COMMENTS RECEIVED FROM EXTERNAL REFEREES AND OTHERS

SIGN 151: Management of stable angina

Invited reviewers:			Declared interests:
AB	Dr Alan Begg	General Practitioner – Honorary Senior Lecturer, University of Dundee, Montrose.	Individual response. Remuneration from self employment - Medical Writer and Editorial Board Member - Guidelines in Practice, British Journal of Cardiology, Primary Care Cardiovascular Journal. Co-Editor of Practical Diabetes. Occasional honorarium from pharmaceutical companies with cardiovascular products for lectures and educational initiatives. Remuneration as a partner in a firm - Partner in Townhead Medical Practice (General Practice) Director of Dunrossie Publishing Company. Shares and securities – Only as part of stocks and shares ISA. Remuneration from consultancy – Occasional pharmaceutical contracts already declared. Non-financial interests – Trustee of CHS Scotland, Trustee of Scottish Heart and Arterial Risk Prevention Group. Non-personal support from commercial healthcare companies – Co-Applicant in ALL-HEART study – funded by National Institute for Health Research.
GB	Mr Geoffrey Berg	Retired Consultant Cardiac Surgeon, Retired from GJNH, Clydebank	Individual response. Remuneration from employment – no employment.

			Remuneration for consultancy work – Previous consultancy with Vascutek (manufacture of vascular grafts), Collagen Solutions Ltd (manufacture of surgical grafts – not used in cardiac surgery)
AC	Mr Andrew Call	Advanced Cardiology Nurse, Raigmore Hospital, Inverness	Individual response.
GD	Mrs Gillian Donaldson	Lead Cardiac Specialist Nurse, NHS Borde5rs, Melrose	Individual response.
JH	Ms Jane Holt	Cardiac Rehab Team Lead Physio, NHS Ayrshire and Arran, Crosshouse	Individual response.
SL	Professor Stephen Leslie	Cardiologist, Raigmore, Inverness	Individual response.
LM	Mrs Lynsey Moir	Advanced Pharmacist, Clinical Cardiology, West Glasgow Ambulatory Care Centre, Glasgow	Individual response.
DM	Dr David Murdoch	Consultant Cardiologist, Queen Elizabeth University Hospital, Glasgow	Individual response.
DN	Professor David Newby	Professor of Cardiology, Royal Infirmary, Edinburgh	Individual response. Remuneration of employment – SIGN have these on record. Remuneration from self employment – SIGN have these on record. Remuneration from consultancy – SIGN have these on record.
AN	Dr Alastair Nimmo	Consultant Anaesthetist, Royal Infirmary of Edinburgh, Edinburgh	Individual response.
NO'D	Mr Nick O'Donnell	Community Pharmacist, Kennyhill Pharmacy, Glasgow	Individual response.
MO	Dr Morag Osborne	Consultant Clinical Psychologist, West Glasgow ACH, Dalnair Street, Yorkhill, Glasgow	Individual response. Remuneration of employment – NHS GGC.
RW	Dr Robin Weir	Consultant Cardiologist, Hairymyres, Glasgow	Individual response.

Open consultation:			
AF	Dr Andrew Flapan	Consultant Cardiologist, Edinburgh Royal Infirmary, Edinburgh	Individual response.
RCGP		Royal College of General Practitioners, Edinburgh	Group/Organisation response (Dr Scott Jamieson, GP, Scottish Council RCGP). Nature of group or organisation – Professional group. How might the statements and recommendations in the draft SIGN guideline impact on your organisations functions – On clinical management of patients attending GP and their follow up.
RCP&S		Royal College of Physicians and Surgeons of Glasgow, Glasgow	Group/Organisation response (Dr Richard Hull, Honorary Secretary). Nature of group or organisation - A multidisciplinary Royal College which supports and represents its membership of surgeons, physicians, dental professionals, specialists in the field of travel medicine and podiatric medicine by setting the highest possible standards of healthcare. How might the statements and recommendations in the draft SIGN guideline impact on your organisations functions - Draft recommendations in this SIGN guideline will have no discernible impact on the function or productivity of our organisation.
SMC		Scottish Medicines Consortium	Group/Organisation response (Christine Hepburn, Principal Pharmaceutical Analyst). Nature of group or organisation – Health technology assessment. How might the statements

			and recommendations in the draft SIGN guideline impact on your organisations functions – SMC has been asked to comment as an interested party. Recommendations in the SIGN guideline should be aligned with SMC advice.

Those submitting comments on behalf of an organisation are not required to complete a declaration of interests.

Section		Comments received	Development group response	Editorial group comments
General				
	AB	The guideline group should be recommended on a comprehensive document. The updated evidence base on the use of stents and revascularisation is appreciated as well as highlighting the evidence gaps. I have tried to indicate where the 'conflict' as I see it has arisen perhaps by trying to reflect the approach taken in NICE CG 95. This was based on the concept of a 'probability' of rule in /out and 'accepting inevitable false negatives and positives'. Do we accept this or do we have the capacity/resources for a comprehensive approach?	*Thank you* *Your comments are noted. We have tried to produce a pragmatic guideline for use in Scotland focussing on the key questions and new evidence.*	
	AF	I promised this comment as a light-hearted consideration "Guidelines are like sausages and they look good and taste good however some caution is required when one understands what they are made from or what goes into them" However this guideline appears to be sound The Chair will recognise the quote and should be congratulated	*Thank you*	
	GB	Congratulations to the guideline development group. One can appreciated the considerable amount of work and expertise required to produce this guideline.	*Thank you*	
	SL	Good to reduced importance of ETT. I would question benefit of ACEi in stable angina – high NNT.	*Noted. This is outside the remit of the update in which only new evidence was considered.*	
	DM	Thought that this would be a bit of a chore but actually enjoyed reading it. Well done.	*Thank you*	
	DN	I would make the following comments which I hope you find helpful. On page 11, the last 2 of the four recommendations may need some rewording. In general, I think the recommendations should reflect current NICE guidance (CG95 update November 2016). "…confirmed diagnosis of chest pain due to stable angina" could perhaps be better phrased to "patients with	*Thank you. This suggested rewording has been added to the text.*	

		known coronary artery disease". They (as NICE suggests) should have a functional test.		
		Also in this context, demonstrating ischaemia can help in the diagnosis, and not just risk stratification.	*Agreed. The text has updated to reflect this.*	
		For the CT coronary angiogram recommendation, it may be worth spelling out the differences between how typical, atypical and non-anginal chest pain should be investigated. The NICE guidance recommends dividing patients into non-anginal chest pain (non-anginal pain with normal ECG) and possible angina (typical or atypical angina, or non-anginal chest with an abnormal ECG).	*Noted. The guideline group feel adequate explanation has been provided in the text preceding the recommendation.*	
		NICE recommend no further testing in the non-anginal chest pain group. Should this be recommended too? Who does require no further testing?	*Thank you. The text has been updated to 'non-anginal'.*	
		Given the current hierarchy of testing, you may want to put the CTCA recommendation above the functional tests.	*The tests have been presented in order of invasiveness.*	
		There is also a question of whether you would want to separate the diagnosis of coronary heart disease from the diagnosis of angina due to coronary heart disease. The former is to determine risk and preventative therapies, and the latter is to treat symptoms and select those for revascularisation.	*This guideline is for the management of stable angina only. No change made.*	
		The mixing of diagnosis and risk stratification may need to be considered and whether these should be separated or not?	*Thank you. The text has been updated*	
		I think you are right not to make and specific recommendations regarding FFR.	*Thank you.*	
		On page 19/20, the main drive for DES seems to be evidence of reduced restenosis. BMS would seem reasonable in large arteries with short stents. Should some text to reflect this be included? Complete DES use for all patients correct?	*Noted, the guideline group does not feel the text needs to be updated to include the suggestions.*	
		On page 25, should the prognostic benefits of revascularisation (second recommendation) not specifically state	*We accept the original evidence offers prognostic benefit of CABG over medical therapy with specific*	

		CABG given the evidence base? There is no definitive evidence for this with PCI.	*anatomical disease. The most recent evidence at the last out of 3 years PCI may be equivalent to CABG. It would therefore be unethical to undertake a study of CABG v PCI, as discussed in the text.*	
		On page 28, do you need to include a recommendation for Transmural Laser Revascularisation. This is rarely if ever used now and certainly not in Scotland. There are other devices, such as coronary sinus occluders, which are beginning used. However, at this stage, I just wonder if this should be removed? Seems of historical interest only.	*Noted, however the guideline group has decided to keep the recommendation.*	
		On page 35, perioperative aspirin is not recommended. Do you mean this for patients with concomitant CAD/stable angina who are already on aspirin? The meaning is a little unclear.	*Thank you. This section has been re-worded for clarity.*	
		On page 35, the second recommendation talks about high thrombotic risk. It is not clear if stable angina is considered high thrombotic risk in comparison to say patients without CAD.	*Thank you. This text has been re-worded.*	
		The text in 6.3.4 does not really describe the benefits of perioperative aspirin in reducing atherothrombotic events and what the magnitude of this is. The text does describe this for bleeding so I think it does need some balance in the text.	*Thank you. The text has been updated to acknowledge this patient group.*	
		On page 35, the practice point could usefully give recommendations for the timing of discontinuation before surgery. 5 days?	*Thank you. This has been updated.*	
	NO'D	Information presented in comprehensive yet concise manner.	*Thank you.*	
	MO	Just a small spelling mistake in my title in the steering group section 11 .3 - Consultant	*Thank you. Title updated.*	
	RCP&S	The college trusts this consultation advice is helpful to the guidance committee and will be happy to elaborate further on specific points if necessary.	*Thank you.*	
	RW	Excellent draft. Usual SIGN format which is easy to follow.	*Thank you.*	
Section 1				

1.1	AB	I would agree that coronary heart disease prevalence and the presentation of patients with new onset or recurrent chest pain is still an important aspect of a general practitioners work. I find the variable use of CHD, CAD and later IHD distracting when reading through the text. The Tayside study referred to was 2002 and the situation has changed dramatically since then.	*Noted.* *Noted and thank you. The guideline will be updated to only use CAD.* *Noted. The guideline group feel this study is still relevant, along with the more recent studies that are also referred to in this section.*	
	RCP&S	The Royal College of Physicians and Surgeons of Glasgow welcomes the Scottish Inter-Collegiate Guidelines Network Guideline on the Management of Stable Angina. Overall it approves of the guidance. It has however asked experts in the field to review the Draft Report and review the literature. There has been discussion of the conclusions with other cardiologists in the field. The College has particular comments relating to the significant change from using the functional test of exercise testing hitherto considered the standard in most district general hospitals to an anatomically defined test such as CT coronary angiography. The authors discuss myocardial perfusion scintigraphy, stress echocardiography and Stress Perfusion Cardiac MR. It is important that the guidance not only recognises and discusses relative effectiveness but also considers availability in localities and cost effectiveness.	*Noted and thank you.* *Thank you. This is an important issue and the guideline has strived to achieve this. See section 3.2, first paragraph and section 9.2.*	
1.1.1	AB	I agree that SIGN 96 (February 2007) in parts requires updating.	*Noted and thank you.*	
1.2.1	AB	The benefits of different revascularisation approaches are still controversial in terms of prognostic benefit.	*Agreed.*	
1.2.2	AB	When the patient presents with classical symptoms and is deemed to be in a high risk category then making a diagnosis (it is a symptomatic diagnosis) tends to be straight forward. The problem is confirming the presence and extent of underlying obstructive coronary heart disease.	*Agreed.*	
	AF	Stable angina is a symptom which is precipitated by exertion and relieved by rest and GTN. The time farm of relief from GTN (very quick 2-3 minutes) can	*Agreed. This is addressed in section 3.1.*	

		be helpful in diagnosis		
1.2.3	AB	This draft will confuse general practitioners on the approach to be taken initially when a patient presents with chest pain - -there is a clear implication that it needs to be managed in primary care.	*Noted. In sections 3.3 and 3.1 reference to assessment and management in secondary care is made. We feel the guideline is clear that an initial diagnosis can be made in primary care.*	
1.3.1	AB	Agreed	*Thank you.*	
1.3.2	AB	Agreed	*Thank you.*	
1.3.3	AB	Should a lack of a recommendation for a drug indication be an absolute barrier to its use in certain circumstances - is the summary of product characteristics not more relevant?	*This section provides a high level summary of the role of SMC.*	
	SMC	The second paragraph should read "The Scottish Medicines Consortium (SMC) provides advice to NHS Boards and their Area Drug and Therapeutics Committees about the status of all newly licensed medicines and all new formulations and new indications of established products...."	*Thank you. Text has been updated.*	
Section 3				
General	AB	That it is a symptom is highlighted. The initial assessment is usually made in primary care but can the definite diagnosis of angina due to underlying obstructive coronary heart disease be made in this setting?	*Thank you.* *Yes a definitive diagnosis can be made in primary care, for example if the patient is known to have CAD and the history is clear.*	
3.1	AB	The patient pathway is important - it says managed in 'primary care setting' then 'further assessment at a cardiology outpatient clinic is desirable' CAD and CHD in same set of bullet points	*Agreed the patient pathway is important. Most initial assessments are made in primary care with most patients referred to secondary care, however this is not appropriate for all patients.* *Thank you and noted. Only CAD will be used.*	
	AF	Stable angina is a symptom which is precipitated by exertion and relieved by rest and GTN. The time farm of relief from GTN (very quick 2-3 minutes) can be helpful in diagnosis	*Noted. No changes made.*	
	GB	I appreciate you have used the NICE guidelines for making a diagnosis of stable angina on clinical assessment but is it appropriate to incorporate to use "relieved by GTN" as one of the features as presumably you would not advocate prescription of GTN as a method for determining the diagnosis?	*In the setting of stable angina evidence in the NICE assessment suggests a response to GNT is useful in determining diagnosis of stable angina. Obviously this should not be the sole determinant. This should also not be confused with unstable symptoms.*	

	GD	other factors – "angina may be precipitated by exertion or cold weather". Already mentioned on exertion above. Should change precipitated by exertion to "precipitated by cold weather or after a meal". Also.... "Patients with suspected angina should have a detailed initial clinical assessment which includes history, examination and an assessment of blood pressure, haemoglobin, thyroid function, cholesterol and glucose levels". I would like to see added in this renal function and LFTS. It has been mentioned in the paragraph above but not in the recommendations. In my experience it is very important to have a full blood picture prior to consultation at RACPC for initiation of any medicine that may be detrimental to renal or liver function and a baseline is required. It would be a good reminder in primary care to have this in recommendations. Also.. ECG should be included as part of the suggested work up in primary care before referral to any clinic. If angina is suspected an ECG is required. As part of our triage for RACPC we assess ECG and on a good few occasions admit directly on basis of ECG/telephone call to pt. Pick up acute ACS.CHB etc.. if you have an ECG from primary care it also allows you to utilise services better. For example if known LBBB would not plan to use ETT slot. Echo may be requested if not had previously.	*Agreed. Text updated. (final bullet point of first list in 3.1)* *The guideline group considered the inclusion of LFTS as part of this guideline update. There was no evidence to support its inclusion. However once a diagnosis has been made there is an option to consider it.* *The guideline group agree the completion of an ECG is important and this can be done in primary or secondary care.*	
	LM	Bullets point 3 & 5 both state angina can be related to or precipitated by exertion (duplicate).	*Thank you and noted. This text has been updated.*	
	NO'D	Presentation point/duplication. Other factors – lists exertion. Is this not already mentioned previously.	*Thank you and noted. This text has been updated.*	
3.1.1	AB	Do we need to define what we mean - -in the atypical case can we be so definite that they should not be assessed further. Ref 21 Did these patients have Angina / Stable coronary heart disease? The work of Sekri N et all HEART 2007;93:458-463 showed that 32.4% of all events during follow up from a rapid access chest pain clinic occurred in those with 'non cardiac chest pain'	*The guideline group feel this definition has been given in section 3.1.1.* *Thank you for bringing this reference to our attention. Based on the NICE data and the broad evidence base the risk of recurrent cardiac events in patients with non-anginal chest pain in low.*	

3.2	AB	Pre-test probability - are you suggesting we consider using a grading process such as the Diamond and Forrester algorithm (NEngl J Med 1979: 300: 1350-8) This influenced NICE but is fraught with problems and reproducibility	*No we are not advocating a grading process. The objective of the guideline is to provide simple, practical guidance in the management of stable angina.* *We would agree with the reviewer that a scoring system to evaluate pre-test probability and determining subsequent investigations is fraught with difficultly and can be difficult to follow.*	
	RCP&S	The one area of this review that always had the potential to be contentious is the use of Exercise Testing in patients. The most important recommendation of the guideline is contained in Annexe 3 where the recommendation is that Exercise Testing should not be used in the investigation and management of patients with suspected coronary artery disease and should be replaced by CT coronary angiography. This replaces a functional test with one that defines anatomy. The usefulness of a diagnostic test depends on its ability to enhance the clinician's ability to distinguish individuals with disease from those without and clarify diagnosis	*Agreed.*	
3.2.1	AB	Agreed	*Thank you.*	
	RCGP	Could we be clear in what setting we think the 12-lead ECG should be done? Is this in primary care or at secondary care?	*As part of the assessment of a patient it is important that the test is done and interpreted accurately. The test can be done in primary or second care.*	
3.2.2	AC	The move away from functional testing is to be welcomed, and the guideline makes clear why a diagnosis of angina should not be made on ETT alone. There should be equal weight to ensuring that angina? CHD is not ruled out on ETT alone.	*Thank you and noted.*	
	AB	Have you made a convincing argument for it not to be used as a first-line investigation. (3.2.7 second recommendation	*The exercise tolerance test has relatively poor sensitivity and specificity for the diagnosis of angina in all patients under investigation for chest pain. The guideline group feel a convincing argument has been made not to recommend the exercise tolerance test as*	

			routine first line in the investigation of patients with suspected angina. The ETT may have a role in specific patient populations and this has been discussed in section 3.2.2	
	AF	I think we need to be clearer hear that symptoms associated with ECG changes may be very helpful in the diagnosis of angina. Detecting coronary disease is different	*Agreed. Stable angina is a diagnosis based on symptoms. Demonstration of ischemia can be helpful in reaching that diagnosis. This guideline deals with the management of stable angina due to obstructive coronary artery disease (CAD) only. The text in section 3.2.2 has been updated.*	
	RCP&S	The advantages of exercise treadmill testing are well summarised in Uptodate.com (latest review August 17)— As a general rule, exercise stress testing provides more information than pharmacologic stress testing for the following reasons ●Exercise testing is more physiologic and mimics the conditions under which the patient's usual symptoms may be replicated. Symptoms induced by pharmacologic stress testing are usually nonspecific and may be side effects of the drug. ●Exercise documents the workload that induces symptoms and ischemia. ●Exercise capacity and hemodynamic responses are predictors of prognosis independent of ischemia. ●Symptoms and ischemia at a low workload indicates a greater likelihood of severe disease and a worse prognosis than does the same degree of ischemia at a high workload. Furthermore, the inability to exercise is itself associated with increased cardiovascular risk. In addition to obtaining the physiologic information related to exercise, exercise ECG testing has several advantages: ●Widely available and accessible	*Thank you.* *The guideline group agrees with your points. All functional tests have limited specificity and sensitivity. The choice of which test to use will be determined by a number of factors including local resource and expertise and this is discussed in the text.* *The demonstration of ischemia using function testing can help in the diagnosis of stable angina in patients with known obstructive CAD, but it has limited utility in the routine evaluation of all patients.* *This is highlighted by the broad range of sensitivity and specificity referred to in the text.*	

		●No requirements for intravenous access or radiation exposure ●Relatively inexpensive, particularly compared with stress testing with imaging ●Extensively validated The SIGN authors comment that the sensitivity and specificity of ETT in establishing a diagnosis of coronary heart disease is dependent on the cohort of patients studied. This is accepted. They state that sensitivity is higher in patients with triple vessel disease and lower in patients with single vessel disease. They accept that the Exercise ECG has a relativity high sensitivity but only moderate specificity for the diagnosis of CHD in women, but do not pass comment as to its sensitivity and specificity in men. The authors quote no specific figures but in Section 3.2.5 on myocardial perfusion scintigraphy, the authors state that MPS is an accurate and non-invasive investigation which reliably predicts the presence of coronary disease. They provide sensitivity figures of 78-88% and specificity figures of 64-73% respectively. It is a matter of opinion whether this can be regarded as an accurate test.	*Thank you. The guideline group agrees there is little to choose between the sensitivity and specificity of these tests. The text has been updated to better reflect this.*	
3.2.3	AB	The test suggest we should be using more of this test.	*Noted. The guideline group did not feel the text reflected this.*	
3.2.4	AB	Was reference 33 CMR or SPECT MPS	*Both.*	
	AF	I am not sure how helpful this is for general use	*Noted.*	
	GB	Last line should be "myocardial perfusion scintigraphy (MPS)" as the first occurence and "myocardial perfusion scintigraphy" should be removed from 3.2.4	*Thank you. Text has been updated.*	
3.2.6	AF	CT and coronary arteriography are static tests. The detect demonstrate coronary disease. This should not be confused with the diagnosis of angina. Some people with CAD will have angina and many will not. However the section should not suggest that CAD = Angina. These tests only diagnose the cause of angina if we are confident the patient has angina	*The guideline group agrees with the reviewers comments. Stable angina is a symptomatic diagnosis. This guideline deals with stable angina due to obstructive coronary artery disease (CAD) only. Confirmation of obstructive CAD can be helpful when there is diagnostic uncertainly. The text has been updated to add clarity to this matter.*	

	RC GP	There is zero mention of the harms of CT-CA. No mention of the 56% chance of incidental finding reported in some papers. This is a critical recommendation of this guideline and we are about to create a huge number of incidentalomas and harms. I cannot see this harm has been costed or quantified. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2799652/ This is a higher risk population for finding incidental results. We do many, many, many ETTs/MPS for these uncertain cases and to switch all to CT-CA as the guideline suggests will cost huge amounts in CT time alone let alone the investigation of the incidental findings falling from this...	*The guideline is not advocating routine use of CT-CA for all patients undergoing investigation for chest pain, just for those patients where there is diagnostic uncertainty.* *We agree that CT-CA has some limitations including a small radiation dose that has reduced over time with technological advances (Mean dose ~4 mSv in SCOT-HEART study). The incidence of incidental findings on CT-CA is reported at 10-20%, mainly pulmonary nodules.(Lu et al. JCCT 2017;373-82)(SCOT-HEART Lancet 2015;385:2383-91)Many of these incidental findings may provide further diagnostic information to guide management e.g. hiatus hernia or do not require further investigation .It should be highlighted that there is a significant resource and harm burden associated with false positive and false negative ETTs that is often overlooked* *The dose of radiation that patients undergoing MPS (9-11mSv) receive is higher that from CT-CA (~4mSv). Overall current evidence would suggest focussed use of CT-CA improves clinical outcomes (SCOT-HEART. Lancet 2015;385:2383-91).*	
3.2.7	AB	Is an objective risk stratification 'score' to be recommended. (third recommendation. This is what informed NICE 95	*No. The guideline group does not advocate a specific scoring system. The objective of the guideline is to provide simple, practical guidance in the management of stable angina.*	
	AF	In patients with a positive ETT it depends on how positive the ETT changes are and I am not clear that emergency investigation or urgent investigation is the issue. Starting anti platelet therapy is the issue and recommending coronary arteriography is sensible and obviously	*Agreed. The text specifies that a 'highly abnormal ETT...' should trigger urgent investigation in section 3.2.2.*	

		should not be months but urgent conveys some degree of risk and the condition stable angina has in general a pretty benign prognosis		
3.3	AB	Should all patients be referred and if so which part of secondary care?	*No. Most initial assessments are made in primary care with most patients referred to secondary care, however this is not appropriate for all patients. It also depends on the local model of care.*	
	GB	You have only one model of care but a plural title	*Thank you. Text has been changed.*	
Section 4				
4.1.1	AB	Beta blockers relieve symptoms (Evidence 1+++) but what is the relevance of the statement in this context 'potential to reduce mortality .. '(Reference 54 - evidence level 3) What about the use of beta blockers in COPD - can they safely be used?	*Thank you. The text has been updated as suggested.* *Thank you. The text has been updated as suggested.*	
	LM	Beta blockers are not contraindicated in first degree heart block (only 2nd or 3rd degree heart block. Beta-clockers are only contraindicated in severe asthma.	*Thank you and noted. The text has been updated.*	
	RC GP	BB post MI remains in doubt with only 1 reasonable (but unblended) trial ever showing benefit (ISIS-1 trial) - in this there was only a 0.7% reduction in mortality. That said, there are 26 studies done showing zero benefit. This is now going out for it's 3rd review by Cochrane. Perez MI, Musini VM, Wright JM. Effect of early treatment with anti-hypertensive drugs on short and long-term mortality in patients with an acute cardiovascular event. Cochrane Database Syst Rev. 2009;(4):CD006743. AlReesi A, MD; AlZadjali N, MD; Perry J, Fergusson D, et al. Do βblockers reduce short term mortality following acute myocardial infarction? A systematic review and meta-analysis. CJEM. 2008;10(3):215-23 Sinert R, Newman DH, Paladino L, Brandler E. Immediate Beta-blockade in Patients with Myocardial Infarctions: Is There Evidence of Benefit? An Evidence-Based Review. Annals of Emergency Medicine. 2010;online,doi:10.1016/j.annemergmed. 2010.03.036	*This guideline deals with stable angina due to obstructive coronary artery disease (CAD) only and not patients with a recent acute event.*	
4.1.2	LM	Verapamil and diltiazem are not contraindicated in first degree heart block (only 2nd or 3rd degree heart block.	*Thank you. The text highlighted is from the previous guideline and was not addressed by the current*	

			update. However, in light of comment we have clarified statement.	
4.1.3	GD	Should it not be added in that guidance that was sent in Jan 2016 about issues with Nicorandil that should not be used first line as was often the case. Drug Safety Update Nicorandil (Ikorel): now second-line treatment for angina - risk of ulcer complications	*Thank you the text and ordering has been changed.*	
	LM	Suggest change the order & have this section as 4.1.4 as nitrates are more commonly used prior to nicorandil	*Thank you and noted. The order has been changed.*	
4.1.5	GD	Nonfatal (Non-fatal) typo	*Thank you. Text has been updated.*	
	LM	Perhaps it is worth mentioning the MHRA warning about ivabradine. The SIGNIFY clinical trial included a pre-specified subgroup analysis of 12,049 participants who had symptomatic angina. In this subgroup, there was a small but significant increase in the combined risk of cardiovascular death or non-fatal heart attack with ivabradine compared with placebo. https://www.gov.uk/drug-safety-update/ivabradine-procoralan-in-the-symptomatic-treatment-of-angina-risk-of-cardiac-side-effects	*Thank you. Text has been updated.*	
	RW	It is correctly stated that in Scotland, the SMC approves ivabradine only for those with angina and intolerant of beta blockers and ratelimiting calcium channel blockers. However, I think it would be useful to insert that the combination of ivabradine with either diltiazem or verapamil (both moderate CYP3A4 inhibitors) is contraindicated and may be harmful (reference: SIGNIFY trial N Engl J Med. 2014 Sep 18;371(12):1091-9)	*Thank you and noted. The text has been updated.*	
4.1.6	LM	R - point 4. Should CCBs not be second line if intolerant to beta-blockers then nitrates, nicorandil or ivabradine third line as with NICE	*Thank you and noted. The recommendations have been updated.*	
	RC GP	Can we be clearer what we think the place (if any) of ranolazine is here? We have states it's not approved by SMC. Could the guideline go so far as to say, it's not recommended for use in stable angina? It is being prescribed in Scotland despite the SMC guidelines through IPTRs and even appears on some formularies. Clarity on this would be very much recommended. Either it is recommended or it is not... (my	*Ranolazine is not recommended by SMC. As such, SIGN is unable to issue any formal recommendation regarding its use (or not). In the absence of a recommendation, we have tried to provide an objective summary of the evidence base.*	

		reviewing of the evidence would suggest the later and I agree with the SMC.)		
	SMC	The last paragraph should say "not recommended by SMC...." instead of "not approved by SMC..."	*Thank you and noted. The text will be updated.*	
4.2.1	RCGP	We have said: Other RCTs have shown that adding CCBs to beta blockers, although safe, offered very little or no benefit in relief of anginal symptoms.83-85. Subsequently we have then said "a calcium channel blocker should be considered." Could we also be clearer and say that a "calcium channel blocker could be considered, although the evidence to support any benefit is conflicting."	*Although there is some conflicting evidence, taken together the data do suggest that calcium channel blockers should be considered.*	
4.2.2	AB	Can the combination of ivabradine and a beta blocker not be used?	*As stated in the text this combination is not currently approved by SMC for use in Scotland.*	
	SMC	The last paragraph should say "not recommended by SMC...." instead of "not approved by SMC..."	*Thank you and noted. The text will be updated.*	
4.3.1	DM	Co-existing atrial fibrillation is frequent in stable coronary disease so a section on anti-thrombotic management in this group would be helpful.	*We agree this is an important issue. However, the detailed management of atrial fibrillation was felt to be outwith the remit of this guideline. Where indications for anti-thrombotic therapy in patients with stable angina, a search of recent literature failed to identify any robust evidence. This has been highlighted as an area for future research.*	
4.3.3	AB	The meta-analysis evidence level is 1++ yet the recommendation is 'should be considered'	*Section 4.3.3. was retained from the previous version of the guideline, no changes have been made. As outlined in the 'Key to evidence statements and recommendations' section SIGN guidelines the word 'should' is used for strong recommendations.*	
	RCGP	"All patients with stable angina should be considered for treatment with angiotensin-converting enzyme inhibitors". Again it's the same issue, we have made a statement recommending something, whilst the narrative clearly shows that the evidence doesn't wholly support this. We should include that 'the evidence to support this is conflicting'.	*Section 4.3.3. was retained from the previous version of the guideline, no changes have been made.*	

Section 5				
5.1	AF	There is a bit missing here about any centre offering revascularisation for angina needs to keep a record of outcomes PROM Surgical Outcomes PCI outcomes Symptoms as well as mortality are important	*It goes without saying that clinical governance is a key component of any local service, be it cardiac or any other specialty. The guideline group felt this was out with the remit of this specific guideline update and may be more suited to general guidance on clinical governance.*	
5.2.1	AB	Stable IHD is introduced in paragraph 3	*Thank you and noted. Text to be updated to CAD.*	
5.2.2	AB	Have you explained what a drug eluting balloon is ?	*Thank you and noted. Text to be updated to include explanation.*	
5.3	GB	Not sure why you would want to use such an old reference (125) and report 2% mortality. The UK mortality rate for elective CABG has been 1% or less for each of the past 10 years. The most recent data is from 2015 with a mortality rate of 0.58%. http://www.bluebook.scts.org/#ActivityRates It may be useful for patients to include a link to these results.	*Thank you and noted. The text has been updated with the more recent reference as suggested.*	
5.3.2	AF	Is this really so ? recent discussion	*Noted.*	
	GB	"Although considered minimally invasive, the procedure still involves a chest incision" - off pump CABG is not minimally invasive. Minimally invasive surgery involves a smaller alternative access to the heart compared to a median sternotomy but may also be off pump or on pump. Off-pump v on-pump is a couple topic and whilst your recommendation may be correct, it doesn't reflect the concern in the broad surgical community. There has been much recent debate about the outcomes of off pump surgery with some authors advocating that surgeons should abandon the technique due to poorer long term outcomes compared to on pump surgery. The frequency of off pump surgery is falling in the Western world, possibly related to long term outcome studies but also due to improved on-pump results with improved patient pre-operative status and anaesthetic techniques. It is further complicated by the use of the "no-touch" technique which may improve the	*Minimally invasive may refer to the size of the incision or less physiological insult, e.g. by not putting the patient on bypass. In this sense, many consider off-pump surgery to be minimally invasive.*	

		outcomes of off pump surgery by avoiding manipulating and clamping the aorta during surgery. The much cited ROOBY trial {Shroyer et al., 2009, New England Journal of Medicine N Engl J Med, 361, 1827-1837} - not referenced by this guideline, has recently reported 5-year results with lower survival and event-free survival; {Shroyer et al., 2017, New England Journal of Medicine N Engl J Med, 377, 623-632}	*Multiple peer reviewers have suggested its inclusion and therefore the text has been updated to include this and a summary of the limitations of the study.*	
	RW	I think the recent ROOBY-FS trial results should be included here, suggesting poorer 5 year survival with off-pump compared to onpump CABG (ref: N Engl J Med. 2017 Aug 17;377(7):623-632)	*Multiple peer reviewers have suggested its inclusion and therefore the text has been updated to include this and a summary of the limitations of the study.*	
5.4	AF	Should all patients be discussed	*No. For patients where the treatment options are clear, for example patients with limiting symptoms and focal single vessel disease, treatment may be offered without MDT discussion. Where doubt exists, patients should be discussed.*	
5.4.4	GB	Typo last character "["	*Thank you. Text updated.*	
5.4.5	AB	Recommendations - -despite all the interventions trials -- although the drug eluting stents are an advance especially in relation to instent re-thrombosis the evidence remains unchanged despite the change in clinical practice that is seen nationally in relation to PCI and CABG.	*Agreed. This may in part reflect the shift in workload from stable angina to re-vascularisation following acute coronary syndrome.*	
5.5.1	AF	Good	*Thank you.*	
	GB	"The Society of Thoracic Surgeons has recommended that aspirin should be stopped for 3-5 days before elective CABG and then restarted early after surgery.176" - this was updated in 2012 {Ferraris et al., 2012, The Annals of Thoracic Surgery, 94, 1761-1781} - "Aspirin discontinuation before purely elective operations in patients without acute coronary syndromes is reasonable to decrease the risk of bleeding." Although it mentions 48 hours for the administration of postoperative Aspirin, the update to your reference quotes "For stable nonbleeding patients, aspirin should be given within 6 to 24 hours of coronary artery bypass graft surgery	*Noted. Although a detailed update of this section was outwith the scope of the current focused guideline update, we agree it is important to update the reference and STS recommendation. The text has been updated as follows "The Society of Thoracic Surgeons has recommended that aspirin should be stopped for 3-5 days before elective CABG and, in stable non bleeding patients, restarted within 6 to 24 hours of coronary artery bypass graft surgery (CABG) to*	

		(CABG) to optimize vein graft patency." This is an important point as early administration of aspirin has the greatest effect on the reduction of graft occlusion.	*optimize vein graft patency. " Update reference to Ferraris et al Ann Thorac Surg 2012;94:1761–8.*	
5.5.2	AB	? allergic to clopidogrel' - should intolerance be mentioned?	*Thank you and noted. This was discussed and the guideline group made a decision not to include this.*	
	AF	Good	*Thank you.*	
	DM	Similar comment as before, some guidance in antithrombotic management in patients with co-existent AF would be very useful.	*Agree. This is of interest however there is no evidence. It is an area for future research.*	
5.8.2	GD	"R Transmyocardial laser revascularisation is not recommended for the treatment of stable angina" You have mentioned this under recommendation not for use in stable angina but this heading is under treatment of refractory angina. I have never heard of it being recommended for any type of angina and would want to know when it may be of benefit not when it shouldn't be considered?..... " TML should only be considered if person on maximum tolerated anti-anginals and there is contraindication to PCI /CABG for refractory angina"	*Although somewhat historical, TML is a treatment for stable refractory angina that was trialled around the time of the original guideline publication. Clinical trials confirmed no benefit. Indeed there was the potential for significant harm. This is summarised in the data. The guideline group felt the potential for harm justified the inclusion and recommendation.*	
5.8.4	JH	I understand that there is a specific cardiac rehab guideline but I feel it would be useful to highlight lifestyle and rehab as a specific management tool of angina.	*Lifestyle and rehab as management tools have been covered in section 7.2, including a specific signpost to SIGN 150 Cardiac rehabilitation guideline.*	
Section 6				
General	AN	"Patients who have postoperative cardiac injury are at increased risk of death; in one series 1.9% mortality at 30 days (95% CI 1.7 to 2.1).190" In that study 1.9 % was the overall mortality for all patients. For patients with a postoperative cardiac injury it was higher. Patients with a peak TnT value of 0.01 ng/mL or less, 0.02, 0.03-0.29, and 0.30 or greater had 30-day mortality rates of 1.0%, 4.0%, 9.3%, and 16.9%, respectively.	*Thank you the text has been amended to reflect this comment (chapter 6 introductory paragraph).*	
6.1	AN	In Table 2, Cardiomyopathy appears twice. "Assessment for surgery should consider the inherent procedural risk…" It would be useful here to refer to Table 3, surgical procedures stratified by cardiac risk level. That table is a slightly modified	6.*1 Thank you. The duplicate "cardiomyopathy" has been removed from table 2. As suggested Table 3 is referenced in text. Table 3 has been updated to table 3 from 2014 ESC guidelines as referenced and these*	

		version of Table 4 in the 2007 ACC/AHA Guidelines on Perioperative Cardiovascular Evaluation and Care for Noncardiac Surgery and the source should be referenced if the table is used. However, the table was not included in the current 2014 ACC/AHA guideline. A more up-to-date equivalent (distinguishing for example between open vascular surgery and endovascular / angioplasty procedures) is Table 3 in the 2014 European Society of Cardiology (ESC) and the European Society of Anaesthesiology (ESA) Guidelines on Non-cardiac Surgery: Cardiovascular Assessment and Management [a]. It would be preferable to use that table. [a] Eur Heart J. 2014 Sep 14; 35(35):2383-431.	*guidelines are now included in reference section (2014 ESC/ESA Guidelines on non-cardiac surgery: cardiovascular assessment and management. European Heart Journal 2014; 35:2383–2431.*	
6.1.1	AB	Second Recommendation - -still a place for exercise tolerance testing as a functional test?	*Noted. No change made.*	
6.2	AN	"Preoperative revascularisation" would be a better title for this section then "Perioperative revascularisation" because it discusses revascularisation before non-cardiac surgery but not combined revascularisation and non-cardiac surgery or revascularisation after non-cardiac surgery. "The Coronary Artery Revascularisation Trial randomly assigned patients at risk for perioperative cardiac complications and clinically significant coronary heart disease to undergo either revascularisation or no revascularisation before elective major non-cardiac vascular surgery.203 At 2.7 years after randomisation, mortality was 22% in the revascularisation group and 23% in the no revascularisation group. These results conflict with the Coronary Artery Surgery Study…" This gives the misleading impression that the Coronary Artery Revascularisation Trial was a trial of CABG against medical therapy. In fact, most of the patients randomised to "revascularisation" in that trial underwent PCI. The decision as to whether to undertake PCI or CABG was decided by the local investigators and "the potential Longterm advantage of CABG among patients with diabetes and multivessel disease was recognized". Patients who underwent CABG had more severe coronary disease than those who	*Thank you. The text has been updated as suggested.* *Thank you. This was a focussed guideline update. The guideline committee did not feel that there had been any major advances in the evidence around pre-operative revascularisation and a formal literature search was not performed on this topic. A minor amendment to text has been made to clarify any potential confusion around evidence.*	

		underwent PCI (Table 2 in the report of the study – figures for numbers of vessels revascularised and completeness of revascularisation.) Therefore, the patients who underwent CABG had more severe disease than those randomised to medical therapy. The authors did not report outcomes separately for CABG and PCI. However, their results were included in a subsequent meta-analysis by Biccard [a] which found a trend to improved long term outcome for preoperative CABG compared to medical therapy: OR 0.64 [0.36, 1.12] but a poorer long term outcome for preoperative PCI compared to medical therapy: OR 1.46 [1.00, 2.13]. Monaco <b> randomized 208 vascular surgery patients to a strategy of either routine or selective preoperative angiography. The routine angiography group had a higher rate of preoperative myocardial revascularization, a higher proportion of revascularization by CABG rather than PCI and significantly lower mortality. In Edinburgh preoperative CABG is currently undertaken for a small number of patients before very major surgery such as open thoracoabdominal aortic aneurysm repair which is associated with a very high risk of perioperative cardiac complications. Some of these patients do not have indications that would justify CABG independent of their non-cardiac surgery. For example, some have stenosis of over 70 % in only two vessels and/or positive stress tests for myocardial ischaemia. I consider that this management is appropriate on the basis of the available evidence. The recommendation in the guideline “The indications used for revascularisation prior to noncardiac surgery should be those used in the nonoperative setting.” is not supported by the available evidence and may result in an appropriate treatment being denied to some patients. Rather, a decision should be made after considering the severity of the coronary disease, the nature and magnitude of the proposed surgery and the consequences of delaying the non-cardiac surgery. In a small number of patients, CABG in the absence of “significant left main stenosis, triple vessel disease in conjunction with left	 *Thank you, response as comment above* *The guideline group note the reviewer’s comments but disagree with the conclusion. The objective of a guideline is to provide the reader with guidance on the best treatment options. In many cases this guidance is reached from extrapolation of study findings in general populations and interpretation requires an evaluation of individual patient factors. For the vast majority and as a general principle, the indications for coronary revascularisation preoperatively are the same as in the non-surgical setting.*	

		ventricular dysfunction, two vessel disease including proximal LAD, and unstable symptomatic CHD despite full medical therapy" may be considered appropriate.		
		"A significantly higher risk of cardiac complications (27%) was found in patients undergoing noncardiac procedures in the first month after CABG.205 This remained higher (17%) until the sixth month following CABG." In the study quoted, the investigators "did not examine the indication for CABG in our study patients". Therefore, it is not known how many, if any, had CABG because noncardiac surgery was planned and how many had urgent CABG for unstable coronary artery disease. Nor do the authors report the indications for the vascular procedures performed within a month of CABG. In particular, they do not report whether some or all of these vascular procedures were emergencies / urgent or whether any of them could have been delayed. This study is a poor basis on which to make a recommendation on the timing of a planned non-cardiac surgical procedure after CABG.	*Thank you. This section was not updated on this occasion as part of the focussed updated.*	
		"Patients who have had PCI and stent insertion are at risk of stent thrombosis if their dual antiplatelet therapy is discontinued.206,207". I wouldn't disagree with that statement but I'm not sure that the two studies referenced demonstrate this. Both found an increased risk of complications if noncardiac surgery is undertaken soon after coronary stent insertion but it isn't clear whether or not antiplatelet drugs had been discontinued in any of the patients who suffered complications in reference 207. In reference 206, "one or both antiplatelet drugs were typically interrupted one to two days before surgery" and an unusually high rate of bleeding complications was attributed to the fact that "The pharmacodynamics of both drugs make stopping either drug 1 to 2 days before surgery ineffective in diminishing the risk of bleeding." In another study[c] 20 of 54 patients who underwent non-cardiac surgery within 30 days of coronary stenting experienced a major adverse cardiac event although dual antiplatelet therapy was apparently continued until the time of surgery in all	*Thank you. As suggested the references (206 and 207) have been replaced with "Iakovou et al JAMA. 2005 May 4;293(17):2126-30."*	

		these cases. Therefore, while I think the statement in your guideline that "If surgery cannot be delayed, dual antiplatelet therapy should be continued if possible.211. Premature discontinuation of antiplatelet therapy is associated with a high risk of stent thrombosis which is often fatal." Is reasonable, it would be desirable to caution readers that despite continuing antiplatelet therapy, the risk of major complications if noncardiac surgery is performed within a few weeks of coronary stenting remains high. Reference 211 is not an appropriate reference here because it relates to cerebral emboli during carotid surgery not coronary stenting or cardiac complications. "The combination of aspirin and clopidogrel increases the risk of bleeding during CABG, which may also be increased postoperatively." This is true but, since this section is about non-cardiac surgery, it would be more relevant to have a statement and references about the increased risk of bleeding in non-cardiac surgery. "Current guidance suggests that elective surgery should be delayed by at least three months (but preferably six) following a PCI, with the greatest risk when surgery is performed early.177" I presume this sentence refers to the insertion of drugeluting stents? "The bleeding risk of the proposed emergency surgical procedure must be extremely high and the disease requiring surgery must be life threatening to justify stopping antiplatelet agents prematurely.176" Is 176 the correct reference here? It is a guideline that recommends that aspirin be stopped before elective CABG. "If emergency or urgent noncardiac surgery is required after percutaneous coronary intervention, dual antiplatelet therapy should be continued whenever possible. If the bleeding risk is unacceptable and antiplatelet therapy is withdrawn, it should be reintroduced as soon as possible after surgery." I presume this refers to surgery within days or weeks of PCI? It would be useful	*The Guideline Committee felt that the text was acceptable as it is.* *As suggested this sentence has been removed* *Thank you. This has been clarified in text.* Thank you. The reference has been updated [Again please use reference for ACC/AHA and ESC guidelines on periop management *Thank you. This has been clarified in the text.*	

		to clarify this. [a] Biccard BM and Rodseth RN (2009). A meta-analysis of the prospective randomised trials of coronary revascularisation before noncardiac vascular surgery with attention to the type of coronary revascularisation performed. Anaesthesia, 64(10), 1105-1113 <b> Monaco M, Stassano P, Di Tommaso L et al. (2009). Systematic strategy of prophylactic coronary angiography improves long-term outcome after major vascular surgery in medium to high risk patients: a prospective, randomized study. J Am Coll Cardiol, 54, 989–996. [c] van Kuijk JP, Flu WJ, Schouten O, Hoeks SE, Schenkeveld L, de Jaegere PP, et al. Timing of noncardiac surgery after coronary artery stenting with bare metal or drug-eluting stents. Am J Cardiol. 2009; 104(9):1229-34.		
6.3	AB	Is this applicable to all those with a previous history of IHD / CAD - -both used in this paragraph	*Thank you and noted. The acronyms have been updated to just CAD.*	
6.3.1	AN	"Initiation of beta blocker therapy with the intention of reducing cardiac complications in patients not previously treated with beta blockers but at high risk of developing cardiac complications has been extensively investigated but is not currently recommended." This is incorrect. Two current international guidelines cover this topic:- The 2014 ACC/AHA guideline (ref 192) recommends that: "In patients with intermediateor highrisk myocardial ischemia noted in preoperative risk stratification tests, it may be reasonable to begin perioperative beta blockers". "In patients with 3 or more RCRI risk factors (e.g., diabetes mellitus, HF, CAD, renal insufficiency, cerebrovascular accident), it may be reasonable to begin beta blockers before surgery" "In patients in whom betablocker therapy is initiated, it may be reasonable to begin perioperative beta blockers long enough in advance to assess safety and tolerability, preferably more than 1 day before surgery" "Betablocker therapy should not be started on the day of surgery" The 2014 European Society of Cardiology(ESC) and the European Society of Anaesthesiology (ESA)	*Response to comment paras 1-3 - Current evidence does not support the routine use of B Blockers in patients undergoing noncardiac surgery. The guideline development group accept that there may be specific (non-routine) situations where this may be appropriate based on clinical judgement. This discussed in the text.* *As comment above*	

		Guidelines on Non-cardiac Surgery: Cardiovascular Assessment and Management[a] recommend that: “Preoperative initiation of betablockers may be considered in patients scheduled for highrisk surgery and who have 2 clinical risk factors or ASA status 3.” “Preoperative initiation of betablockers may be considered in patients who have known IHD or myocardial ischaemia.” “When oral betablockade is initiated in patients who undergo noncardiac surgery, the use of atenolol or bisoprolol as a first choice may be considered.” “Initiation of perioperative highdose betablockers without titration is not recommended.” “Preoperative initiation of betablockers is not recommended in patients scheduled for lowrisk surgery.” The ESC/ESA Guideline on non-cardiac surgery is very relevant to this chapter of the SIGN Guideline and I suggest that it is referenced in your guideline. Both the ACC/AHA and ESC/ESA guideline groups reviewed in detail the evidence for starting beta blockers before non-cardiac surgery and I think that their recommendations are appropriate. I have concerns about the proposed wording of your recommendation: “Routine initiation of perioperative beta blocker to reduce perioperative myocardial infarction in patients undergoing noncardiac surgery is not recommended.” Taken literally, it is hard to argue against because no-one would advocate starting beta-blockers in all patients having non-cardiac surgery. However, I am concerned that it may lead to the impression that there is no place for considering starting beta-blockers before surgery whereas this is something that should be considered in some high risk patients having high risk surgery. The largest study of perioperative beta blockers (and of highest weight in meta-analyses), the POISE study[d], found a reduction in the primary composite endpoint of death, myocardial infarction, or non-fatal cardiac arrest at 30 days in the beta-blocker group but this was offset by increased all-cause mortality and strokes. In this study beta-blockade was initiated two to four hours before surgery with a large dose of metoprolol	*As comment above* *Response to comment para 4 - Thank you. The text has been updated to reflect these comments.*	

		and there was no protocol for the prevention, detection or management of perioperative hypotension (thought to have been the main cause of the increased mortality and strokes) apart from withholding further doses of metoprolol while a patient was hypotensive or if the heart rate was persistently less than 45. This has led to the recommendations that beta-blockade should be started in advance of surgery and at a low dose, as was undertaken in other studies which did not find increased mortality or strokes. The current SIGN guideline recommends: "If betablockers are started perioperatively …Patients should be monitored postoperatively for adverse effects, particularly hypotension and stroke." However, I would suggest that monitoring alone is insufficient and that the recommendation should be along the lines of: If betablockers are started perioperatively …there is an increased risk of perioperative hypotension. Measures to reduce this risk such as withholding other anti-hypertensive drugs should be considered, blood pressure should be carefully monitored after surgery and there should be a protocol for the management of hypotension". [a] Eur Heart J. 2014 Sep 14; 35(35):2383-431. [d] Devereaux PJ, Yang H, Yusuf S, Guyatt G, Leslie K, Villar JC et al. Effects of extended release metoprolol succinate in patients undergoing noncardiac surgery (POISE trial): a randomised controlled trial. Lancet 2008;371:1839–1847.		
6.3.3	LM	Typo - full stop missing after bracket in line 6.	*Thank you. The full stop has been included.*	
6.3.4	AB	Is 5 days discontinuation the standard approach?	*Thank you. The text has been updated to 'at least 3 days' based on the evidence.*	
Section 7				
General	MO	This section is much shorter than the previous guideline. Much of the previous content has been merged into the new cardiac rehabilitation guideline which is correct.	*Thank you*	
7.1	AB	Highlight that the HAD score is a screening tool although it does correlate with other assessment tools specifically for depression and anxiety.	*We have stated that the HAD is a screening tool. We assume our readers realise that these measures would correlate with each other as they are measuring the same psychological variables.*	

	LM	Typo - full stop missing after asthma in P2 L4	*Thank you. The full stop has been included.*	
	MO	I would include the PHQ-9 (Patient Health Questionnaire 9) and GAD-7 (Generalised Anxiety Disorder 7) in the list of assessment tools as they are recommended by NICE and are free from copyright so easily available, validated in cardiac patients and widely used (indeed the 2 questions for screening on depression mentioned later in the guideline are from the PHQ9). I would also be inclined to reference SIGN 150 cardiac rehabilitation section 6.3 here as screening/assessment should be part of a clinical pathway.	*We have included the PHQ9 and GAD7 questionnaires to the guidelines. We agree it would be helpful to signpost to SIGN 150 CR section 6.3- we have added text to this effect to the draft. (Need to include PHQ9 and GAD7 questionnaires in the guideline. Need to add text in 6.3 to refer to SIGN 150 cardiac rehab)*	
	RC GP	The evidence shown simply says when you are not functioning perfectly, you do not feel as well. To then make the leap to say, as a result we should assess you all for low mood is screening (not backed up by UKNSC). There is zero evidence that screening in the method suggested will result in better QOL outcomes. Only when we have applied the WHO/WIlson criteria to this screening (with supporting evidence) can we be confident that we should do this. If you are going to ask us to screen for depression, provide robust evidence you clearly improved QOL by screening for it in those with stable angina versus those who were not screened... As a GP we are there to help people through chronic disease - not label them with another disease in the process.	*Our guideline does not suggest that screening results in better QoL outcomes, and we did not analyse whether screening results in increased QoL. Screening is not conceptualised as a diagnostic tool within this context. It has the function of highlighting the presence or absence, and severity of psychological distress, to inform decisions for onward referral, and establish the presence of risk. Staff would not be expected to "label" patients with any formal mental health diagnosis as we do not anticipate they are largely trained to do so.* *We believe it is clinically well established that psychological screening can be helpful. We have labelled this more clearly as a "4"- expert opinion, and we signpost to SIGN 150, Cardiac Rehabilitation, Section 6.3.*	
7.2	AF	Are they double blind randomised.	*They are RCT.*	
	LM	Typo - P2 L9, space missing after CI	*Thank you. The space has been added.*	
	MO	This section is well written.	*Thank you.*	
7.2.1	AF	do the trials showed sustained benefit and are they randomised (double blind)	*The guideline group feel there is adequate explanation.*	
	MO	This section is well written.	*Thank you.*	

7.2.2	MO	This section is good	*Thank you.*	
7.3	MO	The York beliefs Qnaire was developed in 2003 so could be out of date? The York group (Gill Furze/ Bob Lewin) had thought about updating it but I am not aware of any further versions. Perhaps it would help to email them to ask if you have not done so already?	*Thank you. The original author has recently clarified, via personal correspondence, that there is no further update to the 2003 version.*	
Section 8				
8.2	AB	As cardiac waiting times rise in Scotland (including outpatient appointments) should the adverse effect of this be highlighted.	*The guideline development group were a unclear what evidence there was to support this. In general waiting times, particularly for cardiac surgery, have reduced or remain unchanged since the last guideline. We accept there may be some regional variation.*	
8.3	AB	Agreed. We need a comment that Quality Clusters should ensure that this process continues post the demise of QOF in primary care.	*The guideline group felt that defining the general role of Quality Clusters was outwith the remit of this guideline.*	
8.4	GD	"careres" (Carers) Typo	*Thank you. Text has been updated.*	
	JH	Can be met by the knowledge and skills of a cardiac rehab team.	*Noted. No change made.*	
	LM	Typo line 1 - carers	*Thank you. Text has been updated.*	
8.4.1	NO' D	Section still in development.	*Noted.*	
8.5	GB	There is an excellent patient section of the Society of Cardiothoracic Surgeon website ` https://scts.org/patients/having-heart-surgery/	*Thank you. This will be passed onto the group responsible for developing the patient version of this guideline.*	
	GD	Under BHF paragraph ...."ItaAlso provides".... (It also provides) Typo	*Thank you. Text has been updated.*	
	LM	Typo - BHF paragraph line 2. It also...	*Thank you. Text has been updated.*	
Section 9				
9.2	AB	Is the resources and expertise available for a shift to increased use of CT-coronary angiography although I get the feeling that there is a confusing attempt in the text to play down this necessary shift.	*The NICE guideline included a full cost assessment and a shift to CT-CA was found to be cost effective when used in the diagnosis of patients with suspected angina. The guideline group felt it was outwith the scope of the guideline to provide an assessment of the locally available resource and*	

			expertise across Scotland.	
Section 10				
10.1	GB	Typos in ref 131- Van Dijk D. Cognitive Outcome After Off-Pump and On-Pump Coronary Artery Bypass Graft Surgery<SUBTITLE>A Randomized Trial</SUBTITLE>. JAMA 2002;287(11):1405.	*Thank you. Text has been updated.*	
10.2	LM	Annex number missed off	*Thank you. Text has been updated.*	
	RC GP	I could consider adding: what are the (unintended) harms of diagnosing angina by using CT coronary angiogram; also: what is the benefit (if any) in screening for depression/mood disorders in patients with stable angina versus those who are not screened.	*Thank you. Both topics will be added to the list of recommendations for research with a change to the text for the second.. 'What are the implications and cost effectiveness of CT-CA in investigations of patients with stable angina'.*	
Annexes				
Annex 1	DM	I cannot see that Question 4 (warfarin and aspirin) has been addressed. But maybe I am missing it.	*The guideline group did consider this question and a literature search was performed. No robust contemporary data was identified, hence the inclusion as an important topic for future research.*	
Annex 2	AB	I can see how this flow chart fits in at a given part of the patient pathway but as a general practitioner I do not get the feel of a how to approach the patient in a definitive way throughout that pathway.	*Noted. The guideline group has tried to develop a pathway that is easy to follow.*	
Annex 3	AB	This chart helps understand the process more but the conflict is still whether all patients with symptoms which could possibly be angina in nature are referred for further secondary care assessment to confirm obstructive coronary heart disease. I accept that not all cases of chest pain need to be referred but in practice and with a change in the nature of the disease, I feel that more and more patients come into the 'possible' angina category.	*If there is diagnostic uncertainty and the patient is a candidate for revascularisation then referral to secondary care should be considered. Where patients are not a candidate for invasive investigation/revascularisation then a trial of medical therapy and assessment of the symptomatic response may be more appropriate. This could be undertaken in primary or secondary care.*	
	GD	I like the flow charts but what is constituted as low/medium/high risk ? Are we recommending any risk tool is used ? Very open to individual interpretation if not.	*Other than specific anatomical characteristics, the guideline group do not advocate any specific risk scoring tool in the assessment of patients with stable angina. Risk assessment requires a degree of clinical*	

			interpretation and will depend on a number of features including history, resting 12 lead ECG and where available functional assessment. These factors are all outlined in the text.	
	DM	The algorithm is commendably clear and definite but I am not sure this message comes across as well in the text. CTCA is listed as simply another diagnostic test and it's prominent role only becomes clearer at the fourth recommendation point and after looking at the Annex. Could it be moved up the list of recommendations so that it's clearly seen as the test of first choice in suspected angina ?	*We have tried to describe the investigations in a logical order based on increasing invasiveness and type of test. We agree that this may underplay the importance of CT-CA.*	
	RC GP	I am not clear we have properly considered the harms/costs which will come with CT Coronary angiogram as a first line investigation... have we got enough people to fully support all the incidental findings as a result and the literature to provide to patients on the risks of having this investigation..? https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2799652/ https://www.ncbi.nlm.nih.gov/pubmed/17086525 I'm not sure we have enough resources to support the rate of incidental findings quoted... and as a GP I am not relishing the thought if this all lands back at us to sort with a distressed patient.	*The guideline is not advocating routine use of CT-CA for all patients undergoing investigations for chest pain, just for those with diagnostic uncertainty.* *We agree that CT-CA has some limitations and these have been highlighted in the text. The NICE guideline included a full cost assessment and a shift to CT-CA was found to be cost effective when used in the diagnosis of patients with suspected angina.* *The guideline group felt that an evaluation of local resource and expertise across Scotland was outwith the scope of the guideline.* *There is a significant resource and harm burden associated with false positive and false negative ETT which is often overlooked. Eliminating this additional workload may reduce the distress caused to patients and GPs alike.*	