Summary of:

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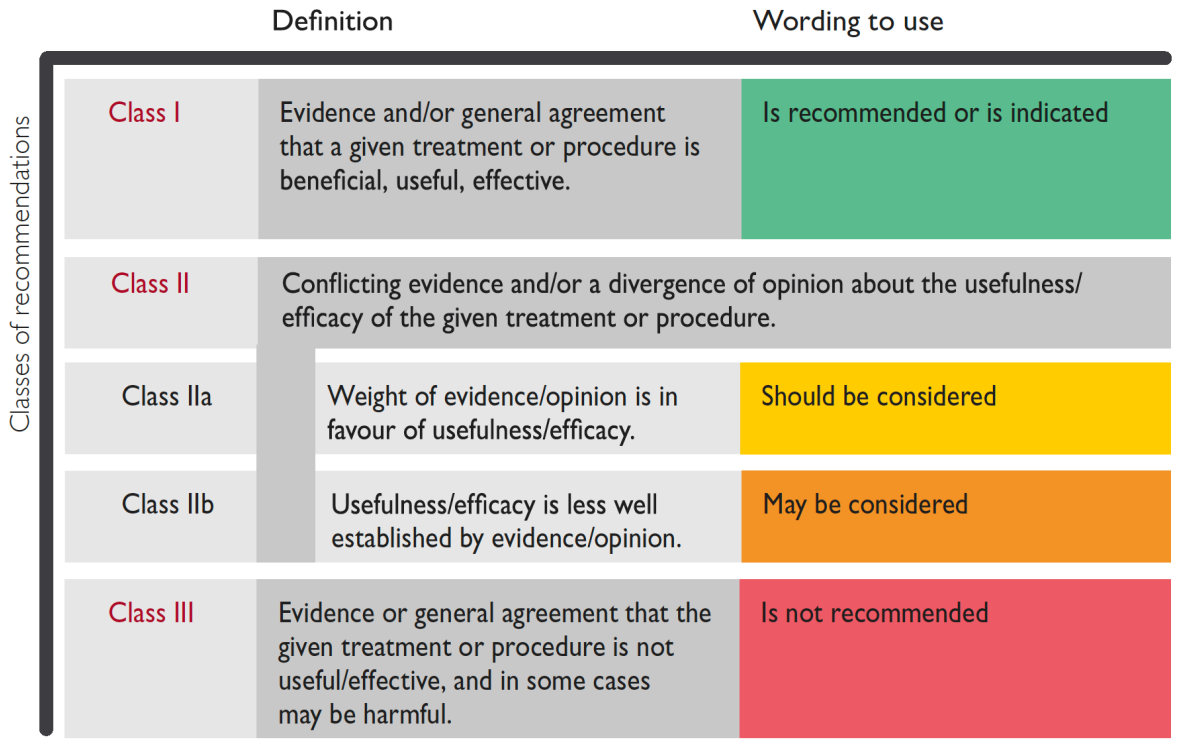
ESC GUIDELINES

2019 ESC Guidelines for the diagnosis and management of chronic coronary syndromes

The Task Force for the diagnosis and management of chronic coronary syndromes of the European Society of Cardiology (ESC)


Definition
Wording to use
Classes of recommendations
Class I
Evidence and/or general agreement that a given treatment or procedure is beneficial, useful, effective.
Is recommended or is indicated
Class II
Conflicting evidence and/or a divergence of opinion about the usefulness/ efficacy of the given treatment or procedure.
Class IIa
Weight of evidence/opinion is in favour of usefulness/efficacy.
Should be considered
Class IIb
Usefulness/efficacy is less well established by evidence/opinion.
May be considered
Class III
Evidence or general agreement that the given treatment or procedure is not useful/effective, and in some cases may be harmful.
Is not recommended
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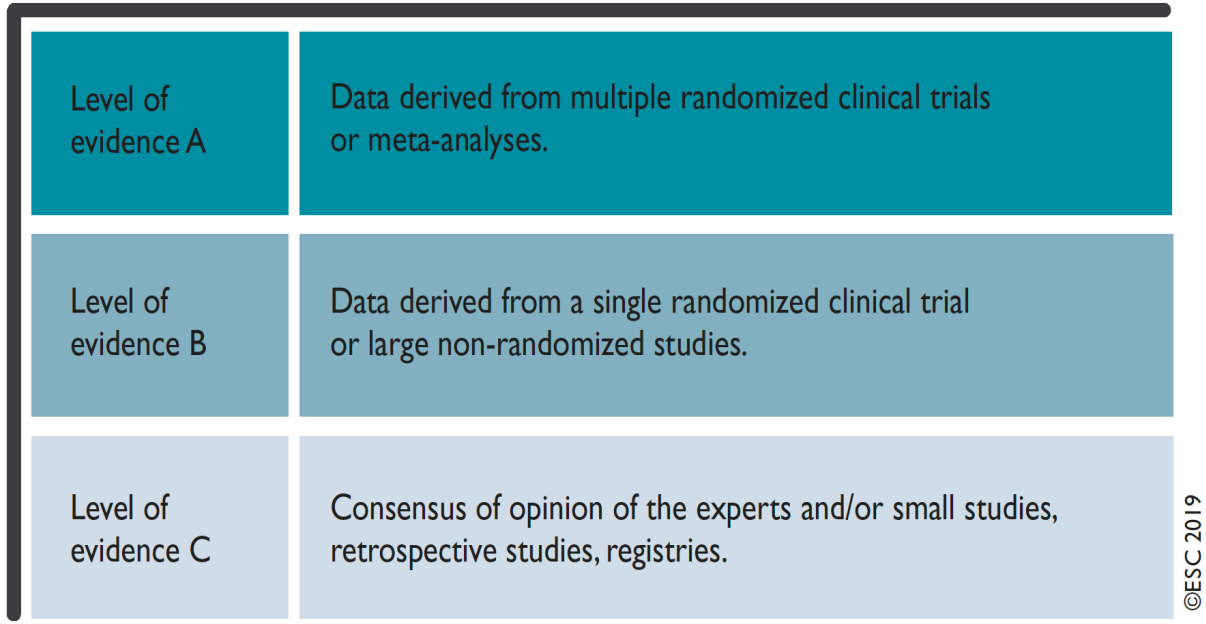
Level of evidence A
Data derived from multiple randomized clinical trials or meta-analyses.
Level of evidence B
Data derived from a single randomized clinical trial or large non-randomized studies.
Level of evidence C
Consensus of opinion of the experts and/or small studies, retrospective studies, registries.
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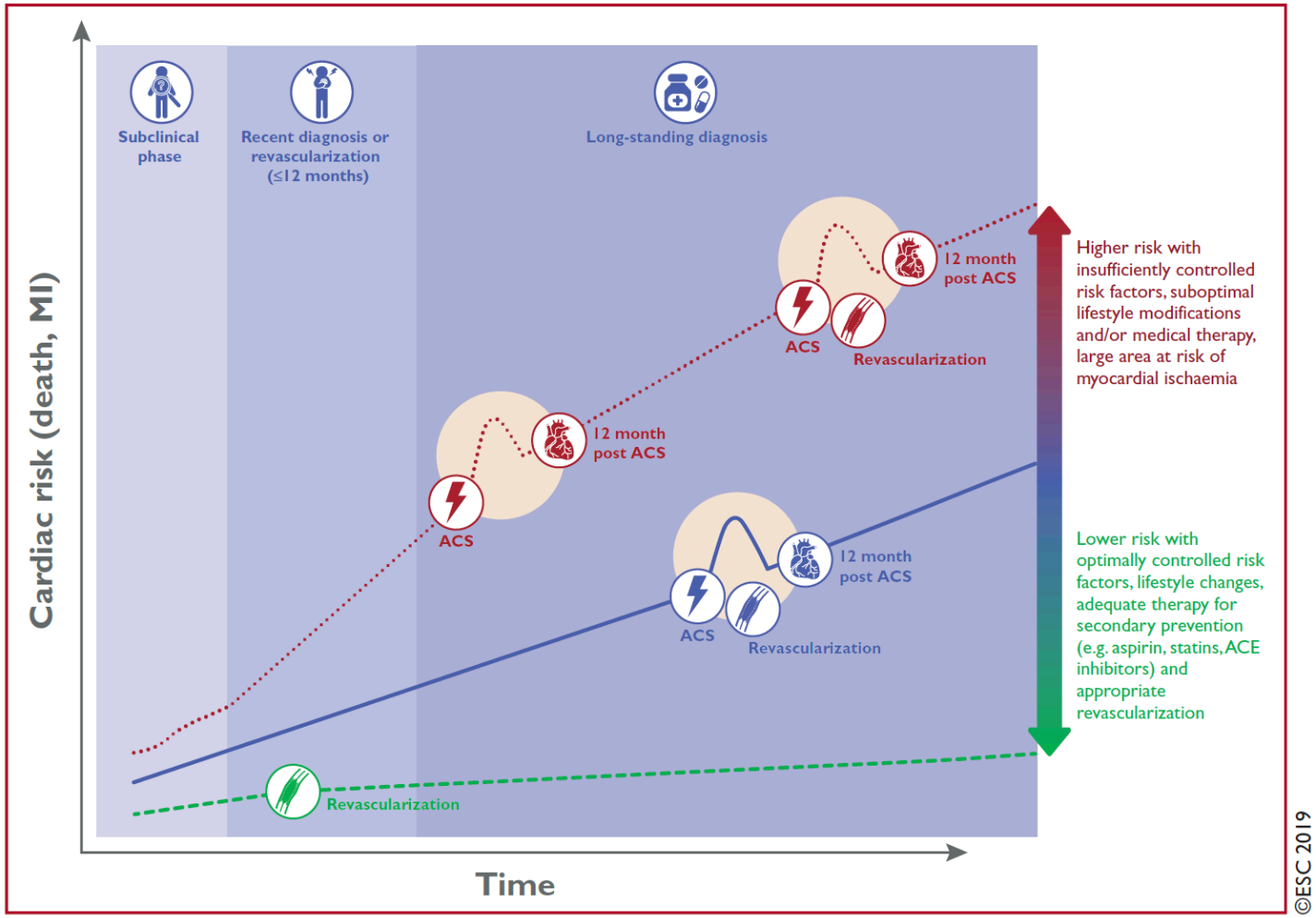


Figure 1 Schematic illustration of the natural history of chronic coronary syndromes. ACE = angiotensin-converting enzyme; ACS = acute coronary syndromes; CCS = chronic coronary syndromes; MI = myocardial infarction.

New/revised concepts in 2019
The Guidelines have been revised to focus on CCS instead of stable CAD.
This change emphasizes the fact that the clinical presentations of CAD can be categorized as either ACS or CCS. CAD is a dynamic process of atherosclerotic plaque accumulation and functional alterations of coronary circulation that can be modified by lifestyle, pharmacological therapies, and revascularization, which result in disease stabilization or regression.
In the current Guidelines on CCS, six clinical scenarios most frequently encountered in patients are identified: (i) patients with suspected CAD and 'stable' anginal symptoms, and/or dyspnoea; (ii) patients with new onset of HF or LV dysfunction and suspected CAD; (iii) asymptomatic and symptomatic patients with stabilized symptoms <1 year after an ACS or patients with recent revascularization; (iv) asymptomatic and symptomatic patients >1 year after initial diagnosis or revascularization; (v) patients with angina and suspected vasospastic or microvascular disease; (vi) asymptomatic subjects in whom CAD is detected at screening.
The PTP of CAD based on age, gender and nature of symptoms have undergone major revisions. In addition, we introduced a new phrase 'Clinical likelihood of CAD' that utilizes also various risk factors of CAD as PTP modifiers. The application of various diagnostic tests in different patient groups to rule-in or rule-out CAD have been updated.
The Guidelines emphasize the crucial role of healthy lifestyle behaviours and other preventive actions in decreasing the risk of subsequent cardiovascular events and mortality.

ACS = acute coronary syndromes; CAD = coronary artery disease; CCS = chronic coronary syndromes; HF = heart failure; LV = left ventricular; PTP = pre-test probability.

New major recommendations in 2019	
Basic testing, diagnostics, and risk assessment	
Non-invasive functional imaging for myocardial ischaemia or coronary CTA is recommended as the initial test for diagnosing CAD in symptomatic patients in whom obstructive CAD cannot be excluded by clinical assessment alone.	I
It is recommended that selection of the initial non-invasive diagnostic test be based on the clinical likelihood of CAD and other patient characteristics that influence test performance, local expertise, and the availability of tests.	I
Functional imaging for myocardial ischaemia is recommended if coronary CTA has shown CAD of uncertain functional significance or is not diagnostic.	I
Invasive angiography is recommended as an alternative test to diagnose CAD in patients with a high clinical likelihood and severe symptoms refractory to medical therapy, or typical angina at a low level of exercise and clinical evaluation that indicates high event risk. Invasive functional assessment must be available and used to evaluate stenoses before revascularization, unless very high grade (>90% diameter stenosis).	I
Invasive coronary angiography with the availability of invasive functional evaluation should be considered for confirmation of the diagnosis of CAD in patients with an uncertain diagnosis on non-invasive testing.	IIa
Coronary CTA should be considered as an alternative to invasive angiography if another non-invasive test is equivocal or non-diagnostic.	IIa
Coronary CTA is not recommended when extensive coronary calcification, irregular heart rate, significant obesity, inability to cooperate with breath-hold commands, or any other conditions make good image quality unlikely.	III

Continued

Antithrombotic therapy in patients with CCS and sinus rhythm	
Addition of a second antithrombotic drug to aspirin for long-term secondary prevention should be considered in patients with a **high risk** of ischaemic events and without high bleeding risk (see options in *section 3.3.2*).	**IIa**
Addition of a second antithrombotic drug to aspirin for long-term secondary prevention may be considered in patients with at least a **moderately increased risk** of ischaemic events and without high bleeding risk (see options in *section 3.3.2*).	**IIb**
Antithrombotic therapy in patients with CCS and AF	
When oral anticoagulation is initiated in a patient with AF who is eligible for a NOAC, a NOAC is recommended in preference to a VKA.	**I**
Long-term OAC therapy (a NOAC or VKA with time in therapeutic range >70%) is recommended in patients with AF and a CHA_2DS_2-VASc score ≥2 in males and ≥3 in females.	**I**
Long-term OAC therapy (a NOAC or VKA with time in therapeutic range >70%) should be considered in patients with AF and a CHA_2DS_2-VASc score of 1 in males and 2 in females.	**IIa**

Antithrombotic therapy in post-PCI patients with AF or another indication for OAC	
In patients who are eligible for a NOAC, it is recommended that a NOAC (apixaban 5 mg b.i.d., dabigatran 150 mg b.i.d., edoxaban 60 mg o.d., or rivaroxaban 20 mg o.d.) is used in preference to a VKA in combination with antiplatelet therapy.	I
When rivaroxaban is used and concerns about high bleeding risk prevail over concerns about stent thrombosis or ischaemic stroke, rivaroxaban 15 mg o.d. should be considered in preference to rivaroxaban 20 mg o.d. for the duration of concomitant single or dual antiplatelet therapy.	IIa
When dabigatran is used and concerns about high bleeding risk prevail over concerns about stent thrombosis or ischaemic stroke, dabigatran 110 mg b.i.d. should be considered in preference to dabigatran 150 mg b.i.d. for the duration of concomitant single or dual antiplatelet therapy	IIa
After uncomplicated PCI, early cessation (≤1 week) of aspirin, and continuation of dual therapy with OAC and clopidogrel, should be considered if the risk of stent thrombosis is low or if concerns about bleeding risk prevail over concerns about risk of stent thrombosis, irrespective of the type of stent used.	IIa
Triple therapy with aspirin, clopidogrel, and an OAC for ≥1 month should be considered when the risk of stent thrombosis outweighs the bleeding risk, with the total duration (≤6 months) decided upon according to the assessment of these risks and clearly specified at hospital discharge.	IIa
In patients with an indication for a VKA in combination with aspirin and/or clopidogrel, the dose intensity of the VKA should be carefully regulated with a target international normalized ratio in the range of 2.0 - 2.5 and with time in therapeutic range >70%.	IIa
Dual therapy with an OAC and either ticagrelor or prasugrel may be considered as an alternative to triple therapy with an OAC, aspirin, and clopidogrel in patients with a moderate or high risk of stent thrombosis, irrespective of the type of stent used.	IIb

Other pharmacological therapy	
Concomitant use of a proton pump inhibitor is recommended in patients receiving aspirin monotherapy, DAPT, or OAC monotherapy who are at high risk of gastrointestinal bleeding.	I
Lipid-lowering drugs: if goals are not achieved with the maximum tolerated dose of statin, combination with ezetimibe is recommended.	I
Lipid-lowering drugs: for patients at very high risk who do not achieve their goals on a maximum tolerated dose of statin and ezetimibe, combination with a PCSK9 inhibitor is recommended.	I
ACE inhibitors should be considered in CCS patients at very high risk of cardiovascular adverse events.	IIa
The sodium-glucose co-transporter 2 inhibitors empagliflozin, canagliflozin, or dapagliflozin are recommended in patients with diabetes mellitus and CVD.	I
A glucagon-like peptide-1 receptor agonist (liraglutide or semaglutide) is recommended in patients with diabetes mellitus and CVD.	I
Screening for CAD in asymptomatic subjects	
Carotid ultrasound IMT for cardiovascular risk assessment is not recommended.	III
Recommendations for treatment options for refractory angina	
A reducer device for coronary sinus constriction may be considered to ameliorate symptoms of debilitating angina refractory to optimal medical and revascularization strategies.	IIb

Exercise ECG is recommendedas the initial test to establish a diagnosis of stable CAD in patients withsymptoms of angina and intermediate PTP of CAD (15–65%), free of anti-ischaemic drugs, unless they cannot exercise or display ECG changes that make the ECG non-evaluable.	I	Exercise ECG is recommended for the assessment of exercise tolerance, symptoms, arrhythmias, BP response, and event risk in selected patients.	I
		Exercise ECG may be considered as an alternative test to rule-in or rule-out CAD when other non-invasive or invasive imaging methods are not available.	IIb
Exercise ECG should be considered in patients on treatment to evaluate control of symptoms and ischaemia.	IIa	Exercise ECG may be considered in patients on treatment to evaluate control of symptoms and ischaemia.	IIb
For second-line treatment it is recommended that long-acting nitrates, ivabradine, nicorandil, or ranolazine are added according to heart rate, BP, and tolerance.	IIa	Long-acting nitrates should be considered as a second-line treatment option when initial therapy with a beta-blocker and/or a non-DHP-CCB is contraindicated, poorly tolerated, or inadequate in controlling angina symptoms.	IIa
For second-line treatment, trimetazidine may be considered,	IIb	Nicorandil, ranolazine, ivabradine, or trimetazidine should be considered as a second-line treatment to reduce angina frequency and improve exercise tolerance in subjects who cannot tolerate, have contraindications to, or whose symptoms are not adequately controlled by beta-blockers, CCBs, and long-acting nitrates.	IIa
		In selected patients, the combination of a beta-blocker or a CCB with second-line drugs (ranolazine, nicorandil, ivabradine, and trimetazidine) may be considered for first-line treatment according to heart rate, BP, and tolerance.	IIb

Changes in major recommendations

2013	Class[a]	2019	Class[a]
In patients with suspected coronary microvascular angina: intracoronary acetylcholine and adenosine with Doppler measurements may be considered during coronary arteriography, if the arteriogram is visually normal, to assess endothelium-dependent and non-endothelium-dependent CFR, and detect microvascular/epicardial vasospasm.	IIb	Guidewire-based CFR and/or microcirculatory resistance measurements should be considered in patients with persistent symptoms, but coronary arteries that are either angiographically normal or have moderate stenoses with preserved iwFR/FFR.	IIa
		Intracoronary acetylcholine with ECG monitoring may be considered during angiography, if coronary arteries are either angiographically normal or have moderate stenoses with preserved iwFR/FFR, to assess microvascular vasospasm.	IIb
In patients with suspected coronary microvascular angina: transthoracic Doppler echocardiography of the LAD, with measurement of diastolic coronary blood flow following intravenous adenosine and at rest, may be considered for non-invasive measurement of CFR.	IIb	Transthoracic Doppler of the LAD, CMR, and PET may be considered for non-invasive assessment of CFR.	IIb

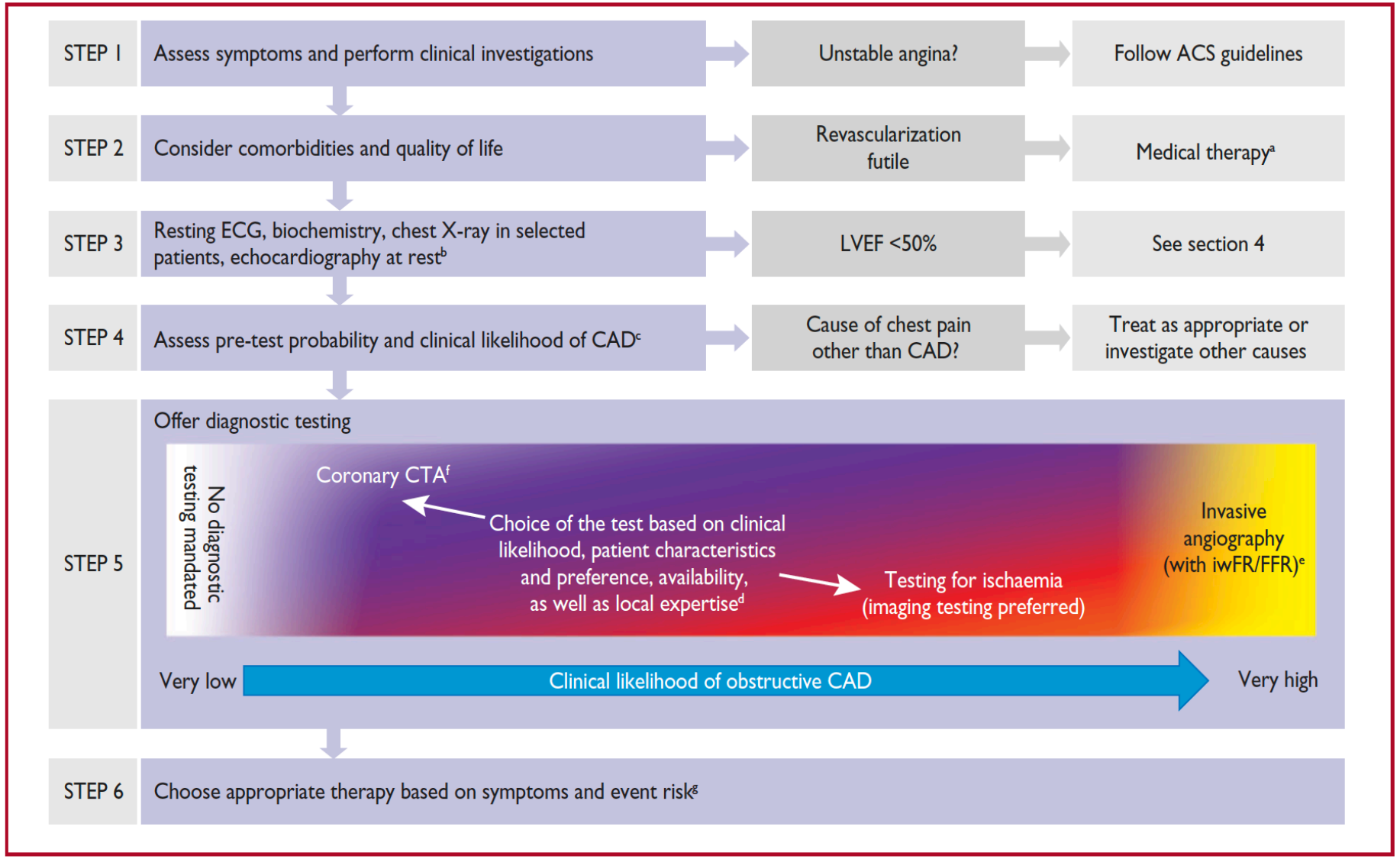

STEP 1
Assess symptoms and perform clinical investigations
Unstable angina?
Follow ACS guidelines
STEP 2
Consider comorbidities and quality of life
Revascularization futile
Medical therapy[a]
STEP 3
Resting ECG, biochemistry, chest X-ray in selected patients, echocardiography at rest[b]
LVEF <50%
See section 4
STEP 4
Assess pre-test probability and clinical likelihood of CAD[c]
Cause of chest pain other than CAD?
Treat as appropriate or investigate other causes
STEP 5
Offer diagnostic testing
No diagnostic testing mandated
Coronary CTA[f]
Choice of the test based on clinical likelihood, patient characteristics and preference, availability, as well as local expertise[d]
Testing for ischaemia (imaging testing preferred)
Invasive angiography (with iwFR/FFR)[e]
Very low
Clinical likelihood of obstructive CAD
Very high
STEP 6
Choose appropriate therapy based on symptoms and event risk[g]

Table 3 Traditional clinical classification of suspected anginal symptoms

Typical angina	Meets the following three characteristics: (i) Constricting discomfort in the front of the chest or in the neck, jaw, shoulder, or arm; (ii) Precipitated by physical exertion; (iii) Relieved by rest or nitrates within 5 min.
Atypical angina	Meets two of these characteristics.
Non-anginal chest pain	Meets only one or none of these characteristics.

Table 4 **Grading of effort angina severity according to the Canadian Cardiovascular Society**

Grade	Description of angina severity	
I	Angina only with strenuous exertion	Presence of angina during strenuous, rapid, or prolonged ordinary activity (walking or climbing the stairs).
II	Angina with moderate exertion	Slight limitation of ordinary activities when they are performed rapidly, after meals, in cold, in wind, under emotional stress, or during the first few hours after waking up, but also walking uphill, climbing more than one flight of ordinary stairs at a normal pace, and in normal conditions.
III	Angina with mild exertion	Having difficulties walking one or two blocks, or climbing one flight of stairs, at normal pace and conditions.
IV	Angina at rest	No exertion needed to trigger angina.

Table 5 **Pre-test probabilities of obstructive coronary artery disease in 15 815 symptomatic patients according to age, sex, and the nature of symptoms in a pooled analysis[64] of contemporary data[7,8,62]**

	Typical		Atypical		Non-anginal		Dyspnoea[a]	
Age	Men	Women	Men	Women	Men	Women	Men	Women
30–39	3%	5%	4%	3%	1%	1%	0%	3%
40–49	22%	10%	10%	6%	3%	2%	12%	3%
50–59	32%	13%	17%	6%	11%	3%	20%	9%
60–69	44%	16%	26%	11%	22%	6%	27%	14%
70+	52%	27%	34%	19%	24%	10%	32%	12%

CAD = coronary artery disease; PTP = pre-test probability.

[a]In addition to the classic Diamond and Forrester classes,[59] patients with dyspnoea only or dyspnoea as the primary symptom are included. The regions shaded dark green denote the groups in which non-invasive testing is most beneficial (PTP >15%). The regions shaded light green denote the groups with PTPs of CAD between 5–15%, in which testing for diagnosis may be considered after assessing the overall clinical likelihood based on the modifiers of PTPs presented in *Figure* 3.

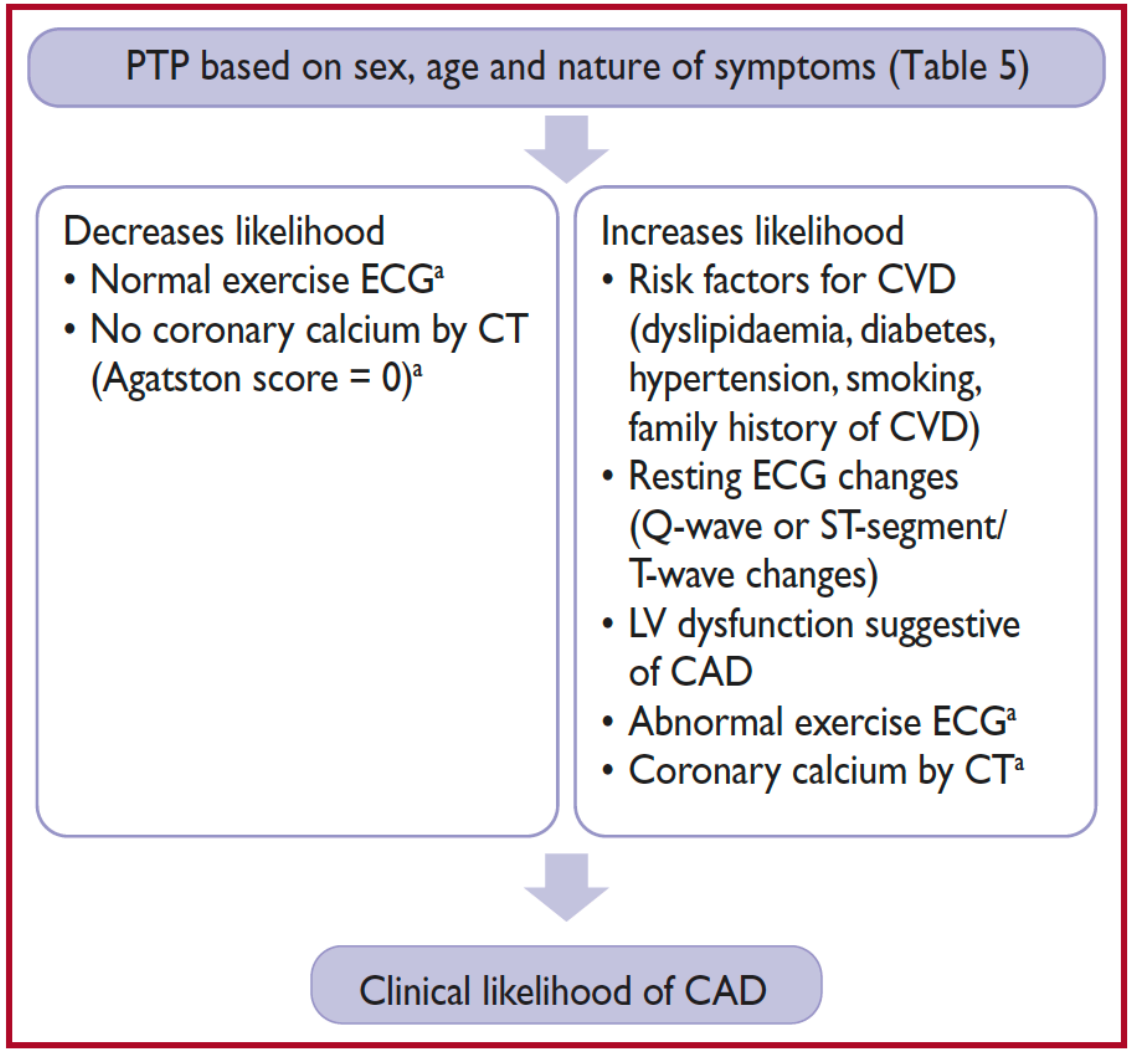


Figure 3 Determinants of the clinical likelihood of obstructive coronary artery disease. CAD = coronary artery disease; CT = computed tomography, CVD = cardiovascular disease, ECG = electrocardiogram, LV = left ventricular; PTP = pre-test probability. [a]When available.

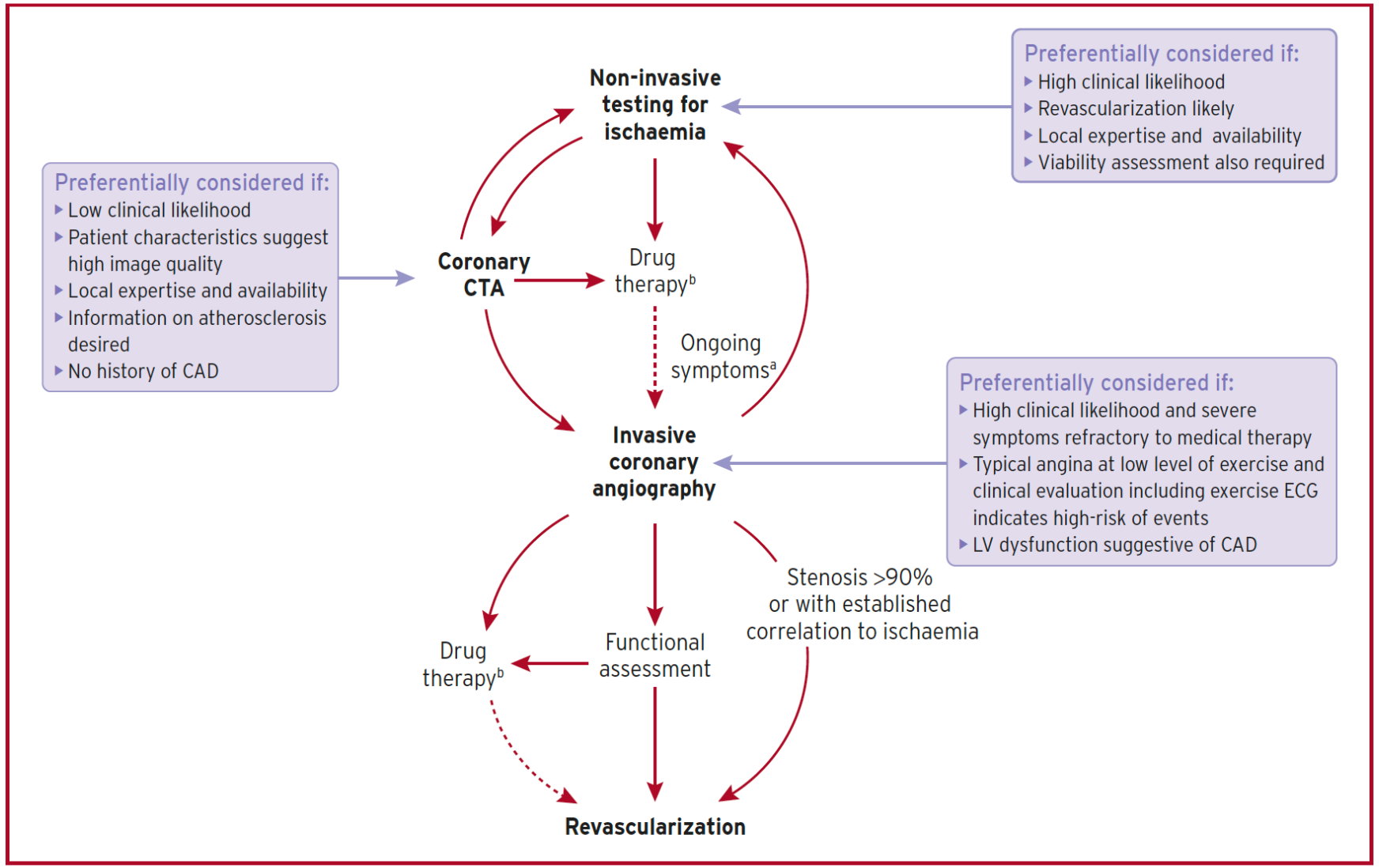


Figure 4 Main diagnostic pathways in symptomatic patients with suspected obstructive coronary artery disease. Depending on clinical conditions and the healthcare environment, patient workup can start with either of three options: non-invasive testing, coronary computed tomography angiography, or invasive coronary angiography. Through each pathway, both functional and anatomical information is gathered to inform an appropriate diagnostic and therapeutic strategy. Risk-factor modification should be considered in all patients. CAD = coronary artery disease; CTA = computed tomography angiography; ECG = electrocardiogram; LV = left ventricular. [a]Consider microvascular angina. [b]Antianginal medications and/or risk-factor modification.

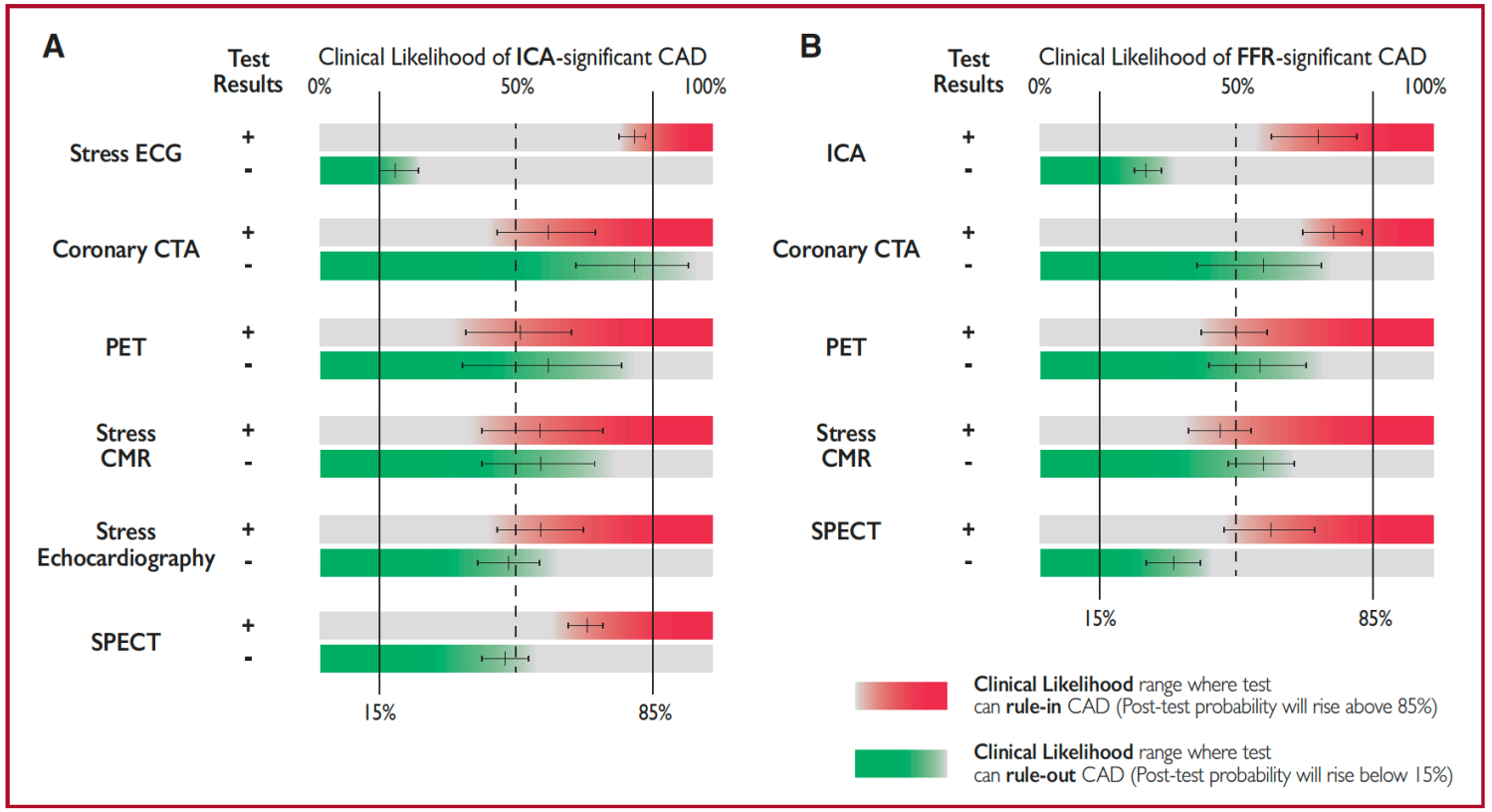


Figure 5 Ranges of clinical likelihood of coronary artery disease in which a given test can rule-in (red) or rule-out (green) obstructive coronary artery disease. (*A*) Reference standard is anatomical assessment using invasive coronary angiography. (*B*) Reference standard is functional assessment using fractional flow reserve. Note in (B) that the data with stress echocardiography and single-photon emission computed tomography are more limited than with the other techniques.[73] The crosshairs mark the mean values and their 95% confidence intervals. Figure adapted from Knuuti *et al.*[73] CAD = coronary artery disease; CMR = cardiac magnetic resonance; CTA = computed tomography angiography; ECG = electrocardiogram; FFR = fractional flow reserve; ICA = invasive coronary angiography; PET = positron emission tomography; SPECT = single-photon emission computed tomography.

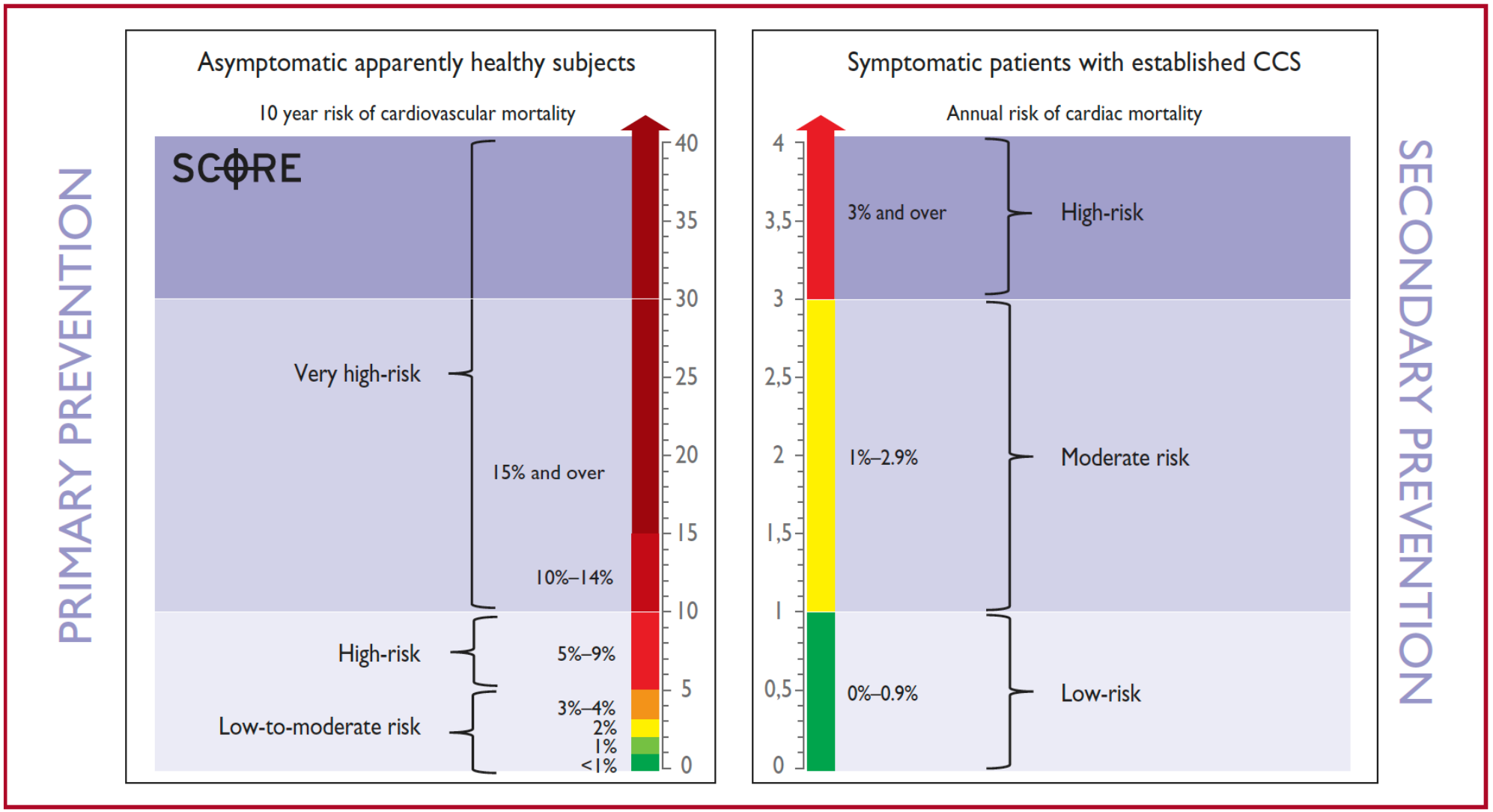


Figure 6 Comparison of risk assessments in asymptomatic apparently healthy subjects (primary prevention) and patients with established chronic coronary syndromes (secondary prevention). Note that in asymptomatic subjects (left panel), SCORE estimates 10 year cardiovascular mortality, while in symptomatic patients (right panel), annual cardiac mortality is estimated. CCS = chronic coronary syndromes; SCORE = Systematic COronary Risk Evaluation.

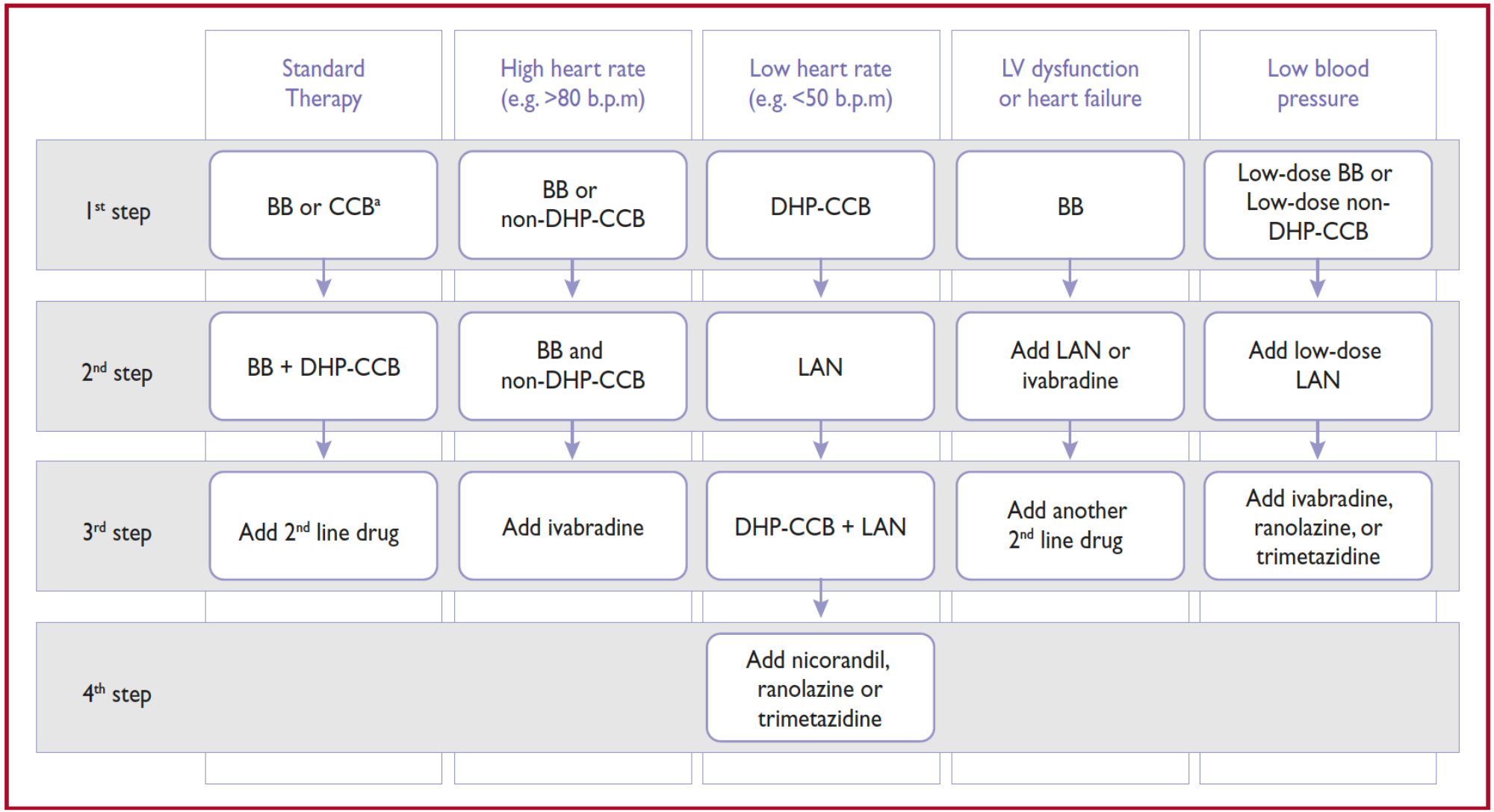


Figure 8 Suggested stepwise strategy for long-term anti-ischaemic drug therapy in patients with chronic coronary syndromes and specific baseline characteristics. BB = beta-blocker; b.p.m. = beats per minute; CCB = [any class of] calcium channel blocker; DHP-CCB = dihydropyridine calcium channel blocker; HF = heart failure; LAN = long-acting nitrate; LV = left ventricular; NDHP-CCB: non-dihydropyridine calcium channel blocker. [a]Combination of a BB with a DHP-CCB should be considered as a first step; combination of a BB or a CCB with a second-line drug may be considered as a first step.

Table 9 Treatment options for dual antithrombotic therapy in combination with aspirin 75 – 100 mg daily in patients who have a high[a] or moderate[b] risk of ischaemic events, and do not have a high bleeding risk[c]

Drug option	Dose	Indication	Additional cautions	References
Clopidogrel	75 mg o.d.	Post-MI in patients who have tolerated DAPT for 1 year		289,290
Prasugrel	10 mg o.d or 5 mg o.d.; if body weight <60 kg or age >75 years	Post-PCI for MI in patients who have tolerated DAPT for 1 year	Age >75 years	289,290,313
Rivaroxaban	2.5 mg b.i.d.	Post-MI >1 year or multivessel CAD	Creatinine clearance 15 - 29 mL/min	297
Ticagrelor	60 mg b.i.d.	Post-MI in patients who have tolerated DAPT for 1 year		291–293,307,314

Treatment options are presented in alphabetical order.

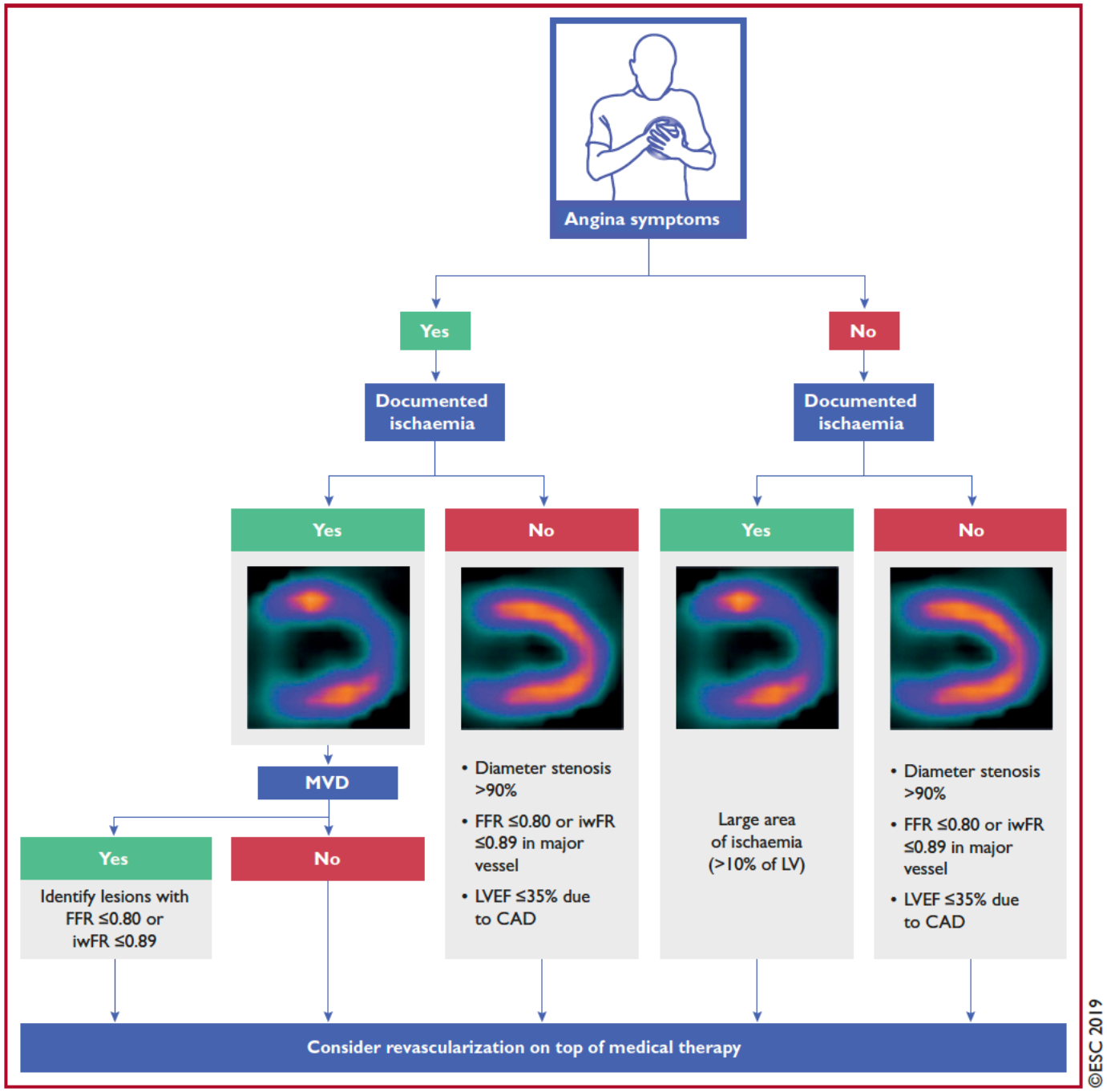
b.i.d. = bis in die (twice a day); CAD = coronary artery disease; CKD = chronic kidney disease; DAPT = dual antiplatelet therapy; eGFR = estimated glomerular filtration rate; HF = heart failure; MI = myocardial infarction; o.d. = omni die (once a day); PAD = peripheral artery disease; PCI = percutaneous coronary intervention.

[a]High risk of ischaemic events is defined as diffuse multivessel CAD with at least one of the following: diabetes mellitus requiring medication, recurrent MI, PAD, or CKD with eGFR 15 - 59 mL/min/1.73 m^2.

[b]Moderately increased risk of ischaemic events is defined as at least one of the following: multivessel/diffuse CAD, diabetes mellitus requiring medication, recurrent MI, PAD, HF, or CKD with eGFR 15 - 59 mL/min/1.73 m^2.

[c]High bleeding risk is defined as history of intracerebral haemorrhage or ischaemic stroke, history of other intracranial pathology, recent gastrointestinal bleeding or anaemia due to possible gastrointestinal blood loss, other gastrointestinal pathology associated with increased bleeding risk, liver failure, bleeding diathesis or coagulopathy, extreme old age or frailty, or renal failure requiring dialysis or with eGFR <15 mL/min/1.73 m^2.

Decision tree for patients undergoing invasive coronary angiography. Decisions for revascularization by percutaneous coronary intervention or coronary artery bypass grafting are based on clinical presentation (symptoms present or absent), and prior documentation of ischemia (present or absent). In the absence of prior documentation of ischemia, indications for revascularization depend on invasive evaluation of stenosis severity or prognostic indications. Patients with no symptoms and ischemia include candidates for transcatheter aortic valve implantation, valve, and other surgery. CAD = coronary artery disease; FFR = fractional flow reserve; iwFR = instantaneous wave-free ratio; LV = left ventricle; LVEF = left ventricular ejection fraction; MVD= multivessel disease.



Proposed algorithm according to patient types commonly observed at chronic coronary syndrome outpatient clinics. The frequency of follow-upmay be subject to variation based on clinical judgement. ACS = acute coronary syndromes; CCS = chronic coronary syndromes; DAPT = dual antiplatelet therapy; ECG = electrocardiogram; LV = left ventricular; MI = myocardial infarction; PCI = percutaneous coronary intervention. A Cardiologist, internist, general practitioner, or cardiovascular nurse.

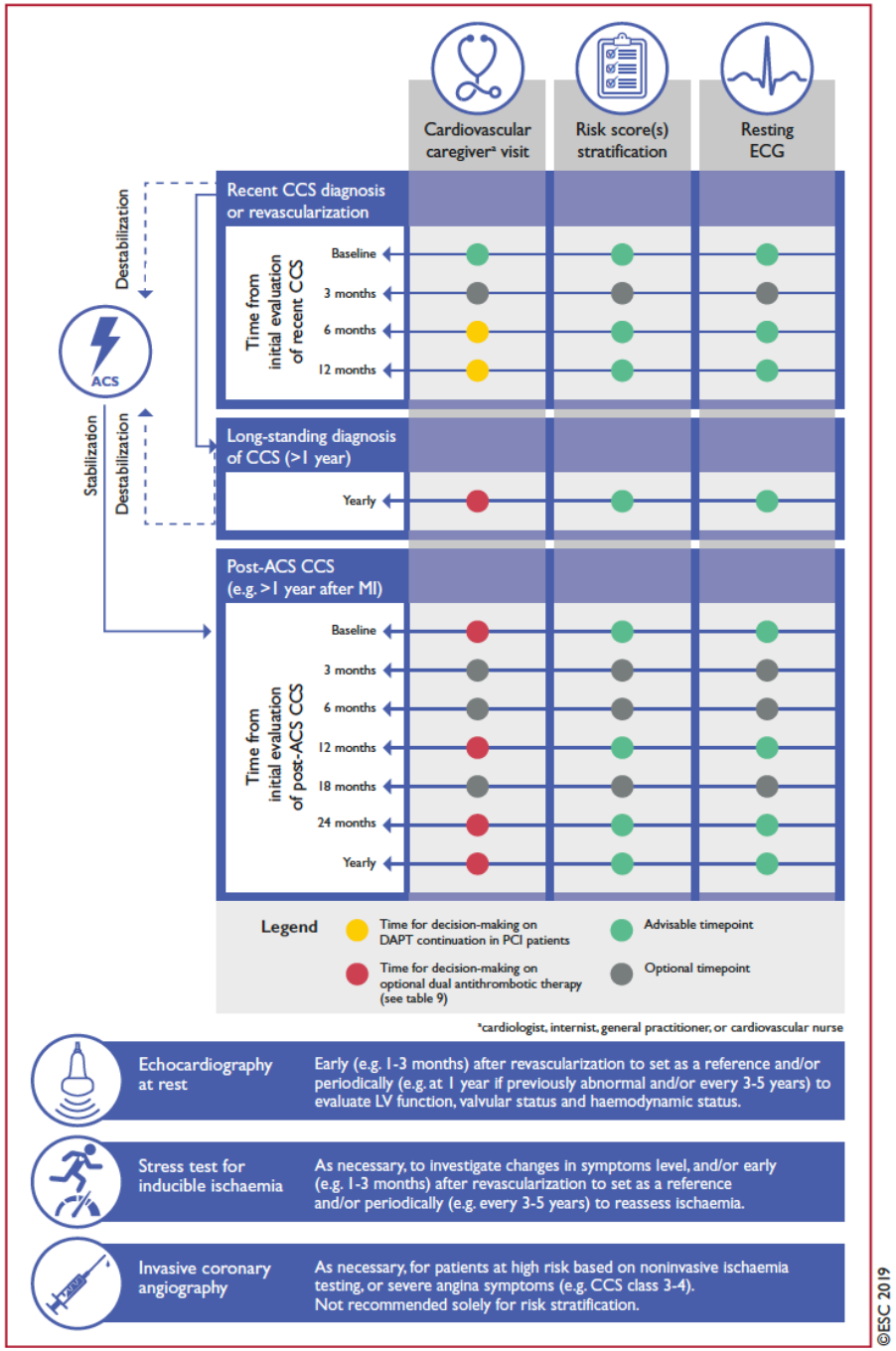


Table 10 **Blood pressure thresholds for the definition of hypertension with different types of blood pressure measurement**[470–472]

Category	Systolic BP (mmHg)		Diastolic BP (mmHg)
Office BP	≥140	and/or	≥90
≥80 years of age	≥160	and/or	≥90
Ambulatory BP			
Daytime (or awake)	≥135	and/or	≥85
Night-time (or asleep)	≥120	and/or	≥70
24 h	≥130	and/or	≥80
Home BP	≥135	and/or	≥85

BP = blood pressure.

Recommendation for sex issues and chronic coronary syndromes

Recommendation	Class[a]	Level[b]
Hormone replacement therapy is not recommended for risk reduction in post-menopausal women.	III	C

[a]Class of recommendation.
[b]Level of evidence.

9 Key messages

(1) Careful evaluation of patient history, including the characterization of anginal symptoms, and evaluation of risk factors and manifestations of CVD, as well as proper physical examination and basic testing, are crucial for the diagnosis and management of CCS.

(2) Unless obstructive CAD can be excluded based on clinical evaluation alone, either non-invasive functional imaging or anatomical imaging using coronary CTA may be used as the initial test to rule-out or establish the diagnosis of CCS.

(3) Selection of the initial non-invasive diagnostic test is based on the PTP, the test's performance in ruling-in or ruling-out obstructive CAD, patient characteristics, local expertise, and the availability of the test.

(4) For revascularization decisions, both anatomy and functional evaluation are to be considered. Either non-invasive or invasive functional evaluation is required for the assessment of myocardial ischaemia associated with angiographic stenosis, unless very high grade (>90% diameter stenosis).

(5) Assessment of risk serves to identify CCS patients at high event risk who are projected to derive prognostic benefit from revascularization. Risk stratification includes the assessment of LV function.

(6) Patients at high event risk should undergo invasive investigation for consideration of revascularization, even if they have mild or no symptoms.

(7) Implementation of healthy lifestyle behaviours decreases the risk of subsequent cardiovascular events and mortality, and is additional to appropriate secondary prevention therapy. Clinicians should advise on and encourage necessary lifestyle changes in every clinical encounter.

(8) Cognitive behavioural interventions such as supporting patients to set realistic goals, self-monitor, plan how to implement changes and deal with difficult situations, set environmental cues, and engage social support are effective interventions for behaviour change.

(9) Multidisciplinary teams can provide patients with support to make healthy lifestyle changes, and address challenging aspects of behaviour and risk.

(10) Anti-ischaemic treatment must be adapted to the individual patient based on comorbidities, co-administered therapies, expected tolerance and adherence, and patient preferences. The choice of anti-ischaemic drugs to treat CCS should be adapted to the patient's heart rate, BP, and LV function.

(11) Beta-blockers and/or CCBs remain the first-line drugs in patients with CCS. Beta-blockers are recommended in patients with LV dysfunction or HF with reduced ejection fraction.

(12) Long-acting nitrates provoke tolerance with loss of efficacy. This requires prescription of a daily nitrate-free or nitrate-low interval of ~10–14 h.

(13) Antithrombotic therapy is a key part of secondary prevention in patients with CCS and warrants careful consideration. Patients with a previous MI, who are at high risk of ischaemic events and low risk of fatal bleeding, should be considered for long-term DAPT with aspirin and either a $P2Y_{12}$ inhibitor or very low-dose rivaroxaban, unless they have an indication for an OAC such as AF.

(14) Statins are recommended in all patients with CCS. ACE inhibitors (or ARBs) are recommended in the presence of HF, diabetes, or hypertension and should be considered in high-risk patients.

(15) Proton pump inhibitors are recommended in patients receiving aspirin or combination antithrombotic therapy who are at high risk of gastrointestinal bleeding.

(16) Efforts should be made to explain to patients the importance of evidence-based prescriptions to increase adherence to treatment, and repeated therapeutic education is essential in every clinical encounter.

(17) Patients with a long-standing diagnosis of CCS should undergo periodic visits to assess potential changes in risk status, adherence to treatment targets, and the development of comorbidities. Repeat stress imaging or ICA with functional testing is recommended in the presence of worsening symptoms and/or increased risk status.

(18) Assessment of myocardial and valvular function and dimensions, as well as a functional test to rule-out significant myocardial silent ischaemia, may be contemplated every 3–5 years in asymptomatic patients with a long-standing diagnosis of CCS.

Recommendations: 'what to do' and 'what not to do'	Class[a]	Level[b]
Basic biochemistry testing in the initial diagnostic management of patients with suspected CAD		
If evaluation suggests clinical instability or ACS, repeated measurements of troponin, preferably using high-sensitivity or ultrasensitive assays, are recommended to rule-out myocardial injury associated with ACS.	I	A
The following blood tests are recommended in all patients:		
• Full blood count (including haemoglobin);	I	B
• Creatinine measurement and estimation of renal function;	I	A
• A lipid profile (including LDL-C).	I	A
It is recommended that screening for type 2 diabetes mellitus in patients with suspected and established CCS is implemented with HbA1c and fasting plasma glucose measurements, and that an oral glucose tolerance test is added if HbA1c and fasting plasma glucose results are inconclusive.	I	B
Assessment of thyroid function is recommended in cases where there is clinical suspicion of thyroid disorders.	I	C
Resting ECG in the initial diagnostic management of patients with suspected CAD		
A resting 12 lead ECG is recommended in all patients with chest pain without obvious non-cardiac cause.	I	C
A resting 12 lead ECG is recommended in all patients during or immediately after an episode of angina suspected to indicate clinical instability of CAD.	I	C
ST-segment alterations recorded during supraventricular tachyarrhythmias should not be used as evidence of CAD.	III	C
Ambulatory ECG monitoring in the initial diagnostic management of patients with suspected CAD		
Ambulatory ECG monitoring is recommended in patients with chest pain and suspected arrhythmias.	I	C
Ambulatory ECG monitoring should not be used as routine examination in patients with suspected CCS.	III	C
Resting echocardiography and CMR in the initial diagnostic management of patients with suspected CAD		
A resting transthoracic echocardiogram is recommended in all patients for: • Exclusion of alternative causes of angina; • Identification of regional wall motion abnormalities suggestive of CAD; • Measurement of LVEF for risk-stratification purposes; • Evaluation of diastolic function.	I	B

Chest X-ray in the initial diagnostic management of patients with suspected CAD		
Chest X-ray is recommended for patients with an atypical presentation, signs and symptoms of heart failure, or suspicion of pulmonary disease.	I	C
Use of diagnostic imaging tests in the initial diagnostic management of symptomatic patients with suspected CAD		
Non-invasive functional imaging for myocardial ischaemia or coronary CTA is recommended as the initial test for diagnosing CAD in symptomatic patients in whom obstructive CAD cannot be excluded by clinical assessment alone.	I	B
It is recommended that selection of the initial non-invasive diagnostic test is done based on the clinical likelihood of CAD and other patient characteristics that influence test performance, local expertise, and the availability of tests.	I	C
Functional imaging for myocardial ischaemia is recommended if coronary CTA has shown CAD of uncertain functional significance or is not diagnostic.	I	B
Invasive angiography is recommended as an alternative test to diagnose CAD in patients with a high clinical likelihood and severe symptoms refractory to medical therapy, or typical angina at a low level of exercise and clinical evaluation that indicates high event risk. Invasive functional assessment must be available and used to evaluate stenoses before revascularization, unless very high grade (>90% diameter stenosis).	I	B

Continued

Coronary CTA is not recommended when extensive coronary calcification, irregular heart rate, significant obesity, inability to cooperate with breath-hold commands, or any other conditions makes good image quality unlikely.	III	C
Coronary calcium detection by computed tomography is not recommended to identify individuals with obstructive CAD.	III	C
Performing exercise ECG in the initial diagnostic management of patients with suspected CAD		
Exercise ECG is recommended for the assessment of exercise tolerance, symptoms, arrhythmias, BP response, and event risk in selected patients.	I	C
Recommendations for risk assessment		
Risk stratification is recommended based on clinical assessment and the result of the diagnostic test initially employed to make a diagnosis of CAD.	I	B
Resting echocardiography is recommended to quantify LV function in all patients with suspected CAD.	I	C
Risk stratification, preferably using stress imaging or coronary CTA (if local expertise and availability permit), or alternatively exercise stress ECG (if significant exercise can be performed and the ECG is amenable to the identification of ischaemic changes), is recommended in patients with suspected or newly diagnosed CAD.	I	B
In symptomatic patients with a high-risk clinical profile, ICA complemented by invasive physiological guidance (FFR) is recommended for cardiovascular risk stratification, particularly if the symptoms are inadequately responding to medical treatment and revascularization is considered for improvement of prognosis.	I	A
In patients with mild or no symptoms, ICA complemented by invasive physiological guidance (FFR/iwFR) is recommended for patients undergoing medical treatment in whom non-invasive risk stratification indicates a high event risk and revascularization is considered for the improvement of prognosis.	I	A
ICA is not recommended solely for risk stratification.	III	C

Recommendations on lifestyle management		
Improvement of lifestyle factors in addition to appropriate pharmacological management is recommended.	I	A
Cognitive behavioural interventions are recommended to help individuals achieve a healthy lifestyle.	I	A
Exercise-based cardiac rehabilitation is recommended as an effective means for patients with CCS to achieve a healthy lifestyle and manage risk factors.	I	A
Involvement of multidisciplinary healthcare professionals (cardiologists, GPs, nurses, dieticians, physiotherapists, psychologists, and pharmacists) is recommended.	I	A
Psychological interventions are recommended to improve symptoms of depression in patients with CCS.	I	B
Annual influenza vaccination is recommended for patients with CCS, especially in the elderly.	I	B
Recommendations on anti-ischaemic drugs in patients with CCS		
General considerations		
Medical treatment of symptomatic patients requires one or more drug(s) for angina/ischaemia relief in association with drug(s) for event prevention.	I	C
It is recommended that patients are educated about the disease, risk factors, and treatment strategy.	I	C
Timely review of the patient's response to medical therapies (e.g. 2–4 weeks after drug initiation) is recommended.	I	C
Angina/ischaemia relief		
Short-acting nitrates are recommended for immediate relief of effort angina.	I	B
First-line treatment is indicated with beta-blockers and/or CCBs to control heart rate and symptoms.	I	A
Nitrates are not recommended in patients with hypertrophic obstructive cardiomyopathy or co-administration of phosphodiesterase inhibitors.	III	B

Recommendations on anti-ischaemic drugs in patients with CCS		
General considerations		
Medical treatment of symptomatic patients requires one or more drug(s) for angina/ischaemia relief in association with drug(s) for event prevention.	I	C
It is recommended that patients are educated about the disease, risk factors, and treatment strategy.	I	C
Timely review of the patient's response to medical therapies (e.g. 2–4 weeks after drug initiation) is recommended.	I	C
Angina/ischaemia relief		
Short-acting nitrates are recommended for immediate relief of effort angina.	I	B
First-line treatment is indicated with beta-blockers and/or CCBs to control heart rate and symptoms.	I	A
Nitrates are not recommended in patients with hypertrophic obstructive cardiomyopathy or co-administration of phosphodiesterase inhibitors.	III	B
Recommendations for event prevention		
Antithrombotic therapy in patients with CCS and in sinus rhythm		
Aspirin 75–100 mg daily is recommended in patients with a previous MI or revascularization.	I	A
Clopidogrel 75 mg daily is recommended as an alternative to aspirin in patients with aspirin intolerance.	I	B
Antithrombotic therapy post-PCI in patients with CCS and in sinus rhythm		
Aspirin 75–100 mg daily is recommended following stenting.	I	A
Clopidogrel 75 mg daily following appropriate loading (e.g. 600 mg, >5 days, or maintenance therapy) is recommended, in addition to aspirin, for 6 months following coronary stenting, irrespective of stent type, unless a shorter duration (1–3 months) is indicated due to the risk or occurrence of life-threatening bleeding.	I	A
Antithrombotic therapy in patients with CCS and AF		
When oral anticoagulation is initiated in a patient with AF who is eligible for a NOAC, a NOAC is recommended in preference to a VKA.	I	A
Long-term OAC therapy (a NOAC or VKA with time in therapeutic range >70%) is recommended in patients with AF and a CHA_2DS_2-VASc score ≥2 in males and ≥3 in females.	I	A

Continued

Antithrombotic therapy in post-PCI patients with AF or another indication for an OAC		
It is recommended that peri-procedural aspirin and clopidogrel are administered to patients undergoing coronary stent implantation.	I	C
In patients who are eligible for a NOAC, it is recommended that a NOAC (apixaban 5 mg b.i.d., dabigatran 150 mg b.i.d., edoxaban 60 mg o.d., or rivaroxaban 20 mg o.d.) is used in preference to a VKA in combination with antiplatelet therapy.	I	A
The use of ticagrelor or prasugrel is not recommended as part of triple antithrombotic therapy with aspirin and an OAC.	III	C
Use of proton pump inhibitors		
Concomitant use of a proton pump inhibitor is recommended in patients receiving aspirin monotherapy, DAPT, or OAC monotherapy who are at high risk of gastrointestinal bleeding.	I	A
Lipid-lowering drugs		
Statins are recommended in all patients with CCS.	I	A
If the goals are not achieved with the maximum tolerated dose of a statin, combination with ezetimibe is recommended.	I	B
For patients at very high risk who do not achieve their goal on a maximum tolerated dose of statin and ezetimibe, combination with a PCSK9 inhibitor is recommended.	I	A
ACE inhibitors		
ACE inhibitors (or ARBs) are recommended in the presence of other conditions (e.g. HF, hypertension, or diabetes).	I	A
Other drugs		
Beta-blockers are recommended in patients with LV dysfunction or systolic HF.	I	A

General recommendations for the management of patients with CCS and symptomatic HF due to ischaemic cardiomyopathy and LV systolic dysfunction		
Recommendations for drug therapy		
Diuretic therapy is recommended in symptomatic patients with signs of pulmonary or systemic congestion to relieve HF symptoms.	I	B
Beta-blockers are recommended as an essential component of treatment due to their efficacy in both relieving angina, and reducing morbidity and mortality in HF.	I	A
ACE inhibitor therapy is recommended in patients with symptomatic HF or asymptomatic LV dysfunction following MI, to improve symptoms and reduce morbidity and mortality.	I	A
An ARB is recommended as an alternative in patients who do not tolerate ACE inhibition or an angiotensin receptor-neprilysin inhibitor in patients with persistent symptoms despite optimal medical therapy.	I	B
An MRA is recommended in patients who remain symptomatic despite adequate treatment with an ACE inhibitor and beta-blocker to reduce morbidity and mortality.	I	A

For devices, comorbidities, and revascularization		
In patients with HF and bradycardia with high-degree atrioventricular block who require pacing, a CRT with a pacemaker rather than right ventricular pacing is recommended.	I	A
An implantable cardioverter-defibrillator is recommended in patients with documented ventricular dysrhythmia causing haemodynamic instability (secondary prevention), as well as in patients with symptomatic HF and an LVEF ≤35%, to reduce the risk of sudden death and all-cause mortality.	I	A
CRT is recommended for symptomatic patients with HF in sinus rhythm with a QRS duration ≥150 ms and LBBB QRS morphology, and with LVEF ≤35% despite optimal medical therapy to improve symptoms and reduce morbidity and mortality. [355,356,383–392,353,354,381–390]	I	A
CRT is recommended for symptomatic patients with HF in sinus rhythm with a QRS duration 130–149 ms and LBBB QRS morphology, and with LVEF ≤35% despite optimal medical therapy to improve symptoms and reduce morbidity and mortality. [355,356,383–392,353,354,381–390]	I	B
Comprehensive risk profiling and multidisciplinary management, including treatment of major comorbidities such as hypertension, hyperlipidaemia, diabetes, anaemia, and obesity, as well as smoking cessation and lifestyle modification, are recommended.	I	A
Myocardial revascularization is recommended when angina persists despite treatment with antianginal drugs.	I	A
Recommendations for patients with a long-standing diagnosis of CCS		
Asymptomatic patients		
A periodic visit to a cardiovascular healthcare professional is recommended to reassess potential changes in the risk status of patients, entailing clinical evaluation of lifestyle-modification measures, adherence to targets of cardiovascular risk factors, and the development of comorbidities that may affect treatments and outcomes.	I	C

Continued

In patients with mild or no symptoms receiving medical treatment, in whom non-invasive risk stratification indicates a high risk, and for whom revascularization is considered for improvement of prognosis, ICA (with FFR when necessary) is recommended.	I	C
Coronary CTA is not recommended as a routine follow-up test for patients with established CAD.	III	C
ICA is not recommended solely for risk stratification.	III	C
Symptomatic patients		
Reassessment of CAD status is recommended in patients with deteriorating LV systolic function that cannot be attributed to a reversible cause (e.g. long-standing tachycardia or myocarditis).	I	C
Risk stratification is recommended for patients with new or worsening symptom levels, preferably using stress imaging or, alternatively, exercise stress ECG.	I	B
It is recommended that patients with significant worsening of symptoms be expeditiously referred for evaluation.	I	C
ICA (with FFR/iwFR when necessary) is recommended for risk stratification in patients with severe CAD, particularly if the symptoms are refractory to medical treatment or if they have a high-risk clinical profile.	I	C
Investigations in patients with suspected vasospastic angina		
An ECG is recommended during angina if possible.	I	C
Invasive angiography or coronary CTA is recommended in patients with characteristic episodic resting angina and ST-segment changes, which resolve with nitrates and/or calcium antagonists, to determine the extent of underlying coronary disease.	I	C

Screening for CAD in asymptomatic subjects		
Total risk estimation using a risk-estimation system such as SCORE is recommended for asymptomatic adults aged >40 years without evidence of CVD, diabetes, CKD, or familial hypercholesterolaemia.	I	C
Assessment of family history of premature CVD (defined as a fatal or non-fatal CVD event, and/or established diagnosis of CVD in first-degree male relatives before 55 years of age or female relatives before 65 years of age) is recommended as part of cardiovascular risk assessment.	I	C
It is recommended that all individuals aged <50 years with a family history of premature CVD in a first-degree relative (<55 years of age in men, <65 years of age in women) are screened for familial hypercholesterolaemia using a validated clinical score.	I	B
Carotid ultrasound IMT for cardiovascular risk assessment is not recommended.	III	A
In low-risk non-diabetic asymptomatic adults, coronary CTA or functional imaging for ischaemia is not indicated for further diagnostic assessment.	III	C
Routine assessment of circulating biomarkers is not recommendedfor cardiovascular risk stratification.	III	B
Recommendations for hypertension treatment in CCS		
It is recommended that office BP be controlled to target values: systolic BP 120–130 mmHg in general and systolic BP 130–140 mmHg in older patients (aged >65 years).	I	A
In hypertensive patients with a recent MI, beta-blockers and RAS blockers are recommended.	I	A
In patients with symptomatic angina, beta-blockers and/or CCBs are recommended.	I	A
The combination of ACE inhibitors and an ARB is not recommended.	III	A

Recommendations for valvular disease in CCS		
ICA is recommended before valve surgery and any of the following: history of CVD, suspected myocardial ischaemia, LV systolic dysfunction, in men aged >40 years and post-menopausal women, or one or more cardiovascular risk factors.	I	C
ICA is recommended in the evaluation of moderate-to-severe functional mitral regurgitation.	I	C
In severe valvular heart disease, stress testing should not be routinely used to detect CAD because of the low diagnostic yield and potential risks.	III	C
Recommendations for active cancer in CCS		
Treatment decisions should be based on life expectancy, additional comorbidities such as thrombocytopenia, increased thrombosis propensity, and potential interactions between drugs used in CCS management and antineoplastic agents.	I	C
If revascularization is indicated in highly symptomatic patients with active cancer and increased frailty, the least invasive procedure is recommended.	I	C
Recommendations for diabetes mellitus in CCS		
Risk factor (BP, LDL-C, and HbA1c) control to targets is recommended in patients with CAD and diabetes mellitus.	I	A
In asymptomatic patients with diabetes mellitus, a periodic resting ECG is recommended for cardiovascular detection of conduction abnormalities, AF, and silent MI.	I	C

Continued

Treatment with ACE inhibitors is recommended in CCS patients with diabetes for event prevention.	I	B
The sodium-glucose co-transporter 2 inhibitors empagliflozin, canagliflozin, or dapagliflozin are recommended in patients with diabetes and CVD.	I	A
A glucagon-like peptide-1 receptor agonist (liraglutide or semaglutide) is recommended in patients with diabetes and CVD.	I	A
Recommendations for CKD in CCS		
It is recommended that risk factors are controlled to target values.	I	A
It is recommended that special attention be paid to potential dose adjustments of renally excreted drugs used in CCS.	I	C
It is recommended that the use of iodinated contrast agents is minimized in patients with severe CKD and preserved urine production to prevent further deterioration.	I	B
Recommendations for elderly patients with CCS		
It is recommended that particular attention is paid to side effects of drugs, intolerance, and overdosing in elderly patients.	I	C
The use of DES is recommended in elderly patients.	I	A
Radial access is recommended in elderly patients to reduce access-site bleeding complications.	I	B
It is recommended that diagnostic and revascularization decisions are based on symptoms, the extent of ischaemia, frailty, life expectancy, and comorbidities.	I	C
Recommendation for sex issues and CCS		
Hormone replacement therapy is not recommended for risk reduction in post-menopausal women.	III	C
Treatment options in refractory angina		
Transmyocardial revascularization is not recommended in patients with debilitating angina refractory to optimal medical and revascularization strategies.	III	A