

### 3-year scoping report

**Topic:** Management of Stable Angina - Literature published since date of SIGN 151 guideline search in 2015

**Date of search:** 4-7 October 2021

**Searched by:** Lorna Thompson

**Key concepts:** stable angina, chronic coronary disease, angina pectoris, myocardial ischaemia

### Summary of findings

The purpose of this 3-year scoping is to identify significant new evidence relating to SIGN 151, and whether any sections of the guideline require updating. A rapid search of the literature was conducted; sources and references are detailed in the box below.

New evidence identified falls into three sections of the current guideline:

- Section 5 – Interventional cardiology. Publications relating to major RCTs (ISCHAEMIA, FAME3 and ORBITA)
- Section 4 – Pharmacological management. New SMC advice on rivaroxaban. (likely of more relevance to prevention guideline)
- Section 3 – Diagnosis and assessment. Incorporation of SHTG HeartFlow advice. Inclusion of [FORECAST](#) trial.

### Chair's comments

#### Discussion with Chair 13/10/2021

The main trial which requires to be incorporated is the FORECAST TRIAL which should be published in full by end 2021. This will require amendments to Section 3 on CT-CA and will need to consider the SHTG Adaptation of NICE HeartFlow assessment.

If a decision is made to update then the opportunity should also be taken to revise the section on interventional procedures. This has no unsafe or concerning recommendations but, being an update of previous version, is structured in a way which does not facilitate full use of key trials ISCHAEMIA, and ORBITA.

### Input from Group Member

Group member Nawwar Al-Attar alerted to the FAME 3 trial– see table covering Guideline Section 5 below

Nawwar Al-Attar also highlighted US and European guidelines which may be informative as below:

- Franz-Josef Neumann, Miguel Sousa-Uva, Anders Ahlsson, et al ESC Scientific Document Group, 2018 ESC/EACTS Guidelines on myocardial revascularization, European Heart Journal, Volume 40, Issue 2, 07 January 2019, Pages 87–165.  
<https://academic.oup.com/ejcts/article/55/1/4/5079878?login=true>
- Gulati M, Levy PD, Mukherjee D, et al 2021 AHA/ACC/ASE/CHEST/SAEM/SCCT/SCMR guideline for the evaluation and diagnosis of chest pain: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. Circulation. 2021:.  
<https://www.ahajournals.org/doi/abs/10.1161/CIR.0000000000001029>

### Relevant evidence and implications for SIGN recommendations

#### SIGN section 5: Interventional cardiology and cardiac surgery

Reference	Details	How does this potentially change current recommendations?
<ul style="list-style-type: none"><li>• <i>Include type of evidence, reference and source of evidence</i></li><li>• <i>Where possible, include hyperlinks to the references</i></li></ul>	<p><i>Include abstract or summary of evidence</i></p>	<ul style="list-style-type: none"><li>• <i>State whether you are referring to a SIGN good-practice point/recommendation or text within the body of the guideline</i></li><li>• <i>State specifically how the new evidence could affect the recommendation</i></li><li>• <i>If you are referring to a recommendation in the SIGN guideline, state whether it is based on evidence or expert opinion</i></li><li>• <i>When making suggestions to SIGN based on your findings, use 'could' rather than 'should' eg 'SIGN could consider this new evidence'</i></li></ul>

<p>Fearon WF, Zimmermann FM, De Bruyne B, Piroth Z, van Straten AH, Szekely L, <b>FAME 3</b> Investigators, et al. Fractional Flow Reserve–Guided PCI as Compared with Coronary Bypass Surgery. <i>New England Journal of Medicine</i>. 2021 Nov 4.</p>	<p>Notified to SIGN by Nawwar Al-Attar</p> <p>It is a multicenter, international, non-inferiority trial, patients with 3v-CAD were randomly assigned to CABG or FFR-guided PCI using current generation zotarolimus-eluting stents. The primary endpoint was the one-year occurrence of all-cause death, myocardial infarction (MI), stroke or repeat revascularization (MACCE). The non-inferiority margin was prespecified as a hazard ratio (HR) of 1.65.</p> <p>In patients with three-vessel coronary artery disease, FFR-guided PCI was not found to be non-inferior to CABG with respect to the incidence of a composite of death, myocardial infarction, stroke, or repeat revascularization at 1 year. (effectively = CABG superior)</p>	<p>Current structure of recommendations does not specifically compare techniques but there is opportunity to outline comparative data and perhaps build on the GPP:</p> <p><i>“A tailored approach to revascularisation is required and the approach should be decided following discussion with the patient and the multidisciplinary ‘Heart Team’. Factors influencing the choice of revascularisation should include burden and complexity of coronary artery disease, presence of diabetes mellitus, age and renal dysfunction.”</i></p>
<p>Fearon WF, Nishi T, De Bruyne B, Boothroyd DB,; FAME 2 Trial Investigators. Clinical Outcomes and Cost-Effectiveness of Fractional Flow Reserve-Guided Percutaneous Coronary Intervention in Patients With Stable Coronary Artery Disease: Three-Year Follow-Up of the FAME 2 Trial (Fractional Flow Reserve Versus Angiography for Multivessel Evaluation). <i>Circulation</i>. 2018 Jan 30;137(5):480-487. <a href="https://pubmed.ncbi.nlm.nih.gov/29097450/">https://pubmed.ncbi.nlm.nih.gov/29097450/</a></p>	<p>A total of 888 patients with stable single-vessel or multivessel coronary artery disease with reduced fractional flow reserve were randomly assigned to PCI plus MT (n=447) or MT alone (n=441). Major adverse cardiac events included death, myocardial infarction, and urgent revascularization.</p> <p>Major adverse cardiac events at 3 years were significantly lower in the PCI group compared with the MT group (10.1% versus 22.0%; p&lt;0.001), primarily as a result of a lower rate of urgent revascularisation (4.3% versus 17.2%; p&lt;0.001). Death and myocardial infarction were numerically lower in the PCI group (8.3% versus 10.4%; p=0.28). Angina was significantly less severe in the PCI group at all follow-up points to 3 years.</p>	<p>This study may inform section 5 around identifying which patients might benefit most from interventional cardiology in addition to medical therapy.</p> <p><b>Recommendation unlikely to change:</b> “Patients with stable angina who remain symptomatic on optimal medical therapy should be considered for revascularisation by coronary artery bypass grafting or percutaneous coronary intervention.”</p>

<p>Xaplanteris P, Fournier S, Pijls NHJ, Fearon WF,; FAME 2 Investigators. Five-Year Outcomes with PCI Guided by Fractional Flow Reserve. N Engl J Med. 2018 Jul 19;379(3):250-259. <a href="https://pubmed.ncbi.nlm.nih.gov/29785878/">https://pubmed.ncbi.nlm.nih.gov/29785878/</a></p>	<p>In patients with stable coronary artery disease, an initial FFR-guided PCI strategy was associated with a significantly lower rate of the primary composite end point of death, myocardial infarction, or urgent revascularization at 5 years than medical therapy alone. Patients without hemodynamically significant stenoses had a favorable long-term outcome with medical therapy alone.</p>	
<p>White HD, O'Brien SM, Alexander KP, Comparison of Days Alive Out of Hospital With Initial Invasive vs Conservative Management: A Prespecified Analysis of the ISCHEMIA Trial. JAMA Cardiol. 2021 Sep 1;6(9):1023-1031. doi: 10.1001/jamacardio.2021.1651. PMID: 33938917; PMCID: PMC8094032. <a href="https://pubmed.ncbi.nlm.nih.gov/33938917/">https://pubmed.ncbi.nlm.nih.gov/33938917/</a></p> <p>Gersh BJ, Bhatt DL. To stent or not to stent? Treating angina after ISCHEMIA—the impact of the ISCHEMIA trial on the indications for angiography and revascularization in patients with stable coronary artery disease. Eur Heart J. 2021 Apr 7;42(14):1389-1393. <a href="https://pubmed.ncbi.nlm.nih.gov/33827132/">https://pubmed.ncbi.nlm.nih.gov/33827132/</a></p>	<p>Prespecified analysis of the ISCHEMIA trial, days alive out of hospital (DAOH) was compared between 5,179 patients with stable coronary disease and moderate or severe ischemia randomised to invasive management or conservative management.</p> <p>DAOH was higher for patients in the conservative management group in the first 2 years but not different at 4 years. DAOH was decreased early in the invasive management group due to protocol-assigned procedures.</p>	<p>This study may inform section 5 around identifying which patients might benefit most from interventional cardiology in addition to medical therapy.</p> <p>Current guideline does not specifically address this other than according to anatomic characteristics.</p>

<p>Al-Lamee R, Thompson D, Dehbi HM, Sen S, et al <b>ORBITA</b> investigators. Percutaneous coronary intervention in stable angina (ORBITA): a double-blind, randomised controlled trial. Lancet. 2018 Jan 6;391(10115):31-40. doi: 10.1016/S0140-6736(17)32714-9. Epub 2017 Nov 2. Erratum in: Lancet. 2018 Jan 6;391(10115):30. <a href="https://pubmed.ncbi.nlm.nih.gov/29103656/">https://pubmed.ncbi.nlm.nih.gov/29103656/</a></p>	<p>Blinded, multicentre randomised trial of PCI versus a placebo procedure for angina relief that was done at five study sites in the UK.</p> <p>There was no significant difference in the primary endpoint of exercise time increment between groups (PCI minus placebo 16.6 s, 95% CI -8.9 to 42.0, p=0.2). ORBITA provides the first placebo-controlled evidence of the efficacy of PCI on angina.</p>	<p><b>This study is referenced in the current guideline. [Info from group Chair 11/10/2021]</b></p> <p>It may inform any revisions which are undertaken to section 5 around identifying which patients might benefit most from interventional cardiology in addition to medical therapy.</p> <p>Current guideline does not specifically address this other than according to anatomic characteristics.</p> <p><b>May prompt reconsideration of PCI recommendation?</b>  “Patients with stable angina who remain symptomatic on optimal medical therapy should be considered for revascularisation by coronary artery bypass grafting or percutaneous coronary intervention.”</p>
<p>McCreanor V, Nowbar A, Rajkumar C, Barnett AG, Francis D, Graves N, Boden WE, Weintraub WS, Al-Lamee R, Parsonage WA. Cost-effectiveness analysis of percutaneous coronary intervention for single-vessel coronary artery disease: an economic evaluation of the <b>ORBITA</b> trial. BMJ Open. 2021 Feb 9;11(2):e044054 <a href="https://pubmed.ncbi.nlm.nih.gov/33563623/">https://pubmed.ncbi.nlm.nih.gov/33563623/</a></p>	<p>A cost-effectiveness analysis comparing PCI with placebo.</p> <p>The ICER for PCI compared with placebo, in patients with single-vessel coronary artery disease and angina on anti-anginal medication, exceeds the threshold of £30,000 used by the National Institute of Health and Care Excellence when undertaking health technology assessment for the NHS context.</p>	<p>This study may inform section 5 around identifying which patients might benefit most from interventional cardiology in addition to medical therapy.</p> <p>Current guideline does not specifically address this other than according to anatomic characteristics.</p> <p><b>May prompt reconsideration of PCI recommendation?</b>  “Patients with stable angina who remain symptomatic on optimal medical therapy</p>

		should be considered for revascularisation by coronary artery bypass grafting or percutaneous coronary intervention.”
<p>Maron DJ, Hochman JS, Reynolds HR, Bangalore S, et al <b>ISCHEMIA</b> Research Group. Initial Invasive or Conservative Strategy for Stable Coronary Disease. N Engl J Med. 2020 Apr 9;382(15):1395-1407.  <a href="https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7263833/">https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7263833/</a></p>	<p>Invasive treatment plus medical therapy does not reduce risk of ischemic cardiovascular events compared to medical therapy alone in patients with stable coronary disease and moderate or severe ischemia</p> <p>Details</p> <ul style="list-style-type: none"> <li>• based on randomized trial</li> <li>• 5,179 adults ≥21 years old (median age 64 years, 77% men) with stable coronary disease and moderate or severe ischemia were randomized to invasive treatment plus medical therapy vs. medical therapy alone</li> <li>• invasive treatment included angiography and subsequent revascularization if appropriate (PCI or coronary-artery bypass grafting [CABG])</li> <li>• medical therapy included pharmacologic interventions (antithrombotic and anti-ischemic medications) and lifestyle interventions (smoking cessation, nutrition, physical activity, weight control, and medication adherence) with angiography if medical therapy failed</li> <li>• 89.6% had history of angina; 35.4% did not have angina in 4 weeks prior to enrollment</li> <li>• 95.6% of invasive treatment plus medical therapy group had angiography, with subsequent revascularization in 79.4% (74% had PCI; 26% had CABG)</li> <li>• primary outcome was composite of cardiovascular death, myocardial infarction,</li> </ul>	<p>This study may inform section 5 around identifying which patients might benefit most from interventional cardiology in addition to medical therapy.</p> <p>Current guideline does not specifically address this other than according to anatomic characteristics.</p>

	<p>or hospitalization for unstable angina, heart failure, or resuscitated cardiac arrest</p> <ul style="list-style-type: none"> <li>• primary outcome was expanded to include hospitalization for unstable angina, heart failure, or resuscitated cardiac arrest following prespecified, protocol-defined procedure to preserve statistical power after slow recruitment</li> <li>• median follow up of 3.2 years</li> <li>• in medical therapy alone group, 25.7% had angiography during follow-up, with subsequent revascularization in 21%</li> <li>• 100% included in analysis</li> <li>• comparing invasive treatment plus medical therapy vs. medical therapy alone (no significant differences) <ul style="list-style-type: none"> <li>○ restricted mean event-free time 4.6 years vs. 4.5 years</li> <li>○ primary outcome rate at 3 years 11.3% vs. 12.7% <ul style="list-style-type: none"> <li>▪ cardiovascular mortality or myocardial infarction 9.7% vs. 11%</li> <li>▪ all-cause mortality 4.3% vs. 4.3%</li> <li>▪ myocardial infarction 7.7% vs. 8.5%</li> </ul> </li> </ul> </li> <li>• medical therapy alone associated with significantly lower primary outcome rates at 6 months and 1 year</li> </ul>	
--	---	--

## Section 4 Pharmacological management

<p>Connolly SJ, Eikelboom JW, Bosch J, et al; <b>COMPASS</b> Investigators. Rivaroxaban with or without aspirin in patients with stable coronary artery disease: an international, randomised, double-blind, placebo-controlled trial. <i>Lancet</i>. 2018 Jan 20;391(10117):205-18</p> <p><a href="https://pubmed.ncbi.nlm.nih.gov/29132879/">https://pubmed.ncbi.nlm.nih.gov/29132879/</a></p>	<p>Patients were randomly assigned (1:1:1) to receive rivaroxaban (2.5 mg orally twice a day) plus aspirin (100 mg once a day), rivaroxaban alone (5 mg orally twice a day), or aspirin alone (100 mg orally once a day).</p> <p>Eligible patients with coronary artery disease had to have had a myocardial infarction in the past 20 years, multi-vessel coronary artery disease, history of stable or unstable angina, previous multi-vessel percutaneous coronary intervention, or previous multi-vessel coronary artery bypass graft surgery.</p> <p>In patients with stable coronary artery disease, addition of rivaroxaban to aspirin lowered major vascular events, but increased major bleeding. There was no significant increase in intracranial bleeding or other critical organ bleeding. There was also a significant net benefit in favour of rivaroxaban plus aspirin and deaths were reduced by 23%.</p>	<p>Query update to section 4.3? Current guideline does not include information on oral anticoagulation <a href="#">SMC advice Feb 2019</a></p> <p>Indication Co-administered with acetylsalicylic acid (ASA) for the prevention of atherothrombotic events in adult patients with coronary artery disease (CAD) or symptomatic peripheral artery disease (PAD) at high risk of ischaemic events</p>
<p>Sorbets E, Steg PG, Young R, Danchin N, Greenlaw N, Ford I, Tendera M, Ferrari R, Merkely B, Parkhomenko A, Reid C, Tardif JC, Fox KM; <b>CLARIFY</b> investigators. <math>\beta</math>-blockers, calcium antagonists, and mortality in stable coronary artery disease: an international cohort study. <i>Eur Heart J</i>. 2019 May 7;40(18):1399-1407.</p>	<p>Beta-blocker use may not reduce 5-year all-cause or cardiovascular mortality in most patients with stable coronary artery disease (CAD) Details</p> <ul style="list-style-type: none"> <li>retrospective cohort study</li> <li>22,006 patients (mean age 63 years, 78% men) with stable CAD from 45 countries had annual follow-up for 5 years starting in 2009-2010</li> <li>78% received beta-blockers; most common were bisoprolol (36%), metoprolol (27%),</li> </ul>	<p>GL Section 4.1.1</p> <p><b>Query – contrasts with this statement:</b> “One observational study suggests a mortality benefit of beta blockers in patients with stable CAD and without a past medical history of MI or heart failure.<sup>56”</sup></p>



	<p>carvedilol (13%), atenolol (12%), and nebivolol (7%)</p> <ul style="list-style-type: none"> <li>• comparing beta-blocker use vs. no beta-blockers at 5 years</li> <li>• overall</li> <li>• all-cause mortality 7.8% vs. 8.4% (not significant)</li> <li>• cardiovascular mortality 5% vs. 5.4% (not significant)</li> <li>• in subgroup of 3,506 patients with myocardial infarction &lt; 1 year prior to enrollment</li> <li>• all-cause mortality 7% vs. 10.3% (p = 0.01)</li> <li>• cardiovascular mortality 4.5% vs. 8.5% (p = 0.0001)</li> <li>• no significant differences in mortality in subgroups with myocardial infarction &gt; 1 year prior to enrollment</li> </ul> <p>Calcium channel blocker use does not appear to reduce 5-year all-cause or cardiovascular mortality in patients with stable coronary artery disease</p> <p>Details</p> <ul style="list-style-type: none"> <li>• based on retrospective cohort study</li> <li>• 22,004 patients (mean age 63 years, 78% men) with stable CAD from 45 countries had annual follow-up for 5 years starting in 2009-2010</li> <li>• 26.7% received calcium channel blockers; most common were long-acting dihydropyridines (79.8%), diltiazem (14.7%), and verapamil (4.9%)</li> <li>• comparing calcium channel blocker use vs. calcium channel blockers at 5 years</li> </ul>	<p>GL Section 4.1.2</p> <p><b>Likely no change to recommendations</b></p> <p>“Beta blockers should be used as first-line therapy for the relief of symptoms of stable angina.”</p> <p>“Rate-limiting calcium channel blockers should be considered where beta blockers are contraindicated.”</p>
--	---	--

	<ul style="list-style-type: none"> <li>• all-cause mortality 8.4% vs. 7.8% (not significant)</li> <li>• cardiovascular mortality 5.3% vs. 5% (not significant)</li> <li>• consistent results in subgroups with history of myocardial infarction stratified by time since infarction</li> </ul>	
<p>Squizzato A, Bellesini M, Takeda A, et al. Clopidogrel plus aspirin versus aspirin alone for preventing cardiovascular events. Cochrane Database Syst Rev. 2017 Dec 14;(12) <a href="https://pubmed.ncbi.nlm.nih.gov/29240976/">https://pubmed.ncbi.nlm.nih.gov/29240976/</a></p>	<p>The available evidence demonstrates that the use of clopidogrel plus aspirin in people at high risk of cardiovascular disease and people with established cardiovascular disease without a coronary stent is associated with a reduction in the risk of myocardial infarction and ischaemic stroke, and an increased risk of major and minor bleeding compared with aspirin alone. According to GRADE criteria, the quality of evidence was moderate for all outcomes except all-cause mortality (low quality evidence) and adverse events (very low quality evidence).</p>	<p>Section 4.3 Possibly more relevant to SIGN 149 Prevention</p> <p><b>Likely no change to recommendation</b> “All patients with stable angina due to atherosclerotic disease should receive long-term standard aspirin and statin therapy.”</p>

### Section 3 Diagnosis and assessment

<p>Scottish Health Technologies Group (2021). HeartFlow FFRCT for estimating fractional flow reserve from coronary CT angiography Glasgow/Edinburgh. NHS Healthcare Improvement Scotland. <a href="https://shtg.scot/our-advice/heartflow-ffrct-for-estimating-fractional-flow-reserve-from-coronary-ct-angiography/">https://shtg.scot/our-advice/heartflow-ffrct-for-estimating-fractional-flow-reserve-from-coronary-ct-angiography/</a></p>	<p>HeartFlow fractional flow reserve computerised tomography (FFRCT) is non-invasive, safe and, by improving specificity, may improve the diagnosis of obstructive versus non-obstructive coronary artery disease (CAD) following computerised tomography-coronary angiography (CT-CA).</p>	<p>New technology - may necessitate update to section 3.2</p>
---	---	---

<p>National Institute for Health and Clinical Excellence. HeartFlow FFRCT for estimating fractional flow reserve from coronary CT angiography.  <a href="https://www.nice.org.uk/guidance/mtg32">https://www.nice.org.uk/guidance/mtg32</a></p>		
<p>Foldyna B, Zeleznik R, Eslami P., Small whole heart volume predicts cardiovascular events in patients with stable chest pain: insights from the <b>PROMISE</b> trial. Eur Radiol. 2021 Aug;31(8):6200-6210.  <a href="https://pubmed.ncbi.nlm.nih.gov/33501599/">https://pubmed.ncbi.nlm.nih.gov/33501599/</a></p>	<p>Compared whole heart volume (WHV) across categories of cardiovascular risk factors and coronary artery disease (CAD) characteristics and determined the association of WHV with MACE (all-cause death, myocardial infarction, unstable angina; median follow-up: 26 months).</p> <p>Small WHV may represent a novel imaging marker of MACE in stable chest pain. In particular, WHV may improve risk stratification in patients with non-obstructive CAD, a cohort with an unmet need for better risk stratification.</p>	<p>New prognostic measure - may necessitate update to section 3.2 if further evidence identified</p>
<p><b>SCOT-HEART</b> Investigators., Newby DE, Adamson PD, et al. Coronary CT angiography and 5- year risk of myocardial infarction. N Engl J Med. 2018 Sep 6;379(10):924-33.  <a href="https://pubmed.ncbi.nlm.nih.gov/30145934/">https://pubmed.ncbi.nlm.nih.gov/30145934/</a></p>	<p>Randomly assigned 4,146 patients with stable chest pain who had been referred to a cardiology clinic for evaluation to standard care plus CTA (2,073 patients) or to standard care alone (2,073 patients). Investigations, treatments, and clinical outcomes were assessed over 3 to 7 years of follow up. The primary end point was death from coronary heart disease or non-fatal myocardial infarction at 5 years.</p> <p>The use of CTA in addition to standard care in patients with stable chest pain resulted in a significantly lower rate of death from coronary heart disease or non-fatal myocardial infarction at 5 years than standard care alone, without resulting</p>	<p>Section 3.2.6  “Computerised tomography-coronary angiography should be considered for the investigation of patients with chest pain in whom the diagnosis of stable angina is suspected but not clear from history alone.”</p> <p>Earlier trial by this group already cited in this section. New trial strengthens this recommendation</p>

	in a significantly higher rate of coronary angiography or coronary revascularisation.	
Curzen N, Nicholas Z, Stuart B, Wilding S, Fractional flow reserve derived from computed tomography coronary angiography in the assessment and management of stable chest pain: the FORECAST randomized trial. Eur Heart J. 2021 Oct 1;42(37):3844-3852. <a href="https://pubmed.ncbi.nlm.nih.gov/34269376/">https://pubmed.ncbi.nlm.nih.gov/34269376/</a>	<p>1,400 patients with stable chest pain in 11 centres were randomized to initial testing with CTCA with selective FFRCT (experimental group) or standard clinical care pathways (standard group). The primary endpoint was total cardiac costs at 9 months. Secondary endpoints were angina status, quality of life, major adverse cardiac and cerebrovascular events, and use of invasive coronary angiography.</p> <p>A strategy of CTCA with selective FFRCT in patients with stable angina did not differ significantly from standard clinical care pathways in cost or clinical outcomes, but did reduce the use of invasive coronary angiography.</p>	<p>Section 3.2.6</p> <p>Query strengthen recommendation?</p> <p>“Computerised tomography-coronary angiography should be considered for the investigation of patients with chest pain in whom the diagnosis of stable angina is suspected but not clear from history alone.”</p> <p>also</p> <p><b>May address research recommendation</b> ‘What are the implications and cost effectiveness of CT-CA in investigation of patients with stable angina?’</p>
Hoffmann U, Ferencik M, Udelson JE, et al; PROMISE Investigators. Prognostic value of noninvasive cardiovascular testing in patients with stable chest pain: insights from the PROMISE trial (Prospective Multicenter Imaging Study for Evaluation of Chest Pain). Circulation. 2017 Jun 13;135(24):2320-32 <a href="https://pubmed.ncbi.nlm.nih.gov/28389572/">https://pubmed.ncbi.nlm.nih.gov/28389572/</a>	<p>In the PROMISE trial (Prospective Multicenter Imaging Study for Evaluation of Chest Pain), patients with stable chest pain and intermediate pretest probability for obstructive coronary artery disease (CAD) were randomly assigned to functional testing (exercise electrocardiography, nuclear stress, or stress echocardiography) or coronary computed tomography angiography (CTA).</p> <p>The discriminatory ability of CTA in predicting events was significantly better than functional testing (c-index, 0.72; 95% CI, 0.68-0.76 versus 0.64; 95% CI, 0.59-0.69; P=0.04).</p>	<p>Section 3.2.6</p> <p>“Computerised tomography-coronary angiography should be considered for the investigation of patients with chest pain in whom the diagnosis of stable angina is suspected but not clear from history alone.”</p> <p>Query - strengthen recommendation?</p>

<p>Budoff MJ, Mayrhofer T, Ferencik M, et al; PROMISE Investigators. Prognostic value of coronary artery calcium in the <b>PROMISE</b> study (Prospective Multicenter Imaging Study for Evaluation of Chest Pain). <i>Circulation</i>. 2017 Nov 21;136(21):1993-2005.</p> <p>Douglas PS, Hoffmann U, Patel MR, et al; PROMISE Investigators. Outcomes of anatomical versus functional testing for coronary artery disease. <i>N Engl J Med</i>. 2015 Apr 2;372(14):1291-300. <a href="https://pubmed.ncbi.nlm.nih.gov/25773919/">https://pubmed.ncbi.nlm.nih.gov/25773919/</a></p>		
<p>Hamon M, Geindreau D, Guittet L, Bauters C, Hamon M. Additional diagnostic value of new CT imaging techniques for the functional assessment of coronary artery disease: a meta-analysis. <i>Eur Radiol</i>. 2019 Jun;29(6):3044-3061. doi: 10.1007/s00330-018-5919-8. Epub 2019 Jan 7 <a href="https://pubmed.ncbi.nlm.nih.gov/30617482/">https://pubmed.ncbi.nlm.nih.gov/30617482/</a></p>	<p>Systematic review - 50 diagnostic studies New functional CT imaging techniques, such as stress CTP and FFRCT, improve diagnostic accuracy of coronary CTA to predict hemodynamically relevant stenosis. • TAG yields poor diagnostic performance. • Combination of CTA and some functional CT techniques (stress CTP and FFRCT) might become a "must" to improve diagnostic accuracy of CAD and to reduce unnecessary invasive coronary angiography.</p>	<p>Section 3.2.6 “Computerised tomography-coronary angiography should be considered for the investigation of patients with chest pain in whom the diagnosis of stable angina is suspected but not clear from history alone.”</p> <p>Query - strengthen recommendation?</p>
<p>Pontone G, Baggiano A, Andreini D, et al. Stress computed tomography perfusion versus fractional flow reserve CT derived in suspected coronary</p>	<p>This study sought to compare the diagnostic accuracy of coronary computed tomography angiography (cCTA) with that of cCTA+fractional flow reserve derived from cCTA datasets (FFRCT) and that of cCTA+static stress-computed</p>	<p>Section 3.2.6 See also <a href="#">SHTG assessment of HeartFlow</a></p>

<p>artery disease: the <b>PERFECTION</b> study. JACC Cardiovasc Imaging. 2019 Aug;12(8 pt 1):1487-97.</p>	<p>tomography perfusion (stress-CTP) in detecting functionally significant coronary artery lesions using invasive coronary angiography (ICA) plus invasive FFR as the reference standard.</p> <p>Both FFRCT and stress-CTP significantly improved specificity and positive predictive values compared to those of cCTA alone. The area under the curve to detect flow-limiting stenoses of cCTA, cCTA+FFRCT, and cCTA+CTP were 0.89, 0.93, 0.92, and 0.90, 0.94, and 0.93 in a vessel-based and patient-based model, respectively, with significant additional values for both cCTA+FFRCT and cCTA+CTP versus cCTA alone (p &lt; 0.001) but no differences between cCTA+FFRCT versus cCTA+CTP</p>	
---	---	--

**Recommendations for research – note any evidence that addresses evidence gaps highlighted in the original guideline under the Recommendations for research section**

<p><b>Reference</b></p> <ul style="list-style-type: none"> <li>• <i>Include type of evidence, reference and source of evidence</i></li> <li>• <i>Where possible, include hyperlinks to the references</i></li> </ul>	<p><b>Details</b></p> <p><i>Include abstract or summary of evidence</i></p>	<p><b>What area for further research does this address?</b></p> <ul style="list-style-type: none"> <li>• <i>A list of these are given in the Recommendations for research section</i></li> </ul>
<p>Blessberger H, Lewis SR, Pritchard MW, Fawcett LJ, Domanovits H, Schlager O, Wildner B, Kammler J, Steinwender C. Perioperative beta-blockers for preventing surgery-related mortality and morbidity in adults undergoing non-cardiac surgery. Cochrane Database Syst Rev. 2019 Sep 26;9(9): <a href="https://pubmed.ncbi.nlm.nih.gov/31556094/">https://pubmed.ncbi.nlm.nih.gov/31556094/</a></p>	<p>The evidence for early all-cause mortality with perioperative beta-blockers was uncertain. We found no evidence of a difference in cerebrovascular events or ventricular arrhythmias, and the certainty of the evidence for these outcomes was low and very low. We found low-certainty evidence that beta-blockers may reduce atrial fibrillation and myocardial infarctions.</p>	<p><i>How effective are beta blockers in the management of patients with stable angina undergoing non-cardiac surgery?</i></p> <p>Updated Cochrane Review – evidence certainty remains low – <b>likely no change to recommendations in section 6.3.1</b></p>

	<p>However, beta-blockers may increase bradycardia (low-certainty evidence) and probably increase hypotension (moderate-certainty evidence). Further evidence from large placebo-controlled trials is likely to increase the certainty of these findings, and we recommend the assessment of impact on quality of life. We found 18 studies awaiting classification; inclusion of these studies in future updates may also increase the certainty of the evidence.</p>	<p>“Routine initiation of perioperative beta-blocker therapy to reduce perioperative myocardial infarction in patients undergoing non-cardiac surgery is not recommended.”</p> <p>“Acute withdrawal of beta blockers in the postoperative period is not recommended.”</p>
<p>Berwanger, O. et al. Atorvastatin for high-risk statin-naïve patients undergoing noncardiac surgery: the Lowering the Risk of Operative Complications Using Atorvastatin Loading Dose (LOAD) randomized trial. <i>Am. Heart J.</i> 184, 88–96 (2017).  <a href="https://pubmed.ncbi.nlm.nih.gov/27892891/">https://pubmed.ncbi.nlm.nih.gov/27892891/</a></p> <p>Putzu A, de Carvalho CM, de Almeida JP, Belletti A, Cassina T, Landoni G, Hajjar LA. Perioperative statin therapy in cardiac and non-cardiac surgery: a systematic review and meta-analysis of randomized controlled trials. <i>Annals of intensive care.</i> 2018 Dec;8(1):1-4.  <a href="https://link.springer.com/article/10.1007/s11239-021-02539-8">https://link.springer.com/article/10.1007/s11239-021-02539-8</a></p>		<p><i>How effective is statin reload in patients with stable angina undergoing non-cardiac surgery?</i></p> <p>There may now be additional evidence. Depending on the applicability of the patient group.</p>

<p>Kim C, Kim JS, Kim H, et al. Consensus Decision-Making for the Management of Antiplatelet Therapy before Non-Cardiac Surgery in Patients Who Underwent Percutaneous Coronary Intervention With Second-Generation Drug-Eluting Stents: A Cohort Study. J Am Heart Assoc. 2021;10(8)  <a href="https://pubmed.ncbi.nlm.nih.gov/33843258/">https://pubmed.ncbi.nlm.nih.gov/33843258/</a></p>	<p>Consensus study</p> <p>Most patients were treated in agreement with a consensus decision about preoperative antiplatelet therapy (APT) based on a referral system among physicians, surgeons, and anesthesiologists. The risk of perioperative adverse events increased if complying with a consensus decision was failed.</p> <p>Arbitrary APT was more frequent when surgery was considered riskier or urgent. Arbitrary APT doubled the risk of a 30-day perioperative NACE. Arbitrary APT was also associated with MACE as well as major bleeding. Arbitrary APT has a consistently deleterious effect on NACE irrespective of the surgical risk, physician's recommendation, and practice of the discontinuation of APT.</p>	<p><i>How effective are antiplatelets in the management of patients with stable angina undergoing non-cardiac surgery and what is the optimum antiplatelet regimen in different patient groups?</i></p> <p>Observational study - may inform intervention in specific patient group.</p>
<p>Kim C, Kim JS, Kim H, Ahn SG, Cho S, Lee OH, Park JK, Shin S, Moon JY, Won H, Suh Y. Patterns of antiplatelet therapy during non-cardiac surgery in patients with second-generation drug-eluting stents. Journal of the American Heart Association. 2020 Jun 2;9(11):e016218.</p>	<p>Among patients undergoing non-cardiac surgery after second-generation drug-eluting stent implantation, preoperative discontinuation of antiplatelet therapy was common and safe in terms of both ischemic and hemorrhagic risk.</p> <p>Discontinuing APT may be associated with lower risk of major bleeding in the certain types of surgery (eg, intra-abdominal)</p>	



<p>Cao D, et al. "Perioperative risk and antiplatelet management in patients undergoing non-cardiac surgery within 1 year of PCI." Journal of Thrombosis &amp; Thrombolysis (2021)  <a href="https://pubmed.ncbi.nlm.nih.gov/33843258/">https://pubmed.ncbi.nlm.nih.gov/33843258/</a></p>	<p>compared with continuing antiplatelet therapy in patients with second-generation drug-eluting stents.</p> <p>Our study supports the notion that discontinuing antiplatelet therapy may be considered an acceptable option for patients undergoing coronary revascularization with second-generation drug-eluting stents before noncardiac surgery unless unduly prolonged (<math>\geq 9</math> days).</p> <p>Observational study  One third of all non-cardiac surgeries occurring within 1 year of PCI were vascular procedures and nearly half were classified as intermediate-to-high risk.</p> <p>High-risk and urgent/emergent procedures tend to occur earlier rather than later in the year post-PCI.</p> <p>Preoperative interruption of antiplatelet therapy was observed in nearly half of the cases and was not associated with an increased risk of major adverse cardiac events.</p> <p>The risk of perioperative ischemic and bleeding events was primarily related to the estimated surgical risk and the urgency of the procedure.</p>	
---	---	--

<p>Howell SJ, et al. "Prospective observational cohort study of the association between antiplatelet therapy, bleeding and thrombosis in patients with coronary stents undergoing noncardiac surgery." <i>British Journal of Anaesthesia</i> 122.2 (2019): 170-179  <a href="https://pubmed.ncbi.nlm.nih.gov/30686302/">https://pubmed.ncbi.nlm.nih.gov/30686302/</a></p> <p>Maznyczka AM, Hobson A, Curzen N, Haworth PA. Should We Interrupt Oral Anticoagulation Before Percutaneous Coronary Intervention? A National Survey of UK Interventional Cardiologists. <i>Heart, Lung &amp; Circulation</i>. 2021 Aug 25.  <a href="https://europepmc.org/article/med/34454839">https://europepmc.org/article/med/34454839</a></p>	<p>Prospective multicentre cohort study OBTAIN showed an increased risk of bleeding with DAPT and found no evidence for protective effects of DAPT from perioperative MACE in patients who have undergone previous PCI.</p> <p>Survey  Abstract not available</p>	
<p>Suzanne H Richards, Lindsey Anderson, Caroline E Jenkinson, Ben Whalley, Karen Rees, Philippa Davies, et al. Psychological interventions for coronary heart disease: Cochrane systematic review and meta-analysis, <i>European Journal of Preventive Cardiology</i>, Volume 25, Issue 3, 1 February 2018, Pages 247–259,  <a href="https://academic.oup.com/eurjpc/article/25/3/247/5926174?login=true">https://academic.oup.com/eurjpc/article/25/3/247/5926174?login=true</a></p>	<p>Thirty-five studies with 10,703 participants (median follow up 12 months) were included. Psychological interventions led to a reduction in cardiovascular mortality (relative risk 0.79, 95% confidence interval [CI] 0.63 to 0.98), although no effects were observed for total mortality, myocardial infarction or revascularisation. Psychological interventions improved depressive symptoms (standardised mean difference [SMD] –0.27, 95% CI –0.39 to –0.15), anxiety (SMD –0.24, 95% CI –0.38 to –0.09) and stress (SMD –0.56, 95% CI –0.88 to –0.24) compared with controls.</p>	<p><i>Do psychological interventions reduce levels of distress, cardiac events or cardiac mortality in patients with stable angina in the long term? Which patient groups benefit most from such interventions (age, sex, ethnicity, deprivation, education, comorbidities)?</i></p> <p>May inform this question, although follow-up period (12 months) may not represent long term outcome.</p>

<p>Tully PJ, Ang SY, Lee EJJ, Bendig E, Bauereiß N, Bengel J, Baumeister H. Psychological and pharmacological interventions for depression in patients with coronary artery disease. <i>Cochrane Database of Systematic Reviews</i> 2021, Issue 12. Art. No.: CD008012. DOI: 10.1002/14651858.CD008012.pub4. Accessed 24 February 2022.</p>	<p>Systematic review and meta-analysis of 37 RCTs. Psychological interventions may result in a reduction in end-of-treatment depression symptoms compared to controls (standardised mean difference (SMD) <math>-0.55</math>, 95% CI <math>-0.92</math> to <math>-0.19</math>; low certainty evidence; 10 trials; <math>n=1226</math>). No effect was evident on medium-term depression symptoms one to six months after the end of treatment (SMD <math>-0.20</math>, 95% CI <math>-0.42</math> to <math>0.01</math>; 7 trials; <math>n=2654</math>). The evidence for long-term depression symptoms and depression response was sparse for this comparison. There is low certainty evidence that psychological interventions may result in little to no difference in end-of-treatment depression remission (odds ratio (OR) <math>2.02</math>, 95% CI <math>0.78</math> to <math>5.19</math>; low certainty evidence; 3 trials; <math>n=862</math>). Pharmacological intervention may have a large effect on end-of-treatment depression symptoms (SMD <math>-0.83</math>, 95% CI <math>-1.33</math> to <math>-0.32</math>; low certainty evidence; 8 trials; <math>n=750</math>). Pharmacological interventions probably result in a moderate to large increase in depression remission (OR <math>2.06</math>, 95% CI <math>1.47</math> to <math>2.89</math>; moderate certainty evidence; 4 trials; <math>n=646</math>).</p>	
<p>Wells A, Reeves D, Capobianco L, Heal C, Davies L, Heagerty A, et al. Improving the Effectiveness of Psychological Interventions for Depression and Anxiety in Cardiac</p>	<p>Anxiety and depression can be effectively managed using group metacognitive</p>	<p><i>What aspects of psychological therapy (for example cognitive, behavioural and relaxation components) are effective in relieving symptoms in patients with stable angina and what is the optimal duration of treatment?</i></p>

<p>Rehabilitation: PATHWAY—A Single-Blind, Parallel, Randomized, Controlled Trial of Group Metacognitive Therapy. <i>Circulation</i>. 2021 Jul 6;144(1):23-33.</p> <p><a href="https://www.ahajournals.org/doi/full/10.1161/CIRCULATIONAHA.120.052428">https://www.ahajournals.org/doi/full/10.1161/CIRCULATIONAHA.120.052428</a></p> <p>Farquhar JM, Stonerock GL, Blumenthal JA. Treatment of anxiety in patients with coronary heart disease: A systematic review. <i>Psychosomatics</i>. 2018 Jul 1;59(4):318-32.</p> <p><a href="https://pubmed.ncbi.nlm.nih.gov/29735242/">https://pubmed.ncbi.nlm.nih.gov/29735242/</a></p>	<p>therapy in patients with cardiovascular disease.</p> <p>The addition of group metacognitive therapy to cardiac rehabilitation is well-tolerated and does not impact negatively on clinic attendance.</p> <p>Metacognitive therapy is deliverable by non-mental health specialists and could improve psychological outcomes for patients with cardiovascular disease.</p>	<p><i>Is interpersonal therapy delivered by therapists with formal training in this therapy more effective than clinical management in relieving symptoms in patients with stable angina?</i></p> <p><i>Which types of relaxation therapy provide most benefit to patients with stable angina and can shorter courses (&lt;9 hours) be designed that deliver equivalent psychological and physical benefits as longer courses?</i></p> <p><i>Which aspects of stress-management interventions are effective at improving outcomes in patients with stable angina?</i></p> <p>Unlikely that these papers answer the very specific points set out in the questions around active components, duration and intensity.</p>
<p>Subedi N, et al. "Implementation of Telerehabilitation Interventions for the Self-Management of Cardiovascular Disease: Systematic Review." <i>JMIR MHealth and UHealth</i> 8.11 (2020): e17957.</p> <p><a href="https://pubmed.ncbi.nlm.nih.gov/33245286/">https://pubmed.ncbi.nlm.nih.gov/33245286/</a></p> <p>Coorey GM, Neubeck L, Mulley J, Redfern J. Effectiveness, acceptability and usefulness of mobile applications for cardiovascular disease self-management: Systematic review with meta-synthesis of</p>	<p>Experimental trials suggest that participants perceive cardiac telerehabilitation to be an acceptable and appropriate approach to improve the reach and utilisation of CR, but pragmatic implementation studies are needed to understand how interventions can be sustainably translated from research into clinical practice</p> <p>Multiple behaviours and cardiovascular disease risk factors appear modifiable in the shorter term with use of mobile apps. Evidence for effectiveness requires larger,</p>	<p><i>What self-management interventions are effective at improving outcomes in patients with stable angina?</i></p> <p>There appear to be many reviews looking at this question for chronic disease broadly or T2D/Heart Failure. Stable angina less so.</p>

<p>quantitative and qualitative data. Eur J Prev Cardiol. 2018 Mar;25(5):505-521. doi: 10.1177/2047487317750913. Epub 2018 Jan 9. PMID: 29313363.  <a href="https://pubmed.ncbi.nlm.nih.gov/29313363/">https://pubmed.ncbi.nlm.nih.gov/29313363/</a></p> <p>Osokpo O and Riegel B. "Cultural factors influencing self-care by persons with cardiovascular disease: An integrative review." International Journal of Nursing Studies 116.(2021): 103383.  <a href="https://pubmed.ncbi.nlm.nih.gov/31353026/">https://pubmed.ncbi.nlm.nih.gov/31353026/</a></p>	<p>controlled studies of longer duration, with emphasis on process evaluation data to better understand important system- and patient-level characteristics.</p>	
<p>Palmer MJ, Machiyama K, Woodd S, Gubijev A, Barnard S, Russell S, Perel P, Free C. Mobile phone-based interventions for improving adherence to medication prescribed for the primary prevention of cardiovascular disease in adults. Cochrane Database of Systematic Reviews 2021, Issue 3. Art. No.: CD012675. DOI: 10.1002/14651858.CD012675.pub3. Accessed 24 February 2022.</p>	<p>Systematic review and meta-analysis, 14 RCT (n=25,633). Participants were recruited from community-based primary and tertiary care or outpatient clinics. The interventions varied widely from those delivered solely through short messaging service (SMS) to those involving a combination of modes of delivery, such as SMS in addition to healthcare worker training, face-to-face counselling, electronic pillboxes, written materials, and home blood pressure monitors. Some interventions only targeted medication adherence, while others additionally targeted lifestyle changes such as diet and exercise.</p> <p>There is low-certainty evidence on the effects of mobile phone-delivered interventions to increase adherence to medication prescribed for the primary prevention of CVD. Trials of BP self-</p>	<p><i>What strategies are effective, in primary and secondary care, at improving medication adherence in patients with stable angina?</i></p> <p>Some evidence of benefit of mobile phone interventions - Further trials of these interventions are warranted.</p>

<p>Maddison R, Jiang Y, Stewart R, Scott T, Kerr A, Whittaker R, Benatar J, Rolleston A, Estabrooks P, Dale L. An Intervention to Improve Medication Adherence in People With Heart Disease (Text4HeartII): Randomized Controlled Trial. JMIR mHealth and uHealth. 2021 Jun 9;9(6):e24952.</p> <p>Thompson D, et al. "Achieving optimal adherence to medical therapy by telehealth: Findings from the ORBITA medication adherence sub-study." Pharmacology Research &amp; Perspectives 9.1 (2021): e00710. <a href="https://pubmed.ncbi.nlm.nih.gov/33570248/">https://pubmed.ncbi.nlm.nih.gov/33570248/</a></p> <p>Divchev D, Stockl G and study investigators. "Effectiveness and Impact on Adherence of a New Fixed-Dose Combination of Ivabradine and Metoprolol in a Wide Range of Stable Angina Patients in Real-Life Practice." Cardiology &amp; Therapy 8.2 (2019): 317-328. <a href="https://pubmed.ncbi.nlm.nih.gov/31410662/">https://pubmed.ncbi.nlm.nih.gov/31410662/</a></p> <p>Kvarnström K, Westerholm A, Airaksinen M, Liira H. Factors Contributing to Medication</p>	<p>monitoring with mobile-phone telemedicine support reported modest benefits. One trial at low risk of bias reported modest reductions in LDL cholesterol but no benefits for BP. There is moderate-certainty evidence that these interventions do not result in harm.</p>	<p>2014 Cochrane review cited in current guideline has not been updated. <a href="https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD000011.pub4/full">https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD000011.pub4/full</a></p> <p>It may be a literature search could identify relevant new evidence around telemed interventions and medication formulations – as well as qualitative aspects as to reasons for non-optimal medication use.</p> <p><b>Potential to develop of a recommendation outlining principles/strategies perhaps?</b></p>
---	---	--

<p>Adherence in Patients with a Chronic Condition: A Scoping Review of Qualitative Research. <i>Pharmaceutics</i>. 2021 Jul;13(7):1100.</p> <p>Pouls BP, Vriezekolk JE, Bekker CL, Linn AJ, van Onzenoort HA, Vervloet M, van Dulmen S, van den Bemt BJ. Effect of interactive eHealth interventions on improving medication adherence in adults with long-term medication: systematic review. <i>Journal of Medical Internet Research</i>. 2021;23(1):e18901.</p> <p>Nardi WR, Loucks EB, Springs S, Operario D, Kronish IM, Gaudiano BA, Sun S. Mindfulness-based interventions for medication adherence: A systematic review and narrative synthesis. <i>Journal of Psychosomatic Research</i>. 2021 Jul 26:110585.</p>		
<p>Ohanyan A, et al. "Investigating patients' views on screening for depression in cardiac practice: A qualitative interview study." <i>Journal of Psychosomatic Research</i> 144.(2021): 110419.  <a href="https://pubmed.ncbi.nlm.nih.gov/33765518/">https://pubmed.ncbi.nlm.nih.gov/33765518/</a></p> <p>Löwe, B., Blankenberg, S., Wegscheider, K., König, H., Walter, D., Murray, A., . . . Kohlmann, S. (2017). Depression screening with patient-targeted feedback in cardiology:</p>	<p>We found that depression screening is endorsed by patients with CHD in this study sample. Standardized routine screening procedures could serve as a useful tool to combat stigmatization, and encourage patients to display symptoms of depression towards cardiologists.</p> <p>Patient-targeted feedback in addition to screening has a significant but small effect on depression severity after 6 months and may encourage patients to take an active</p>	<p><i>What is the benefit (if any) of screening for depression/mood disorders in patients with stable angina versus those who are not screened?</i></p> <p>DEPSCREEN-INFO RCT may be informative but this is not specific to stable angina.</p>

<p>DEPSCREEN-INFO randomised clinical trial. British Journal of Psychiatry, 210(2), 132-139. doi:10.1192/bjp.bp.116.184168</p> <p>Lehmann M, et al. "Suicidal ideation in patients with coronary heart disease and hypertension: Baseline results from the DEPSCREEN-INFO clinical trial." Clinical Psychology &amp; Psychotherapy 25.6 (2018): 754-764. Ovid MEDLINE(R). Web. 08 <a href="https://pubmed.ncbi.nlm.nih.gov/27908896/">https://pubmed.ncbi.nlm.nih.gov/27908896/</a></p> <p>Lowe B, et al. "Depression screening with patient-targeted feedback in cardiology: DEPSCREEN-INFO randomised clinical trial." British Journal of Psychiatry 210.2 (2017): 132-139 <a href="https://pubmed.ncbi.nlm.nih.gov/28806775/">https://pubmed.ncbi.nlm.nih.gov/28806775/</a></p>	<p>role in the self-management of depression.</p> <p>A patient-targeted feedback in addition to depression screening in cardiology is cost-effective with a high probability. This underpins the use of the patient-targeted feedbacks and the PHQ-9 that are both freely available and easy to implement in routine care.</p>	
--	--	--

**Potentially important new evidence** – note any new important evidence in the field that may be relevant for the update but that hasn't been mentioned in the original guideline

<b>Reference</b> <ul style="list-style-type: none"> <li>• Include type of evidence, reference and source of evidence</li> <li>• Where possible, include hyperlinks to the references</li> </ul>	<b>Details</b> <i>Include abstract or summary of evidence</i>	<b>Why might this be important to include in the guideline?</b>
See evidence identified for Section 3		New functional CT imaging techniques, such as stress CTP and FFRCT, may improve diagnostic accuracy of coronary CTA.



**Consultation feedback** (to be completed by PM)

Former members of the SIGN 151 guideline development group were invited to comment on the report and the proposed areas for update.

Reviewer	Comments
Prof Nawwar Al-Attar, Consultant Cardiac and Transplant Surgeon, Golden Jubilee National Hospital, Clydebank	Notification of: <ul style="list-style-type: none"><li data-bbox="723 400 936 427">• FAME-3 trial</li><li data-bbox="723 435 2000 462">• American College of Cardiology guideline for the evaluation and diagnosis of chest pain (2021)</li><li data-bbox="723 470 1839 497">• European Society of Cardiology guideline on myocardial revascularisation (2019)</li></ul>

## Concluding remarks

The literature search has identified new evidence which informs on revascularisation outcomes and, where appropriate, the appropriate revascularisation choices for people with stable coronary artery disease. While SIGN 151 recommends either PCI or bypass surgery for most patients requiring revascularisation, newer evidence adds further stratification to circumstances where advantage may or may not accrue for specific approaches. There is also new evidence suggesting invasive treatment may not reduce cardiovascular risk compared with medical therapy for stable coronary disease, which could support the development of clearer guidance on which patients might benefit most from interventional cardiology.

New evidence on pharmacological therapy is likely to have little impact on SIGN 151's recommendations. Most do not change the current recommendations, relate to secondary prevention in people with stable CVD and could be addressed in the review of SIGN 149.

Several studies suggest new functional CT imaging techniques (eg stress CTP and fractional flow reserve computerised tomography) may increase diagnostic accuracy compared with standard CTCA. The FORECAST trial showed no difference in cost or clinical outcomes associated with FFRCT but reduced use of invasive coronary angiography. Consideration of this evidence may allow a careful balancing of benefits and harms to arrive at recommendations on these newer technologies for NHSScotland. SHTG and NICE have published on FFRCT and they help to address the research recommendation from SIGN 151 -'What are the implications and cost effectiveness of CT-CA in investigation of patients with stable angina?'

The recommendation is: some recommendations will change in the light of the new evidence and selected elements of the guideline should be reviewed

## Decision

On 19 May 2022 the Work Programme Committee recommended:

This guideline is in need of review and has been accepted onto the SIGN guideline programme.
--

## Annex 1

### Evidence sources

Resource	Results
<a href="#">Dynamed</a>	<p>Maron DJ, Hochman JS, Reynolds HR, Bangalore S, et al <b>ISCHEMIA</b> Research Group. Initial Invasive or Conservative Strategy for Stable Coronary Disease. N Engl J Med. 2020 Apr 9;382(15):1395-1407. <a href="https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7263833/">https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7263833/</a></p> <p>Sorbets E, Steg PG, Young R, Danchin N, Greenlaw N, Ford I, Tendera M, Ferrari R, Merkely B, Parkhomenko A, Reid C, Tardif JC, Fox KM; CLARIFY investigators. <math>\beta</math>-blockers, calcium antagonists, and mortality in stable coronary artery disease: an international cohort study. Eur Heart J. 2019 May 7;40(18):1399-1407. <a href="https://pubmed.ncbi.nlm.nih.gov/30590529/">https://pubmed.ncbi.nlm.nih.gov/30590529/</a></p> <p>Fearon WF, Nishi T, De Bruyne B, Boothroyd DB,; FAME 2 Trial Investigators. Clinical Outcomes and Cost-Effectiveness of Fractional Flow Reserve-Guided Percutaneous Coronary Intervention in Patients With Stable Coronary Artery Disease: Three-Year Follow-Up of the FAME 2 Trial (Fractional Flow Reserve Versus Angiography for Multivessel Evaluation). Circulation. 2018 Jan 30;137(5):480-487. <a href="https://pubmed.ncbi.nlm.nih.gov/29097450/">https://pubmed.ncbi.nlm.nih.gov/29097450/</a></p> <p>Xaplanteris P, Fournier S, Pijls NHJ, Fearon WF,; FAME 2 Investigators. Five-Year Outcomes with PCI Guided by Fractional Flow Reserve. N Engl J Med. 2018 Jul 19;379(3):250-259. <a href="https://pubmed.ncbi.nlm.nih.gov/29785878/">https://pubmed.ncbi.nlm.nih.gov/29785878/</a></p> <p>Ferrari R, Ford I, Fox K, Challeton JP, Correges A, Tendera M, Widimský P, Danchin N; <b>ATPCI</b> investigators. Efficacy and safety of trimetazidine after percutaneous coronary intervention (ATPCI): a randomised, double-blind, placebo-controlled trial. Lancet. 2020 Sep 19;396(10254):830-838. doi: 10.1016/S0140-6736(20)31790-6. Epub 2020 Aug 30. <a href="https://pubmed.ncbi.nlm.nih.gov/32877651/">https://pubmed.ncbi.nlm.nih.gov/32877651/</a></p>

BMJ Best Practice

SCOT-HEART Investigators., Newby DE, Adamson PD, et al. Coronary CT angiography and 5- year risk of myocardial infarction. N Engl J Med. 2018 Sep 6;379(10):924-33.

<https://pubmed.ncbi.nlm.nih.gov/30145934/>

Al-Lamee R, Thompson D, Dehbi HM, Sen S, et al ORBITA investigators. Percutaneous coronary intervention in stable angina (ORBITA): a double-blind, randomised controlled trial. Lancet. 2018 Jan 6;391(10115):31-40. doi: 10.1016/S0140-6736(17)32714-9. Epub 2017 Nov 2. Erratum in: Lancet. 2018 Jan 6;391(10115):30.

<https://pubmed.ncbi.nlm.nih.gov/29103656/>

Connolly SJ, Eikelboom JW, Bosch J, et al; COMPASS Investigators. Rivaroxaban with or without aspirin in patients with stable coronary artery disease: an international, randomised, double-blind, placebo-controlled trial. Lancet. 2018 Jan 20;391(10117):205-18

<https://pubmed.ncbi.nlm.nih.gov/29132879/>

Hamon M, Geindreau D, Guittet L, Bauters C, Hamon M. Additional diagnostic value of new CT imaging techniques for the functional assessment of coronary artery disease: a meta-analysis. Eur Radiol. 2019 Jun;29(6):3044-3061. doi: 10.1007/s00330-018-5919-8. Epub 2019 Jan 7 <https://pubmed.ncbi.nlm.nih.gov/30617482/>

Celeng C, Leiner T, Maurovich-Horvat P, et al. Anatomical and functional computed tomography for diagnosing hemodynamically significant coronary artery disease: a meta-analysis. JACC Cardiovasc Imaging. 2019 Jul;12(7 pt 2):1316-25.

<https://pubmed.ncbi.nlm.nih.gov/30219398/>

Pontone G, Baggiano A, Andreini D, et al. Stress computed tomography perfusion versus fractional flow reserve CT derived in suspected coronary artery disease: the PERFECTION study. JACC Cardiovasc Imaging. 2019 Aug;12(8 pt 1):1487-97

<https://pubmed.ncbi.nlm.nih.gov/30343073/>

Hoffmann U, Ferencik M, Udelson JE, et al; PROMISE Investigators. Prognostic value of noninvasive cardiovascular testing in patients with stable chest pain: insights from the PROMISE trial (Prospective Multicenter Imaging Study for Evaluation of Chest Pain). Circulation. 2017 Jun 13;135(24):2320-32

<https://pubmed.ncbi.nlm.nih.gov/28389572/>

Budoff MJ, Mayrhofer T, Ferencik M, et al; PROMISE Investigators. Prognostic value of coronary artery calcium in the PROMISE study (Prospective Multicenter Imaging Study for Evaluation of Chest Pain). *Circulation*. 2017 Nov 21;136(21):1993-2005.

<https://pubmed.ncbi.nlm.nih.gov/28847895/>

Squizzato A, Bellesini M, Takeda A, et al. Clopidogrel plus aspirin versus aspirin alone for preventing cardiovascular events. *Cochrane Database Syst Rev*. 2017 Dec 14;(12)

<https://pubmed.ncbi.nlm.nih.gov/29240976/>

Anderson L, Brown JP, Clark AM, et al. Patient education in the management of coronary heart disease. *Cochrane Database Syst Rev*. 2017 Jun 28;(6)

<https://pubmed.ncbi.nlm.nih.gov/28658719/>

Wright JT Jr, Williamson JD, Whelton PK, et al; SPRINT Research Group. A randomized trial of intensive versus standard blood-pressure control. *N Engl J Med*. 2015 Nov 26;373(22):2103-16.

<https://pubmed.ncbi.nlm.nih.gov/26551272/>

Douglas PS, Hoffmann U, Patel MR, et al; PROMISE Investigators. Outcomes of anatomical versus functional testing for coronary artery disease. *N Engl J Med*. 2015 Apr 2;372(14):1291-300.

<https://pubmed.ncbi.nlm.nih.gov/25773919/>

McKavanagh P, Lusk L, Ball PA, et al. A comparison of cardiac computerized tomography and exercise stress electrocardiogram test for the investigation of stable chest pain: the clinical results of the CAPP randomized prospective trial. *Eur Heart J Cardiovasc Imaging*. 2015 Apr;16(4):441-8.

<https://pubmed.ncbi.nlm.nih.gov/25473041/>

. van Nunen LX, Zimmermann FM, Tonino PA, et al; FAME Study Investigators. Fractional flow reserve versus angiography for guidance of PCI in patients with multivessel coronary artery disease (FAME): 5-year follow-up of a randomised controlled trial. *Lancet*. 2015 Nov 7;386(10006):1853-60.

<https://pubmed.ncbi.nlm.nih.gov/26333474/>

Guidelines and guidance	
<a href="#">Previous HIS projects/advice/guidance relating to this topic</a>	Calvert, J; Campbell, E; Deogaonkar, R; Graham, S; Heggeland, M; Kandulu, J; Kelly, J; MacGann, T (2021). HeartFlow FFRCT for estimating fractional flow reserve from coronary CT angiography Glasgow/Edinburgh. NHS Healthcare Improvement Scotland. <a href="https://shtg.scot/our-advice/heartflow-ffrct-for-estimating-fractional-flow-reserve-from-coronaryct-angiography/">https://shtg.scot/our-advice/heartflow-ffrct-for-estimating-fractional-flow-reserve-from-coronaryct-angiography/</a>
<a href="#">NICE</a>	National Institute for Health and Clinical Excellence. HeartFlow FFRCT for estimating fractional flow reserve from coronary CT angiography. <a href="https://www.nice.org.uk/guidance/mtg32">https://www.nice.org.uk/guidance/mtg32</a>
<a href="#">HTW</a>	Nil
<a href="#">HTA database</a>	Nil
Additional searching (if required)	
<a href="#">Cochrane library (for 2021 refs)</a>	<p>White HD, O'Brien SM, Alexander KP, Comparison of Days Alive Out of Hospital With Initial Invasive vs Conservative Management: A Prespecified Analysis of the ISCHEMIA Trial. JAMA Cardiol. 2021 Sep 1;6(9):1023-1031. doi: 10.1001/jamacardio.2021.1651. PMID: 33938917; PMCID: PMC8094032. <a href="https://pubmed.ncbi.nlm.nih.gov/33938917/">https://pubmed.ncbi.nlm.nih.gov/33938917/</a></p> <p>Gersh BJ, Bhatt DL. To stent or not to stent? Treating angina after ISCHEMIA-the impact of the <b>ISCHEMIA</b> trial on the indications for angiography and revascularization in patients with stable coronary artery disease. Eur Heart J. 2021 Apr 7;42(14):1389-1393. <a href="https://pubmed.ncbi.nlm.nih.gov/33827132/">https://pubmed.ncbi.nlm.nih.gov/33827132/</a></p> <p>McCreanor V, Nowbar A, Rajkumar C, Barnett AG, Francis D, Graves N, Boden WE, Weintraub WS, Al-Lamee R, Parsonage WA. Cost-effectiveness analysis of percutaneous coronary intervention for single-vessel coronary artery disease: an economic evaluation of the ORBITA trial. BMJ Open. 2021 Feb 9;11(2):e044054 <a href="https://pubmed.ncbi.nlm.nih.gov/33563623/">https://pubmed.ncbi.nlm.nih.gov/33563623/</a></p> <p>Curzen N, Nicholas Z, Stuart B, Wilding S, Fractional flow reserve derived from computed tomography coronary angiography in the assessment and management of stable chest pain: the FORECAST randomized trial. Eur Heart J. 2021 Oct 1;42(37):3844-3852. <a href="https://pubmed.ncbi.nlm.nih.gov/34269376/">https://pubmed.ncbi.nlm.nih.gov/34269376/</a></p>

	<p>Foldyna B, Zeleznik R, Eslami P,. Small whole heart volume predicts cardiovascular events in patients with stable chest pain: insights from the PROMISE trial. Eur Radiol. 2021 Aug;31(8):6200-6210. <a href="https://pubmed.ncbi.nlm.nih.gov/33501599/">https://pubmed.ncbi.nlm.nih.gov/33501599/</a></p>
--	---