current stance with regards to LAAO.</p> <p>APGAF believes that it is important that this algorithm is reworked and its conclusions made consistent with existing clinical evidence and NICE guidelines..</p>	

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113	SH	Arrhythmia Alliance, The Heart Rhythm Charity	2	FULL	44	4.1.2 Algorithm 1	<p>(a) It is suggested that a NOAC may be considered as an alternative to anticoagulation. This is confusing as it is not clear whether this means NOACs should only be used for non-valvular AF patients not currently using warfarin. A-A would suggest the diagram is altered to support published guidance for dabigatran, rivaroxaban and apixaban (TA 249, TA 256, TA 275) in which NOAC are considered equally to warfarin.</p> <p>(b) The NOAC option box appears 'lower' than the LAAO box. We feel this could be mis-leading to clinicians, suggesting that LAAO should only be considered when anticoagulation is contraindicated or not tolerated. We would suggest the algorithm is adjusted.</p>	<p>Thank you for your comments</p> <p>(a) We agree that NOACS are only an alternative to VKA for non-valvular AF. The anticoagulation algorithm has been clarified and the heading altered to make it clear that it refers only to non-valvular AF. The algorithm also refers to the use of the NOACS in accordance with the existing STAs, which relate to non-valvular AF. The decision to commence either VKA or NOAC has been made clearer to be an equal choice in the algorithm decision tree, within the existing STA restraints</p> <p>(b) The algorithm has been altered to make this clear.</p> <p>c) We agree that the NICE interventional procedure guidance 349 recommended that the procedure may</p>

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							<p>(c) In respect of the following statement: <i>'Do not offer left atrial appendage occlusion (LAAO) as an alternative to anticoagulation unless anticoagulation is contraindicated or not tolerated'</i>, this contradicts the NICE Interventional Guidance 349: <i>'This procedure can be offered routinely as a treatment option for people with non-valvular atrial fibrillation provided that doctors are sure that: the patient understands what is involved (particularly that the procedure can cause life-threatening complications in a small number of people) and agrees to the treatment, and the results of the procedure are monitored.'</i></p> <p>LAAO is being commissioned under NICE Interventional Guidance 349 'Commissioning through Evaluation' initiative if the doctor and patient agree, and the patient is informed of the risks and benefits of the procedure. We are concerned that these guidelines suggest limited access to LAAO and thus request this restriction – for which no new data has been offered – is removed. LAAO is an option for patients with non-valvular AF, those at increased risk of stroke and for informed patients who would benefit from consideration of this stroke-prevention treatment.</p>	<p>be used provided that normal arrangements are in place for clinical governance, consent and audit. This enabled the GDG to make the recommendation that LAAO can be considered if anticoagulation is contraindicated or not tolerated. We do not believe that our recommendation contradicts the NICE interventional guidance (IPG) 349, rather it provides further guidance as to whom it may be most appropriate to offer LAAO based expert opinion of the current clinical and economic evidence base.</p> <p>The Interventional procedure guidance included one RCT (PROTECT-AF trial) that was included in the guideline review (Holmes 2009). This clinical guideline also had the 2.3 year followed up for this trial (Reddy 2013). The recommendation was also based on findings of an economic evaluation (published after the IPG) that found great uncertainty that the intervention was cost effective. A strong recommendation in favour of routine use of LAAO for all population groups would require evidence indicating a high likelihood that the intervention is cost effective. To note the IPG guidance did not look at different populations of AF within their recommendation.</p> <p>This issue was discussed once again by the GDG following your comments. The GDG remain of the</p>

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							<p>(d) We would urge NICE to reposition the 'quality of anticoagulation control' box, to avoid confusion in suggesting Vit K antagonist as a first line therapy. We are not aware of clinical data to support this, nor does it appear in NICE STA for alternative OAC (TA249, TA256, TA275).</p> <p>(e) A-A is pleased to see the guideline recommendation: <i>'Do not offer aspirin monotherapy solely for stroke prevention to people with atrial fibrillation. Only consider dual antiplatelet therapy with aspirin and clopidogrel for stroke prevention if anticoagulation is contraindicated or not tolerated and the person has a CHA2DS2VASc score of 2 or above.'</i></p> <p>(f) NICE Guideline CG138 (2012) recommends that patients are guided by their clinician on the benefits and impact of different therapy options. Patients are then able to make informed decisions about the future of their care. We feel strongly that this should be incorporated as part of the algorithm.</p> <p>(g) Finally with regards to the algorithm, in order to address the above concerns over clarity of layout and meaning, we have included some suggested amendments in an algorithm diagram at the end of this document.(sent separately)</p>	<p>opinion that the treatment is appropriate for patients in whom anticoagulation is contraindicated or not tolerated, and that until longer term follow-up is available, its use should be restricted to this group.</p> <p>d). This has been clarified in the algorithm</p> <p>e). Thank-you for this comment. After comments from other stakeholders, the recommendation referring to the use of aspirin and clopidogrel has been removed from the final guidance. This was because there was concern firstly that after removal of aspirin from the guidance, patients might inappropriately be channelled towards the aspirin / clopidogrel combination and secondly that there would be very few patients in whom all forms of anticoagulation were contraindicated who would not also have a contraindication to aspirin / clopidogrel. The removal of the recommendation does not preclude the use of the combination and indeed its use is still discussed in the LETR.</p> <p>f). A new recommendation (recommendation 1.5.4) has been added to this effect and the algorithm altered accordingly</p>

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								g). The algorithm has been clarified and simplified.
253	SH	British Hypertension Society	3	FULL	45	Algorithm 2	Fine	Thank you for your comment.
38	SH	Royal College General Practitioners	28	FULL	45	Algorithm 2	Would you describe rate control here for those who like these flow charts as working documents. Is it rate that matters or absence of symptoms?	Thank you for your comment. We don't include operational definitions within the algorithm. However, we have updated the LETR section to include a definition of rate control in sections 14.2.4
254	SH	British Hypertension Society	4	FULL	46	Algorithm 3	Seems not very clear. BCS and HRUK to comment more, but the algorithm seems to say what not to do, not what to do. PAF rhythm control not easy and a recommendation for specialist referral isn't in the algorithm.	Thank you for your comment. The algorithm has been simplified and clarified. We have endeavoured within the constraints of the evidence and the recommendations to make the tone more positive. While we would agree that in many cases management of paroxysmal AF is more difficult and specialist referral may be warranted, the GDG did not think that this was necessarily a requirement for all patients with PAF and did not think that this warranted a specific recommendation
114	SH	Arrhythmia Alliance, The Heart Rhythm	3	FULL	46	4.1.4 Algorithm	(a) There is no clear indicator of who and when to offer class I AADs to; just a reference of who not to. We recommend a clear consideration of flecainide as equivalent to beta blocker in patients with structurally normal hearts and a low	Thank you for your comment. (a)Thank you for your comment. We agree that this is a shortcoming and that the recommendations are substantially based on which drugs should be avoided

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		Charity				3	<p>CHA2DS2VASc score.</p> <p>(b) In the updated 2012 ESC AF Guidelines, intervention using ablation techniques, in physically active individuals with PAF and no or minimal heart disease, is recommended as a possible first line option. However, the algorithm suggests that drug therapy must be considered and trialled prior to consideration of ablation. Clinical data shows that earlier intervention with ablation in this specific AF population gives better success rates and improves patient outcomes (to return to SR and for their QOL). A-A would ask the Committee to include an option for ablation as a first line option for AF patients with the onset of paroxysmal AF, who are symptomatic, active, and with no or few co-morbidities.</p>	<p>in particular situations. However, the limitation is the lack of evidence. While some GDG members were entirely sympathetic to the views expressed on a preference for Ic agents in patients with normal hearts, there was not an evidence base to justify this practice as a recommendation. The recommendation to trial beta blockers first was based on a strategy of least harm, rather than clinical efficacy. This is the same approach as recommended in the 2010 ESC guideline.</p> <p>b) The evidence for first line ablation is limited and contradictory. The GDG considered it reasonable to recommendation that patients try drug therapy first (if not contraindicated). However, the guideline does recommend that they are then offered the next treatment option (ablation) in a timely fashion (<4 weeks) if this is not successful and/or tolerated.</p>
4	SH	Royal Brompton & Harefield NHS FT	1	FULL	47	Algorithm	The algorithm would flow better if the outcome of the "Is AF permanent" decision box could be swapped with NO on the left and YES on the right. This makes sense temporally when reading the algorithm which asks one to consider catheter ablation for non-permanent AF and to prioritise this over pace and AVN ablate.	Thank you for your comment. We agree with you and have edited algorithm 4 appropriately.
5	S	Royal	2	FU	47	Alg	In the YES part of the same algorithm box, the	Thank you for your comment. We agree with you and

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	H	Brompton & Harefield NHS FT		LL		orit hm	bottom arrow linking" consider a pace and AVN ablate strategy" to "When considering" Could be omitted with an explanation box below it, like in the "NO" path	have edited algorithm 4 appropriately.
281	SH	All Party Parliamentary Group on Atrial Fibrillation	5	FULL	47	9-17	APGAF welcomes the recommendation to provide patients with a "personalised package of care" and "psychological support if needed". However the guidance is currently unclear as to what a package of care should include or what information support networks provide. In order to ensure that these recommendations are translated into effective support for patients, it is important that further clarity is provided as to what a personalised package of care and psychological support would entail.	Thank you for your comment. This has been clarified as part of the amendment to the old recommendation7.
115	SH	Arrhythmia Alliance, The Heart Rhythm Charity	4	FULL	47	9-17	A-A welcomes the recommendation for: ' <i>personalised package of care</i> ' and information, including, ' <i>psychological support if needed</i> '. This will ensure the best quality of life and outcomes for the patient.	Thank you for your feedback.
255	SH	British Hypertension Society	5	FULL	47	Algorithm 4	Seems OK but opening paragraph about "ablate and pace" sets the wrong tone. PVI is important, much more frequently performed than "ablate and pace" so should be given more prominence	Thank you for your comment. The algorithm has now been altered to reflect this.
39	S	Royal	2	FU	47	4.1.	What about anticoagulation after ablation	Thank you for this comment. The GDG did not

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	H	College General Practitioners	9	LL		5		specifically review the evidence on this question.
41	SH	Royal College General Practitioners	31	FULL	47	Line 12	To include stroke risk assessment	Thank you. We have amended the wording of the first bullet point to read 'stroke awareness and measures to prevent stroke' which is inclusive of stroke risk assessment.
116	SH	Arrhythmia Alliance, The Heart Rhythm Charity	5	FULL	48	1-5	A-A supports the recommendation for: ' <i>support networks</i> ' although we feel signposting is important to ensure the uptake of this recommendation.	Thank you for your comment. We agree and have updated the recommendation accordingly.
178	SH	Royal Pharmaceutical Society	1	FULL	48	3-4	<p>The Royal Pharmaceutical Society welcomes the update to the NICE clinical guidelines on the management of atrial fibrillation.</p> <p>We would suggest that it may be useful to clarify which groups of healthcare professionals should be providing the individual elements of the personalised package of care and information. For example, as experts in medicines, pharmacists are well placed to provide practical advice on anticoagulation to patients (in line with NICE clinical guideline 144).</p>	Thank you for your comment. NICE guidelines predominately make recommendations on treatment and processes of care rather than specifying roles of different healthcare professionals. The GDG on this occasion did not prioritise a question pertaining to which health care professional is best suited to deliver the service.

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283	SH	All Party Parliamentary Group on Atrial Fibrillation	7	FULL	48	8-9	APGAF welcomes the recommendation to “Refer people promptly at any stage if treatment fails to control the symptoms of atrial fibrillation and referral for many specialised management is needed”. However, it is currently unclear as to what is understood to be “specialised management”. It is important that this is clarified.	Thank you for your comment. The GDG define “specialist management” as the investigation and further assessment/treatment by a health care professional (such as a cardiologist or nurse with an interest in arrhythmia) with appropriate expertise.
117	SH	Arrhythmia Alliance, The Heart Rhythm Charity	6	FULL	48	8-9	A-A is pleased to see the recommendation: ‘ <i>Refer people promptly at any stage if treatment fails to control the symptoms of atrial fibrillation and referral for more specialised management is needed</i> ’. However, we feel the guideline would benefit from greater clarity on which ‘group’ would meet the criteria for ‘ <i>specialised management</i> ’.	Thank you for your comment. The GDG agreed that it was difficult to list every patient group that might benefit from referral. The GDG provided a generic statement about referral if ‘treatment fails to control symptoms’ and further specialist advice is required. We have amended the footnote to give it greater clarity.
42	SH	Royal College General Practitioners	32	FULL	48	16	To include after ablation	Thank you for this comment. The GDG did not specifically review the evidence on this question
44	SH	Royal College General Practitioners	34	FULL	49	6	I thought that a recent study suggested that the mean time to therapeutic range was 6 weeks and so 50% will be more than this ? would 8 weeks not be better	Thank you for your comment. This was a GDG consensus recommendation and they agreed to exclude measurements for at least the first 6 weeks of treatment. The time specified is to highlight that the loading period should not be included in a TTR

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								calculation.
118	SH	Arrhythmia Alliance, The Heart Rhythm Charity	7	FULL	49	14	In algorithm 1 we do not believe it is reasonable to offer rate control to everyone in the first instance as the suggestion is that only if this fails then rhythm control is considered. Although there is a box suggesting some patient groups in whom an initial rate control strategy could be offered this box does not include young people presenting with persistent AF, or people who already have adequate rate control and have symptoms. The same issue is presented on page 54, line 24 of the full document.	Thank you for your comment. The recommendation has been combined to clarify that rate control is first line and then lists some examples of exceptions. The GDG would like to acknowledge that these are some examples and do not cover all situations. This is not an exhaustive list and we have added a bullet point saying "for whom a rhythm based strategy would be more suitable 1.6.1 last bullet point.
47	SH	Royal College General Practitioners	37	FULL	50	1	? to add and at annual review for hypertension, IHD, Diabetes, stroke and CKD	Thank you for your comment. Recommendation 1 on Identification and diagnosis was not updated as part of the current guideline update, as described in the section on guideline update on page 11 of the full guideline.
147	SH	MEDTRONIC LIMITED	2	FULL	50	2 to 10	Medtronic would like to present very recent and important evidence than is presented in the guidance from 2006 or in the draft updates guidance in support of broader use of . Implantable Loop Recorders with specific AF detection algorithms (Medtronic Reveal XT and Medtronic Reveal Linq) for the detection of Paroxysmal AF in patients with Cryptogenic Stroke and that the guidance reflect this evidence in the section 4.3.3 we suggest "OR AN IMPLANTABLE LOOP RECORDER	Thank you for your comment. Recommendations 2 and 3 on Identification and diagnosis was not updated as part of the current guideline update, as described in the section on guideline update on page 11 of the full guideline.

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							<p>1. Sinha et al 'CRYSTAL AF; 'In 25% to 30% of stroke patients the cause cannot be determined, cryptogenic stroke. The purpose of this study is to identify the incidence of AF and the time to AF in patients with cryptogenic stroke using an insertable cardiac monitor". Design published in American Heart Journal volume 160, number 1, July 2010. Results: presented at a late-breaking science session at the American Stroke Association's International Conference, February 2014: The Reveal ICM discovered AF in 6.4 times more patients than standard care at 6 months (p=0.0006). The trial found that compared to standard care (including electrocardiograms, Holter monitors and other short term diagnostic tests over the follow up period, the Reveal ICM detected AF in 7.3 times more patients at 12 months (p<0.0001) and 8.8 times more patients at 36 months. When followed for 36 months, 30% of the patients in the ICM arm had AF detected. "Compared to standard care continuous monitoring is superior when attempting to diagnose AF in this at-risk population and ICM's offer these patients</p>	

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							<p>new hope. We know that patients with cryptogenic stroke are at increased risk of a subsequent stroke and finding AF allows us to put patients on medication that should be more effective at preventing these second strokes” quotes from Richard A. Bernstein, Professor of Neurology, North Western University, Director of Stroke Program at North Western Memorial Hospital, Chicago USA.</p> <p>2. Ritter et al “Occult Atrial Fibrillation in Cryptogenic Stroke, detection by 7 day ECG v Implantable Cardiac Monitors (ICM), published in Stroke AHA Journals 2013. Methods: 60 patients were included. ICM implanted 13 days after the qualifying event and 7 day Holter monitoring was applied after the implant of the ICM. Results: Intermittent AF (iAF) was detected in 17% of patients by the ICM. Only 1 patient (1.7%) had iAF detected by the Holter monitor as well. Conclusions: ICM offer a greater diagnostic yield than 7-day Holter monitoring</p> <p>3. Cotter et al “The incidence of Atrial Fibrillation detected by implantable loop recorders in unexplained stroke” published in</p>	

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							<p>"Neurology 2103". Methods: 51 patients with cryptogenic stroke were implanted with ILR's following appropriate vascular and cardiac imaging and at least 24 hours of cardiac monitoring. Results: The median (range) of monitoring prior to AF detection was 48 (0 to 158) days. And AF was detected in 25.5% of patients. Conclusion: In Patients with unexplained stroke AF was detected by ILR in 25.5%.</p> <p>4. Rojo- Martinez et al "High Performance in the Implantable Holter in detecting Occult paroxysmal AF in patients with cryptogenic stroke with a suspected embolic mechanism". Methods: Reveal XT was implanted in all patients in whom the exact cause of stroke was not established (101 patients). Results: Paroxysmal AF was detected in 33.7% of patients</p> <p>5. Etgen et al "Insertable Cardiac Event Recorder in detection of AF in Cryptogenic Stroke". Methods: All patients with Cryptogenic stroke and were eligible for OAV were offered an Insertable Cardiac Event recorder. Regular follow up for 1 year recorded the incidence of AF. Results: An implantable event recorder was inserted in</p>	

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							22 eligible patients. At 1 year the AF detection rate was 27%	
156	SH	NHS Trafford CCG	1	FULL	51	14	<p>Page 144 line 26 provides supporting evidence for this statement.</p> <p>Dual antiplatelet versus antiplatelet monotherapy</p> <p><i>Two RCTs^{5,192} in people with AF, of whom 13-15% had a prior stroke, showed that dual antiplatelet therapy had a beneficial effect on reducing the risk of ischaemic stroke compared with single antiplatelet therapy. However, no difference was detected in the risk for all-cause mortality, haemorrhagic stroke, or systemic emboli. Conversely, dual antiplatelet therapy increased the risk of major bleeding.</i></p> <p>Dual antiplatelet versus anticoagulant monotherapy</p> <p><i>One RCT⁶ showed that dual antiplatelet therapy increases the risk of ischaemic</i></p> <p>Is Dual Antiplatelet recommendation safe if reason that anticoagulation contraindicated due to high risk of bleeding . Appears to be based on conflicting evidence base and does not consider wider evidence base about the bleeding risks of using dual antiplatelets in vascular patients (eg</p>	Thank you for your comment. We agree and the GDG after extensive debate have removed this recommendation on dual antiplatelet.

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							<p>MATCH and CHARISMA trials)</p> <p>In the Active A STUDY⁵⁵ Primary endpoint of CVA NNT=42 over 3 years BUT major bleeding NNH= 42 over 3 years</p> <p>NICE draft guidance admits there is a high degree of uncertainty as to which strategy would be optimal in major bleeding outcome.</p> <p>In the Active W study⁶ it was an open randomisation study and patients were eligible to take Warfarin ie a completely different cohort to Active A where the patients were included if unsuitable for Warfarin</p> <p>eg PU within 6 months Hx cerebral haemorrhage Alcohol abuse Platelets < 50 x 109</p> <p>Conclusions that dual antiplatelet therapy should be considered if anticoagulation was contraindicated is therefore not evidence based if contraindicated on grounds of bleeding risk.</p> <p>There is a considerable risk that prescribers will</p>	

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							<p>take the current draft guidance literally (from the summary guidance) and when worried about bleeding risks with Anticoagulants then feel reassured that NICE says OK to give dual antiplatelets.</p> <p>“real “ patients and “clinical trial” patients are very different and the current guidance is highly likely to cause serious numbers of bleeding complications across the UK. The recommendation that if using dual antiplatelets prescribers should consider the need for gastroprotection to reduce risk is hidden in the 418 page full document and not highlighted in the summary document that most busy prescribers will read. Also need to consider use of other medicines which increase risk other than NSAID e.g. SSRI / Bisphosphonate / Steroid use</p> <p>No treatment is the pragmatic clinical decision made in clinical practice for many patients at high risk of bleeding and this should be an option following informed decision making.</p>	

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162	SH	NHS Trafford CCG	7	FULL	51	17	Is use of CHADSVASc in line with manufacturers licence for patients with CHADS2 of 0 but CHADSVASc>1?	Thank you for your comment. We are defining criteria for anticoagulation.
51	SH	Royal College General Practitioners	41	FULL	51	18	And ablation	Thank you for this comment. The GDG did not specifically review the evidence on this question.
160	SH	NHS Trafford CCG	5	FULL	51	22	<p><i>For people with an increased risk of bleeding the benefit of anticoagulation may not always outweigh the bleeding risk, and careful monitoring of bleeding risk is important.</i></p> <p>Guidance is needed around when the bleeding risk outweighs the benefit of anticoagulant. Use of HASBLED is recommended in line 21- can this guide when the risk outweighs the benefit</p>	Thank you for this comment. We can completely understand the desire to have a clearly stated HASBLED value as a “cut-off” for anticoagulant use. This was discussed by the GDG and it was not thought possible to adopt this approach. The contraindications to anticoagulation need to be considered against the degree of stroke risk and hence any “cut-off” value would vary with the stroke risk of the individual patient. The GDG considered that in the majority of patients stroke risk would outweigh bleeding risk. For example, the net clinical benefit (NCB) balancing ischaemic stroke reduction against serious bleeding (eg Intracranial bleeding) is positive in favour of oral anticoagulation or patients with ≥1 stroke risk factors, irrespective of CHA2DS2-VASc or HAS-BLED strata [Friberg et al Circulation 2012, Olesen et al Thromb Haemostat 2011, Banerjee

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								et al.,Thromb Haemostat. The GDG viewed the main value of the HASBLED score as assisting in the identification of potentially reversible bleeding risk factors. This is expressed in the existing recommendations.
282	SH	All Party Parliamentary Group on Atrial Fibrillation	6	FULL	52	1-5	It is encouraging that the guideline identifies the need to establish support networks, providing patients with further information. This is of particular importance, as an APGAF survey of over 650 patients found that 52 percent did not believe that they received any information about the range of treatment and therapy options available to them.. However, it is important that further detail is provided about what information NHS services should provide, and what patients can expect. It is important that these information packs provide patients with details on available options as well as explaining their rights as detailed under the NHS Constitution.	Thank you for your comment. We agree and have amended the recommendation to include 'who to contact for advice if needed' and given examples of support networks.
280	SH	All Party Parliamentary Group on Atrial Fibrillation	4	FULL	52	19-21	APGAF welcomes the decision to move the CHADS2 to CHA2D2-VASc. The CHA2DS2-VASc. Scoring scheme has been shown to outperforming the CHADS2 in identifying truly low-risk patients with AF, and is comparable at identifying high-risk patients.	Thank you for your comment.
119	S	Arrhythmia	8	FU	52	19-	To clarify the CHA2DS2-VASc scoring thresholds	Thank you we have amended this to improve the

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	H	ha Alliance, The Heart Rhythm Charity		LL		21	we recommend the guideline states: 'Female = '1' in all circumstances, except in women under 65 years; it could then be recommended that treatment should be considered for all people with CHA2DS2-VASc of '1' or more.	clarity by adding an additional recommendation to clarify which low risk patients should not have anticoagulation.
191	SH	Boehringer Ingelheim	11	FULL	52151	73	<p>The licensed indication for dabigatran has been updated in SPC 14 (December 2013). We would request that this new wording on indication is acknowledged:</p> <ul style="list-style-type: none"> Prevention of stroke and systemic embolism in adult patients with non-valvular atrial fibrillation(NVAF) with one or more risk factors, such as prior stroke or transient ischaemic attack(TIA), age ≥ 75 years, heart failure(NYHA Class \geq II), diabetes mellitus, hypertension 	Thank you for your comment. This was beyond the scope of the guideline.
137	SH	AntiCoagulation Europe	2	FULL	53	general	<p>24. refers to 'calculating persons time in therapeutic range (TTR) at each visits' As the NOACS do not need to be monitored in the same way as warfarin, patients may prefer to commence treatment on a NOAC to avoid monitoring challenges.</p> <p>25. Indication here is that people may have no option than to start with VKA therapy, and if they are unable to attain TTR, only then will other treatment options be considered?</p> <p>Could this be open to interpretation by prescribers</p>	Thank you for your comment. It has been made clearer on revision that following a decision to commence anticoagulation that this may be with either a VKA or a NOAC. A new recommendation has been added (recommendation 1.5.4) to discuss the options for anticoagulation with the patient. We anticipate that part of this discussion would encompass the need for monitoring with VKA. Obviously the issue of monitoring of control only applies to VKA. The initial choice of anticoagulant and subsequent implications

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							or will the NICE version of AF guidelines be the term of reference where all current therapies are listed in section 1.5 – 'Interventions to prevent stroke'	for monitoring has been clarified in a simplification of the anticoagulation algorithm.
54	SH	Royal College General Practitioners	44	FULL	53	11	Harmful alcohol?	<p>Thank you. In relation to your point regarding harmful alcohol consumption: The 'alcohol' criterion refers to alcohol excess/abuse. For the validation paper a numerical figure was stated as this was needed for a statistical validation. Other published validations have used 'hospitalisation for alcohol excess' and the outcome is unchanged. Different studies define harmful alcohol differently, and therefore we are unable to give an exact definition.</p> <p>Risk scores need to be pragmatic. The GDG agreed to align with the definition used in the 2012 ESC guidelines i.e. alcohol excess or abuse, which is essentially an intake where the clinician assesses there would be an impact on health or bleeding risk.</p>
157	SH	NHS Trafford CCG	2	FULL	53	21	Does this need to make clearer that HAS BLED only validated for Warfarin not NOACS?	Thank you for your comment. The HAS-BLED score has been validated with NOACs and this has been clarified in the LETR in the bleeding risk chapter (Chapter 10).

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212	SH	Resuscitation Council (UK)	20	FULL	53-54	11-17 10-12	Would it not be useful to recommend that measures to reduce bleeding risk may improve the safety of anticoagulation in some people?	Thank you for your comment. We feel that the recommendation do state such measures. Please see section 10 on how to use HAS-BLED score, to address the correctable risk factors for bleeding
57	SH	Royal College General Practitioners	47	FULL	54	1	Why not just recommend an annual stroke risk assessment using CHADVASc for everyone with AF?? And also if they develop concurrent medical problems such as d,hf,,cvd or stroke?	The GDG felt that everybody with AF should have an annual review, and a separate review for those whose status changes.
59	SH	Royal College General Practitioners	49	FULL	55	3	What is unsuccessful rate control?	Thank you for your comment. We have added a definition to the text in the linking evidence to recommendations section 14.2.4
213	SH	Resuscitation Council (UK)	21	FULL NICE	55?	7-9?	Are you recommending consideration of amiodarone use in this way for all people undergoing cardioversion? This will be a major change of clinical strategy and if applied widely will result in much greater use of amiodarone and adverse effects therefrom. At present most people use amiodarone to promote rhythm control in people whose AF has relapsed or proved resistant to an initial cardioversion without amiodarone. Is there really an adequate evidence base for such a radical change of strategy?	Thank you for this comment. The GDG shared these reservations and did not wish to recommend that amiodarone should be routinely used in association with cardioversion. The evidence, nonetheless, suggests a benefit in maintaining sinus rhythm and hence the GDG recommended that it should be "considered". The LETR already expresses reservations on the use of amiodarone in this situation and the recommendation makes clear that these benefits and risks should be discussed with the patient. The GDG did not think that they were able to

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								be proscriptive of the situations when amiodarone should and should not be used, but nonetheless some examples of where it might be more appropriate are included in the linking evidence to recommendation section (LETR).
120	SH	Arrhythmia Alliance, The Heart Rhythm Charity	9	FULL	55	30	Dronedarone should not be continued in patients with AF persisting for longer than 6 months according to its license. This needs to be made clear in the document.	Thank you for your comment. The dronedarone recommendation is from a NICE technology appraisal that has been incorporated ad verbatim into the guideline.
149	SH	MEDTROPIC LIMITED	4	FULL	56	30	Left Atrial Ablation. Medtronic would like the CGD to reconsider the phrase "consider left atrial ablation" to "offer" left atrial ablation given the current body of evidence for this patient group	Thank you for your comment. After careful consideration, we do not agree that this should be offered to everyone with continuing symptoms post drug therapy. There is no evidence that it reduces mortality or stroke. Furthermore patients and clinicians will need to consider the severity of symptoms and risk of the procedure when making their decision.
62	SH	Royal College General Practitioners	52	FULL	58	28	For rate control	Thank you for your comment. We agree and have updated this accordingly.
63	SH	Royal College General Practitioners	53	FULL	60	17	This para recommends targeted screening and should be added as suggested at annual review of those people with concomitant conditions in primary care	Thank you for your comment. Section 5.1 on 'Identification and diagnosis' was not updated as part of the current guideline. Please see page 11 of the full guideline for a description of what was covered

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		ers						during this update.
214	SH	Resuscitation Council (UK)	22	FULL	60	32–33	The wording here suggests a failure to recognise or acknowledge that 'near-syncope' is a very specific symptom and is only one of many forms of 'dizziness'. Some people with AF (especially paroxysmal AF) experience near-syncope. Many other people with AF experience other forms of dizziness that would not be referred to as near-syncope, so it seems unlikely that the term 'near-syncope' was used to mean any type of 'dizziness'. Similarly chest pain is only one of several types of chest discomfort that may be experienced by people with AF, so it is not just terminology that varies among different studies: it is actual symptoms that were included.	Thank you for your comment. Section 5.1.1 on 'Identification and diagnosis' was not updated as part of the current guideline. Please see page 11 of the full guideline for a description of what was covered during this update.
215	SH	Resuscitation Council (UK)	23	FULL	61–63	12–25 19–21	Checking for an irregular pulse alone will miss all those with similar symptoms and with atrial flutter and a regular ratio (2:1 or occasionally 3:1 or greater) of AV conduction. This is touched on in lines 19–21. A sentence stating that unexplained regular tachycardia should also be assessed further by 12-lead ECG would largely address this.	Thank you for your comment. Section 5 on 'Identification and diagnosis' was not updated as part of the current guideline. Please see page 11 of the full guideline for a description of what was covered during this update.
146	SH	MEDTRONIC LIMITED	1	FULL	63–65	10 to 25	Medtronic would like to highlight more recent evidence than is presented in the guidance from 2006 or has been reviewed for the updated draft guidance in support of broader use of Implantable Loop Recorders for the detection of AF as an alternative to 7 day Holter monitoring in appropriate	Thank you for your comment. Chapter 5 on 'Identification and diagnosis' was not updated as part of the current guideline. Please see page 11 of the full guideline for a description of what was covered during this update.

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							<p>patients. Implantable Loop Recorders with specific AF detection algorithms (Medtronic Reveal XT and Medtronic Reveal Linq) provide a higher diagnostic yield for the detection of AF than Holter monitors.</p> <ol style="list-style-type: none"> 1. Camm et al "Usefulness of continuous electrocardiographic monitoring for atrial fibrillation", American Journal of Cardiology 2012 110; 270-276 "Many trials have confirmed that most paroxysmal AF (PAF) episodes are asymptomatic, many patients are completely asymptomatic and electrocardiographic (ECG) monitoring with Holter devices has limited sensitivity. "Continuous monitoring of AF is a powerful tool to detect silent paroxysmal AF in patients without previously documented arrhythmic episodes such as those with cryptogenic stroke or other episodes" 2. Hindricks et al "Performance of a New Leadless Implantable Cardiac Monitor in Detecting and Quantifying Atrial Fibrillation Results of the XPECT Trial" published in Circulation. Methods: 247 patients were implanted with an ICM and compared with core lab classification of the surface ecg. Results: The XPECT study has shown that Reveal[®] XT has an atrial fibrillation 	

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							<p>detection performance with 96.1% sensitivity and 97.4% negative predictive value compared with simultaneous Holter monitoring</p> <p>3. Ritter et al "Occult Atrial Fibrillation in Cryptogenic Stroke, detection by 7 day ECG v Implantable Cardiac Monitors (ICM), published in Stroke AHA Journals 2013. Methods: 60 patients were included. ICM implanted 13 days after the qualifying event and 7 day Holter monitoring was applied after the implant of the ICM. Results: Intermittent AF (iAF) was detected in 17% of patients by the ICM. Only 1 patient (1.7%) had iAF detected by the Holter monitor as well. Conclusions: ICM offer a greater diagnostic yield than 7-day Holter monitoring</p>	
216	SH	Resuscitation Council (UK)	24	FULL	63	19–24	<p>This wording is really confusing and potentially misleading to people. Line 19 appears to give people inappropriate permission to diagnose AF on the basis of an irregular pulse alone, but few healthcare professionals would ever be able to make a confident clinical distinction between AF and multiple extrasystoles as a cause of an irregular pulse by recognising cannon waves in the</p>	<p>Thank you for your comment. Chapter 5 on 'Identification and diagnosis' was not updated as part of the current guideline. Please see page 11 of the full guideline for a description of what was covered during this update.</p>

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							venous pulse if the extrasystoles were ventricular. The recommendation in lines 23–24 is correct and the contradictory first sentence on line 19 requires re-wording.	
218	SH	Resuscitation Council (UK)	26	FULL	64	36-40	A good recommendation regarding common sense choice of recorder, but people may reasonably ask how they are to estimate/suspect the frequency of episodes of AF that are asymptomatic!	Thank you for your comment. Chapter 5 on Identification and diagnosis was not updated as part of the current guideline update, as described in the section on guideline update on page 11 of the full guideline.
6	SH	Novacor SAS	1	FULL	64	37-39	I propose the following wording 'use a 24-hour ambulatory ECG monitor only in those who report multiple symptomatic episodes each day.' 'in all other cases use an automatic and patient activated event recorder ECG. Higher yields will be achieved by using a device with automatic AF detection. Monitoring should be for a minimum of 7 days or until the device provides feedback to the patient that sufficient AF has been detected to make a positive diagnosis. I believe that there is a serious risk of false negative results from 24 hour ambulatory ECG monitoring and as paroxysms are often asymptomatic this false reassurance could lead to a resistance to further testing and therefore to long-term suboptimal care.	Thank you for your comment. Chapter 5 on 'Identification and diagnosis' was not updated as part of the current guideline. Please see page 11 of the full guideline for a description of what was covered during this update.

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							A recently published study “Noninvasive Cardiac Event Monitoring to Detect Atrial Fibrillation After Ischemic Stroke: A Randomized, Controlled Trial” Peter Higgins et al <i>Stroke</i> . 2013;44:2525-2531 Clearly demonstrates the need for extended monitoring of high risk patients.	
217	SH	Resuscitation Council (UK)	25	FULL	64	30	This sentence doesn't make sense. Insert 'that' after 'AF'.	Thank you for your comment. Section 5.3.3 on 'Identification and diagnosis' was not updated as part of the current guideline. Please see page 11 of the full guideline for a description of what was covered during this update.
219	SH	Resuscitation Council (UK)	27	FULL	68	12-13	The need may be to identify cardiac abnormalities as well as to exclude them.	Thank you for your comment. Section 5.4.4 on 'Identification and diagnosis' was not updated as part of the current guideline. Please see page 11 of the full guideline for a description of what was covered during this update.
220	SH	Resuscitation Council (UK)	28	FULL	69	10	Typo: 'need' not 'needs' but 'should' would be more correct English. There are several other typos or errors of punctuation in this section.	Thank you for identifying the typographical errors. These have been corrected.
284	SH	All Party Parliamentary	8	FULL	77	16.2.	The Guidelines refer to “Time in therapeutic range (TTR), quality of life and stroke and thromboembolic complications were considered the	Thank you for your comment. Whilst the GDG agreed with your point regarding quality of life, they questioned how this would be effectively assessed

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		Group on Atrial Fibrillation				4	critical outcomes for this review. However consideration for choice of therapy within the document or algorithm does not appear to further reference consideration of quality of life. APGAF would recommend that after assessing risk, consideration of appropriate therapy should also include "quality of life" factors for the individual.	and achieved. In light of this we have not edited the guideline or recommendations.
121	SH	Arrhythmia Alliance, The Heart Rhythm Charity	10	FULL	77	16.2.4	<p>(a) A-A recommends that the guideline reflects how after assessing an individual's risk, the decision about their therapy option(s) should factor in the impact upon their 'quality of life'.</p> <p>(b) We are pleased to see the reference to a '<i>personalised package of care</i>' and that this includes '<i>support networks</i>.' To support this we would like to see further definition of the 'package', i.e. where patients can seek reliable and quality information and support, regardless of where they live.</p> <p>We would happily help NICE develop further information on this.</p>	<p>Thank you for your comments.</p> <p>a) Quality of life is not routinely measured, and the decision about the patient's therapy would be a shared decision.</p> <p>b) This recommendation has been amended to include "who to contact for advice if needed", and an example of a support network.</p> <p>c) Thank you we have made the NICE implementation team aware of your kind offer.</p>
158	SH	NHS Trafford CCG	3	FULL	77	6.24	Would like to see reference to patient decision aids for decisions about Anticoagulation	Thank you for your comment. The Medicines and Prescribing team at NICE are developing a patient decision tool to support the implementation of this guideline.

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							<p>eg</p> <p>http://sdm.rightcare.nhs.uk/pda/stroke-prevention-for-atrial-fibrillation/</p> <p>http://patients.dartmouth-hitchcock.org/health_information/health_encyclopedia/abl2009#abl2010</p> <p>http://www.npc.nhs.uk/therapeutics/cardio/atrial/resources/pda_af.pdf</p>	
192	SH	Boehringer Ingelheim	12	FULL	77	Section 6.2.4 Point 8	<p>Quote: "NICE has produced guidance on the components of good patient experience-in adults NHS services. Follow the recommendations in Patient experience in adult NHS services (NICE clinical guideline 138) (NEW 2014)".</p> <ul style="list-style-type: none"> Please note that within NICE clinical guideline 138: Patient experience in adult NHS services: <p>Point 5, Page 5, states that "patients are supported by healthcare professionals to understand relevant treatment options, including benefits, risks and potential consequences".</p>	<p>Thank you for your comment. The Patient Experience guidance is cross referred to within the AF guideline.</p> <p>In addition to this, a new recommendation (1.5.4) has been added pertaining to patient choice for anticoagulation.</p>

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							Point 7, Page 5, states that “patients are made aware that they have the right to choose, accept or decline treatment and these decisions are respected and supported” Point 1.3.3 on Page 11 states “Give the patient information about relevant treatment options they are entitled to, even if these are not provided locally”	
122	SH	Arrhythmia Alliance, The Heart Rhythm Charity	11	FULL	87	7.2.41	We would ask that NICE define who can be considered an ‘AF specialist’.	Thank you for your comment. The GDG would define an “AF specialist” as a cardiologist or nurse with an interest in arrhythmias. This has been added to the relevant linking evidence to recommendation section of the full guideline.
65	SH	Royal College General Practitioners	54	FULL	94	Table heading	? events per year so annual event rate	Thank you for your comment. This is the number of events over the number of people so in fact not an annual event rate. However, the heading in the row above has been corrected to events/people.
221	SH	Resuscitation Council (UK)	29	FULL	113 and elsewhere	4 and elsewhere	The abbreviation HR would mean heart rate rather than hazard ratio to many clinicians, so particularly in the setting of a clinical guideline on AF printing ‘hazard ratio’ in full would be preferable,	Thank you for your comment. You are correct to point out that the meaning of HR could be mistaken. This has been changed to read ‘hazard ratio’.
269	SH	Bayer Healthcare	6	Full	115		Under ‘trade-off between clinical benefits and harms’ the draft guideline states “ <i>The GDG considered the role of gender in risk stratification of</i>	Thank you for bring this to our attention. We appreciate that the text in the LETR may have led to some confusion. The GDG considered the role of

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							<p><i>patients with no other risk factors. They were of the opinion that any effect of gender in this group was small and that a CHA₂DS₂-VASc score of 1 should be regarded as low risk groups, not meriting anticoagulation</i>.</p> <p>This emboldened statement appears to be at odds with the proceeding text which reads: <i>"In summary, the GDG agreed that the initial clinical decision step should use the CHA₂DS₂-VASc score to determine the low risk patients who do not require anticoagulant therapy. These low risk patients are defined as those age <65 with lone AF irrespective of gender (thus, this includes those with a CHA₂DS₂-VASc score=0 if male, or a CHA₂DS₂-VASc score=1, if female). Subsequent to this step, stroke prevention could be offered to those AF patients with one or more stroke risk factors."</i></p> <p>Recommendation 12 also suggests considering anticoagulation for men with a CHA₂DS₂-VASc score of 1.</p> <p>We suggest that the statement should read <i>"...and that a CHA₂DS₂-VASc score of 1 in females, and 0 in males, should be regarded as low risk groups not meriting anticoagulation"</i></p>	gender in risk stratification of patients with no other risk factors. They were of the opinion that any effect of gender in this group was small and that a CHA ₂ DS ₂ -VASc score of 1 in women (that is women under the age of 65 with no other risk factors) should both be regarded as a low risk group, not meriting anticoagulation. We have amended the text to provide clarification, taking your comment into account.
66	S	Royal	5	FU	115	Par	Where is the evidence for men with CHADSVASC	Thank you for your comment. The SPORTIF, RELY,

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	H	College General Practitioners	5	LL		a 3	1??	ARISTOTLE and AVERROES trials all include AF patients with a single risk factor (some had CHA2DS2-VASc=1). This has now been noted in the LETR.
68	SH	Royal College General Practitioners	57	FULL	116	3	Again conflict when economics only CHADSVASc score 2	Thank you for your comment. The line you reference does not appear to correspond to your comment. In reference to the third paragraph, we explain here that the optimal threshold of giving anticoagulation is at CHADSVASC of 1 if the only objective is to reduce thromboembolic events (i.e. not taking into account bleeds or associated costs). This risk threshold is slightly lower than that indicated to be most likely to be cost effective when the trade off with bleeding events and costs have been accounted for. For the lowest bleeding risk group, there was great uncertainty in the results of economic analysis, with only a slightly higher probability that initiation of anticoagulation at CHADSVASC 2 would be more cost effective than initiation at a CHADSVASC of 1. The GDG took all the evidence, its limitations and uncertainty of findings into account when forming the recommendations. We hope this response provides clarification to your query.
223	SH	Resuscitation Council (UK)	31	FULL	118	17-18	The chapter addresses use of other anticoagulants as well as warfarin.	Thank you for your comment. The introduction now refers to anticoagulants.

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222	SH	Resuscitation Council (UK)	30	FULL	118	17	...platelet inhibitors, not anti-platelet agents	Thank you for your comment. The GDG do not agree and feel that anti-platelet agent is the accepted term in the anticoagulation field.
69	SH	Royal College General Practitioners	58	FULL	118	17	Evidence from older trials includes only higher risk patients	Thank you. We acknowledge your point. All available and appropriate studies were included when the GDG reviewed the evidence in order to answer the question posed. The GDG asked for the removal of studies that looked at aspirin against fixed dose warfarin from the 1990s (as warfarin is not used in this manner and it seemed inappropriate to use such clinical practice when evaluating the literature).
70	SH	Royal College General Practitioners	59	FULL	120		Review of papers numbers of patients, stroke risk and mean age are important for comparison. Included in some but not all	Thank you for your comment. We agree and this has been updated accordingly.
71	SH	Royal College General Practitioners	60	FULL	127		Tables ? comparison of annual event rates	Thank you for your comment. These are the clinical GRADE tables that include number of patients with the outcome and relative risk or hazard ratios. These tables do not include annual event rates of these outcomes.
190	SH	Boehringer	10	FULL	135	5	For the outcome of 'all cause mortality'; anticoagulation has been highlighted as the optimal	Thank you for your comment. NICE already has guidance (technology appraisal) in the area and it was

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		Ingelheim					strategy for stroke prevention in AF. In terms of relative effects of anticoagulants, all 3 NOACs reduce 'all cause mortality' by approximately 10% vs. warfarin.	not appropriate to review individual NOACs within this guideline. The technology appraisals have been incorporated in this guideline.
189	SH	Boehringer Ingelheim	9	FULL	135	11 16-17	<ul style="list-style-type: none"> We support the acknowledgement that anticoagulation is the optimal strategy for ischaemic stroke prevention in AF. However, the statement regarding haemorrhagic strokes that anticoagulation is the 'least optimal strategy' fails to acknowledge that all 3 NOACs (dabigatran, rivaroxaban, apixaban) statistically significantly reduce haemorrhagic stroke vs. warfarin. 	Thank you for your comment. We acknowledge your second point and emphasize that the statement refers to anticoagulation as a class of drugs. NICE already has guidance (technology appraisal) in the area and it was not appropriate to review individual NOACs within this guideline. The technology appraisals have been incorporated in this guideline.
130	SH	Daiichi Sankyo UK	2	FULL	144	Section 9.2.4 /14	As anticoagulation is not contraindicated in patients on dual antiplatelet therapy (i.e., already on aspirin and clopidogrel for acute coronary syndrome), guidance should be included on managing the risk of stroke in these patients.	<p>Thank you for your comment. We agree that this is an important question. The GDG did consider the issue of single or dual antiplatelet therapy in combination with anticoagulation. Only one RCT was identified in this area (DeWilde 2013). This study is discussed in the LETR on page 146. The GDG did not feel confident to make a generalised recommendation based on this single study.</p> <p>In this situation, any recommendation would have been largely based on GDG consensus. The GDG were aware that this area had already been</p>

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								considered in detail recently by another guideline group, considering secondary prevention following myocardial infarction (http://guidance.nice.org.uk/CG172) that made a detailed set of recommendations regarding combinations of anticoagulant and single and dual antiplatelet therapy.
271	SH	Bayer Healthcare	8	Full	144	26	<p>Recommendation 14</p> <p>We suggest that the risk of bleeding should also be taken into account when considering dual antiplatelet therapy (as is the case in recommendations 11 and 12 relating to anticoagulation). In the 'recommendations and links to evidence section' (p146) it states that <i>"[the network meta-analysis] also showed that dual antiplatelet therapy potentially carried high risks of bleeding (with much uncertainty in this parameter). Therefore patients undertaking this strategy will need to be assessed for bleeding risk and gastric protection"</i></p>	Thank you for the comment. We agree that bleeding risk should be taken into consideration. However, the GDG have removed this recommendation.
163	SH	NHS Trafford CCG	8	FULL	145	26	<p>GDG recognised that some patients might still need to take aspirin for indications other than AF. Question being asked by prescribers is whether antiplatelets should be continued for secondary prevention of MI when patient anticoagulated for NVAf. ESC guidelines say no- Should this be</p>	Thank you for your comment. The GDG agreed that patients who chose not to undertake stroke risk modification for AF should be able to receive aspirin monotherapy. The guideline does not recommend aspirin monotherapy for AF but the GDG did not wish to deny aspirin monotherapy for those requiring

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							clarified in the guidance?	<p>aspirin for non-AF conditions.</p> <p>Please note the NICE MI secondary prevention guideline has recently been updated and was published in November 2013 and can be found here: http://guidance.nice.org.uk/CG172</p> <p>We have added a cross reference to CG172 (recommendations 1.3.22 to 1.3.29) to the relevant point in the linking evidence to recommendation section of the guideline (section 9.2.4).</p>
131	SH	Daiichi Sankyo UK	3	FULL	151-152	Recommendations 15-20.	With regard to the recommendations listed for antithrombotic therapy, guidance should be provided in relation to dosing for patients already receiving treatment with a NOAC for VTE. There is currently no mention of this in the draft guideline.	Thank you for your comment. Dosing of NOACs for VTE was not within the scope of this guideline on AF.
285	SH	All Party Parliamentary Group on Atrial Fibrillation	9	FULL	151	2	Antithrombotic therapy- in the list of recommendations and guides for considerations when selecting an antithrombotic therapy, it may be helpful to include warfarin within the tables so all OAC are read and interpreted with the same considerations.	Thank you. This guideline has fully incorporated the guidance from published technology appraisals and the wording of the recommendations cannot be changed.
123	SH	Arrhythmia Alliance,	12	FULL	151	2	In the list of recommendations and guides for current NICE approved OAC, it may be helpful to include warfarin so that it is shown in line with all	Thank you. This guideline has fully incorporated the guidance from published technology appraisals and the wording of the recommendations cannot be

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		The Heart Rhythm Charity					options.	changed.
3	SH	College of Emergency Medicine	2	FULL	166	10.2.4 recommendation 21/general	<p>a) There is no qualification of 'harmful alcohol consumption'; the HAS-BLED suggests more than 8 drinks/week – this is within DOH suggested safe limits.</p> <p>b) Additionally, there is little direction on what constitutes sufficient level of bleeding risk to warrant changes in management. There is suggestion that stroke risk generally outweighs bleeding risk- if this is so then calculating risk does not affect management</p>	<p>Thank you.</p> <p>In relation to your point regarding harmful alcohol consumption, point a): The 'alcohol' criterion refers to alcohol excess/abuse. For the validation paper a numerical figure was stated as this was needed for a statistical validation. Other published validations have used 'hospitalisation for alcohol excess' and the outcome is unchanged. Different studies define harmful alcohol differently, and therefore we are unable to give an exact definition.</p> <p>Risk scores need to be pragmatic. The GDG agreed to align with the definition used in the 2012 ESC guidelines i.e. alcohol excess or abuse, which is essentially an intake where the clinician assesses there would be an impact on health or bleeding risk.</p> <p>In relation to point b) of your comment - we agree with the reviewer's comment. The GDG considered that in the majority of patients stroke risk would outweigh bleeding risk. For example, the net clinical benefit (NCB) balancing ischaemic stroke reduction against serious bleeding (e.g. intracranial bleeding) is positive in favour of oral anticoagulation or patients with</p>

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								≥1 stroke risk factors, irrespective of CHA2DS2-VASc or HAS-BLED strata [Friberg et al Circulation 2012, Olesen et al Thromb Haemostat 2011, Banerjee et al Thromb Haemostat. The GDG viewed the main value of the HASBLED score as assisting in the identification of potentially reversible bleeding risk factors. So we would agree with the reviewer's comment that calculating bleeding risk will not necessarily change management - but it does serve to focus attention on correcting potentially reversible risk factors.
224	SH	Resuscitation Council (UK)	32	FULL	169	5-6 and 8	It is probably the frequency rather than the regularity of assessment that is needed (not'...are needed').	Thank you for your comment which relates to the clinical introduction of section 11.1. The GDG prioritised a review question relating to the effectiveness of systematic monitoring rather than how often. The grammar has been corrected, thank-you.
108	SH	Royal College of Pathologists & British Society for Haematology	12	FULL	169	11.2	Appendix C referred to could not be opened despite downloading latest software	Thank you for your comment. We apologise that you were unable to access appendix C. We have liaised with NICE's Web Editor and reported your difficulties.
263	S	Roche	4	FU	170	3	We are surprised that no evidence regarding	Thank you for your comment. This was not prioritised

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	H	Diagnosticians		LL			frequency and type of monitoring was included in the review. For INR control, there is evidence that more frequent testing was associated with higher TTR (Samsa & Matchar J Thromb Thrombolysis 2000; 9:283–292). Higher TTR is associated with fewer adverse events (e.g. Wan et al. Circulation 2008; 118:97-106 or Gallagher et al. Thromb Haemost 2011; 106:968–977). A significant number of RCTs exist that compare different monitoring strategies, in particular more frequent INR self-monitoring with clinic visits. Meta-analysis of these studies indicate that self-monitoring is more effective in increasing TTR and reducing thromboembolic events compared to monitoring in clinics (e.g. Heneghan et al. Lancet 2012; 379:322-334 and evidence discussed in the diagnostic assessment for self-monitoring referred to in comment 2).	by the guideline development group for review in this guideline.
225	SH	Resuscitation Council (UK)	33	FULL	171	5-6	Incorrect use of English	Thank you for your comment, the English has been corrected.
272	SH	Bayer Healthcare	9	Full	171 172	17	Recommendations 24-27 In the full version of this guideline it is not clear that the above recommendations are only applicable to people taking vitamin k antagonists; there is no need for routine monitoring of coagulation	Thank you for your comment. This has been clarified so the full guideline reflects the NICE guideline.

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							parameters during treatment with NOACs. In the NICE version of the guideline these recommendations are preceded by a subheading entitled " <i>Assessing anticoagulation control with vitamin K antagonists</i> ". We suggest that a similar subheading should be included in the full version of the guideline.	
132	SH	Daiichi Sankyo UK	4	FULL	171	17	<p>Recommendation 24 within this list states that calculations of TTR should exclude measurements taken within the first 6-weeks of treatment, and that TTR should be calculated over a maintenance period of at least 6 months.</p> <p>It is unclear whether the 6-weeks of initial treatment is additive (i.e., patients require a trial of warfarin for 7.5 months) or inclusive (i.e., patients should have a trial of warfarin for 6 months with the INRs during the first 6 weeks excluded.) We would like clarity on this issue.</p>	Thank you for your comment. There is no suggestion of a trial period. The guideline development group were indicating that the loading period measurements should not be included in any TTR calculation.
133	SH	Daiichi Sankyo UK	5	FULL	171	17	We question the evidence behind the 6-month trial of warfarin. We understand the rationale for measurements to be excluded during the first 6 weeks after warfarin has been initiated; however, if a patient is unstable on warfarin after the first 6-8 weeks, they may remain to be unstable for the entire duration of 6 months.	Thank you for your comment. It is not suggested that there is a 6 month trial; it was felt that 6 months is a reasonable time-frame over which to assess TTR, any such period will be arbitrary.

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							We feel that a TTR measurement at 3-4 months may be more appropriate, rather than the 6 months as written in the guideline, so that these patients may benefit by using alternative stroke prevention strategies at an earlier time point should their INR not be controlled within range.	
134	SH	Daiichi Sankyo UK	6	FULL	171	17	Recommendation 25 within this list defines “poor anticoagulation control”. As the text above this list of recommendations indicate that no clinical or economic evidence is available to support this, can you please explain how you have arrived at these definitions?	Thank you for your comment. This recommendation was derived from the consensus opinion of the GDG.
135	SH	Daiichi Sankyo UK	7	FULL	171	17	<p>We welcome the draft guidelines in using scoring systems to assess a patient's risk of stroke (CHA₂DS₂-VASc) and bleeding (HASBLED).</p> <p>A scoring system that appears to have been overlooked (perhaps due to a paucity of data) in these draft guidelines is the SAME-TT₂R₂ score that can predict poor INR control and aid decision-making by identifying those patients with AF who would do well on VKA (SAME-TT₂R₂ score = 0-1), or conversely, those who are likely to have poor anticoagulation control with a VKA (a score ≥2) and where a NOAC could be a better option. We feel</p>	<p>Thank you for your comment.</p> <p>This score was discussed by the GDG. However, this score was not published at the time the GDG set the protocol for this question. In addition the validation study was only published after our final cut-off date for included publications. This score has been included in one of the guidelines research recommendations (Appendix P).</p>

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							that the GDG may want to incorporate this scoring system into the guidelines.	
188	SH	Boehringer Ingelheim	8	FULL	172	3 to 5	<p>Quote: "If poor anticoagulation control cannot be improved, evaluate the risks and benefits of alternative stroke prevention strategies and discuss these with the person".</p> <ul style="list-style-type: none"> This statement differs from the Technology Appraisal for dabigatran etexilate (TA249) which states that patients should not need to trial warfarin before being offered dabigatran: "It also accepted that it was not reasonable to expect all patients to try warfarin first, with the associated risks, for the purpose of selecting out a subgroup for whom dabigatran was less cost effective". Reference: www.nice.org.uk/ta249. Page 33, section 4.19, line 7. Furthermore, TA249 states; "The Committee concluded that evidence for stratifying by INR control was insufficient to exclude the minority of people with very good control from the recommendation of dabigatran as a potential treatment option, and that the ICER for the whole population should be the basis of the recommendation". 	<p>Thank you for your comment. It was never the intention of the guideline to suggest that patients should come to NOACs after trialling vitamin K antagonists.</p> <p>The initial choice between vitamin K antagonists and NOACs has been made clear with an additional recommendation. There is an existing initial statement at the start of section 1.5 that "Anticoagulation may be with apixaban, dabigatran etexilate, rivaroxaban or a vitamin K antagonist."</p> <p>The algorithm has similarly been clarified and it is now clear that patients can come to NOACs through either of two pathways, either through an initial intention to treat with NOACs or through an initial decision to treat with a vitamin K antagonist and the subsequent demonstration that they have poor anticoagulant control.</p>

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							<ul style="list-style-type: none"> Reference: www.nice.org.uk/ta249. Page 35, section 4.20, lines 9-12. 	
124	SH	Arrhythmia Alliance, The Heart Rhythm Charity		FULL	172	27	A-A welcomes the included notice of pending guidelines for INR self-monitoring along with further criteria on lifestyle when monitoring.	Thank you for your comment.
184	SH	Boehringer Ingelheim	4	FULL	172	25 to 28	<p>Quote: "...after the initial stabilisation of dose, a minimum of 60% of people under the care of the anticoagulation service should be within therapeutic range at a given point in time. Although, they stated that over 65% would be desirable".</p> <ul style="list-style-type: none"> Boehringer Ingelheim supports the use of individual TTR measurement rather than use of centre based TTR. This section appears to suggest that non-attainment of TTR (and therefore suboptimal stroke prevention) is acceptable in 40% of patients. This is not indicative of individual patient TTR, which is mentioned in this section under 'poor anticoagulation control' which is stated to be 'TTR less than 65%'. 	Thank you for your comment. This is a quote from the NICE topic advisory group from the NICE anticoagulation commissioning guide. The quote has been reproduced within the linking evidence to recommendation section of the guideline. As you point out it applies to a population based assessment of quality of anticoagulation. The guideline through its recommendations moves on from this to endorse the concept of individual patient based assessment of TTR and the GDG recommended that alternatives were considered when an individual's TTR falls below 65% (recommendation 1.5.12.) which is in accordance with the views you have put forward.
185	SH	Boehringer	5	FULL	173	6 to 9	Quote: "Anticoagulation clinics often assess patients who are not reaching the recommended	Thank you for your comment. A new recommendation has been added which covers your point.

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		Ingelheim					<p>TTR and these patients need more frequent monitoring. It is therefore difficult to recommend a frequency for regular monitoring as all patients are different and optimal frequency for an individual will depend on that individual's level of control".</p> <ul style="list-style-type: none"> We feel this statement should acknowledge patient choice - patients may choose not to participate in more frequent testing and should be offered the choice of alternative anticoagulant strategies which do not require INR monitoring. 	
187	SH	Boehringer Ingelheim	7	FULL	173	20 to 21	<p>Quote: "Bleeding risk and effective INR control remains an important determinant of cost effectiveness of stroke prevention using anticoagulation".</p> <ul style="list-style-type: none"> We suggest that the point at which NOACs become more cost effective should be acknowledged here. 	Thank you for your comment. NOAC thresholds are outside the scope of the guideline.
186	SH	Boehringer Ingelheim	6	FULL	173	25 to 26	<p>Quote: "It was acknowledged that at least 20 INR results would be optimal to determine a patient's TTR but this could take up to a year to accumulate".</p> <ul style="list-style-type: none"> We would suggest that this would be a huge burden on patients and does not take 	<p>Thank you for your comment. We would make two points in response.</p> <p>The first is that the statement quoted suggested an ideal which the GDG acknowledged as impractical and suggested as a compromise calculating TTR over</p>

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							patient quality of life into consideration.	<p>a 6 month period. We would acknowledge that this shorter period is still a potential burden for the patient.</p> <p>The second point is that a new recommendation has been added (recommendation 1.5.4 that the options for anticoagulation should be discussed with the patient and we would anticipate that the need for monitoring and scrutiny of TTR values would be one of the factors which would be addressed in this discussion.</p>
274	SH	Bayer Healthcare	11	Full	174	1	<p>Recommendation 30</p> <p>This recommendation includes that for people taking an anticoagulant, the quality of anticoagulation control should be reviewed at least annually.</p> <p>Use of the phrase 'anticoagulation control' denotes some form of monitoring of coagulation parameters, which would not be relevant during treatment with NOACs.</p> <p>We suggest that the word "control" is removed from this recommendation, referring then to <i>the "quality of anticoagulation"</i>, which is applicable to both VKAs and NOACs. Quality will therefore not be restricted to international normalised ratio control, but all aspects of anticoagulation.</p>	Thank you for your comment. The word "control" has been removed from the recommendation.
276	S	Bayer	1	Full	174	1	Recommendation 30.	Thank you for your comment. The word "control" has

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	H	Healthcare	3				<p>This recommendation covers the need to <i>“review the need for anticoagulation and the quality of anticoagulation control at least annually or more frequently if clinically relevant events occur”</i>. The current wording implies that a review should be precipitated by an ‘event’ however there are other considerations which should prompt a review of anticoagulation needs, but which may not be classified as ‘events’, such as a change in haemorrhagic risk, an indication for concomitant medication, or a change in renal or hepatic function.</p> <p>Bearing in mind this comment, and that described in order number 11, we suggest that recommendation 30 should read <i>“for people who are taking an anticoagulant, review the need for anticoagulation and the quality of anticoagulation at least annually, or more frequently if clinically indicated.”</i></p> <p>This suggested amendment should also be included in the stroke prevention algorithm on p44 of the full guideline as depicted in the alternative algorithm shown in order numbers 3 and 4.</p>	been removed from the recommendation.
79	SH	Boston Scientific	4	FULL	176-181	21-22-4-8	<p>c) The evidence used is not up-to-date</p> <p>A complete literature review of the Watchman™ device is provided in addition to this document for</p>	Thank you for your comment and the information within the literature review. We have checked the clinical studies within the literature review and it includes only one RCT on the PROTECT-AF trial that we have included within the guideline review. As the

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							<p>the Development Group attention [attachment #1]</p> <ol style="list-style-type: none"> 1. The PROTECT-AF RCT (Holmes, 2009) has reported on longer-term follow-up (1588 patient- years or 2.3 years) and has been published in 2013 [Reddy VY, Doshi SK, Sievert H, Holmes D et al. on behalf of the PROTECT AF Investigators Percutaneous Left Atrial Appendage Closure for Stroke Prophylaxis in Patients With Atrial Fibrillation 2.3-Year Follow-up of the PROTECT AF (Watchman Left Atrial Appendage System for Embolic Protection in Patients With Atrial Fibrillation) Trial Circulation 2013;127:720-729) <p>The clinical evidence statement does not take into account the more up-to-date PROTECT-AF 4-year results which have shown that WATCHMAN LAAC device provided superior outcomes over warfarin in primary efficacy and promising all-cause mortality reductions in patients with non-valvular Atrial Fibrillation (AF).</p> <ul style="list-style-type: none"> • 40% relative reduction of primary efficacy events • 60% relative reduction for CV mortality • 34% relative reduction for all-cause mortality 	<p>attached report states, there was only one economic evaluation (Singh 2013) which was peer reviewed in a journal and not an abstract. This has been included in the review of the evidence in the guideline. In line with the economic review protocol, we would exclude budget impact analyses and abstracts.</p> <p>1. We have updated the review to include the Reddy study and 2.3 year follow up data. We have not been able to include the 4 year results as they have not yet been published. However, we have added a comment in the LETR to acknowledge that they are awaiting publication.</p> <p>2. Thank you for bringing our attention to the review by Professor Cramm. This literature review was not included as it was published after our literature search cut-off date. Having looked at this review it only includes the PROTECT-AF trial by Holmes et al that has been included in our review.</p> <p>Quality of evidence: The evidence for outcomes was evaluated and presented using an adaptation of the 'Grading of Recommendations Assessment, Development and Evaluation (GRADE) toolbox (see section 3.4.4 and 3.4.5 for further information on GRADE). The overall quality of evidence for each outcome was considered taking into account: risk of</p>

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							<p>The 4-year results are awaiting publication and were presented at the Heart Rhythm Congress in 2013 ("Reddy VY, Sievert H, Holmes D et al. for the Protect AF investigators. Long Term Results of PROTECT AF: The Mortality Effects of Left Atrial Appendage Closure versus Warfarin for Stroke Prophylaxis in AF. Heart Rhythm 2013, Late Breaking Clinical Trials"</p> <p>2. A recent paper by Professor Camm et al is a peer-reviewed literature review published in 2013 including a up-to-date evidence of LAAO (Reference: Heart Rhythm 2014;11:514–521) This review summarises the latest clinical evidence of non-pharmacological approaches for stroke risk reduction e.g. left atrial appendage closure and the relevance for clinical practice. The authors conclude that "it is now appropriate to consider these techniques for patients with AF who are at high risk for stroke for whom effective conventional or novel anticoagulant therapy is not available or who present problems in managing drug treatment".</p>	<p>bias, inconsistency, indirectness and imprecision. The outcomes in table 39 have been downgraded due to risk of bias and imprecision. The GDG agreed that there was a high risk of bias due to both arms receiving warfarin and more than 10% drop outs (further information on risk of bias in section 3.4.6). Serious or very serious imprecision was detected in all outcomes as the confidence intervals crossed the default minimally important difference (MID) (0.75 and/or 1.25). Please refer to section 3.4.9 for further information on imprecision. The outcome was downgraded once for risk of bias to moderate and then to low if serious imprecision (crossed one MID) or to very low if crossed both MIDs.</p>

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							<p>Quality of the evidence:</p> <p>We also strongly disagree with the statement in Table 39 on page 180 that the evidence is 'low to very low quality evidence'. It is a very subjective statement which is not backed up by any justification, other than to state that there are not as many patients as in a (AF) drug trial. It is an unfair comparison and a more relevant benchmark would be to compare the Watchman/LAAC evidence to other device trials such as RCTs for implantable cardioverter defibrillators (ICDs) and Afib ablation trials.</p> <p>We would like to highlight that this was a randomised controlled trial with adequate power to determine non-inferiority to warfarin. Bayesian analysis is becoming more accepted as a statistical method for studies with large amounts of historical data (in this case, decades of use of warfarin), while limiting the exposure of experimental therapies to large numbers of patients. For example, the FDA has issued a guidance document on Bayesian analysis being a preferred method in cases where significant historical data exists and provides a well-informed platform with which to design a study.</p>	

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							<p>Moreover, we have carried out an analysis of the Watchman evidence using the GRADE (Grading of Recommendations Assessment, Development and Evaluation) scoring system (http://www.gradeworkinggroup.org/intro.htm) and found that the level is MODERATE. There are 4 levels in grading the quality of the evidence in GRADE: High; Moderate; Low and Very Low</p> <p>We couldn't copy our analysis in this table so we have attached it (attachment #2 – GRADE analysis of the quality of evidence)</p>	
80	SH	Boston Scientific	5	FULL	176	19 (Table 37)	<p>The Population included as part of the PICO analysis includes 2 subgroups: patients who cannot take anticoagulants and people who can take anticoagulants.</p> <p>However the evidence presented in the Full guideline includes only the second group (people who can take anti-coagulants). It is of critical importance to include the first group (people who cannot take anticoagulants) as it is the population for whom it is recommended in the current draft, in</p>	<p>Thank you for your comment. The GDG agreed that the protocol population should report people who can and cannot take anticoagulants separately. The review only includes people who can take anticoagulants as no RCT evidence was found in people that could not take anticoagulants. The registry and ASA Plavix study were not included as they were not RCTs. However, LAAO was thought to offer a major advance in patients at risk of stroke and who are unable to take any form of anticoagulation. Although there was no RCT evidence relating to</p>

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							<p>the NHS England commissioning.</p> <p>We would kindly request the GDG to consider the evidence available on the contraindicated population and the ASAP registry.</p> <p>NICE Clinical Guideline methods indicate that non-RCT evidence can be included when there is no RCT available.</p> <p>The ASA Plavix (ASAP) study evaluated the feasibility of implanting the WATCHMAN Device in patients contraindicated to warfarin. The device was implanted in 150 patients with a mean CHADS2 score of 2.8 who were then prescribed clopidogrel and aspirin for 6 months. After 6 months, aspirin therapy was continued indefinitely. The implantation was successful in 95% of patients. In a mean 14.2 months of follow up, there was an observed 1.7% rate of ischemic stroke in patients who received WATCHMAN, this compares to an expected rate of 7.3% based on CHADS2 score ie a 77% reduction in ischemic events compared to historical control with aspirin alone and a 64% reduction in ischemic events compared to historical control with aspirin plus clopidogrel Reference: Reddy et al. JACC 2013; 61(25):2551–6.</p>	<p>patients with a contra-indication to anticoagulation, the GDG noted that there was non-randomised clinical trial (ASA Plavix) evidence relating to this group and that there was no reason to believe that the RCT evidence could not be extrapolated to this group. The GDG agreed that it was appropriate to make a recommendation that LAAO should be considered in this population of patients unable to take any form of anticoagulation. We have updated the text to clarify this point.</p>

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125	SH	Arrhythmia Alliance, The Heart Rhythm Charity	13	FULL	181	12.2.4 14	<p>We would like clarification from NICE about the suggested contradiction between recommendations for LAAO referred to in IPG 349 and within this guideline, in which it states: <i>'Do not offer left atrial appendage occlusion (LAAO) as an alternative to anticoagulation unless anticoagulation is contraindicated or not tolerated.</i> A-A can find no new evidence within the updated AF Guidelines to suggest a change in trial data.</p> <p>A-A requests that NICE amends the statement on page 16 (and reference to this in Algorithm 1 page 44): <i>'Patients and healthcare professionals have rights and responsibilities as set out in the NHS 34 Constitution for England – all NICE guidance is written to reflect these. Treatment and care should take into account individual needs and preferences. Patients should have the opportunity to make informed decisions about their care and treatment, in partnership with their healthcare professionals'</i> to correctly reflect IPG 349 and the NHS Constitution for England.</p>	<p>Thank you for your comment.</p> <p>We agree that the NICE interventional procedure guidance 349 recommended that the procedure 'may' be used provided that normal arrangements are in place for clinical governance, consent and audit. This enabled the GDG to make the recommendation that LAAO can be considered if anticoagulation is contraindicated or not tolerated. We do not believe that our recommendation contradicts the NICE interventional guidance (IPG) 349, rather it provides further guidance as to whom it may be most appropriate to offer LAAO based expert opinion of the current clinical and economic evidence base.</p> <p>The Interventional procedure guidance included one RCT (PROTECT-AF trial) that was included in the guideline review (Holmes 2009). This clinical guideline also had the 2.3 year followed up for this trial (Reddy 2013). The recommendation was also based on findings of an economic evaluation (published after the IPG) that found great uncertainty that the intervention was cost effective. A strong recommendation in favour of routine use of LAAO for all population groups would require evidence indicating a high likelihood that the intervention is cost effective. To note the IPG guidance did not look at different populations of AF within their</p>

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								<p>recommendation.</p> <p>This issue was discussed again by the GDG following your comments. The GDG remain of the opinion that the treatment is appropriate for patients in whom anticoagulation is contraindicated or not tolerated, and that until longer term follow-up is available, its use should be restricted to this group.</p> <p>With regard to your last point, we are aware the IPG349 says 'Patients should be considered for alternative treatments to reduce the risk of thromboembolism associated with AF, and should be informed about these alternatives'. We have added a new recommendation to the guideline which says 1.5.4. 'Discuss the options for anticoagulation with the person and base the choice on their clinical features and preferences'. Whilst this recommendation relates to anticoagulation, it would encompass further discussions should anticoagulation be contra-indicated.</p> <p>We have also cross referred to the NICE Patient experience guideline (CG138) http://www.nice.org.uk/nicemedia/live/13668/58283/58283.pdf within the AF guideline.</p>
88	S	BRITISH	6	FU	181	14	Recommendation 55: The recommendation to	Thank you for your comment. The GDG felt that the

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	H	HEART RHYTHM SOCIETY (FORMERLY HRUK)		LL			consider LAAO could be expanded to be more specific to include patients at high risk of stroke. For example 'consider LAAO in patients with atrial fibrillation at high risk of thromboembolic stroke (CHA ₂ DS ₂ -VASc score of 2 or more) with a contraindication to oral anticoagulation (intolerance, previous significant bleed, high bleeding risk)'.	recommendation adequately covered the point you are raising.
82	SH	Boston Scientific	7	FULL	183	Other Considerations	It is important to note that the Watchman device (referenced in this table for costings) is the only device with significant clinical evidence available. The studies referenced, as well as the ones included here, studied the Watchman™ device exclusively.	Thank you for your comment.
226	SH	Resuscitation Council (UK)	34	FULL	184	3-5 5	The reduction of atrial contribution to the cardiac output is due to loss of effective atrial contraction as well as loss of synchronisation of contraction between the atria and ventricles. Also the ventricular rate may be rapid but it is the ventricular rhythm that is irregular.	Thank you, we agree and have amended the text.
227	SH	Resuscitation Council (UK)	35	FULL	184	13	Most rate-controlling drugs slow the rate of conduction through the AV node, not just the maximum rate of conduction.	Thank you for your comment. We agree with your statement but would contend that it is the maximum rate of conduction through the A-V node which determines ventricular response rate.
228	SH	Resuscitation Council (UK)	36	FULL	184	23	Pulmonary vein isolation, not pulmonary vein ablation!	Thank you. We agree and have amended the text accordingly.

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229	SH	Resuscitation Council (UK)	37	FULL	191	6	Incorrect use of English	Thank you. The sentence has been amended.
83	SH	BRITISH HEART RHYTHM SOCIETY (FORMERLY HRUK)	1	FULL	195	6	Recommendation 33: We would disagree with this recommendation as a blanket statement for the treatment of paroxysmal and non-paroxysmal AF. Whilst we realise the importance of offering rate control to patients with PAF during an episode and to patients with persistent AF, the recommendation of rate control as a 'first line strategy' may be disadvantageous for patients who would benefit from early cardioversion or a rhythm control approach. The recommendation could potentially delay or in some cases discourage this treatment.	Thank you for your comment. We have amended recommendation 33 to include some examples of when rate control should not be first line.
230	SH	Resuscitation Council (UK)	38	FULL	230	1-2	Lumping 'calcium channel blockers' together in this statement is inappropriate. Dihydropyridine agents would not be considered for chemical cardioversion and whether or not verapamil or diltiazem have any worthwhile effect is also questionable.	Thank you for your comment. This study compared verapamil to flecainide and we have updated the text accordingly.
231	SH	Resuscitation Council (UK)	39	FULL	232	First box - recommendation	As noted elsewhere this appears to recommend routine use of amiodarone before and after cardioversion. This is a radical departure from most current UK practice. Inflicting amiodarone therapy and the need for monitoring and the harms caused by amiodarone. See paragraph at top of page 260.	Thank you for this comment. The GDG shared these reservations and did not wish to recommend that amiodarone should be routinely used in association with cardioversion. The evidence, nonetheless, suggests a benefit in maintaining sinus rhythm and hence the GDG recommended that it should be

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						mentation 41		“considered”. The linking evidence to recommendation (LETR) section already expresses reservations on the use of amiodarone in this situation and the recommendation makes clear that these benefits and risks should be discussed with the patient. The GDG did not think that they were able to be proscriptive of the situations when amiodarone should and should not be used, but nonetheless some examples of where it might be more appropriate are included in the linking evidence to recommendation section (LETR).
182	SH	Boehringer Ingelheim	2	FULL	234	8	<p>Quote: “As it may take some time to achieve therapeutic international normalised ratio for 3 consecutive weeks, some patients may wait months before cardioversion is attempted. As it is perceived that patients are more likely to successfully cardiovert the shorter the time they have been in AF, strategies to facilitate early cardioversion have been explored”.</p> <ul style="list-style-type: none"> Published evidence from UK hospital states shorter time to cardioversion is possible with dabigatran compared to warfarin, with associated cost saving. Reference: Choo WK, et al. Dabigatran improves efficiency of an elective direct current cardioversion service. Br J Cardiol 2014;21(1). Pre-published online 4th 	Thank you for your comment. This is a partial update of NICE clinical guideline 36 and it is outside of our remit to comment on recommendations that have not been updated.

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				FULL	46		<p>February 2014. Available at: http://bicardio.co.uk/2014/02/dabigatran-improves-the-efficiency-of-an-elective-direct-current-cardioversion-service/</p> <p>Algorithm 3 (rhythm control strategies) page 46:</p> <ul style="list-style-type: none"> We would suggest dabigatran be added in restoration of sinus rhythm as an alternative anticoagulant – “where a minimal period of precardioversion anticoagulation is indicated due to patient choice or bleeding risks”. Dabigatran is the only NOAC to have specific mention of cardioversion within its SPC. This states; “patients with atrial fibrillation can stay on dabigatran while being cardioverted”. Reference: Pradaxa Summary of Product Characteristics. Current version available online at: http://www.medicines.org.uk/emc/ 	
126	SH	Arrhythmia Alliance, The Heart Rhythm Charity	14	FULL	234	15.3.1 Line 8-11 and	<p>A-A would like to offer information from the following source in support of using dabigatran to ensure faster times to cardioversion, successful outcomes and reduction in associated costs: <i>Choo, W.K., (2014) Dabigatran improves efficiency of an elective direct current cardioversion service. The</i></p>	Thank you for your comment. This is a partial update of NICE clinical guideline 36 and it is outside of our remit to comment on sections that have not been updated.

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						Fig 3	<i>British Journal of Cardiology [Online]. 21 (1),</i> available from: http://bjcardio.co.uk/2014/02/dabigatran-improves-the-efficiency-of-an-elective-direct-current-cardioversion-service/	
232	SH	Resuscitation Council (UK)	40	FULL	236	21–22	Other important clinical reasons for a minimal period of pre-cardioversion anticoagulation have been omitted and should be included.	Thank you for your comment. This is a partial update of NICE clinical guideline 36 and it is outside of our remit to comment on recommendations that have not been updated.
85	SH	BRITISH HEART RHYTHM SOCIETY (FORMERLY HRUK)	3	FULL	257–8	25	Recommendation 50: The recommendation is not supported by evidence in patients with atrial fibrillation and is extrapolated data from the CAST study which used class Ia drugs in high risk patients post MI in an attempt to suppress ventricular arrhythmia and showed harm for those treated with class I drugs. This recommendation therefore rules out a moderately effective treatment for patients with minor structural or coronary artery disease in whom by default amiodarone is the only recommended drug.	Thank you for your comment. This was discussed at length by the GDG who sympathised with the comment and agreed with the observation that recommendations are based on extrapolations from the CAST study. The GDG considered it appropriate to maintain the current wording based on a number of considerations <ul style="list-style-type: none"> • That patient safety should be the primary concern and that it was better to err on the side of safety given the seriousness of the problems observed in the CAST study • A difficulty in defining what is meant by minor coronary disease • A recognition that if coronary disease was present, this could change with time in an unpredictable fashion. • Internal consistency with the pill in the pocket

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								recommendation from the 2006 guideline. However, the GDG were aware of some existing practices in relation to investigation for possible coronary disease before commencing class Ic drugs and thought these inappropriate. For this reason, the recommendation has been changed to refer to "known" coronary disease.
84	SH	BRITISH HEART RHYTHM SOCIETY (FORMERLY HRUK)	2	FULL	257	25	Recommendation 44: There is very little evidence to support the use of a beta-blocker as first line therapy for long term rhythm control. The one study quoted (Kuhlkamp 2000) compared metoprolol CR/XL with placebo for maintenance of sinus rhythm post cardioversion for persistent AF and was rated low quality evidence. There have been no efficacy studies of beta-blockers in paroxysmal AF.	Thank you for your comment. The GDG weighed up the balance between the benefits of sinus rhythm maintenance against the side effects reported. The GDG agreed that the harm of the numerous side effects of drugs for rhythm control potentially outweighed the benefits. They recommended that if this treatment option is considered then beta-blockers would be the drug of first choice as they have the lowest side effects reported. In practice, in many cases patients will already have received beta blockers as part of a rate control strategy and under these circumstance a decision might be made to progress directly to another drug category. Associated comorbidities and patient preferences would need to be considered. However, we have amended the recommendation from 'offer' to 'consider' reflecting the evidence.
233		Resuscita	4	FU	262	sect	It would have been helpful to investigate and advise	Thank you for your comment. This is a partial update

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	SH	Health Council (UK)	1	LL		16.3.4	on whether or not the safety of a pill-in-the pocket strategy with class 1c drugs can/should be improved by prior testing in a controlled setting. For example a relatively large dose of 200–300mg Flecainide may be needed for optimal p-i-p effectiveness but may cause potentially hazardous QT prolongation in a few people, who could be identified by prior challenge in a hospital setting. Even if there is no evidence base for such an approach, raising awareness of it may enhance the quality of clinical practice.	of NICE clinical guideline 36 and it is outside of our remit to comment on sections that have not been updated.
148	SH	MEDTRONIC LIMITED	3	FULL	296	24 to 25	<p>“17.4 3. Evidence statements.</p> <ul style="list-style-type: none"> • No Evidence” <p>Medtronic refers to the statements in economic evidence on page 298. <i>“a key limitation of all models looking at catheter ablation was the implicit assumption that restoration of sinus rhythm via left atrial catheter ablation would necessarily lead to a reduced risk of stroke”. This was not considered a reasonable assumption given the lack of evidence demonstrating that a reduction in AF correlates with a reduction in stroke risk. The group felt that as the clinical review did not find evidence to support this assumption, results of such models should</i></p>	<p>Thank you for your comment.</p> <p>We have removed the bullet point in 17.4.3 for consistency of style in this chapter. To note these evidence statements on page 298 only relate to the comparison of surgical ablation compared to left atrial catheter ablation. Evidence regarding the cost effectiveness of ablation as a first line option appears earlier in the chapter (17.2.3).</p> <p>The cost effectiveness study you cite was published after the cut-off date for includable studies for the guideline. However, from the information quoted, the inclusion of this study would have not changed the conclusions or recommendation. Firstly, the ICER found was above £20,000 (both in the base case and the sensitivity analysis cited). This suggests that drug</p>

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							<p><i>be interpreted with caution”.</i></p> <p>We would like to bring your attention to two studies which show catheter ablation to be cost effective without assuming a reduction in stroke.</p> <ol style="list-style-type: none"> 1. Reynolds et al 2009 Treatment of atrial fibrillation with antiarrhythmic drugs or radiofrequency ablation: two systematic literature reviews and meta-analyses (already cited in the draft guidance) supported by 2. Reynolds et al “Cost effectiveness of cryoballoon ablation for the management of paroxysmal atrial fibrillation” published in 2014. <p>A quote from the 2014 study, Cryoballoon ablation compared with drug therapy, results in greater QALYs (3.565 vs. 3.404), and greater costs (£21 162 vs. £17 627). These results yield an ICER of £21 957 per QALY gained. One-way sensitivity analyses (Figure 3) showed that the model result was the most sensitive to the time horizon used, the costs of follow-up care in patients with recurrent AF, and the total cost of the ablation procedure. Assuming the same risk of stroke for patients in sinus rhythm and those with recurrent AF had little impact upon the results, with the ICER</p>	<p>therapy is likely to be more cost effective than ablation. Secondly, the study you cite appears to have similar findings to those reviewed, i.e. results were in particular sensitive to time horizon and potentially had the effect been extrapolated over a longer horizon the ICER would reduce. Such limitations of the included evidence were taken into account when forming recommendations, i.e. the results of the evaluations were interpreted with caution keeping findings of sensitivity analyses in mind. The study you cite appears to support this stance and the developers have not amended the statement.</p>

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							<p>increasing slightly to £24 265 per QALY gained.” The above result takes a 5 year time horizon which is concurrent with AF Guideline time horizon expecting efficacy to be sustained beyond five years. In light of this new evidence we would like the CGC to reconsider the statement “<i>The group felt that as the clinical review did not find evidence to support this assumption, results of such models should be interpreted with caution</i>”.</p>	
127	SH	Arrhythmia Alliance, The Heart Rhythm Charity	15	FULL	297	2	<p>(a) As ablation is a specialised procedure, not well known by non-specialist, it would be helpful to clarify who should discuss this treatment option with the patient.</p> <p>(b) The recommendations suggests that drug therapy is always first line choice therapy. However, in the group of patients experiencing the recent onset of lone AF, who are active and otherwise healthy, there may be the benefit of improved outcomes, if ablation is considered as a possible first line option.</p>	<p>Thank you for your comment.</p> <p>(a) NICE clinical guidelines have not usually named professionals.</p> <p>(b) The evidence for first line ablation is limited and contradictory. The GDG considered it reasonable to recommend that patients try drug therapy first (if not contraindicated). This guideline does recommend that they are then offered the next treatment option (ablation) in a timely fashion (<4 weeks) if this is not successful and/or tolerated.</p>
86	SH	BRITISH HEART RHYTHM	4	FULL	297	2	<p>Recommendation 53: This recommendation is based on one study (Boersma 2012) which compared catheter ablation vs. surgical ablation for</p>	<p>Thank you for your comment. We agree and the recommendation has been changed accordingly.</p>

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		SOCIETY (FORMERLY HRUK)					patients with persistent AF. This study by definition included patients 'less amenable to catheter ablation' and 2/3 of patients had already failed a previous catheter ablation procedure. Whilst surgical ablation could be considered as an option for patients with challenging persistent AF based on their profile, there are few surgical centres in the UK performing stand-alone thoracoscopic ablation whilst catheter ablation for persistent AF is more commonly performed with reasonable outcome data. The recommendation infers that surgical ablation is perhaps preferable over catheter ablation and we would suggest that this statement is re-written to say 'consider left atrial catheter ablation or surgical ablation for people with persistent AF'	
152	SH	MEDTRONIC LIMITED	7	FULL	297	2	Medtronic welcomes the updated recommendation for Left Atrial Ablation	Thank you for your comment.
153	SH	MEDTRONIC LIMITED	8	FULL	316	1	Medtronic welcomes the updated recommendation for Pace and Ablate	Thank you for your comment.
87	SH	BRITISH HEART RHYTHM SOCIETY	5	FULL	317	1	Recommendation 55: It is disappointing that the GDG have not considered the specific role of resynchronisation pacing (CRT) compared with single site right ventricular pacing following AV	Thank you for your comment. It was outside of our scope to consider different types of pacing.

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		(FORMERLY HRUK)					nodal ablation, particularly for those patients with pre-existing LV dysfunction. Among patients undergoing AV junction ablation for chronic AF, the PAVE trial (Doshi 2005) randomised patients to either RV apical pacing or biventricular pacing. Those with RV apical pacing had a deterioration in LVEF that was avoided by those with biventricular pacing with the latter group having improved exercise capacity. Other reports have demonstrated that for those patients who develop heart failure after AV node ablation, upgrading them to a biventricular device improves symptoms and LV function. We believe the role of resynchronisation pacing prior to AV nodal ablation, particularly for patients with pre-existing LV dysfunction should be considered in the guidance	
234	SH	Resuscitation Council (UK)	42	FULL	319	First box - recommendation 56	Where a pace-and-ablate strategy is adopted for people with paroxysmal AF (perhaps after failed left atrial ablation) it is important to ensure that the pacemaker is programmed to provide atrial pacing, which in a few patients will reduce the occurrence of PAF, but as far as possible to avoid unnecessary RV pacing, which will tend to encourage further AF.	Thank you for your comment. We agree but recommendations as to choice of pacemaker and pacing mode lie outside the scope of the guideline.
154	SH	MEDTRONIC	9	FULL	319	1	Medtronic welcomes the updated recommendation for Pace and Ablate	Thank you for your comment.

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		LIMITED						
155	SH	MEDTRONIC LIMITED	10	FULL	320	2	Medtronic welcomes the updated recommendation for Pace and Ablate	Thank you for your comment.
235	SH	Resuscitation Council (UK)	43	FULL	322-353	general	This section contains 30 pages that focus on pharmacological and other therapies to achieve rate control or restoration of sinus rhythm but makes no mention of the importance of correcting physiological and biochemical abnormalities that may be driving the heart rate or potentially preventing effective rhythm control. If a person is hypovolaemic or in uncontrolled heart failure attempts to suppress the heart rate alone will be ineffective and potentially dangerous unless the underlying physiological abnormality is treated also. It is really important to emphasise this. Correction of electrolyte abnormality (especially hypokalaemia) is a crucial component of a safe and effective approach to rhythm control. Correction of hypoxia is mentioned in relation to AF after cardiothoracic surgery but not in this section.	Thank you for your comment. We agree and this point has already been made in bullet points 2 and 4 of the introduction. However, we have now expanded on this further at the end of this paragraph.
236	SH	Resuscitation Council (UK)	44	FULL	323	table 102	'Calcium rate limiting antagonists' should be replaced with 'rate-limiting calcium channel blockers'.	Thank you for your comment. We have edited this accordingly.

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237	SH	Resuscitation Council (UK)	45	FULL	350	para 2, 3 rd bullet point	Having used 'arrhythmia' throughout the previous 349 pages the word 'dysrhythmia' has now been used instead – suggest change to 'arrhythmia' for consistency.	Thank you for your comment. We have changed this for consistency.
89	SH	BRITISH HEART RHYTHM SOCIETY (FORMERLY HRUK)	7	FULL (short)	15	2	The guideline recommends offering anticoagulation with a novel anticoagulant or a vitamin K antagonist and links to the recent technology appraisals for these new agents. Uptake and prescribing of the novel anticoagulants has not been uniform throughout the UK despite fairly robust evidence for their benefits due to cost implications. Patients in certain areas of the UK may have no or limited access to these agents except in circumstances where inadequate anticoagulation control with a vitamin K antagonist has been the case despite the NICE recommendations. The current guideline may not be explicit enough in its recommendations to address this issue.	Thank you. NICE already has guidance (technology appraisal) in the area and it was not appropriate to review individual NOACs within this guideline. The technology appraisals have been fully incorporated in this guideline.
181	SH	Boehringer Ingelheim	1	FULL and NICE	General	General	NOACs are underrepresented as a class throughout the guideline. As both NOACs and warfarin are considered as first line anticoagulation strategies they should be acknowledged equally throughout the guideline. All three NOACs have received full NICE guidance (TA 249, TA 256, TA 275) as alternative treatment options to warfarin,	Thank you for your comment. We have incorporated the NICE technology appraisals into the guideline and given them equal emphasis with vitamin K antagonists in the revised algorithm.

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							which is recognised in the full guideline.	
264	SH	Bayer Healthcare	1	FULL and NICE	General	General	<p>In general we support the recommendations included in this clinical guideline. In particular, the delivery of a personalised package of care and information, the use of risk stratification tools to guide management decisions, and a clear emphasis on the importance of appropriately managed interventions to reduce the risk of stroke in people with atrial fibrillation (AF), all of which will be instrumental in reducing the acknowledged shortfall in current anticoagulant uptake.</p> <p>We do have a few observations and areas for clarification which we have outlined in our comments below.</p>	Thank you for your comment. We are pleased that in general you support the recommendations in the guideline. We will address each of your comments in turn.
96		NHS Sheffield CCG	6	FULL and NICE	General	General	<p>It would be helpful if NICE could resolve the apparent disparity between this draft AF guideline and the NICE recommendations for the 2014/15 QOF. This draft AF guideline recommends the use of CHA2DS2-VASc scoring whereas QOF indicator AF4 (NICE indicator reference NM46) specifies the use of CHADS2 in a primary care setting. We note that NICE as part of the guideline development has appraised the use of CHA2DS2-VASc versus CHADS2. However, this would present two different concurrent versions of NICE recommended clinical practice in primary care settings, and implying</p>	Thank you for your comment. We anticipate the QOF will be reconsidered in the context of the changes to the guideline.

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							different absolute stroke risk thresholds for offering / considering anticoagulation.	
210	SH	Resuscitation Council (UK)	18	FULL and NICE	general	general	The guidelines do not make clear whether they apply to atrial flutter as well as AF. There is just one reference to atrial flutter in relation to thromboembolic risk but no reference to the fact that these are different rhythms with different causes and potentially different responses to treatment, with rhythm control being a highly effective strategy in the majority of people with atrial flutter and rate control being a poor second-best option for many patients. Even if this was considered outside the scope of the guideline and its update, a clear statement acknowledging the exclusion of this important clinical element and the reason for its exclusion would be helpful.	Thank you for your comment. We agree and have added some wording to the introduction for chapter 17 and linking evidence to recommendation section 13.2.4.
211	SH	Resuscitation Council (UK)	19	FULL and NICE	general	general	Some spelling errors and many errors of punctuation are scattered throughout the documents and for some readers will be distracting and will reduce the credibility of the content. Examples include repeated incorrect spelling of 'dronedarone', numerous unhyphenated compound adjectives and incorrect use of a hyphen in 'Ambulatory ECG' and when 'beta blocker' is used as a noun: 'beta-blocker' should be hyphenated only when used as a compound adjective. Otherwise 'beta blocker' or 'beta-adrenoceptor	Thank you for your feedback. The spelling errors and punctuation have been corrected.

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							blocker' are correct. It is surprising that NICE has, largely, omitted the hyphen from cost-effective erroneously but has inserted an incorrect hyphen in cost-effectiveness!	
111	SH	Royal College of Pathologists & British Society for Haematology	15	FULL and NICE	354/26	27-31/1.7.5	<p>Recommendation for using Heparin is a continuation of current practice with no evidence basis. The use of Heparin/LMWH is unlicensed for this indication.</p> <p>In past heparin was used in these situations as it was the only short half-life anticoagulant available. This situation has now changed with the availability of new oral anticoagulants. Even if anticoagulation is being considered for short term, awaiting full review, new oral anticoagulants should be an option in this situation</p>	Thank you for your comment, this is outside the scope of the update of the guideline.
129	SH	Daiichi Sankyo UK	1	FULL and NICE	NICE: page 16 Full : 44	NICE: section 1.5 Full : line 1	In the NICE version of the draft guidelines, the interventions listed as options for treatment (the novel oral anticoagulants and vitamin K antagonists) are listed with equal weighting. However, the treatment algorithm in the full guideline appears to preferentially recommend treatment with VKAs, followed by second-line treatment with NOACs. To avoid confusion, we recommend that the treatment algorithm is amended to reflect the wording in the NICE guideline.	Thank you for your comment. We agree and have updated the algorithm.

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165	SH	The Stroke Association	2	NICE	General	General	The wording used in the recommendations for the Novel Oral Anticoagulants includes detail on joint decision making and discussion of risks and benefits of the treatment e.g. 1.5.4. It is suggested that similar wording is used in the recommendations for other treatments, to promote informed joint decision making in all practice.	Thank you for your comment. Where possible the GDG have adopted the approach you have suggested.
81	SH	Boston Scientific	6	NICE			d) In December 2013, the U.S. FDA Circulatory System Devices Panel of the Medical Devices Advisory Committee voted favorably by a majority, Yes: 13, No: 1, that the benefits of the WATCHMAN Left Atrial Appendage Closure device outweigh the risks. The FDA Panel was further asked if there is reasonable assurance that the device is safe, the Panel voted Yes: 13, No: 1. On the question of reasonable assurance of efficacy, the Panel voted Yes: 13, No: 1. The FDA will take into account the Panel's vote in its decision on approval of the WATCHMAN device. Approval is expected in the first half of 2014	Thank you for your comment. The GDG agreed to change the order of the recommendations 1.15.19 before 1.5.18.
238	SH	Bristol-Myers Squibb and Pfizer	1	NICE	General	General	Overall, we welcome this update to the guideline and support the new recommendations that we believe will drive improvements in patient outcomes in atrial fibrillation (AF) through, for example: <ul style="list-style-type: none"> The recommendation for a personalised package of care and information The assessment of stroke and bleeding 	Thank you for your comment.

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							<p>risks using validated tools (CHA2DS2-VASc and HAS-BLED)</p> <ul style="list-style-type: none"> The recommendation enabling the opportunity to choose between all 4 oral anticoagulants (OACs) <p>However, the Bristol-Myers Squibb Pfizer Alliance has a number of concerns that we believe could be addressed with some minor clarifications and we have described these below.</p>	
249	SH	Bristol-Myers Squibb and Pfizer	12	NICE	General	General	<p>Whilst we recognise that this is a clinical guideline and therefore not subject to the same legal and funding requirements associated with NICE technology appraisals. However, this guideline refers to a number of technology appraisals.</p> <p>We therefore suggest that it would be useful to reiterate NHS obligations to implement NICE guidance within 3 months and to remind the NHS that NICE assessments should not be duplicated locally.</p>	<p>Thank you for your comment. This is relevant to the Technology Appraisals only, and hence we have not included this wording in the guideline.</p> <p>We have passed on your concerns to the implementation team.</p>
139	SH	British Medical Association	1	NICE	General	General	<p>This is an extensive re-write of existing recommendations and it is considerably more complex. We suspect that most GPs will no longer be comfortable with managing Atrial Fibrillation (AF) in primary care.</p>	<p>Thank you for your comment. Where possible we have tried to make this guideline less complex by avoiding subdivision of atrial fibrillation (for example, paroxysmal, persistent, and permanent). We have further clarified the algorithm in line with the</p>

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								consensus of stakeholder comments.
75	SH	National AF Clinical Policy Forum (NAFCPF)	3	NICE	General	General	The NAFCPF notes that there seem to be regional inconsistencies in local guidance on which part of the patient pathway should be responsible for making the decision on which anticoagulant should be used in the treatment of any given patient. The NAFCPF are aware of both areas where it is recommended that this decision should always be taken by the GP as well areas where clinicians have been advised that this decision should be taken exclusively in the secondary care setting. We recognise that tackling this variation most likely falls beyond the scope of this guideline, however, any clarity that could be provided by this document on the scope of responsibilities of different parts of the patient pathway would go a long way in addressing the confusion which may currently exist in the NHS.	Thank you for your comment. This is an implementation issue, and we have highlighted this point to the NICE implementation team.
209	SH	Resuscitation Council (UK)	17	NICE		deleted 1.5.1.6	Although continuing surveillance and review of treatment should be provided for people with both paroxysmal and permanent AF the harsh reality of the situation is that this does not always happen. If the guideline states that it should happen, that can then form the basis of quality standards for and audit of the management of patients with AF both in general practice and in secondary care. As far as we can see, the only statement about review in the new guideline relates to review of stroke risk.	Thank you for your comment. Recommendations 1.5.17 and 1.5.18 suggest reviews for those on anticoagulants and those with identified risk factors.

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260	SH	Roche Diagnostics	1	NICE	general		We congratulate the guideline development group on this very comprehensive and up-to-date guideline and welcome the update on anticoagulation by inclusion of the verbatim recommendations from relevant technology guidance.	Thank you for your feedback.
164	SH	The Stroke Association	1	NICE	General	General	We welcome the opportunity to comment on this draft guideline for atrial fibrillation (AF). The link between AF and stroke is well established and the Cardiovascular Disease Outcomes Strategy estimates that by improving uptake of anti-thrombotic therapy 2,100 lives could be saved per year and there could be 7,100 fewer strokes per year.	Thank you for your comment.
20	SH	Royal College General Practitioners	9	NICE		1.1.3	Will 24hr ECG detect evidence in people with suspected asymptomatic episodes?	Thank you for your comment. Recommendation 1.1.3 was not updated as part of the current guideline and the evidence was not reviewed. Please see page 11 of the full guideline for a description of what was covered during this update.
22	SH	Royal College General Practitioners	11	NICE		1.1.5	This is very helpful	Thank you for your comment.
25	SH	Royal College General Practitioners	14	NICE		1.4.2	Also what is harmful alcohol and CKD 4 and 5	Thank you. In relation to your point regarding harmful alcohol consumption: The 'alcohol' criterion refers to alcohol

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		ers						<p>excess/abuse. For the validation paper a numerical figure was stated as this was needed for a statistical validation. Other published validations have used 'hospitalisation for alcohol excess' and the outcome is unchanged. Different studies define harmful alcohol differently, and therefore we are unable to give an exact definition.</p> <p>Risk scores need to be pragmatic. The GDG agreed to align with the definition used in the 2012 ESC guidelines i.e. alcohol excess or abuse, which is essentially an intake where the clinician assesses there would be an impact on health or bleeding risk.</p> <p>In relation to the point about abnormal renal function we would suggest defining abnormal renal function as e.g. serum creatinine >200, or creatinine clearance <30mls/min, or need for dialysis.</p> <p>Also please see the draft consultation CKD guideline http://www.nice.org.uk/nicemedia/live/13712/66658/66658.pdf (page 54) - due for publication 23rd July 2014. Table 27 provides a classification of CKD GFR and ACR categories. We have cross reference to this draft in the LETR section of 10.2.4 'other considerations box'.</p>
28	S	Royal	1	NIC		1.5.	I need to find the evidence for men with	

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	H	College General Practitioners	7	E		2	CHADSVASC of 1. The numbers of such low risk patients included in the trials would have been very low. It would be important to confirm that they would have the option to have a NOAC as well as warfarin.	Thank you for your comment. The SPORTIF, RELY, ARISTOTLE and AVERROES trials all includes AF patients with a single risk factor (some had CHA2DS2-VASc=1)
26	SH	Royal College General Practitioners	15	NICE		1.4.4	However consideration should be given to correctable causes of falls including orthostatic hypotension and social factors	Thank you for your comment. Please refer to section 10 where this is mentioned.
248	SH	Bristol-Myers Squibb and Pfizer	11	NICE	9	General	<p>We support the recommendation for prompt referral to specialist management if treatment fails to control the symptoms. We suggest that the guideline should clarify that the preferred setting for the routine management of AF patients is primary or community care.</p> <p>We note that the recommendations outlined in NICE's <i>CMG49: Support for commissioning: anticoagulation therapy</i> state that: "The novel oral anticoagulants can be readily prescribed in primary care by GPs and a dedicated monitoring service is not needed. Commissioners should consider rationalising anticoagulation services over time as increasing numbers of people are prescribed these new drugs."</p>	The GDG felt that AF patients should be referred promptly and be managed with an appropriate level of expertise. Whilst it may be true that the majority of patients may be managed well in primary care, others require specialist management (either in primary or secondary). The guideline did not review service configurations or optimal commissioning structures, as these would be highly influenced by local factors.
12	S	Royal	1	NI	9		Personalised package of care information I think	Thank you. We have amended the wording of the first

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	H	College General Practitioners		CE			that the first bullet point should be stroke risk assessment because it is difficult to deal with the rest if this is not clearly stated	bullet point to read 'stroke awareness and measures to prevent stroke' which is inclusive of stroke risk assessment.
13	SH	Royal College General Practitioners	2	NICE	9		Superscript point 1 re referral after cardioversion. If it hasn't worked then why do we need to refer everyone back within 4 weeks? If it is required it this should be included in the hospital pathway and not involving another new referral from primary care	Thank you for your comment. It was not the intention of the guideline to recommend that all patients should be referred back within 4 weeks of failed cardioversion. The need for repeat referral would depend on circumstances. For example, a patient who was symptomatically well on a rate control strategy would not require re-referral. However, if further treatment is required, most particularly consideration of ablation, it is important that this should occur expeditiously. The wording of the footnote has been clarified.
166	SH	The Stroke Association	3	NICE	9		The prioritisation of personalised packages of care and information is important to enable people to make informed decisions about their care and lifestyle.	Thank you for your comment.
167	SH	The Stroke Association	4	NICE	9		The prioritisation of assessment of stroke and bleeding risk is important to enable an informed discussion between people with AF and clinicians about anticoagulation. These informed discussions are vital when making decisions about the right treatment for an individual.	Thank you for your comment.
14	SH	Royal College	3	NICE	10	Stroke	Does this also include after ablation?	Thank you for this comment. The GDG did not specifically review the evidence on this question.

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		General Practitioners				risk final bullet		
15	SH	Royal College General Practitioners	4	NICE	10	Bleeding risk	What is harmful alcohol consumption?	<p>Thank you. Risk scores need to be pragmatic. The 'alcohol' criterion refers to alcohol excess/abuse. For the validation paper a numerical figure was stated as this was needed for a statistical validation. Other published validations have used 'hospitalisation for alcohol excess' and the outcome is unchanged. As different studies define harmful alcohol differently, and therefore we are unable to give an exact definition.</p> <p>The GDG agreed to align with the definition used in the 2012 ESC guidelines i.e. alcohol excess or abuse, which is essentially an intake where the clinician assesses there would be an impact on health or bleeding risk.</p>
16	SH	Royal College General Practitioners	5	NICE	10	Bleeding risk	Please consider adding CKD 4 and 5	<p>Thank you for your comment</p> <p>In relation to the point about CKD 4 and 5 we would suggest defining abnormal renal function as (e.g.). Serum creatinine >200, or creatinine clearance <30mls/min, or need for dialysis).</p> <p>Also please see the draft consultation CKD guideline http://www.nice.org.uk/nicemedia/live/13712/66658/66658.pdf (page 54) - due for publication 23rd July</p>

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								2014. Table 27 provides a classification of CKD GFR and ACR categories. We have cross reference to this draft in the LETR section of 10.2.4 'other considerations box'.
17	SH	Royal College General Practitioners	6	NICE	10	Assessing anticoag control	What is at each visit ? Continuous monitoring of TTR	Thank you for your comment. The recommendation states that the TTR should be calculated at each visit.
168	SH	The Stroke Association	5	NICE	10		We agree with the prioritisation of interventions to prevent stroke as AF increases the risk of stroke by five times and reduction of this risk is vital to prevent mortality and disability.	Thank you for your comment
246	SH	Bristol-Myers Squibb and Pfizer	9	NICE	10 16	1.5.1	<p>We note that page 10 of the NICE guideline and page 16 (1.5.1) highlight the priorities for intervention recommending anticoagulation. This is followed on page 10 by a section on assessing anticoagulation control with VKAs, which may imply that VKAs are the only choice for anticoagulation.</p> <p>We suggest that the priority for implementation should reflect recommendation 1.5 by adding that anticoagulation may be with apixaban, dabigatran etexilate, rivaroxaban or a vitamin K</p>	Thank you for your comment. We agree and have added a line under the heading 'anticoagulation' stating 'Anticoagulation may be with apixaban, dabigatran etexilate, rivaroxaban or vitamin k antagonist'.

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							antagonist.	
18	SH	Royal College General Practitioners	7	NICE	11	Pace and ablate	Has this been missed off?	Thank you for your comment. This section refers to the ten selected key priorities for implementation and not the full list of recommendations. There were no recommendations on pace and ablate selected as a key priority for implementation.
194	SH	Resuscitation Council (UK)	2	NICE FULL FULL	11 and 19 and 20 48 51	1.5 1.5. 14 23 25	The term 'Platelet inhibitor' is preferable to 'Antiplatelet'	Thank you for your comment. The GDG feel that anti-platelet agents is the accepted term in the anticoagulation field.
19	SH	Royal College General Practitioners	8	NICE	12	1.1 .1	Why has And at annual review of people with hypertension, IHD, stroke and CKD been missed off?	Thank you for your comment. Recommendation 1.1.1 on Identification and diagnosis was not updated as part of the current guideline update, as described in the section on guideline update on page 11 of the full guideline.
195	SH	Resuscitation Council (UK)	3	NICE FULL	13 50	1.1. 4 line s 18– 21	We suggest rewording for clarity. Heart failure and heart murmur are not examples of structural heart disease but are examples of the triggers that should raise suspicion thereof.	Thank you for your comment. Recommendation 1.1.4 on Identification and diagnosis was not updated as part of the current guideline update, as described in the section on guideline update on page 11 of the full guideline.

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21	SH	Royal College General Practitioners	10	NICE	13	1.1.4	First bullet seems so all encompassing that it includes everyone with AF which is then excluded by 1.1.5 so I wonder why it is included as the first bullet?	Thank you for your comment. Recommendation 1.1.4 on Identification and diagnosis was not updated as part of the current guideline update, as described in the section on guideline update on page 11 of the full guideline.
262	SH	Roche Diagnostics	3	NICE	14		The description of the personalised package of care could contain more details. As a very significant proportion of AF patients require anticoagulation and the relevant sections of the guideline have undergone major update. the personalised care package should therefore highlight the choice of anticoagulation therapy and options of self-monitoring for patient on long-term vitamin K antagonist which affect the majority of patients.	Thank you for your comment. The GDG believe there is adequate information within the recommendation 1.2.1. The guideline cross refers to the NICE diagnostic guidance on self-monitoring coagulometers.
140	SH	British Medical Association	2	NICE	14	1.3	Despite section 1.3 'Referral for specialised management: Refer people promptly at any stage if treatment fails to control the symptoms of AF and referral for more specialised management is needed', most patients will be referred in order to gain specialist advice on the desirability of the more modern treatments.	Thank you. Following reviewing the evidence the GDG recommended that there should be timely onward referral of patients who remain symptomatic despite their initial care package. The GDG wanted to ensure that patients were promptly referred if their initial care package (for whatever reason) had not helped to control their symptoms or when further management requires onward referral (this would be inclusive of further specialist advice about type of treatment). Please see the linking evidence to recommendation section 7.2.4 of the full guideline.
23	SH	Royal College General	12	NICE	14	1.2.1	Also to include stroke risk assessment	Thank you. We have amended the wording of the first bullet point to read 'stroke awareness and measures to prevent stroke' which is inclusive of stroke risk

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		Practitioners						assessment.
169	SH	The Stroke Association	6	NICE	14	1.2.1	<p>We agree with the guidance on personalised care and information. Particularly the guidance on ensuring people have information on psychological support and support networks, as these have been identified as areas of unmet need in stroke survivors in the Stroke Association's report "Feeling Overwhelmed": http://www.stroke.org.uk/sites/default/files/files/Feeling%20Overwhelmed_Final_2_5mb.pdf</p> <p>We suggest that all information should be delivered in a format accessible to the person and that this guidance should be included in the recommendations. People need to be able to understand the information they are given, otherwise there is little point giving it. This could mean providing information in a person's first language, in easy words and pictures or in audio. This point is particularly important for people with AF who are stroke survivors as aphasia and cognitive difficulties are common.</p> <p>We would recommend that the bullet on measures to prevent stroke goes into more detail about the measures that should be covered, including information about lifestyle risk factor reduction.</p>	<p>Thank you for your comments, suggestions and information. We did not review evidence pertaining to stroke survivors so we are unable to include the reference you provide us with.</p> <p>With regard to recommendation 1.2.1, this is not an exhaustive list however we have edited the recommendation to include 'stroke awareness', 'who to contact for advice if needed' and 'support networks (for example, cardiovascular charities)'.</p> <p>We have liaised with the NICE editor who will include reference to The Stroke Association at the back of the NICE AF Information for the Public (IFP) version as a source of advice and information.</p>

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							<p>It is recommended that the following additional bullet points are added to the list of personalised care and information to be documented and delivered:</p> <ul style="list-style-type: none"> • Clear guidance about who to contact if they experience an issue with their condition or medication. • Stroke prevention services • Guidance on managing AF with co-morbidities 	
196	SH	Resuscitation Council (UK)	4	NICE FULL FULL	14 48	1.3.1 line s 7–9 line s 9–11	We suggest that this recommendation should advise referral to a heart rhythm specialist, or at least make reference to the importance of considering the most appropriate choice of specialist service. Simply making generic referral to a cardiologist may not be the best option for the patient or the most cost-effective option.	Thank you for your comment. The GDG define “specialist management” as the investigation and further assessment/treatment by a health care professional (such as a cardiologist with an interest in arrhythmia) with appropriate expertise.
170	SH	The Stroke Association	7	NICE	14	1.3.1	We suggest re-defining prompt referral for the purposes of these guidelines. If people wait 4 weeks following their final failed treatment or 4 weeks after the recurrence of AF following cardioversion followed by a potential waiting list for the specialist management service, then scheduling	Thank you for your comment. The GDG feels that the 4 week target is a reasonable one, and is an improvement upon current practice.

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							an appointment in the future and getting specialist management – this is potentially a long wait between final failed treatment or recurrence of AF following cardioversion. A long wait is negative from a patient experience point of view, as well as a stroke risk reduction point of view.	
73	SH	National AF Clinical Policy Forum (NAFCPF)	1	NICE	15	1-9	<p>The NAFCPF fully supports the move away from CHADS₂ to CHA₂DS₂-VASc stroke risk score. Despite the fact that CHADS₂ still features in the AF QOF indicators, the CHA₂DS₂-VASc scoring scheme has been shown to outperform CHADS₂ in identifying truly low-risk patients with AF, and is at least as good as, and possibly better in identifying high risk patients.</p> <p>While the NAFCPF supports the inclusion of recommendation 1.4.1, we believe that the recommendation might be extended to include a comment on the desirability of a change of emphasis when undertaking stroke risk assessment of patients with AF. In line with the recommendations of the European Society of Cardiology, we propose that the recommendation de-emphasises the artificial categorization of AF patients into low, moderate and high risk strata – practice associated with the use of the CHADS₂ scheme. Instead, the recommendation should emphasise that, with the move towards CHA₂DS₂-</p>	Thank you. We agree. We have added a new recommendation to emphasise this point.

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							VASc, the focus need to be on the identification of truly low-risk patients with AF (CHA ₂ DS ₂ -VASc = 0). Only these truly low-risk patients do not require any antithrombotic therapy.	
145	SH	UK Clinical Pharmacy Association: Haemostasis Anticoagulation & Thrombosis (HAT) Group Cardiac Group	2	NICE	15	1-9	The UKCPA fully supports the move away from CHADS ₂ to CHA ₂ DS ₂ -VASc stroke risk score. Despite the fact that CHADS ₂ still features in the AF QOF indicators, the CHA ₂ DS ₂ -VASc scoring scheme has been shown to outperform CHADS ₂ in identifying truly low-risk patients with AF, and is at least as good as, and possibly better in identifying high risk patients.	Thank you for your comment.
91	SH	NHS Sheffield CCG	1	NICE	15	1.4.1	Recommendation to use CHADSVASC in place of CHADS ₂ . Currently the QoF clinical indicator for AF uses the CHADS ₂ score and this is retained for 14/15: http://www.nhsemployers.org/SiteCollectionDocuments/2014_15_Summary_of_QOF_changes_mh141113.pdf There is thus a disparity between the	Thank you for your comment. We anticipate the QOF will be reconsidered in the context of the changes to the guideline. .

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							recommendation in this guideline, the QoF measure for 14/15 and the scoring tool available on the GP practice clinical computer system. This needs to be recognised and the disparity resolved if implementation of the change in risk calculator tool is to be effective in primary care over the next year.	
161	SH	NHS Trafford CCG	6	NICE	15	1.4.1	Link to CHADSVASc/HASBLED/EHRA: HASBLED – need to define when score for abnormal renal and liver function	<p>Thank you.</p> <p>In relation to the point about abnormal renal function we would suggest defining abnormal renal function as e.g. serum creatinine >200, or creatinine clearance <30mls/min, or need for dialysis.</p> <p>Also please see the draft consultation CKD guideline http://www.nice.org.uk/nicemedia/live/13712/66658/66658.pdf (page 54) - due for publication 23rd July 2014. Table 27 provides a classification of CKD GFR and ACR categories. We have cross reference to this draft in the LETR section of 10.2.4 'other considerations box'</p> <p>For abnormal liver function, this could be defined as rise of liver enzymes >2x ULN (Upper Limit of Normal), or known liver cirrhosis.</p>
24	SH	Royal College General Practitioners	13	NICE	15	1.4.1	Also after ablation	Thank you for your comment. There may be rare situations where asymptomatic AF should undergo catheter ablation for example when heart failure is thought to be the result of AF. Therefore although

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		ers						symptoms underpin the basis of all rhythm control (ablation is only one form of this) it would not be reasonable to expose rare patients who might benefit prognostically from rhythm control.
97	SH	Royal College of Pathologists & British Society for Haematology	1	NICE	15	1.4.2	HASBLED risk factors should be defined in the guideline. Eg harmful alcohol consumption (original HASBLED defined 8units/wk OR should it be the standard limit of 21 and 14 units/wk for M and F respectively). Also define uncontrolled HT (? >160mmHg, systolic)	<p>Thank you. The 'alcohol' criterion refers to alcohol excess/abuse. For the validation paper a numerical figure was stated as this was needed for a statistical validation. Other published validations have used 'hospitalisation for alcohol excess' and the outcome is unchanged. As different studies define harmful alcohol differently, and therefore we are unable to give an exact definition.</p> <p>Risk scores need to be pragmatic. The GDG agreed to align with the definition used in the 2012 ESC guidelines i.e. alcohol excess or abuse, which is essentially an intake where the clinician assesses there would be an impact on health or bleeding risk.</p> <p>Please see the NICE guideline (CG127) on hypertension published in August 2011, page 10/36 provides definitions. http://www.nice.org.uk/nicemedia/live/13561/56008/56008.pdf</p>
98	SH	Royal College of Pathologi	2	NICE	15	1.4.2	HASBLED: The criteria for Poor control of INR (whether < 60% in the original HASBLED score; Pisters R et al, chest/138/5/Nov 2010) or >70% as	Thank you for your comment. Regarding labile INR, the GDG agree it is acceptable to define this as (for example) TTR <60%, as with Pisters et al.

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		sts & British Society for Haematology					quoted as good INR control in ESC guidelines 2012 update (Camm et al E Heart J, 33,2719-2747)	
99	SH	Royal College of Pathologists & British Society for Haematology	3	NICE	15	1.4.2	HASBLED: score only identified Renal failure, Prior major bleeding and age>65 yrs as significant in univariate analysis. Hypertension, stroke, antiplatelet agent and alcohol use were not found to have significant impact on bleeding risk. (Pisters R et al, Chest/138/5/Nov 2010)	Thank you. This is a literal interpretation of the first validation paper which is a relatively small cohort (and hence isn't powered for all risk factors). The methodological section of the paper is worth reading as the risk factors used for HAS-BLED were initially identified in the EHS cohort and considered concomitantly with bleeding risk factors identified in systematic reviews. Other larger validations have proven the impact of the HAS-BLED risk factors on bleeding risk.
100	SH	Royal College of Pathologists & British Society for Haematology	4	NICE	15	1.4.2	HASBLED,HEMORR2HAGES AND ATRIA RISK SCORES DEMONSTRATE POOR AGREEMENT AND LOW TO MODERATE DISCRIMATORY ABILITY (Burgess et al, J Thrombosis and Haemast 2013; 11:1647-54)	Thank you for your comment. The Burgess et al paper was in a heterogeneous general anticoagulation cohort, which included both AF and non-AF patients, and therefore it could be expected that there would be poor agreement. HAS-BLED has been shown to outperform other scores in various independent trial and real world AF cohorts, and has been well- validated for AF.
101	SH	Royal College of Pathologi	5	NICE	15	1.4.2	Suggested comment to be added: 'There is no well validated and robust score for assessing bleeding risk and this is a research area. Until more	Thank you. The NICE version of the guideline contains only the recommendations.

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		sts & British Society for Haematology					evidence is available HASBLED score can be used to make clinical decisions and counselling patient'	<p>The linking evidence to recommendation section of the guideline section 10.2.4 'trade off between benefits and harms' notes 'The review found that the bleeding risk scores were generally poor at discriminating between risk groups, with HAS-BLED and HEMORR2HAGES score having a c-statistic of more than 0.7 in only 2 studies (refs 338,380), whilst all reported studies using the ATRIA score had a c-statistic of less than 0.7. The GDG considered that other factors such as applicability should be considered when making recommendations. The GDG agreed that if a bleeding risk score was used then it should be the HAS-BLED score as the other scores are more complex, miss important risk factors or include risk factors that are impractical (for example genetic information)'.</p> <p>The GDG did not prioritise this as an area for a future research recommendation.</p>
102	SH	Royal College of Pathologists & British Society for Haematology	6	NICE	15	1.4.3	Recommendation should define 'increased risk of bleeding'. If recommending use of HASBLED score, increased risk has been defined as HASBLED >3	Thank you for this comment. We can understand the wish to demarcate patients using HASBLED to identify those at increased bleeding risk. This was discussed by the GDG and it was not thought appropriate to adopt this approach. There is a danger that a designation of "increased risk" will be used to withhold anticoagulation whereas contraindications to anticoagulation need to be considered against the degree of stroke risk and hence any "cut-off" value

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								would vary with the stroke risk of the individual patient. The GDG considered that in the majority of patients stroke risk would outweigh bleeding risk. The GDG viewed the main value of the HASBLED score as assisting in the identification of potentially reversible bleeding risk factors.
171	SH	The Stroke Association	8	NICE	15	1.4.3	We believe that the discussion of the benefits and risks of anticoagulation with is vital to making a joint decision that is right for the individual. We suggest that the guidance also includes providing information in an accessible format, as detailed in Comment 4.	Thank for your comment. The Medicines and Prescribing team at NICE are developing a patient decision tool to support the implementation of this guideline.
92		NHS Sheffield CCG	2	NICE	15	1.4.4	'Do not withhold anticoagulation solely because the person is at risk of having a fall' - this recommendation is welcomed as local information suggests this as one of the factors that clinicians consider as a contra-indication to anticoagulation.	Thank you for your comment.
172	SH	The Stroke Association	9	NICE	15	1.4.4	We support the recommendation that anticoagulation should not be withheld solely because the person is at risk of having a fall.	Thank you for your comment.
138	SH	AntiCoagulation Europe	3	NICE	16		NOACS and VKA options clearly stated. Reference to current NICE assessment of self testing devices helpful for patients currently on VKA for AF	Thank you for your comments.

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74	SH	National AF Clinical Policy Forum (NAFCPF)	2	NICE	16	1-8	<p>Recommendation 1.5 correctly states that anticoagulation may be with apixaban, dabigatran etexilate, rivaroxaban or vitamin K antagonist – the four first line treatment options as recommended by NICE.</p> <p>Unfortunately, the NAFCPF has been made aware that many NHS organisations' prescribing protocols make it mandatory for prescribers to initiate all new AF patients, for whom anticoagulation for the prevention of AF-related stroke is recommended, on warfarin for a specified period of time.</p> <p>In these areas, patients do not have access to the full range of NICE-recommended therapies at the time of initiation, placing local organisations in breach of the NHS Constitution. While we note that the use of novel oral anticoagulants can be associated with cost implications, local NHS organisations should recognise that treatment with warfarin may not be suitable for certain groups of patients and making them undergo 'warfarin stress testing' might place them at risk.</p> <p>In order to identify those patients for which warfarin may not be suitable, NICE may wish to recommend the use of SAME-TT₂R₂ – a validated practical</p>	<p>Thank you for your comments. Your feedback on the prescribing of anticoagulants has been passed onto the NICE implementation team.</p> <p>In relation to SAME-TT₂R₂ .this score was discussed by the GDG. However, this score was not published at the time the GDG set the protocol for this question. In addition the validation study was only published after our final cut-off date for included publications. This score has been included in one of the guidelines research recommendations (Appendix P).</p> <p>The NICE version of the guideline provides the reader with the recommendations rather than additional narrative text. Recommendation 1.5.4 has been added and says 'Discuss the options for anticoagulation with the person and base the choice on their clinical features and preferences'.</p>

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							<p>scoring tool for assessing the likelihood of poor international normalised ratio (INR) control in AF patients initiated on warfarin.</p> <p>However, given that the current NICE guidance does not differentiate between the four first line treatments for the prevention of AF-related stroke, we would like to see recommendation 1.5 expanded to put greater emphasis on the importance of patient choice in the selection of the most appropriate treatment. While we recognise that references to the need for an informed discussion with the clinician are featured in the sections on separate treatments (1.5.3, 1.5.4 and 1.5.5), we would argue for the inclusion of a prominent overarching paragraph on the importance of patient choice near the beginning of recommendation 1.5.</p> <p>This paragraph should make it clear that, the decision to start treatment with any anticoagulant should be made after an informed discussion between the clinician and the patient about their preferences for treatment. It is known that patients' beliefs about their health, their medical conditions, treatment options and healthcare they receive are key determinants of whether or not they accept recommended treatment in general and may be</p>	

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							particularly important for stroke prevention in AF, which requires life-long adherence to treatment which can have potentially serious side-effects.	
197	SH	Resuscitation Council (UK)	5	NICE	16	1.5	The guideline offers no advice on choice of NOAC. We recognise that this is because there are no good comparative studies on which to base advice. However we think that it would be helpful to those who are not familiar with NOACs to include a simple statement to that effect and perhaps mention some of the attributes of the NOACs that may be taken into account when making a choice.	Thank you for your comment. Medicines and Prescribing team at NICE are developing a patient decision tool to support the implementation of this guideline.
240	SH	Bristol-Myers Squibb and Pfizer	3	NICE	16	1.5	Although recommendations 1.5.3 to 1.5.8 state that the NOACs should be used in line with their marketing authorisation, we suggest that the distinction between valvular versus non-valvular atrial fibrillation (NVAF) should be clarified in this guideline. The European Society of Cardiology (ESC) updated guidelines for AF (2012) suggest that for valvular AF patients, treatment should be with VKA therapy, whilst the NOACs should be the preferred treatment for the majority of NVAF patients.	Thank you for your comment. We are in agreement and have altered the anticoagulation algorithm to make clear that it applies to patients with non-valvular AF. We also make it clear that NOACs should only be used in accordance with the existing NICE STAs.
244	SH	Bristol-Myers Squibb and Pfizer	7	NICE	16	1.5	We support the decision not to re-evaluate the clinical and economic evidence for the NOACs. However, we believe that the benefits associated	Thank you for your comment. This guideline has fully incorporated the guidance from published technology appraisals and the wording of these recommendations

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							<p>with the NOACs, which were recognised in the individual appraisals, have not been adequately captured in this guideline. In light of the benefits offered by the NOACs, and since NICE has found all 3 of the NOACs to be cost-effective options versus warfarin, we suggest that it would be appropriate for the guideline to recommend the use of NOACs as preferable for the majority of NVAF patients requiring anticoagulation, in line with the ESC updated guidelines (2012) for the management of AF.</p> <p>Furthermore, we would like to highlight that apixaban is the only NOAC to have demonstrated superior improvements compared to warfarin in stroke/systemic embolism rates, mortality and major bleeding rates (Granger et al., 2011).</p>	cannot be changed.
245	SH	Bristol-Myers Squibb and Pfizer	8	NICE	16	1.5	<p>We suggest that additional factors should be taken into account to inform the decision about which anticoagulant to prescribe.</p> <p>Firstly, we note that NICE commissioning support guidance 49 (CMG49) suggests that <i>"a person who has been referred to an anticoagulation service to start anticoagulation therapy should be assessed within 2 weeks."</i> In alignment with CMG49, we suggest that the guideline should recommend</p>	<p>Thank you for your comments.</p> <p>In relation to your first point, this is in line with the HTA already published by NICE. We have not defined time windows but the commissioning guide does specify speed to intervention. Many of those found to be in AF have been in this state for some time.</p> <p>In relation to points two, three and four recommendation 1.5.4. says 'Discuss the options for anticoagulation with the person and base the choice</p>

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				NICE	10	N/A	<p>that anticoagulation treatment should be initiated within the shortest clinically appropriate window. We also suggest that an alternative strategy should be considered if it is not possible to start anticoagulation therapy within 2 weeks.</p> <p>Second, we note that whilst regular anticoagulation monitoring is required for those prescribed VKA therapy, it is not required for the NOACs. We suggest that the absence of the requirement for regular anticoagulation monitoring should be considered as part of the prescribing decision.</p> <p>Thirdly, apixaban, dabigatran etexilate, rivaroxaban and VKAs have different characteristics and variable impact on patients. Therefore, we feel it is important to reiterate the need for an informed discussion between clinician and patient, upfront in section 1.5, as well as under recommendations 1.5.4, 1.5.6 and 1.5.8.</p> <p>Finally, as part of this consideration, we highlight the recognition that the first 6 weeks of anticoagulation with VKA might not be straightforward with the recommendation to 'exclude the first 6 weeks of treatment' (when calculating the person's time in therapeutic range.</p>	on their clinical features and preferences'.

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							<p>This aspect is in our view worthy of consideration and discussion with the patient at the time of choosing the appropriate anticoagulation.</p> <p>In summary, we suggest that 1.5 should recommend an informed discussion about all the treatment options available, taking into account timeliness of anticoagulation treatment, the requirement for regular anti-coagulation monitoring and patient's values and preferences, to ensure that the patient is prescribed the most appropriate anticoagulant for their needs.</p>	
93		NHS Sheffield CCG	3	NICE	16	1.5	<p>'Anticoagulation may be with apixaban, dabigatran etexilate, rivaroxaban or a vitamin K antagonist.' – the guideline then goes onto include recommendations from the separate NICE TAs for the NOACs without further comment. The choice between the 3 NOACs remains an issue for primary care clinicians. Thus it would be useful to expand this opening statement to provide more explicit guidance on the choice of NOACs. The NICE TAs were produced at different times e.g. dabigatran needs to be considered compared with warfarin whereas apixaban needs to be considered as a choice compared with warfarin, dabigatran and rivaroxaban. This introduces some confusion in</p>	<p>Thank you for your comments. The medicine prescribing team at NICE are developing a patient decision tool to support the implementation of this guideline.</p>

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							interpretation.	
27	SH	Royal College General Practitioners	16	NICE	16	1.5	Would it be helpful to include on the top line Except for those people with AF and valvular heart disease?	<p>Thank you. The existing recommendations already emphasise that use of the NOACs should be in accordance with their existing STAs. The recommendations are reproduced in the guideline and it is made clear that their use does not extend to non-valvular AF.</p> <p>However, in relation to the anticoagulation algorithm in the full guideline (which summarises the recommendations on anticoagulation including NOACs) the heading of the algorithm has been amended to make it clear that it refers to people with non-valvular AF.</p>
103	SH	Royal College of Pathologists & British Society for Haematology	7	NICE	16	1.5	Suggested comment to be added: ' patients <65 years with sole AF and no other risk factors irrespective of gender do not require anticoagulation for AF due to very low risk of stroke. These patients should be reviewed for assessment of risk factors on periodic basis'	Thank you for your comment. We agree and have added a new recommendation 1.5.1 for people with AF who do not need stroke prevention therapy.
173	SH	The Stroke Association	10	NICE	16	1.5	In this point the term "vitamin K antagonist" is used, however Warfarin is specifically referred to in the guidance on Novel Oral Anticoagulants. Consistency throughout the document would be appreciated.	Thank you for your comment. This guideline has fully incorporated the guidance from the published technology appraisals and the wording of these recommendations cannot be changed.

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104	SH	Royal College of Pathologists & British Society for Haematology	8	NICE	16	1.5.3	NICE TAG 275 is contradictory to the AF guidance. It recommends anticoagulation on the basis of CHADS risk factors and not the CHADSVASC recommended in the current guidance (a 66 year old male with h/o vascular disease will not be eligible for apixaban as per section 1.5.3 though will be eligible for anticoagulation as per the guideline)	<p>Thank you for your comment. The NICE guidance makes reference to the TA recommendations, which refer to '... with one or more stroke risk factors'.</p> <p>This guideline has fully incorporated the guidance from the published technology appraisals and the wording of these recommendations cannot be changed.</p>
141	SH	British Medical Association	3	NICE	16	1.5.4	We are concerned that GPs without a particular special interest in this subject will not be able to counsel patients to the required standards as detailed in 1.5.4, 1.5.6, and 1.5.8	Thank you for your comments. NICE already has guidance (technology appraisal) in the area and it was not appropriate to review individual NOACs with this guideline. The technology appraisals have been fully incorporated in this guideline.
239	SH	Bristol-Myers Squibb and Pfizer	2	NICE	16	1.5, 1.5.4, 1.5.6, 1.5.8	<p>Whilst we acknowledge that the recommendations included in the consultation are extracted from consecutively introduced individual technology appraisals, we are concerned that this creates variable and potentially misleading recommendations for the 3 NOACs. When deciding to commence treatment with apixaban, comparison with <u>warfarin, dabigatran etexilate and rivaroxaban</u> is encouraged. This differs to the other NOACs, wherein only comparison to warfarin is recommended:</p> <ul style="list-style-type: none"> 1.5.4: The decision about whether to start 	Thank you for your comment. This guideline has fully incorporated the guidance from the published technology appraisals and the wording of these recommendations cannot be changed.. However, the GDG have added a recommendation that the option for anticoagulation should be discussed and based on clinical features and preferences.

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							<p>treatment with apixaban should be made after an informed discussion between the clinician and the person about the risks and benefits of apixaban <u>compared with warfarin, dabigatran etexilate and rivaroxaban</u>.</p> <ul style="list-style-type: none"> 1.5.6: The decision about whether to start treatment with dabigatran etexilate should be made after an informed discussion between the clinician and the person about the risks and benefits of dabigatran etexilate <u>compared with warfarin</u>. 1.5.8: The decision about whether to start treatment with rivaroxaban should be made after an informed discussion between the clinician and the person about the risks and benefits of rivaroxaban <u>compared with warfarin</u>. <p>A general recommendation should be considered on informed discussion relating to all oral anticoagulants prior to the individual NOAC recommendations. The recommendation to compare with all other available anticoagulants should then be applied consistently in 1.5.4, 1.5.6 and 1.5.8.</p>	
9	S	ABPI	2	NIC	16	9	The draft guideline includes the NOACs as initial	Thank you for your comment. We agree and have

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	H	SAFI (Stroke Prevention in Atrial Fibrillation Initiative)		E	17 18 19		<p>treatment options for stroke prevention in Atrial Fibrillation, alongside warfarin, in line with individual health technology appraisal recommendations.</p> <p>We support this decision to recommend all three NOACs (or a vitamin K antagonist) as options for stroke prevention in non-valvular AF.</p> <p>However, we are concerned that the algorithm summarising the treatment approach does not accurately reflect the accompanying written guidelines. Specifically, the written guidelines position the three NOACs and VKA side by side as potential treatment options however the algorithm suggests that Vitamin K antagonists are considered over NOACs as the first-line treatment approach. We would recommend that the algorithm is amended accordingly to avoid confusion.</p>	amended the algorithm.
105	SH	Royal College of Pathologists & British Society for Haematology	9	NICE	17	1.5.5	<p>The criteria set for use of Apixaban/Rivaroxaban are different from Dabigatran. This has resulted from the design of the original studies and when CHADS score was in use. Different criteria for the same condition and intention of treatment will result in significant confusion. The individual TAG criteria (TAG 275, 249 and 256) should all be excluded from the draft AF guidance and only the CHADSVASC scoring should be used for decision</p>	<p>Thank you for your comment. We acknowledge your point.</p> <p>This guidance has fully incorporated the guidance from the published technology appraisals and the wording of these recommendations cannot be changed.</p>

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							regarding anticoagulation	
261	SH	Roche Diagnostics	2	NICE	19		We welcome the reference to the on-going diagnostic assessment on point-of-care coagulometers (the CoaguChek XS system and the INRatio2 PT/INR monitor) for self-monitoring coagulation status in people on long-term vitamin K antagonist therapy who have atrial fibrillation or heart valve disease. We would find it very beneficial for the reader if the final recommendations (due to be published by July 2014) could be included in the final guideline in verbatim. Given the timing of the final guidance on self-monitoring, there is an opportunity to accomplish an up-to-date guideline without a significant delay in publication.	Thank you for your comments. We are unable to include the suggested recommendations as these are published after the guideline is submitted and published.
109	SH	Royal College of Pathologists & British Society for Haematology	13	NICE	19	1.5.10	Recommended TTR 65% ESC guidelines 2012 recommend TTR 70% (Camm et al E Heart J, 33,2719-2747)	Thank you for your comment. The GDG agreed to define labile INR as being (for example) TTR <60%, as with Pisters et al., Chest 138, 5.
29	SH	Royal College General Practitioners	18	NICE	19	1.5.12	If poor control with a vitamin K antagonist cannot be improved?? We cannot assess control with a NOAC	Thank you for your comment. This recommendation has been modified.

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174	SH	The Stroke Association	11	NICE	19	1.5.12	We agree that evaluating risks and benefits of alternative stroke prevention strategies and discussing these with the person where anticoagulation control is poor is vital. It recognises the importance of stroke prevention while also ensuring people are treated as individuals.	Thank you for your comment.
243	SH	Bristol-Myers Squibb and Pfizer	6	NICE	19	1.5.13	<p>The current version of the AF guideline (CG36) recommends aspirin monotherapy as a treatment for stroke prevention, and this is no longer recommended in the draft guideline under consultation.</p> <p>We are supportive of the decision to no longer recommend aspirin monotherapy for stroke prevention in NVAf. However, we are concerned about the large number of patients already on aspirin and continuing to be given aspirin monotherapy for the purpose of stroke prevention in NVAf, a treatment that is no longer recommended in the guideline. This draft guideline makes no suggestions as to how these patients should be managed as a result of this change in recommendations.</p> <p>We suggest in the context of this indication, that clear recommendations are included in this guideline ensuring that patients currently</p>	<p>Thank you. The GDG have been very aware of this issue, as indeed have the NICE implementation team. A joint discussion was held between the two on this topic. The GDG considered adding a recommendation to the guideline to address the issue of patients on existing aspirin therapy with an indication for anticoagulation, who did not wish to convert to anticoagulant therapy. Whatever way this was worded, it still seemed to be a partial endorsement of aspirin. The GDG were of the opinion that there was a strong possibility that this would be misused as a justification for maintaining aspirin therapy and that this was not warranted.</p> <p>The guideline acknowledges that patients may need to be on aspirin for reasons other than stroke prevention. The GDG believed that in the AF population as a whole, there would frequently be justification for the use of aspirin for other reasons - but they wished to distinguish this from the false security of the use of aspirin for stroke prevention.</p>

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							<p>managed with aspirin only (for stroke prevention in non-valvular atrial fibrillation) are duly considered for anticoagulation where appropriate. Specific mention of apixaban may be considered, given the strong evidence base to support its benefits compared to aspirin.</p> <p>The AVERROES trial included patients (n=5,599) who were unable to take or unsuitable for VKA treatment and patients were randomised to aspirin or apixaban. The trial was stopped early (mean follow up of 1.1 years) because apixaban significantly reduced the risk of stroke or systemic embolism (55% reduction) compared to aspirin. There were no significant differences in key safety outcomes, including major bleeding or intracranial haemorrhage (ICH).</p>	The GDG were well aware of the AVERROES study and that many patients considered unsuitable for a VKA can successfully take a non-VKA oral anticoagulant. However, further consideration, comparison or recommendation of specific non-VKA oral anticoagulants is beyond the scope of this guideline.
106	SH	Royal College of Pathologists & British Society for Haematology	10	NICE	19	1.5.13	<p>Aspirin may be appropriate for following group of patients</p> <ol style="list-style-type: none"> 1. Those who decline any oral anticoagulation (patient choice after appropriate counselling) 2. Patients who cannot tolerate aspirin-clopidogrel combination 3. Patients who have contraindication or not suitable for any OAC (eg pt with renal impairment and inability to understand 	<p>Thank you for this comment. Aspirin should be only considered where other conditions suggest the use of aspirin as the benefit in AF alone is the same as CVD primary prevention and this is no longer recommended.</p> <p>Also as demonstrated by Walraven et al (2009) in Effect of Age on Stroke Prevention therapy in patients with atrial fibrillation: the atrial fibrillation investigators.</p>

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							regular dose changes of warfarin)	Stroke; a Journal of Cerebral Circulation. 2009; 40(4):1410-1416
107	SH	Royal College of Pathologists & British Society for Haematology	11	NICE	19	1.5.13	Suggested addition: Aspirin monotherapy is not recommended in most patients with AF requiring anticoagulation. It may however be the only option in some patients where anticoagulation is unacceptable or unsuitable due to various clinical reasons. These patients should preferably be discussed with specialist centres before deciding against oral anticoagulation. Patient should be informed that aspirin monotherapy has a lower efficacy in stroke prevention but similar risk of bleeding when compared with OAC.	Thank you for your comment. We agree. The guideline advises against use of aspirin monotherapy for stroke prevention in favour of OAC for the majority of patients. There will always be select groups where clinical judgement will dictate optimal care.
175	SH	The Stroke Association	12	NICE	19	1.5.13	We agree with this recommendation as there is no evidence that this treatment reduces the risk of stroke in people with AF.	Thank you for your comment. We are pleased that you agree with the recommendation.
142	SH	British Medical Association	4	NICE	19	1.5.9	The requirement to formally assess the amount of time spent with adequate anticoagulation over the preceding 6 months was not part of anticoagulation national enhanced service and if it is incorporated into locally commissioned services in future then we believe that this will result in an increased cost to	Thank you for this comment. The NICE Commissioning Guide, Support for Commissioning Anticoagulation Therapy, published in May 2013 states: <i>The Topic Advisory Group agreed that the following 4</i>

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							the NHS. Many CCGs have introduced restrictions on the use of non-warfarin anticoagulants which are considerably more restrictive than these guidelines	<p><i>measures should be used to monitor the overall quality of INR control in people taking vitamin K antagonists. Commissioners may wish to consider the audit requirements for the following measures, including frequency of data collection and formal reporting measures.</i></p> <p><i>Service time in therapeutic range</i> <i>Time within target INR range is an accepted indicator of the standard of anticoagulation therapy [6]. The Topic Advisory Group agreed that after the initial stabilisation of dose, a minimum of 60% of people under the care of an anticoagulation service should be within therapeutic range at a given point in time. The Topic Advisory Group agreed that it would be desirable that 65% of people should be within therapeutic range. Time in therapeutic range for people in the first 6 weeks on treatment should not be included in these calculations.</i></p> <p>We would therefore suggest that the recommendation for monitoring time in therapeutic range is already in place. In the Commissioning Guide, time in therapeutic range is recommended largely as a means of monitoring the quality of an anticoagulant service. We believe that the extension of the principle to assess quality of anticoagulation in the individual patient is a logical development.</p>

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								<p>It is our understanding that time in therapeutic range is readily available from a number of the software programmes used to guide anticoagulant dosing, so the recommendation does not necessarily incur a major additional workload.</p> <p>Your second point relates to implementation of the NOACs. More specifically to the STAs for the NOACs, but a recommendation has been added to this guideline (recommendation 1.5.4) to consider all forms of anticoagulation.</p>
10	SH	ABPI SAFI (Stroke Prevention in Atrial Fibrillation Initiative)	3	NICE	19	26	<p>The draft guideline, in contrast to the current AF NICE Guideline (CG36), states that aspirin monotherapy should no longer be offered for stroke prevention to people with AF</p> <p>We welcome this change in guidance relating to the use of aspirin monotherapy. However, we are concerned about the large population of patients who are on a treatment that is no longer recommended by NICE and for whom there is no guidance on how these patients should now be managed. We would recommend that such advice be included in the guideline.</p>	<p>Thank you. The GDG have been very aware of this issue, as indeed have the NICE implementation team. A joint discussion was held between the two on this topic. The GDG considered adding a recommendation to the guideline to address the issue of patients on existing aspirin therapy with an indication for anticoagulation, who did not wish to convert to anticoagulant therapy. Whatever way this was worded, it still seemed to be a partial endorsement of aspirin. The GDG were of the opinion that there was a strong possibility that this would be misused as a justification for maintaining aspirin therapy and that this was not warranted.</p> <p>The guideline acknowledges that patients may need to be on aspirin for reasons other than stroke prevention. The GDG believed that in the AF population as a whole, there would frequently be</p>

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								justification for the use of aspirin for other reasons - but they wished to distinguish this from the false security of the use of aspirin for stroke prevention. We anticipate the QOF will be reconsidered in the context of the changes to the guideline.
270	SH	Bayer Healthcare	7	NICE	20		Recommendation 1.5.14 We suggest that the risk of bleeding should also be taken into account when considering dual antiplatelet therapy (as is the case in recommendations 1.5.1 and 1.5.2 relating to anticoagulation). In the 'recommendations and links to evidence' section of the full guideline (p146) it states that <i>"[the network meta-analysis] also showed that dual antiplatelet therapy potentially carried high risks of bleeding (with much uncertainty in this parameter). Therefore patients undertaking this strategy will need to be assessed for bleeding risk and gastric protection."</i>	Thank you for your comment. The GDG agree with your point, this recommendation has been removed.
273	SH	Bayer Healthcare	10	NICE	20		Recommendation 1.5.17 This recommendation includes that for people taking an anticoagulant, the quality of anticoagulation control should be reviewed at least annually. Use of the phrase 'anticoagulation control' denotes some form of monitoring of coagulation parameters, which would not be relevant during treatment with	Thank you for your comment. The word control has been removed from this recommendation.

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							<p>NOACs.</p> <p>We suggest that the word 'control' is removed from this recommendation, referring then to the <i>"quality of anticoagulation"</i>, which is applicable to both VKAs and NOACs. Quality will therefore not be restricted to international normalised ratio control, but all aspects of anticoagulation.</p>	
275	SH	Bayer Healthcare	12	NICE	20		<p>Recommendation 1.5.17</p> <p>This recommendation covers the need to <i>"review the need for anticoagulation and the quality of anticoagulation control at least annually or more frequently if clinically relevant events occur"</i>.</p> <p>The current wording implies that a review should be precipitated by an 'event' however there are other considerations which should prompt a review of anticoagulation needs, but which may not be classified as 'events', such as a change in haemorrhagic risk, an indication for concomitant medication, or a change in renal or hepatic function.</p> <p>Bearing in mind this comment, and that described in order number 10, we suggest that recommendation 1.5.17 should read <i>"for people who are taking an anticoagulant, review the need for anticoagulation and the quality of anticoagulation at least annually, or more frequently if clinically indicated."</i></p>	Thank you for your comment. The recommendation has been reworded.

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							This suggested amendment should also be included in the stroke prevention algorithm on p44 of the full guideline as depicted in the alternative algorithm shown in order numbers 3 and 4.	
76	SH	Boston Scientific	1	NICE	20	1.5.18/ 1.5.19	<p>The wording of this section on left atrial appendage closure (LAAC) is unnecessarily negative and does not reflect:</p> <ul style="list-style-type: none"> a) NICE own review as part of Interventional Procedures Programme; b) the current NHS England commissioning statement on LAAC; c) the up-to-date and extensive clinical evidence on the Watchman left atrial appendage occlusion device including 2 randomised controlled trials with thousands of patients, and 2 registries. d) The FDA Panel review, which occurred in December 2013, was very confident in the technology and voted overwhelmingly in favour of a positive approval for Watchman LAAC <p>We would recommend that 1.5.18 is rewritten to reflect the previous NICE guidance, NHS England statement and more up-to-date evidence base. Our suggestion would be: Left atrial appendage occlusion (LAAO) is recommended as an alternative to anticoagulation for patients who are contraindicated or for whom long-term oral-anticoagulation is not tolerated.</p>	Thank you for your comment. After careful consideration we do not agree that recommendation 1.5.18 should change. However, we have amended the text in this chapter to give a more positive attitude to the technique and switched the order of the two recommendations. We will address each of your points in turn below.

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							We will take a), b) and c) in turn	
77	SH	Boston Scientific	2	NICE	20	1.5.18/ 1.5.19	<p>a) NICE Interventional Procedure Guidance 349 published in June 2010 states that: <i>“Current evidence suggests that percutaneous occlusion of the left atrial appendage (LAA) is efficacious in reducing the risk of thromboembolic complications associated with non-valvular atrial fibrillation (AF). With regard to safety, there is a risk of life-threatening complications from the procedure, but the incidence of these is low. Therefore, this procedure may be used provided that normal arrangements are in place for clinical governance, consent and audit.”</i></p> <p>This guidance was very positive as it recommends ‘normal arrangements’ of care, despite being published more than 3 years ago before many of the trials reported and before the long-term follow-up from the landmark randomised controlled trial PROTECT-AF.</p> <p>Section c) will look more closely about the evidence which has not been included in the overview</p>	<p>Thank you for your comment. We agree that the NICE interventional procedure guidance 349 recommended that the procedure <u>may</u> be used provided that normal arrangements are in place for clinical governance, consent and audit. This enabled the GDG to make the recommendation that LAAO can be considered if anticoagulation is contraindicated or not tolerated. The Interventional Procedure Guidance included one RCT (Holmes 2009) that we have included in our review. We have also included the recent report from Reddy 2013 that includes 2.3 year outcomes. The recommendation was also based on findings of an economic evaluation (published after the IPG) that found great uncertainty that the intervention was cost effective. A strong recommendation in favour of routine use of LAAO for all population groups would require evidence indicating a high likelihood that the intervention is cost effective.</p>

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								We have responded to the comment about evidence not included in the overview in section c below.
78	SH	Boston Scientific	3	NICE	20	1.5.18/ 1.5.19	<p>b) NHS England specialised services has published its statement on left atrial appendage closure highlighting that:</p> <p><i>There is a small minority of patients who cannot take anticoagulants, usually because of bleeding risk as a consequence of anticoagulation, and also a very small group of patients who have a recurrent embolic stroke despite adequate anticoagulation. Those patients with AF who are unable to take anticoagulants require an alternative treatment to reduce their risk of stroke. This is the group of patients for whom therapeutic percutaneous left atrial appendage occlusion (LAAO) may be indicated.</i></p> <p>A similar statement could be used in the Clinical Guideline in order to align it to commissioning recommendations and clarify the advice for NHS clinicians, patients and commissioners.</p>	Thank you for your comment. We agree with this comment and believe that this is reflected in the recommendations.
94		NHS Sheffield CCG	4	NICE	20	1.5.14	<p>'Only consider dual antiplatelet therapy with aspirin and clopidogrel for stroke prevention if anticoagulation is contraindicated or not tolerated and the person has a CHA2DS2-VASc score of 2 or above.' – the evidence for this from the full</p>	Thank you for your comment. After careful consideration the GDG have deleted the recommendation pertaining to dual antiplatelet therapy.

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							guideline (p148) is stated to be low to moderate quality evidence. Dual antiplatelet therapy increases the bleeding risk and polypharmacy in patients who are likely to be taking a number of other medications. Aspirin monotherapy may be a suitable choice for some patients, in line with patient centred care.	<p>The GDG agreed that patients who chose not to undertake stroke risk modification for AF should be able to receive aspirin monotherapy. The guideline does not recommend aspirin monotherapy for AF but the GDG did not wish to deny aspirin monotherapy for those requiring aspirin for non-AF conditions.</p> <p>In addition a recommendation has been added 1.5.4. 'Discuss the options for anticoagulation with the person and base the choice on their clinical features and preferences'.</p>
30	SH	Royal College General Practitioners	19	NICE	20	1.5.14	What are the contraindications to OAC that are not also to anti platelet therapy except allergy?	Thank you for your comment. We have now deleted this recommendation.
250	SH	Bristol-Myers Squibb and Pfizer	13	NICE	20	1.5.17	We support the recommendation for an annual review of anticoagulation as outlined in this recommendation. However, a clear distinction should be made between the regular monitoring required for patients on warfarin versus the holistic, annual review required for all OAC patients. Additionally, we suggest that this annual review should be more formally required and documented within an annual audit to ensure that the management of AF is optimally managed.	Thank you for your comment about the annual review being 'more formally required'. This is an implementation issue and we have passed your comment onto the NICE implementation team.
110	S	Royal	1	NICE	20	1.5.	Annual review should include,	Thank you for your comment. This would be the

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	H	College of Pathologists & British Society for Haematology	4	E		17	<ol style="list-style-type: none"> 1. Reassessment of stroke risk 2. Reassessment of bleeding risk 3. Assessment of renal function 4. Incidence of adverse events relating to anticoagulation since last review 5. Assessment of TTR in last 12 months (quality of INR control) 6. Assessment of compliance 7. Discuss availability of alternative anticoagulant <p>The above are the NICE recommendations from commissioning of anticoagulation therapy (NICE CMG 49)</p>	expectation of the GDG. Please see the linking evidence to recommendation section 11.2.4 (second part, page 174) 'trade-off between clinical benefits and harms' box. We have clarified the text and also added a cross reference to the CMG48 commissioning guidance. In addition, section 11.2.4 (first part, page 172) of the guideline also refers to the CMG48 (within the linking evidence to recommendation section) where we quote verbatim the points cited from CMG48 'monitoring by the healthcare professional section 5.4.3'.
144	SH	UK Clinical Pharmacy Association: Haemostasis Anticoagulation & Thrombosis (HAT) Group	1	NICE	20	1.5.17	<p>Page 172 of the full guidance provides further information on what should be included in a review of anticoagulation therapy; for user / reader accessibility this information should more clearly feature in the NICE guidance:</p> <ul style="list-style-type: none"> • Assessment of renal function • Incidence of adverse events relating to anticoagulation therapy since last review • Assessment of compliance • Choice of alternative anticoagulant <p>Also the focus of the monitoring appears to be Vitamin K antagonists; attention should also be given to the newer oral anticoagulants monitoring</p>	Thank you for your comments. We agree and have added some text on the importance of monitoring renal function particular for NOACs to the LETR on section 11.2.4. The recommendations can also be found in section 11.2.4.

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							requirements.	
2	SH	College of Emergency Medicine	1	NICE	21	1.6.2/ general	Rhythm control is to be offered to all new onset AF in the 2014 guideline; however, while the anticoagulation is clearly defined, the choice of rhythm control is not when the patient is haemodynamically stable and minimally symptomatic (a great majority of the patients that present to Emergency Departments). In particular there is no guidance between electrical vs pharmacological cardioversion in this group (within the 48 hour window), and no guidance regarding timing of cardioversion outside of this.	Thank you for your comment. We have updated the recommendations in the acute AF section to address this. Recommendation 1.3.1 gives guidance on timely referral.
31	SH	Royal College General Practitioners	20	NICE	21	1.6.2	New onset AF ? is this clear for primary care, need clear new onset of symptoms rather than new diagnosis	Thank you for your comment. New onset AF is defined as a patient presenting to medical care with atrial fibrillation whose new or changing symptoms suggest that the episode of AF commenced less than 48 hours prior to presentation. We have updated the acute chapter introduction and the glossary accordingly.
95		NHS Sheffield CCG	5	NICE	21	1.6.3	'Offer a beta-blocker ---' we are unclear whether the term beta-blocker includes sotalol. The full guideline (p204) implies that sotalol would not be considered. It would be helpful for this to be more explicit in the NICE version.	Thank you for your comment. We agree and have amended the recommendation accordingly.
198	SH	Resuscitation Council (UK)	6	NICE FULL	21 54 204	1.6.5 37 Firs	We suggest including a caution here. Recommending the combination of beta blockade and diltiazem with no caveat will generate a potential risk of severe and potentially dangerous	Thank you for your comment. The GDG were sufficiently concerned about the interaction between verapamil and beta blockers to word the original recommendation 37 with this in mind. By contrast, the

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				FULL		box	<p>bradyarrhythmia (especially in those with evidence of AV conduction disease) and severe and potentially fatal heart failure (especially in those who have LV impairment or current or previous heart failure).</p> <p>Also the wording recommends dual therapy if symptoms are not controlled, but makes no mention of whether or not this is attributable to failure to achieve rate control. In some people monotherapy may control rate but not control symptoms because those symptoms are not due to the fast heart rate alone. This is a group of people highly likely to be harmed if diltiazem is then added to a beta blocker.</p>	<p>GDG were of the opinion that the combination of a beta blocker with diltiazem is successfully used in many patients.</p> <p>The guideline does not necessarily seek to iterate all cautions, contra-indications and interactions expressed in drug datasheets or in the BNF. Nonetheless, in view of the expressed concern, we have added a sentence to the LETR cautioning the use of a beta blocker / diltiazem combination in patients with LV impairment. It would be unusual to need to use combination therapy to further reduce A-V node conduction in patients with existing A-V node conduction but a caveat has also been expressed on this point.</p> <p>Thank you for the second point, that continuing symptoms should be due to poor rate control. The recommendation has been altered accordingly.</p>
199	SH	Resuscitation Council (UK)	7	NICE FULL	2144	1.6.638	This is much-needed. Thank you. There is also a need for caution in those taking long-term amiodarone for rhythm control. It is not uncommon for them to later develop permanent AF, which may or may not be recognised, but then to be left on amiodarone when other rate-controlling drugs would be safer and need less clinical and laboratory monitoring.	Thank you for this comment. We believe it is implicit in the current wording of the recommendation that amiodarone should not be used in patients with permanent AF, when the only reason for using it would be rate control.
205	SH	Resuscitation Council	13	NICE	22 and	1.6.8–1.6.	These deletions seem to leave a gap in the guidelines. 'Conventional' electrical cardioversion remains an option and is stated to be regarded as	Thank you for your comment. NICE already has guidance (technology appraisal) in the area and it was not appropriate to review individual NOACs within this

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		(UK)			43	10 deleted 1.3.3.1 and 1.3.3.2	being equally effective as TOE-guided cardioversion, yet there appears to be no recommendation regarding optimal anticoagulation for people having conventional cardioversion. As part of this there is increasing evidence that NOACs allow cardioversion to occur safely, and clearly reduce the delays imposed by unpredictable time taken to achieve warfarin control.	guideline. The technology appraisals have been fully incorporated. In addition, the GDG did not prioritise effectiveness of anticoagulation with cardioversion.
200	SH	Resuscitation Council (UK)	8	NICE	23	1.6.12-1.6.14	Greater clarity on the distinction between a pure beta blocker and sotalol, and when to use each, is needed. Some people still use sotalol as first-line therapy rather than a cardioselective beta blocker, often without awareness of the pharmacology of sotalol or regard to its added risks. When small doses of sotalol or large doses of a pure beta blocker are not tolerated the patients are often labelled as 'intolerant of beta blockers' when smaller doses of a cardioselective beta blocker may be well-tolerated and therapeutically useful.	Thank you for this helpful comment. We have clarified these recommendations to make it clear that the preference in the recommendation is for a "standard" beta blocker other than sotalol. The term "standard" in this sense was also used in the 2006 guideline. The potential adverse effect of sotalol and the distinction between beta blocking and class III doses of sotalol are already described in the LETR.
32	SH	Royal College General Practitioners	21	NICE	23	1.6.12 and 13	It would be helpful to have an idea of which B Blocker because with the 2 together it may appear that sotalol is first choice (which it may be for rhythm rather than rate control)	Thank you for your comment. We have clarified these recommendations to make it clear that the preference in the recommendation is for a "standard" beta blocker other than sotalol. The term "standard" in this sense was also used in the 2006 guideline. The potential adverse effect of sotalol and the distinction between beta blocking and class III doses

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								of sotalol are already described in the LETR.
201	SH	Resuscitation Council (UK)	9	NICE FULL	2355	2543	For clarity we suggest change of wording from 'who do not have a history of, or current, heart failure' to 'who do not have heart failure or a history of heart failure'	Thank you for your comment. It is outside of our remit to amend this recommendation which has been incorporated from an existing NICE technology appraisal.
33	SH	Royal College General Practitioners	23	NICE	25	1.6.24	? need for LA Ablation or AV node ablation after pacing	Thank you for this comment. The recommendation is referring to A-V node ablation. This is in fact referred to in the first part of the recommendation ("When considering a pace and atrioventricular node ablate strategy.....") and we think it would be repetitious to repeat the A-V node ablation in the second part of the recommendation.
143	SH	British Medical Association	5	NICE	26	1.7.5	In primary care most patients who are diagnosed with AF have not presented with symptoms of the condition but are found by routine pulse palpation undertaken as part of a clinical examination. As such they are likely to have been in AF for some time. Given this, and the fact that even with multiple risk factors for stroke, the risk of stroke within the time-frame required to establish effective oral anticoagulation is small on an individualised basis, we are surprised at the recommendation to offer heparin pending the establishment of a therapeutic INR. This intervention is very unpopular with	Thank you. The risk of stroke is accentuated in the early period following initiation of warfarin (increased by >70% - the following reference might be of interest to you, 'Azoulay et al Eur Heart J 2014') and strokes related to AF have a high mortality and morbidity. Thus, the use of SC heparin would ameliorate this risk This is normal clinical practice.

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							patients, and requires considerable staff time either to administer the injections or to teach self-administration.	
34	SH	Royal College General Practitioners	24	NICE	26	1.7.5	Would we offer everyone newly diagnosed with AF heparin or is this only for those who are haemodynamically unstable or who may have cardioversion? This is covered I suppose by 1.7.7	Thank you for your comment. Yes, pending establishment of therapeutic INRs on warfarin. If a NOAC is used, there is no need.
202	SH	Resuscitation Council (UK)	10	NICE	26	1.7.3 and 1.7.4	It would be good to have a statement recommending that a beta blocker is not used as first-line therapy for pharmacological cardioversion when a rhythm control strategy has been chosen. It is not uncommon for people to prescribe an oral beta blocker for an acute episode of AF in the hope that it may achieve rhythm control, and then to accept some rate control as a suboptimal outcome, when pharmacological cardioversion with flecainide would have achieved a much more prompt and better outcome for many.	Thank you for your comment. The wording of recommendation 1.7.2 and 1.7.3 has been revised with further clarification regarding selection of rate or rhythm control. While we understand and sympathise with these views, we accept that there may in some clinical circumstance be a dual role for beta blockers in relation to rate and rhythm control. Therefore, the GDG did not think it appropriate to rigidly restrict their use to one or other situation.
203	SH	Resuscitation Council (UK)	11	NICE FULL FULL	2758361	1.9.11021	Formatting of bullet points requires correction. The correct term is calcium-channel blocker, not calcium antagonist.	Thank you for your feedback. We have used the term rate limiting calcium-channel blocker and we have standardised this across the guideline.
176	SH	The Stroke	13	NICE	28	2.1	We agree with the recommendation for more research on CBT for people with AF.	Thank you for your comment. Post-stroke psychological support needs to be very different to AF

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		Association					<p>We suggest a recommendation for more research into a stepped care model of psychological care was detailed in NHS Stroke Improvement's document "Psychological care after stroke": http://system.improvement.nhs.uk/ImprovementSystem/ViewDocument.aspx?path=Cardiac/National/Website/Stroke/Psychological+support+resource/StrokePsychologicalSupport+FINAL.pdf</p> <p>Economic modelling of this approach suggests that an investment of around £69,000 this type of service may deliver a benefit of around £108,000 to the NHS and social care in around two years:</p> <p>http://system.improvement.nhs.uk/ImprovementSystem/ViewDocument.aspx?docId=22444&Title=Microsoft_PowerPoint_-_Psychological_care_after_stroke-Economic_modelling_GUIDE</p>	CBT; the former is more of a PTSD approach, whereas CBT for long-term AF is about patient empowerment from the start.
204	SH	Resuscitation Council (UK)	12	NICE	29	2.2	We suggest rewording this title. It is the people who are aged 75 or over, not the AF.	Thank you for your comment. This has been reworded to say "aged 75 and over with atrial fibrillation".
35	SH	Royal College	25	NICE	29	2.2	Drug treatment for RATE CONTROL	Thank you for your comment. We have amended this title accordingly.

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		General Practitioners						
36	SH	Royal College General Practitioners	26	NICE	30	2.4	If we are considering concordance then there may be an outcome difference between a once daily NOAC and a twice daily	Thank you for your comment. NICE already has guidance (technology appraisal) in the area and it was not appropriate to review individual NOACs within this guideline. The technology appraisals have been fully incorporated into the guideline.
177	SH	The Stroke Association	14	NICE	31	2.5	This recommendation for more research into stroke risk assessment is vital as stroke risk is five times higher in people with AF compared with the general population.	Thank you for your comment.
206	SH	Resuscitation Council (UK)	14	NICE	43	deleted 1.3.3.3	This deletion seems to leave no guidance for treatment in the group of people whose cardioversion is not so urgent as to be covered by 1.7.1 but in whom cardioversion cannot be postponed safely for at least 3 weeks (the reality is that achieving good warfarin control for a minimum of 3 weeks may delay the cardioversion for much longer than that) and who are admitted to a hospital with no staff or facilities for TOE-guided cardioversion. If transfer to another hospital for TOE-guided cardioversion is regarded as the optimal strategy for these people it would be helpful if the guideline stated that explicitly.	Thank you for this comment. This recommendation has been deleted because the 2014 guideline adopts a different care pathway. The Guideline Development Group did not review this question and are not confident that the evidence remains the same.
207	S	Resuscitation	15	NICE	44	deleted	A welcome and much-needed change. Thank you.	Thank you for your feedback.

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	H	Council (UK)				d 1.3. 3.5		
208	SH	Resuscitation Council (UK)	16	NICE	46	deleted 1.5. 1.5	This has removed from the guideline acknowledgement that most people with heart failure and left ventricular systolic dysfunction should be taking a beta blocker as part of the treatment of that problem, so amiodarone would be considered as additional rhythm-control therapy when paroxysmal AF recurs despite beta blockade, or when beta blockade is contra-indicated.	Thank you for your comment. We agree it has removed the option of a beta blocker for this treatment.

These organisations were approached but did not respond:

Academic Cardiology
Action Heart
Aintree University Hospital NHS Foundation Trust
Airedale NHS Trust
Alder Hey Children's NHS Foundation Trust
Alere
Allocate Software PLC
AMORE health Ltd
AMORE Studies Group
Aneurin Bevan Health Board
Anglia Stroke and Heart Network
AOP Orphan Pharmaceuticals
Association of Anaesthetists of Great Britain and Ireland

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Association of British Healthcare Industries
Association of British Insurers
Association of Chartered Physiotherapists in Cardiac Rehabilitation
Astrazeneca UK Ltd
Bard Limited
Barnsley Hospital NHS Foundation Trust
BBOLMC
Berkshire Local Pharmaceutical Committees
Betsi Cadwaladr University Health Board
BIOTRONIK UK Ltd.
Birmingham & Brunel Consortium
Black Country Cancer and Cardiac Network
Blood Pressure UK
Boots
Bradford District Care Trust
Bradford Districts Clinical Commissioning Group
Brighton and Sussex University Hospital NHS Trust
British Association for Nursing in Cardiovascular Care
British Association of Critical Care Nurses
British Association of Stroke Physicians
British Cardiovascular Society
British Geriatrics Society
British Medical Journal
British National Formulary
British Nuclear Cardiology Society
British Nuclear Medicine Society
British Pacing and Electrophysiology Group
British Paramedic Association
British Pharmacological Society
British Psychological Society
British Red Cross
British Society for Heart Failure
BUPA Foundation
C. R. Bard, Inc.
Caledonian Medical LTD

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Cambridge University Hospitals NHS Foundation Trust
 Camden Link
 Capsulation PPS
 Capsulation PPS
 Cardiac and Stroke Networks in Lancashire & Cumbria
 Cardiff and Vale NHS Trust
 CardioLogic Ltd
 Cardiomyopathy Association, The
 Care Quality Commission (CQC)
 CIS' ters
 Clarity Informatics Ltd
 Cochrane Heart Group
 Countess of Chester Hospital NHS Foundation Trust
 County Durham Primary Care Trust
 Coventry and Warwickshire Cardiac Network
 Covidien Ltd.
 Croydon Clinical Commissioning Group
 Croydon Health Services NHS Trust
 Croydon University Hospital
 Cumberland Infirmary
 Cumbria Partnership NHS Trust
 David Lewis Centre, The
 Department of Health, Social Services and Public Safety - Northern Ireland
 Different Strokes
 East and North Hertfordshire NHS Trust
 East Kent Hospitals University NHS Foundation Trust
 East Midland Ambulance Services NHS
 East Midlands Ambulance Service NHS
 Education for Health
 Epsom & St Helier University Hospitals NHS Trust
 Ethical Medicines Industry Group
 European Heart Rhythm Association
 Faculty of Intensive Care Medicine
 Faculty of Sport and Exercise Medicine
 Five Boroughs Partnership NHS Trust

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GE Healthcare
George Eliot Hospital NHS Trust
Great Western Hospitals NHS Foundation Trust
Greater Manchester and Cheshire Cardiac and Stroke Network
Guidant Corporation
Guy's and St Thomas' NHS Foundation Trust
Health & Social Care Information Centre
Health and Care Professions Council
Healthcare Improvement Scotland
Healthcare Infection Society
Healthcare Inspectorate Wales
Healthcare Quality Improvement Partnership
Healthwatch East Sussex
Heart Rhythm UK
HEART UK
Herts Valleys Clinical Commissioning Group
Hindu Council UK
Hockley Medical Practice
Humber NHS Foundation Trust
ICD Patient and Family Heart Support Group
Independent Healthcare Advisory Services
Institute of Biomedical Science
Integrity Care Services Ltd.
Johnson & Johnson
Lancashire Care NHS Foundation Trust
Leeds Community Healthcare NHS Trust
Leeds North Clinical Commissioning Group
Leeds South and East Clinical Commissioning Group
Leeds Teaching Hospitals NHS Trust
Local Government Association
London Ambulance Service NHS Trust
London Clinic
Luton and Dunstable Hospital NHS Trust
MA Healthcare
Maidstone and Tunbridge Wells NHS Trust

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Maquet UK Ltd
Medicines and Healthcare products Regulatory Agency
Mid Staffordshire NHS Foundation Trust
Ministry of Defence (MOD)
Monash Health
National Association of Primary Care
National CLAHRC stroke Group
National Clinical Guideline Centre
National Collaborating Centre for Cancer
National Collaborating Centre for Mental Health
National Collaborating Centre for Women's and Children's Health
National Deaf Children's Society
National Institute for Health Research Health Technology Assessment Programme
National Institute for Health Research

National Patient Safety Agency
National Public Health Service for Wales
Newcastle upon Tyne Hospitals NHS Foundation Trust
NHS Barnsley Clinical Commissioning Group
NHS Bassetlaw CCG
NHS Central Lancashire
NHS Connecting for Health
NHS County Durham and Darlington
NHS Cumbria Clinical Commissioning Group
NHS Direct
NHS England
NHS England - Greater Manchester
NHS Fylde & Wyre CCG
NHS Greater Manchester Commissioning Support Unit
NHS Halton CCG
NHS Health at Work
NHS Health Check
NHS Heywood, Middleton & Rochdale CCG
NHS Improvement
NHS London

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NHS Luton CCG
NHS Medway Clinical Commissioning Group
NHS Newcastle
NHS Pathways
NHS Plus
NHS Portsmouth Clinical Commissioning Group
NHS South Cheshire CCG
NHS Southern Derbyshire CCG
NHS Wakefield CCG
NHS Warwickshire North CCG
NHS West Hampshire CCG
NHS West Lancashire CCG
NHS West Suffolk CCG
Norfolk and Norwich University Hospital
North East Lincolnshire Care Trust Plus
North Essex Partnership Foundation Trust
North of England Cardiovascular Network
North of England Commissioning Support
North Trent Network of Cardiac Care
North West London Hospitals NHS Trust
Nottingham City Council
Oxford Health NHS Foundation Trust
Oxford University Hospitals NHS Trust
Oxfordshire Clinical Commissioning Group
P.M.S
Pan London Acute Medicine Network
Papworth Hospital NHS Foundation Trust
Parkwood Healthcare
Peninsula Heart & Stroke Network
PERIGON Healthcare Ltd
Peterborough Primary Care Trust
PharmaPlus Ltd
PHE Alcohol and Drugs, Health & Wellbeing Directorate
PrescQIPP NHS Programme
Primary Care Cardiovascular Society

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Primary Care Partnerships
 Primary Care Pharmacists Association
 Primrose Bank Medical Centre
 Progressive Supranuclear Palsy Association
 Public Health Agency
 Public Health Wales NHS Trust
 Pulmonary Fibrosis Yahoo Group
 Queen Elizabeth Hospital
 Queen Elizabeth Hospital King's Lynn NHS Trust
 Regional Public Health Agency for Northern Ireland
 Robert Jones & Agnes Hunt Orthopaedic & District Hospital NHS Trust
 Royal Berkshire NHS Foundation Trust
 Royal College of Anaesthetists
 Royal College of General Practitioners in Wales
 Royal College of Midwives
 Royal College of Midwives
 Royal College of Obstetricians and Gynaecologists
 Royal College of Paediatrics and Child Health
 Royal College of Paediatrics and Child Health , Gastroenterology, Hepatology and Nutrition
 Royal College of Physicians
 Royal College of Physicians and Surgeons of Glasgow
 Royal College of Psychiatrists
 Royal College of Radiologists
 Royal College of Surgeons of England
 Royal Free London NHS Foundation Trust
 Royal Society of Medicine
 Royal United Hospital Bath NHS Trust
 Sanofi
 Scottish Intercollegiate Guidelines Network
 SEE BETSI CADWALADR - North Wales NHS Trust
 Sheffield Teaching Hospitals NHS Foundation Trust
 Shropshire and Staffordshire Cardiac Network
 Social Care Institute for Excellence
 Society and College of Radiographers
 Society for Academic Primary Care

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Society for Cardiothoracic Surgery of Great Britain and Ireland
 Sorin Biomedica U K Ltd.
 South Central Cardiovascular Network
 South East Coast Ambulance Service
 South East Staffordshire and Seisdon Penninsula CCG
 South London & Maudsley NHS Trust
 South London Cardiac and Stroke Network
 South West London Elective Orthopaedic Centre
 South West Yorkshire Partnership NHS Foundation Trust
 South Western Ambulance Service NHS Foundation Trust
 Southern Health NHS Foundation Trust
 Southport and Ormskirk Hospital NHS Trust
 Spacelabs Healthcare
 St Bartholomews Hospital
 St John Ambulance
 St Jude Medical UK Ltd.
 St Mary's Hospital
 Staffordshire and Stoke on Trent Partnership NHS Trust
 Stockport Clinical Commissioning Group
 Sue Ryder
 Surrey Heart & Stroke Network
 Tameside Hospital NHS Foundation Trust
 The Ashley Jolly SADS Trust
 The Association of the British Pharmaceutical Industry
 The British Society for Haematology
 The Patients Association
 The Princess Alexandra Hospital NHS Trust
 The Rotherham NHS Foundation Trust
 Torbay and Southern Devon Health and Care NHS Trus
 Translucency Ltd.
 UK Health Forum
 UK Lung Cancer Coalition
 UK National Screening Committee
 UK Specialised Services Public Health Network
 Unison

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University Hospital Aintree
University Hospital Birmingham NHS Foundation Trust
University Hospitals Birmingham
University Hospitals Coventry and Warwickshire NHS Trust
Walsall Local Involvement Network
Wandsworth Clinical Commissioning Group
WELSH ASSOCIATION OF STROKE PHYSICIANS
Welsh Government
Welsh Kidney Patients Association
West Midlands Ambulance Service NHS Trust
Western Sussex Hospitals NHS Trust
Westminster Local Involvement Network
Wigan Borough Clinical Commissioning Group
Wirral University Teaching Hospital NHS Foundation Trust
Worcestershire Acute Hospitals Trust
Worcestershire Health and Care NHS Trust
Worcestershire LINK
Wrightington, Wigan and Leigh NHS Foundation Trust
York Hospitals NHS Foundation Trust

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