Arvand Pharmed

State-of-Art: Management of patients with CCS

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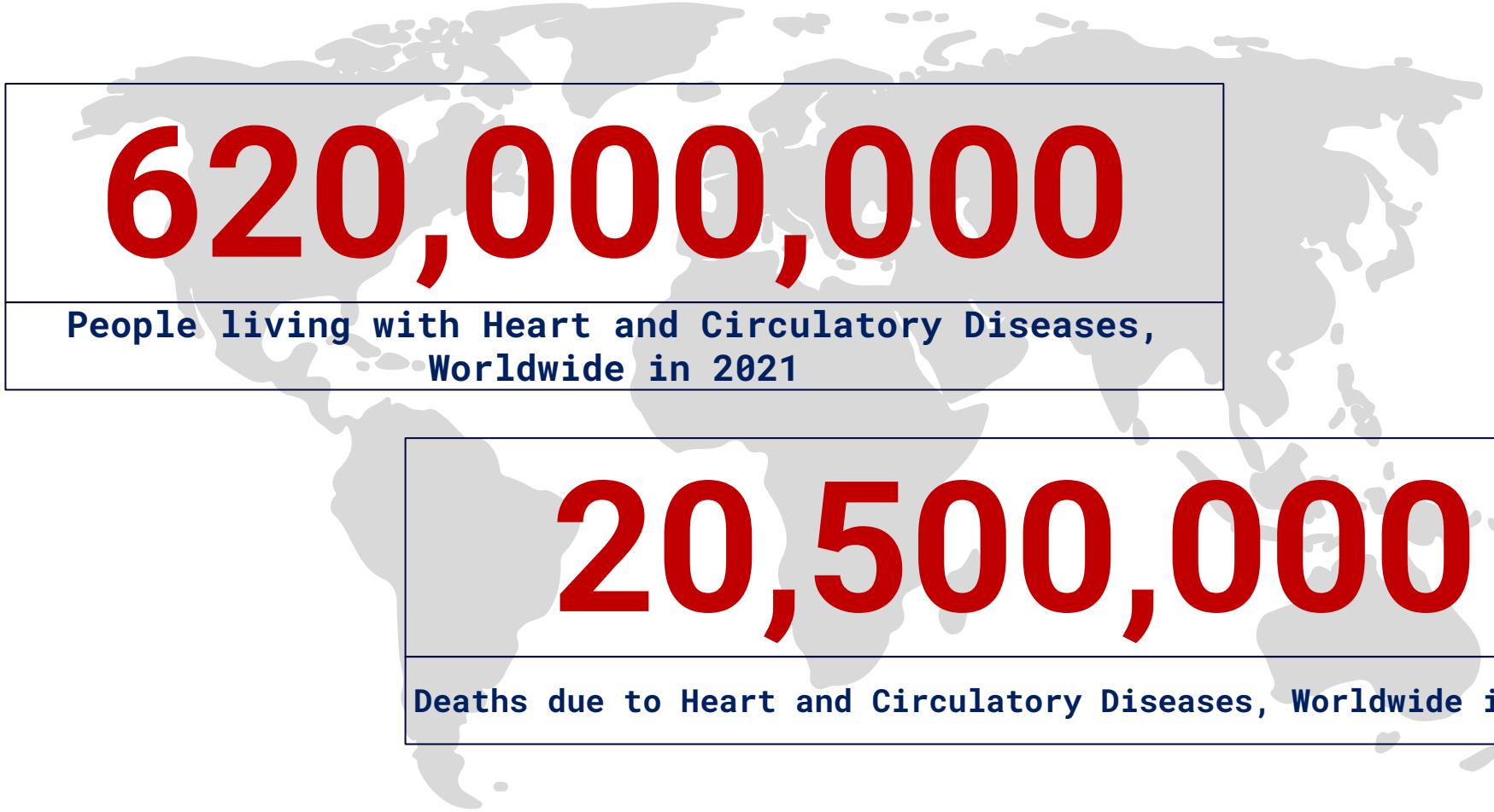
Introduction

Epidemiology & Definition



620,000,000

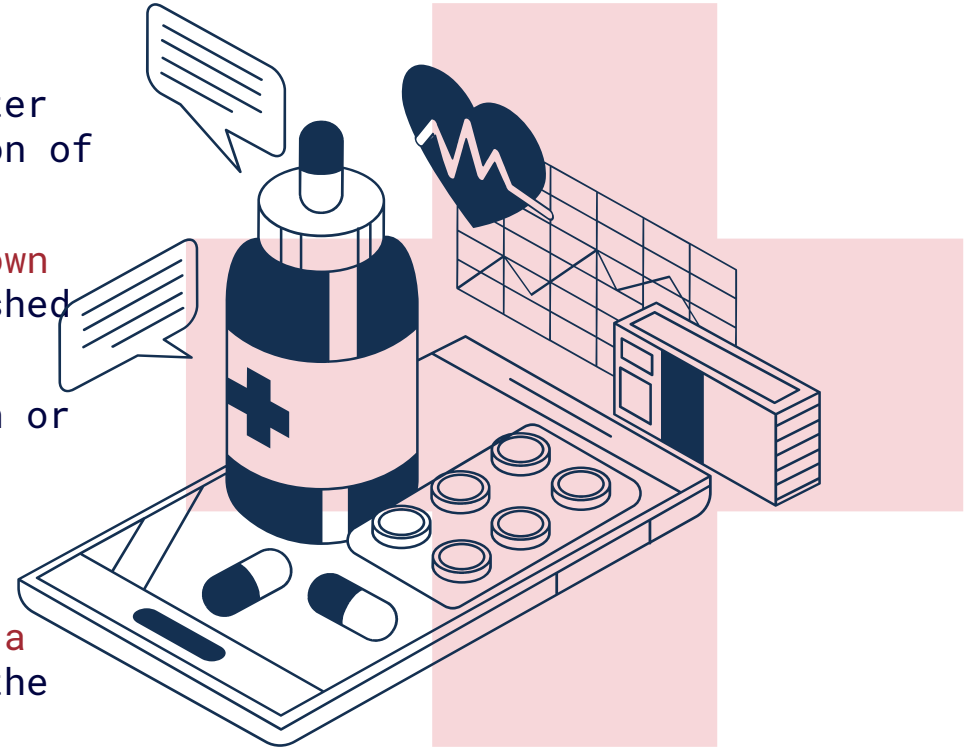
People living with Heart and Circulatory Diseases, Worldwide in 2021

20,500,000

Deaths due to Heart and Circulatory Diseases, Worldwide in 2021

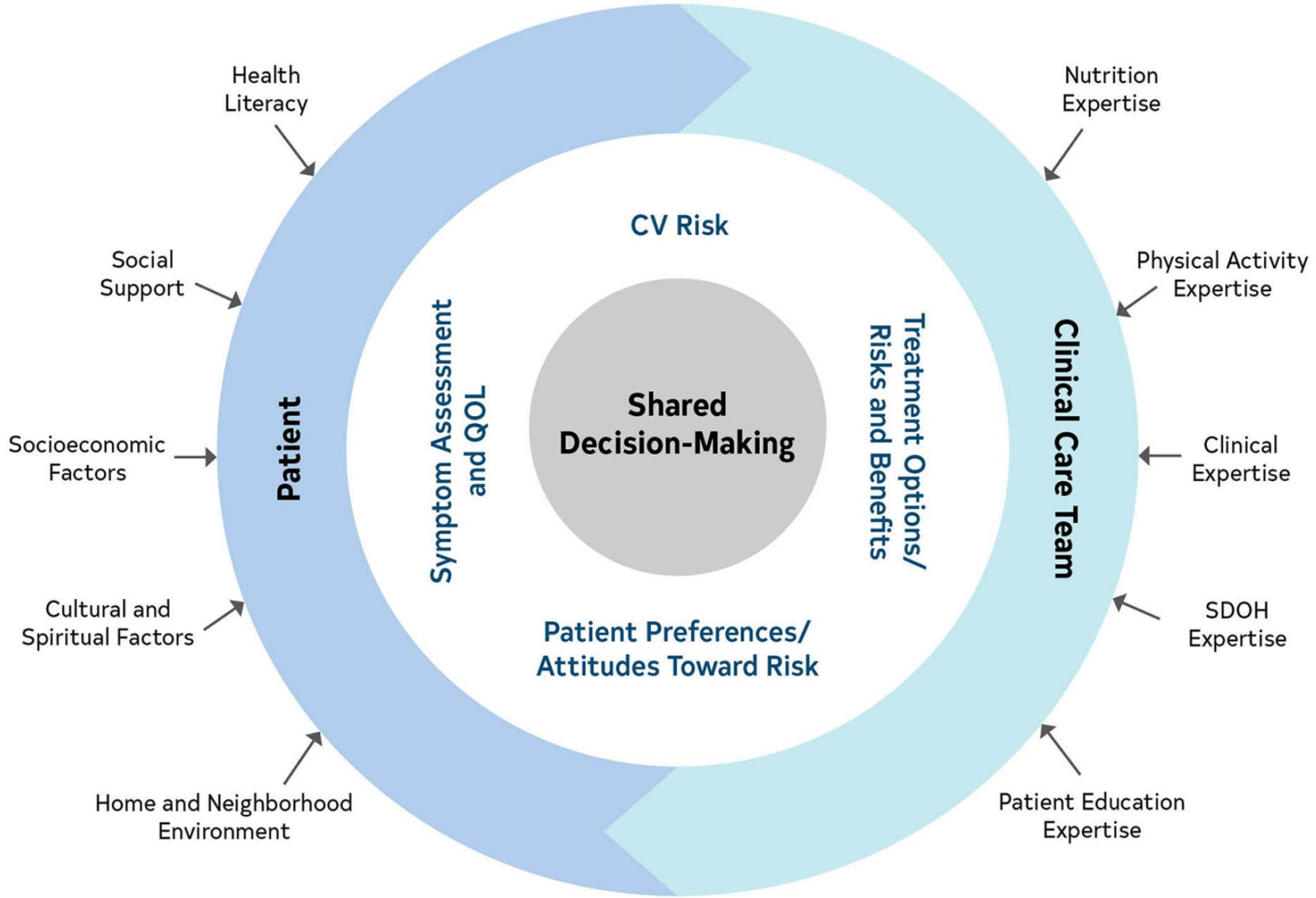
CCD DEFINITION

- Patients discharged after admission for an ACS event or after coronary revascularization procedure and after stabilization of all acute cardiovascular issues.
- Patients with left ventricular systolic dysfunction and known or suspected coronary artery disease or those with established cardiomyopathy deemed to be of ischemic origin.
- Patients with stable angina symptoms medically managed with or without positive results of an imaging test.
- Patients with angina symptoms and evidence of coronary vasospasm or microvascular angina.
- Patients diagnosed with CCD based solely on the results of a screening study and the treating clinician concludes that the patient has coronary disease.



Emphasis is on **team-based**, **patient centered** care that considers **social determinants of health** along with associated costs while incorporating **shared decision-making** in risk assessment, testing, and treatment.

Domains to Consider When Seeing a Patient With CCD



02

Evaluation, Diagnosis, & Risk Stratification

Diagnostic Evaluation for Risk Management

2023 AHA Diagnostic Evaluation

In patients with CCD, if there is an opportunity to do so, clinicians should **first intensify GDMT** and defer testing. In patients with CCD, assessing the severity of ischemia may be useful to guide clinical **decision-making** regarding the use of **ICA** and for intensification of preventive and anti-ischemic therapy.

ICA: **invasive coronary angiography**

GDMT: **guideline-directed management and therapy**

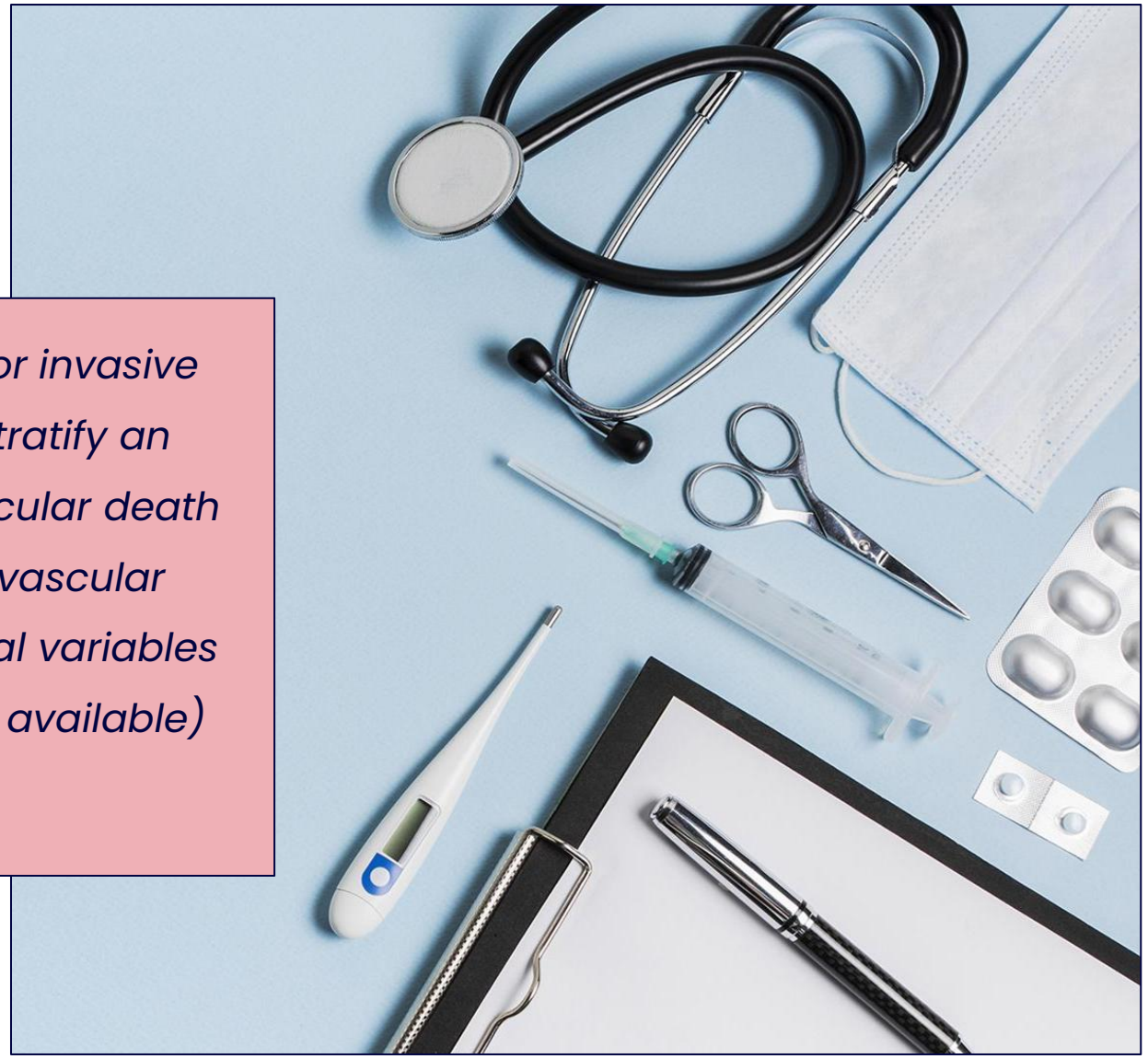
2023 AHA Guideline for Diagnostic Evaluation

Recommendations for Diagnostic Evaluation
Referenced studies that support the recommendations are summarized in the Online Data Supplement.

COR	LOE	RECOMMENDATIONS
1	B-NR	1. In patients with CCD and a change in symptoms or functional capacity that persists despite GDMT, stress positron emission tomography/single photon emission CT myocardial perfusion imaging (PET/SPECT MPI), cardiovascular magnetic resonance (CMR) imaging, or stress echocardiography is recommended to detect the presence and extent of myocardial ischemia, estimate risk of major adverse cardiovascular events (MACE), and guide therapeutic decision-making.*[1-23]
1	B-R	2. In patients with CCD and a change in symptoms or functional capacity that persists despite GDMT, invasive coronary angiography (ICA) is recommended for guiding therapeutic decision-making with the goal of improving anginal symptoms.*[24-28]
2a	B-R	3. In patients with CCD and a change in symptoms or functional capacity that persists despite GDMT, when selected for rest/stress nuclear MPI, PET is reasonable in preference to SPECT, if available, to improve diagnostic accuracy and decrease the rate of nondiagnostic test results.*[29]
2a	B-NR	4. In patients with CCD and a change in symptoms or functional capacity that persists despite GDMT, exercise treadmill testing can be useful to determine whether the symptoms are consistent with angina pectoris, assess the severity of symptoms, evaluate functional capacity, and guide management.*[26,30-32]
2a	B-NR	5. In patients with CCD undergoing stress PET MPI or stress CMR imaging, the addition of myocardial blood flow reserve (MBFR) can be useful to improve diagnostic accuracy and enhance risk stratification.*[18-23]
2a	B-NR	6. In patients with CCD and a change in symptoms or functional capacity that persists despite GDMT, and who have had previous coronary revascularization, coronary CT angiography (CCTA) is reasonable to evaluate bypass graft or stent patency (for stents ≥3 mm).*[33-37]

*Modified from the 2021 AHA/ACC/Multisociety Guideline for the Evaluation and Diagnosis of Chest Pain.[38]

Risk Stratification



*In patients with CCD, the results of non-invasive or invasive testing **alone** are **insufficient** to accurately risk stratify an individual's annual future risk of future cardiovascular death or nonfatal MI. Clinicians should **integrate** cardiovascular test results with demographic, social, and medical variables and use **validated** risk prediction models (where available) to estimate the annual cardiovascular risk.*

The ultimate goals for treatment of CCD are to **prolong survival** and **improve QOL**. To do this, treatments should target a reduction in cardiac death, nonfatal ischemic events, progression of atherosclerosis, & symptoms & functional limitations of CCD while engaging patients in shared **decision-making** considering their preferences, potential complications of procedures/ medications, and costs to the health
care system.

2023 AHA Guideline for Risk Stratification

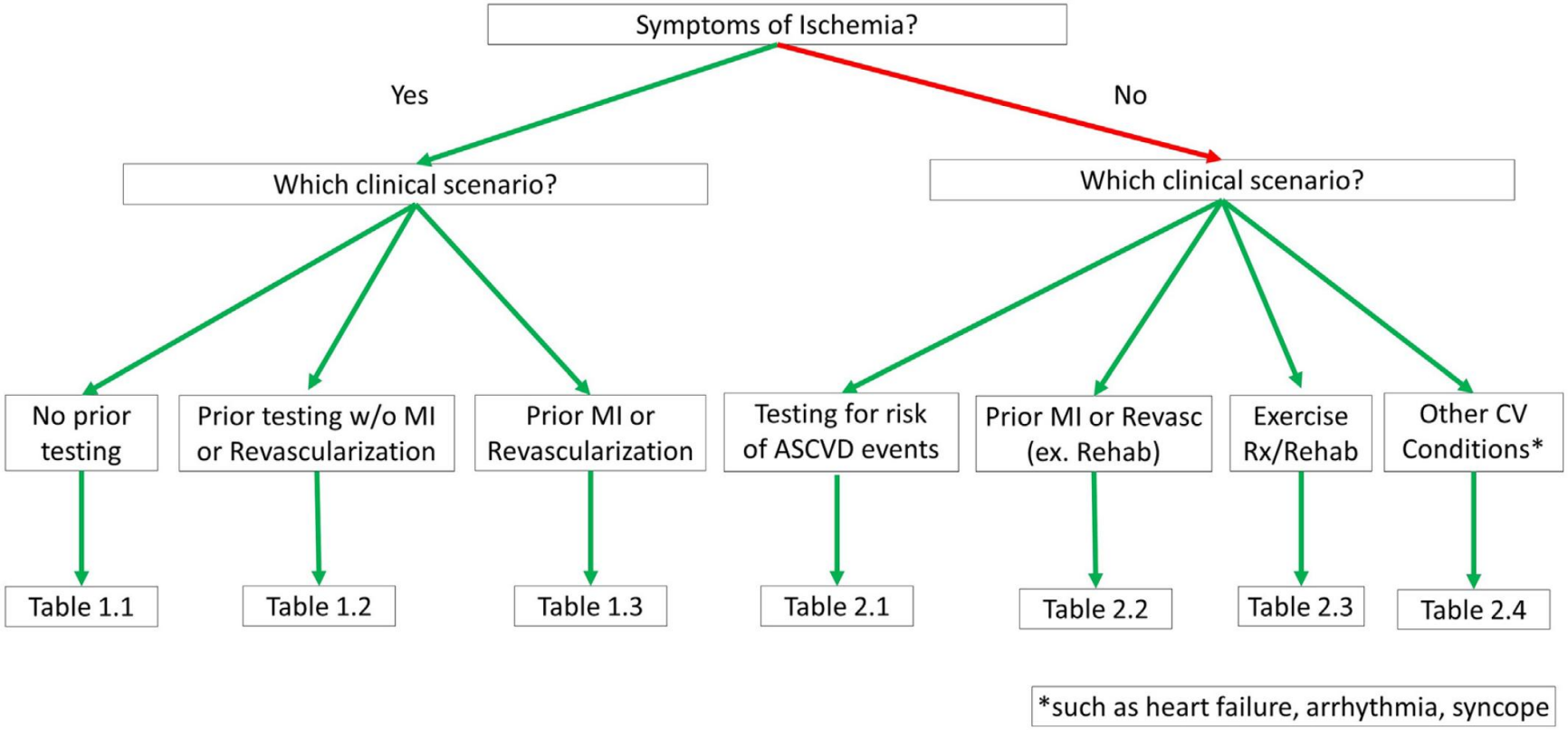
Recommendations for Risk Stratification and Relationship to Treatment Selection
Referenced studies that support the recommendations are summarized in the Online Data Supplement.

COR	LOE	RECOMMENDATIONS
		Risk Stratification and Prognosis
1	B-NR	1. In patients with CCD, it is recommended that risk stratification incorporate all available information, including noninvasive, invasive, or both cardiovascular diagnostic testing results or use validated risk scores to classify patients as low (<1%), intermediate (1%-3%), or high (>3%) yearly risk for cardiovascular death or nonfatal MI.[1-4]
		Relationship to Treatment
1	A	2. In patients with CCD, optimization of GDMT is recommended to reduce MACE.*[5-7]
1	A	3. In patients with CCD with newly reduced LV systolic function, clinical heart failure, or both, ICA is recommended to assess coronary anatomy and guide potential revascularization.[8,9]
3: No benefit	A	4. In patients with CCD, ICA for risk stratification is not routinely recommended in patients without LV systolic dysfunction, heart failure, stable chest pain refractory to GDMT, and/or noninvasive testing suggestive of significant (>50%) left main disease.[5-7,10,11]

*Modified from the 2021 AHA/ACC/Multisociety Guideline for the Evaluation and Diagnosis of Chest Pain.[12]

AHA Multimodality Appropriate Use Criteria

for the Detection and Risk Assessment of CCD



Flowchart of appropriateness Tables

Symptomatic with No Prior Testing

TABLE 1.1 Symptomatic Patients With No Known CCD and No Prior Testing

Clinical Scenario Text	ECG Treadmill	Stress Nuclear MPI	Stress Echo	Stress CMR	CAC	CCTA	Cath	No Test
1. ■ Less-likely anginal symptoms with a noncardiac explanation	R (3)	R (2)	R (2)	R (2)	R (3)	R (1)	R (1)	A (8)
2. ■ Less-likely anginal symptoms, age <50 y and 0 or 1 CV risk factor	M (4)	R (3)	R (3)	R (3)	M (4)	R (3)	R (1)	A (7)
3. ■ Less-likely anginal symptoms, age 50 y or above and/or ≥2 CV risk factors	M (6)	M (6)	M (6)	M (5)	M (6)	M (5)	R (2)	M (4)
4. ■ Likely anginal symptoms, age <50 y and 0 or 1 CV risk factor	A (7)	A (7)	A (7)	A (7)	M (6)	A (7)	R (3)	R (3)
5. ■ Likely anginal symptoms, age 50 y or above and/or ≥2 CV risk factors	A (7)	A (8)	A (8)	A (7)	M (5)	A (7)	A (7)	R (1)

CV risk factors: diabetes mellitus, smoking, family history of premature CAD, hypertension, dyslipidemia.

A = Appropriate; CAC = coronary artery calcium; CAD = coronary artery disease; cath = cardiac catheterization; CCD = chronic coronary disease; CCTA = coronary computed tomography angiography; CMR = cardiac magnetic resonance; CV = cardiovascular; ECG = electrocardiogram; echo = echocardiography; M = May Be Appropriate; MPI = myocardial perfusion imaging; R = Rarely Appropriate.

Prior Testing without MI or Revascularization

TABLE 1.2 Symptomatic Patients Without Known CCD and With Prior Testing*

Clinical Scenario Text	ECG Treadmill	Stress Nuclear MPI	Stress Echo	Stress CMR	CAC	CCTA	Cath	No Test
6. ■ Abnormal ECG	M (4)	A (8)	A (8)	A (8)	M (5)	A (8)	M (5)	M (4)
7. ■ Normal ET		M (6)	M (6)	M (6)	M (5)	M (6)	R (3)	M (5)
8. ■ Inconclusive ET		A (8)	A (8)	A (7)	M (5)	A (8)	M (5)	R (3)
9. ■ Abnormal ET		A (8)	A (8)	A (7)	M (4)	A (8)	A (8)	M (5)
10. ■ Normal stress imaging†	R (1)	R (2)	R (2)	R (2)	M (4)	A (7)	M (5)	M (6)
11. ■ Mild ischemia on stress imaging†	R (1)	R (3)	R (3)	R (3)	R (3)	A (7)	M (6)	M (5)
12. ■ Inconclusive stress imaging†	R (1)	M (5)	M (5)	M (5)	M (4)	A (8)	M (6)	R (3)
13. ■ Moderate to severe ischemia on stress imaging†	R (1)	R (1)	R (1)	R (1)	R (2)	A (7)	A (9)	M (4)
14. ■ CCTA with no CAD or up to 49% stenosis (CAD-RADS 0-2)	M (4)	M (5)	M (5)	M (5)	R (1)		R (2)	M (6)
15. ■ CCTA with moderate stenosis 50%-69% (CAD-RADS 3)	M (6)	A (7)	A (7)	A (7)	R (1)		A (7)	M (5)
16. ■ CCTA with severe stenosis ≥70% (CAD-RADS 4-5)	M (5)	M (6)	M (6)	M (6)	R (1)		A (8)	M (5)
17. ■ CCTA inconclusive (CAD-RADS N)	A (7)	A (8)	A (8)	A (8)	R (1)		A (7)	R (3)
18. ■ CAC score = 0 (CAC-DRS 0)	M (5)	M (6)	M (6)	M (6)		M (5)	R (1)	M (5)
19. ■ CAC score 1-99 (CAC-DRS 1)	M (6)	M (5)	M (6)	M (5)		M (5)	R (3)	M (5)
20. ■ CAC score 100-299 (CAC-DRS 2)	A (7)	A (7)	A (7)	A (7)		A (7)	M (5)	M (4)
21. ■ CAC score ≥300 (CAC-DRS 3)	A (7)	A (7)	A (7)	A (7)		M (6)	M (6)	R (3)
22. ■ Invasive coronary angiography with mild or no CAD and/or normal invasive physiological testing‡	R (2)	M (3)	R (2)	M (4)	R (1)	R (1)		A (7)
23. ■ Invasive coronary angiography with intermediate severity and/or invasive physiological testing not done‡	M (5)	A (7)	A (8)	A (7)	R (1)	R (1)		M (4)
24. ■ Invasive coronary angiography with obstructive CAD and/or abnormal invasive physiological testing‡	R (2)	M (4)	M (4)	M (4)	R (1)	R (1)		M (4)

If grayed out, rating not applicable

*Refers to sequential testing being done as part of a continued patient evaluation or application of recent testing results in the reevaluation of a patient

†Stress imaging could be SPECT, PET, echo, or CMR.

‡Refers to diagnostic angiography, not percutaneous coronary intervention

A = Appropriate; ASCVD = atherosclerotic cardiovascular disease; CAC = coronary artery calcium score; CAC-DRS = Coronary Artery Calcium Data and Reporting System; CAD = coronary artery disease; CAD-RADS = Coronary Artery Disease-Reporting and Data System; cath = cardiac catheterization; CCD = chronic coronary disease; CCTA = coronary computed tomography angiography; CMR = cardiac magnetic resonance; CTCA = computed tomography coronary angiography; ECG = electrocardiogram; echo = echocardiography; ET = exercise stress test; M = May Be Appropriate; MPI = myocardial perfusion imaging; PET = positron emission tomography; R = Rarely Appropriate; SPECT = single-photon emission tomography.

Prior MI or Revascularization

TABLE 1.3 Symptomatic Patients With Prior MI or Revascularization

Clinical Scenario Text	ECG Treadmill	Stress Nuclear MPI	Stress Echo	Stress CMR	CAC	CCTA	Cath	No Test
25. ■ Incomplete revascularization	M (4)	A (8)	A (8)	A (7)	R (1)	R (3)	M (6)	M (4)
26. ■ Prior PCI, symptoms similar to prior ischemic episode and/or anginal symptoms	M (5)	A (8)	A (8)	A (8)	R (1)	M (5)	A (7)	M (5)
27. ■ Prior PCI, nonanginal symptoms	M (5)	M (6)	M (6)	M (6)	R (1)	M (5)	R (3)	M (6)
28. ■ Prior CABG, symptoms similar to prior ischemic episode and/or anginal symptoms	M (4)	A (8)	A (8)	A (8)	R (1)	M (6)	A (7)	M (5)
29. ■ Prior CABG, nonanginal symptoms	M (5)	M (6)	M (6)	M (6)	R (1)	M (6)	R (3)	M (5)
30. ■ Prior MI, no revascularization, symptoms similar to prior ischemic episode and/or anginal	M (5)	A (8)	A (8)	A (8)	R (1)	A (7)	A (7)	R (3)
31. ■ Prior MI, no revascularization, nonanginal symptoms	M (5)	M (6)	M (6)	M (6)	R (1)	M (6)	M (5)	M (5)
32. ■ Assessment of myocardial viability	R (1)	A (8)	A (7)	A (8)	R (1)	R (1)	R (1)	
33. ■ Prior to cardiac rehabilitation, coronary disease (no new or worsening symptoms)	A (7)	M (5)	M (5)	M (4)	R (1)	R (2)	R (1)	M (4)

If grayed out, rating not applicable.

A = Appropriate; CABG = coronary artery bypass graft; CAC = coronary artery calcium score; cath = cardiac catheterization; CCTA = coronary computed tomography angiography; CMR = cardiac magnetic resonance; ECG = electrocardiogram; echo = echocardiography; M = May Be Appropriate; MPI = myocardial perfusion imaging; MI = myocardial infarction; PCI = percutaneous coronary intervention; R = Rarely Appropriate.

Testing for Risk of ASCVD Events

TABLE 2.1 Asymptomatic Patients Without Known ASCVD

Clinical Scenario Text	ECG Treadmill	Stress Nuclear MPI	Stress Echo	Stress CMR	CAC	CCTA	Cath	No Test
34. ■ Low ASCVD risk <5%*	R (2)	R (1)	R (1)	R (1)	M (4)	R (1)	R (1)	A (8)
35. ■ Borderline ASCVD risk 5% to 7.5%	M (4)	R (2)	R (2)	R (2)	A (7)	R (2)	R (1)	A (7)
36. ■ Borderline ASCVD risk 5% to 7.5% with risk-enhancing factors†	M (4)	R (3)	R (3)	R (3)	A (7)	R (3)	R (1)	A (7)
37. ■ Intermediate ASCVD risk 7.5% to 20% with or without risk-enhancing factors†	M (5)	R (3)	R (3)	R (3)	A (8)	R (3)	R (1)	M (5)
38. ■ High ASCVD risk >20%	M (5)	M (4)	M (4)	M (4)	M (6)	M (4)	R (2)	M (5)

*Risk calculated using the ASCVD risk estimator.
†See Table C, Risk-Enhancing Factors.

A = Appropriate; ASCVD = atherosclerotic cardiovascular disease; CAC = coronary artery calcium score; cath = cardiac catheterization; CCTA = coronary computed tomography angiography; CMR = cardiac magnetic resonance; ECG = electrocardiogram; echo = echocardiography; M = May Be Appropriate; MPI = myocardial perfusion imaging; R = Rarely Appropriate.

Prior MI or Revascularization

TABLE 2.2 Asymptomatic Patients With Prior Revascularization or MI

	Clinical Scenario Text	ECG Treadmill	Stress Nuclear MPI	Stress Echo	Stress CMR	CAC	CCTA	Cath	No Test
39.	■ Incomplete revascularization	M (5)	M (6)	M (6)	M (6)	R (1)	M (4)	R (2)	M (5)
40.	■ Prior high-risk PCI	M (4)	M (6)	M (5)	M (5)	R (1)	M (4)	R (3)	M (5)
41.	■ <5 y after CABG	R (2)	R (2)	R (2)	R (2)	R (1)	R (3)	R (1)	A (7)
42.	■ >5 y after CABG	M (4)	M (4)	M (4)	M (4)	R (1)	M (4)	R (2)	A (7)
43.	■ <2 y after PCI	R (2)	R (2)	R (2)	R (2)	R (1)	R (2)	R (1)	A (7)
44.	■ >2 y after PCI	M (5)	M (5)	M (5)	M (5)	R (1)	M (4)	R (1)	A (7)
45.	■ Patients at high risk for or with a history of silent ischemia*	M (4)	A (7)	A (7)	A (7)	R (1)	M (5)	R (3)	M (5)
46.	■ Assessment of myocardial viability	R (1)	A (7)	M (6)	A (7)	R (1)	R (1)	R (1)	
47.	■ Isolated evaluation of bypass graft patency	R (3)	M (5)	M (5)	M (5)	R (1)	A (7)	R (3)	M (6)

If grayed out, rating not applicable.

*Diabetes mellitus with accelerated progression of CAD, chronic kidney disease, peripheral artery disease, prior brachytherapy, in-stent restenosis, saphenous vein graft intervention.[43]

A = Appropriate; CABG = coronary artery bypass graft; CAC = coronary artery calcium score; cath = cardiac catheterization; CCTA = coronary computed tomography angiography; CMR = cardiac magnetic resonance; ECG = electrocardiogram; echo = echocardiography; M = May Be Appropriate; MI = myocardial infarction; MPI = myocardial perfusion imaging; PCI = percutaneous coronary intervention; R = Rarely Appropriate.

Exercise Program or Cardiac Rehabilitation

TABLE 2.3 Asymptomatic Patients Undergoing Assessment of an Exercise Program or Cardiac Rehabilitation

	Clinical Scenario Text	Exercise ECG	Stress Nuclear MPI	Stress Echo	Stress CMR	CAC	CCTA	Cath	No Test
48.	■ Prior to initiation of an unsupervised exercise program, without known CCD	M (6)	R (3)	R (3)	R (3)	R (3)	R (1)	R (1)	A (7)
49.	■ Prior to initiation of an unsupervised exercise program, with known CCD	A (7)	M (5)	M (5)	M (4)	R (1)	R (2)	R (1)	M (4)
50.	■ Prior to cardiac rehabilitation	A (7)	M (4)	M (4)	M (4)	R (1)	R (2)	R (1)	M (5)

A = Appropriate; CAC = coronary artery calcium score; cath = cardiac catheterization; CCD = chronic coronary disease; CCTA = coronary computed tomography angiography; CMR = cardiac magnetic resonance; ECG = electrocardiogram; echo = echocardiography; HFpEF= heart failure with preserved ejection fraction; HFrEF = heart failure with reduced ejection fraction; M = May Be Appropriate; MI = myocardial infarction; MPI = myocardial perfusion imaging; R = Rarely Appropriate.

Other Conditions

TABLE 2.4 Other Cardiovascular Conditions in Patients Without Symptoms of Ischemia

Clinical Scenario Text	ECG Treadmill	Stress Nuclear MPI	Stress Echo	Stress CMR	CAC	CCTA	Cath	No Test
Newly-Diagnosed Heart Failure (Resting LV Function Previously Assessed but No Prior CAD Evaluation)								
51. ■ Newly diagnosed HFpEF	M (4)	A (7)	A (8)	A (7)	R (3)	A (7)	M (6)	R (3)
52. ■ Newly diagnosed HFrEF	M (4)	A (7)	A (8)	A (8)	R (2)	A (7)	A (8)	R (1)
53. ■ Screening for transplant vasculopathy	R (3)	A (7)	A (7)	A (7)	R (1)	A (7)	A (8)	
Evaluation of Arrhythmias Without Ischemic Equivalent (No Prior Cardiac Evaluation)								
54. ■ Infrequent PVCs	M (4)	R (2)	R (2)	R (2)	R (2)	R (1)	R (1)	A (8)
55. ■ Frequent PVCs or nonsustained VT	A (7)	A (7)	A (7)	A (7)	R (3)	M (6)	M (5)	M (4)
56. ■ Paroxysmal supraventricular tachycardia	M (5)	R (2)	R (3)	R (3)	R (1)	R (2)	R (1)	M (5)
57. ■ New-onset atrial fibrillation/flutter	M (5)	R (3)	R (3)	R (3)	R (2)	R (3)	R (1)	M (5)
58. ■ Prior to initiation of antiarrhythmic therapy in patients with high global CAD risk	M (6)	A (7)	A (7)	A (7)	R (3)	A (7)	R (3)	R (3)
59. ■ Exercise-induced VT	A (7)	A (7)	A (8)	A (7)	R (2)	A (7)	A (7)	R (1)
60. ■ Sustained VT	A (7)	A (7)	A (7)	A (7)	R (2)	A (7)	A (7)	R (1)
61. ■ Ventricular fibrillation	M (4)	A (7)	A (7)	A (7)	R (1)	A (7)	A (8)	R (1)
Syncope Without Ischemic Equivalent								
62. ■ Initial evaluation suggests CV abnormalities	A (7)	A (7)	A (7)	A (7)	R (3)	M (6)	M (5)	R (3)
63. ■ Initial evaluation suggests other etiology	M (4)	R (3)	M (4)	R (3)	R (2)	R (2)	R (1)	M (6)
Cardio-oncology								
64. ■ Prior chest radiation, no symptoms, >5 y ago	M (4)	M (4)	M (6)	M (5)	M (6)	M (6)	R (2)	M (5)

If grayed out, rating not applicable

A = Appropriate; CAC = coronary artery calcium score; CAD = coronary artery disease; cath = cardiac catheterization; CCTA = coronary computed tomography angiography; CMR = cardiac magnetic resonance; CV = cardiovascular; ECG = electrocardiogram; echo = echocardiography; HFpEF= heart failure with preserved ejection fraction; HFrEF = heart failure with reduced ejection fraction; M = May Be Appropriate; MPI = myocardial perfusion imaging; PVC = premature ventricular contraction; R = Rarely Appropriate; VT = ventricular tachycardia.

03

Treatment

CCD Management & Treatment

2023 AHA Guideline for Lipid Management

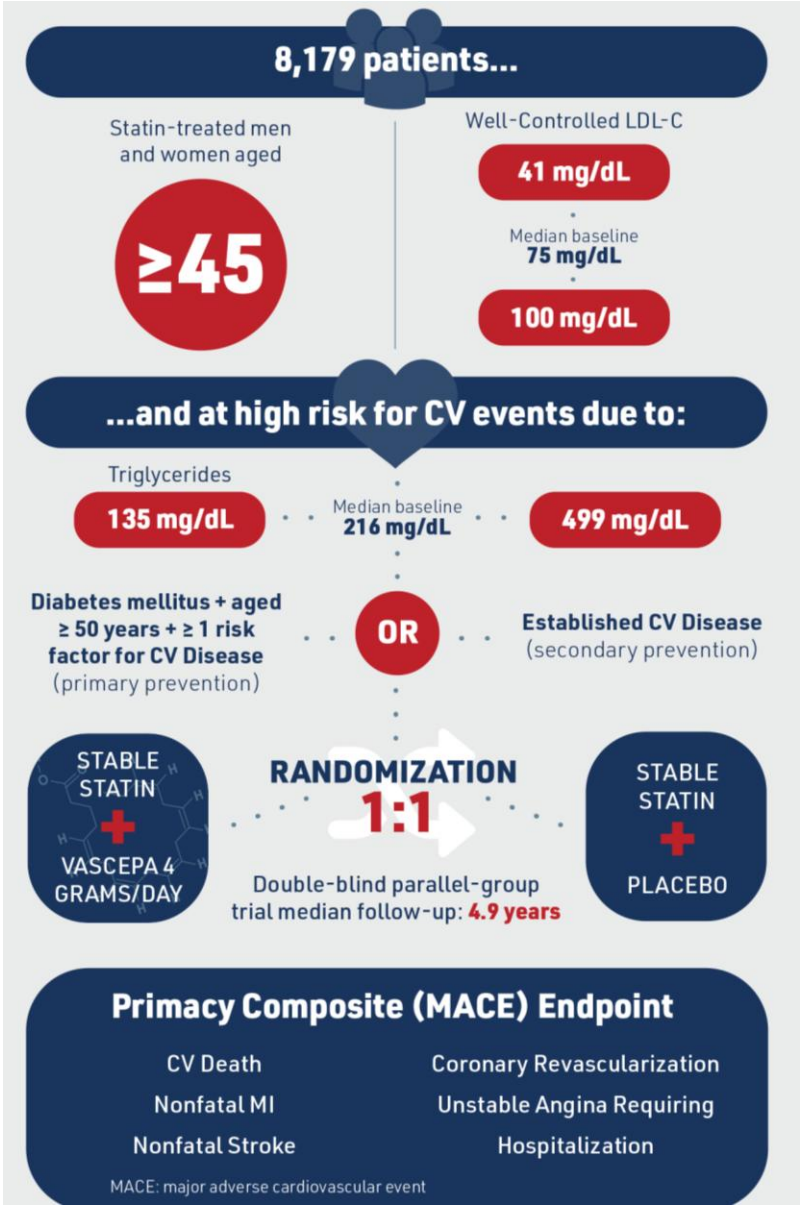
COR	LOE	RECOMMENDATIONS
1	A	1. In patients with CCD, high-intensity statin therapy is recommended with the aim of achieving a ≥50% reduction in LDL-C levels to reduce the risk of MACE.*[1-3]
1	A	2. In patients in whom high-intensity statin therapy is contraindicated or not tolerated, moderate-intensity statin therapy is recommended with the aim of achieving a 30% to 49% reduction in LDL-C levels to reduce the risk of MACE.*[2,4-8]
1	A	3. In patients with CCD, adherence to changes in lifestyle and effects of lipid-lowering medication should be assessed by measurement of fasting lipids in 4 to 12 weeks after statin initiation or dose adjustment and then every 3 to 12 months thereafter based on need to assess response or adherence to therapy.*[2,9-11]
Cost Value Statement: High Value	B-NR	4. In patients with CCD, the use of generic formulations of maximally tolerated statin therapy is projected to be cost saving.[12,13]
2a	B-R	5. In patients with CCD who are judged to be at very high risk (Table 10) and on maximally tolerated statin therapy with an LDL-C level ≥70 mg/dL (≥1.8 mmol/L), ezetimibe can be beneficial to further reduce the risk of MACE.*[14-19]
Cost Value Statement: High Value	B-NR	6. In patients with CCD, addition of generic ezetimibe to maximally tolerated statin therapy in appropriately selected patients is projected to be of high economic value at US prices.[12,20,21]
2a	A	7. In patients with CCD who are judged to be at very high risk (Table 10) and who have an LDL-C level ≥70 mg/dL (≥1.8 mmol/L), or a non-high-density lipoprotein cholesterol (HDL-C) level ≥100 mg/dL (≥2.6 mmol/L), on maximally tolerated statin and ezetimibe, a PCSK9 monoclonal antibody can be beneficial to further reduce the risk of MACE.*[22-29]
Cost Value Statement: Uncertain	B-NR	8. In patients with CCD who are very high risk, the use of PCSK9 monoclonal antibodies is projected to be of uncertain economic value at US prices[12,20,21,30,31]
2b	B-R	9. In patients with CCD on maximally tolerated statin therapy with an LDL-C level <100 mg/dL (<2.6 mmol/L) and a persistent fasting triglyceride level of 150 to 499 mg/dL (1.7–5.6 mmol/L) after addressing secondary causes, icosapent ethyl may be considered to further reduce the risk of MACE and cardiovascular death.[32]
2b	B-R	10. In patients with CCD who are not at very high risk and on maximally tolerated statin therapy with an LDL-C level ≥70 mg/dL (≥1.8 mmol/L), it may be reasonable to add ezetimibe to further reduce the risk of MACE.*[14,15,18,19]

Lipid Management

REDUCE-IT trial randomized patients with established ASCVD or diabetes plus additional risk factors, triglyceride levels between **150 mg/dL and 499 mg/dL**, and an LDL-C level of <100 mg/dL on background statin therapy to either **4 g/day of icosapent ethyl** (purified EPA only) or mineral oil placebo.

25%
Decrease in MACE.

20%
Decrease in CV death.



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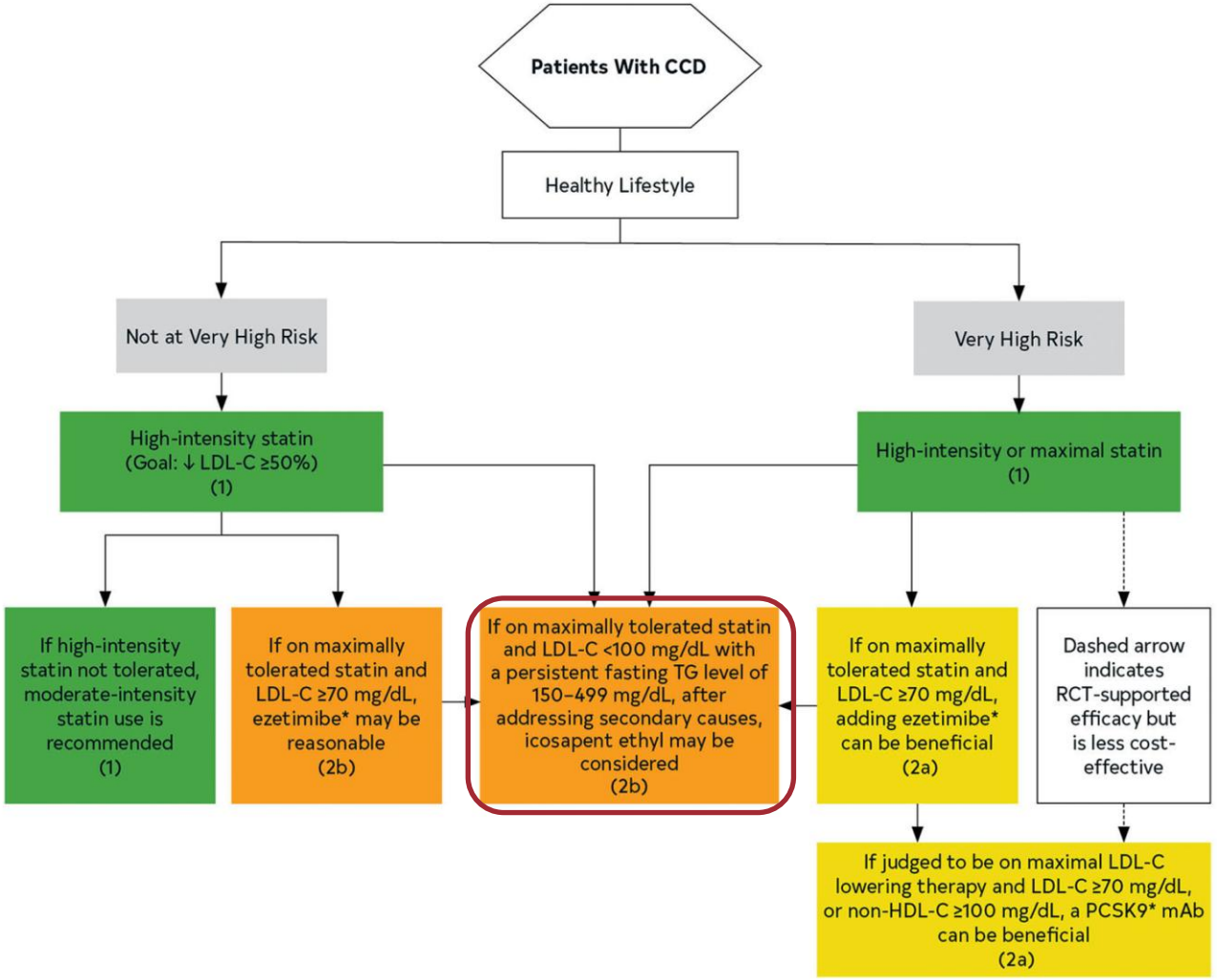

2023 AHA Guideline for Lipid Management

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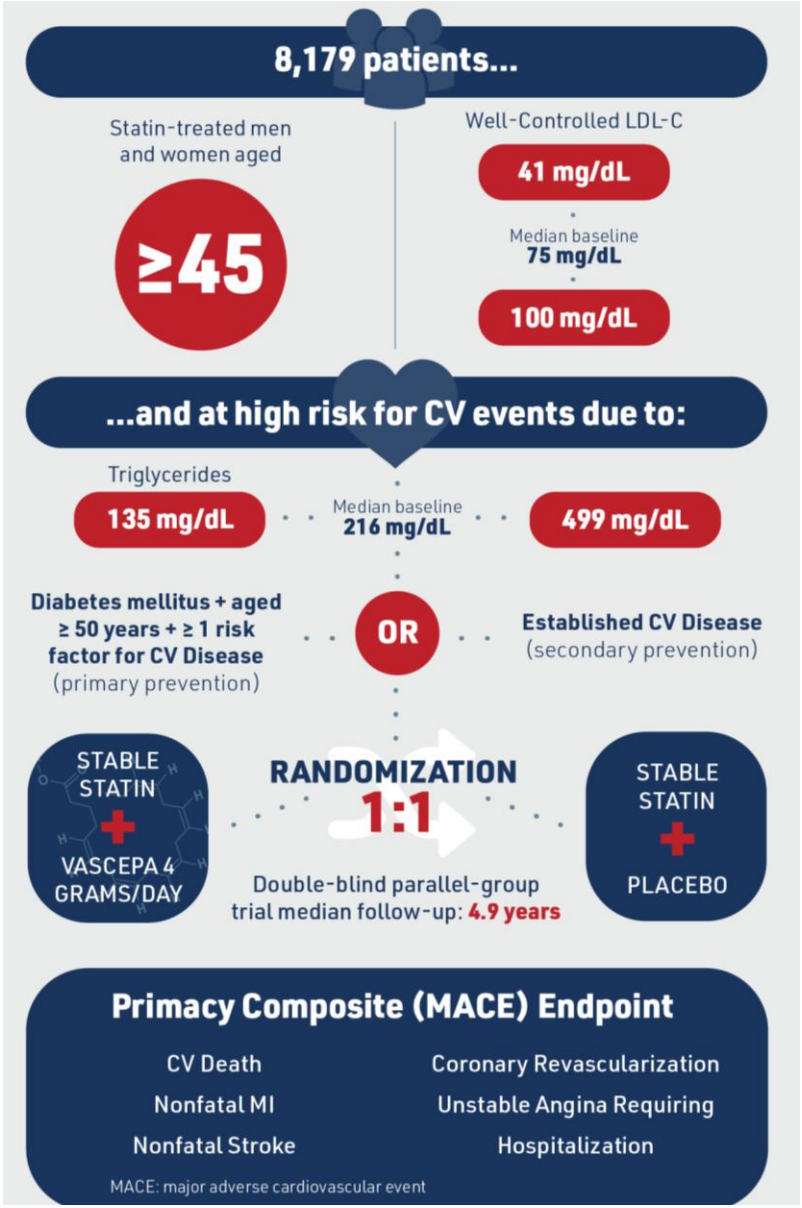
1	A	1. In patients with CCD, high-intensity statin therapy is recommended with the aim of achieving a ≥50% reduction in LDL-C levels to reduce the risk of MACE.*[1-3]
1	A	2. In patients in whom high-intensity statin therapy is contraindicated or not tolerated, moderate-intensity statin therapy is recommended with the aim of achieving a 30% to 49% reduction in LDL-C levels to reduce the risk of MACE.*[2,4-8]
1	A	3. In patients with CCD, adherence to changes in lifestyle and effects of lipid-lowering medication should be assessed by measurement of fasting lipids in 4 to 12 weeks after statin initiation or dose adjustment and then every 3 to 12 months thereafter based on need to assess response or adherence to therapy.*[2,9-11]
Cost Value Statement: High Value	B-NR	4. In patients with CCD, the use of generic formulations of maximally tolerated statin therapy is projected to be cost saving.[12,13]
2a	B-R	5. In patients with CCD who are judged to be at very high risk (Table 10) and on maximally tolerated statin therapy with an LDL-C level ≥70 mg/dL (≥1.8 mmol/L), ezetimibe can be beneficial to further reduce the risk of MACE.*[14-19]
Cost Value Statement: High Value	B-NR	6. In patients with CCD, addition of generic ezetimibe to maximally tolerated statin therapy in appropriately selected patients is projected to be of high economic value at US prices.[12,20,21]
2a	A	7. In patients with CCD who are judged to be at very high risk (Table 10) and who have an LDL-C level ≥70 mg/dL (≥1.8 mmol/L), or a non-high-density lipoprotein cholesterol (HDL-C) level ≥100 mg/dL (≥2.6 mmol/L), on maximally tolerated statin and ezetimibe, a PCSK9 monoclonal antibody can be beneficial to further reduce the risk of MACE.*[22-29]
Cost Value Statement: Uncertain	B-NR	8. In patients with CCD who are very high risk, the use of PCSK9 monoclonal antibodies is projected to be of uncertain economic value at US prices[12,20,21,30,31]
2b	B-R	9. In patients with CCD on maximally tolerated statin therapy with an LDL-C level <100 mg/dL (<2.6 mmol/L) and a persistent fasting triglyceride level of 150 to 499 mg/dL (1.7–5.6 mmol/L) after addressing secondary causes, icosapent ethyl may be considered to further reduce the risk of MACE and cardiovascular death.[32]
2b	B-R	10. In patients with CCD who are not at very high risk and on maximally tolerated statin therapy with an LDL-C level ≥70 mg/dL (≥1.8 mmol/L), it may be reasonable to add ezetimibe to further reduce the risk of MACE.*[14,15,18,19]

Lipid Management

REDUCE-IT trial randomized patients with established ASCVD or diabetes plus additional risk factors, triglyceride levels between **150 mg/dL and 499 mg/dL**, and an LDL-C level of <100 mg/dL on background statin therapy to either **4 g/day of icosapent ethyl** (purified EPA only) or mineral oil placebo.

25%
Decrease in MACE.

20%
Decrease in CV death.



Dietary supplements containing omega-3 fatty acids (ie, fish oil) are widely used for presumed cardioprotective benefits. However, low-dose omega-3 fatty acid supplementation does not reduce MACE in patients with CCD.

The only omega-3 fatty acid formulation that can be recommended in patients with CCD is icosapent ethyl (EPA only).

2023 AHA Guideline for SGLT2i Indications

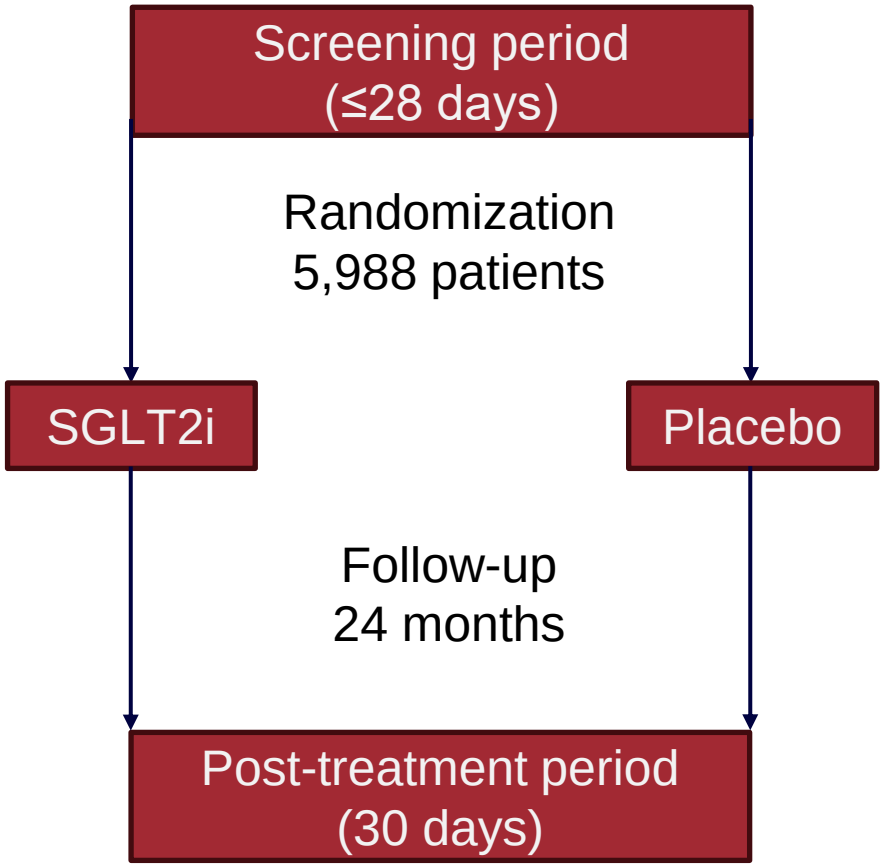
Recommendations for Use of SGLT2 Inhibitors and GLP-1 Receptor Agonists
Referenced studies that support the recommendations are summarized in the Online Data Supplement.

COR	LOE	RECOMMENDATIONS
1	A	1. In patients with CCD who have type 2 diabetes, the use of either an SGLT2 inhibitor[1-8] or a GLP-1 receptor agonist[9-17] with proven cardiovascular benefit is recommended to reduce the risk of MACE.
Cost Value Statement: High Value	B-NR	2. In patients with CCD and type 2 diabetes, addition of a GLP-1 receptor agonist at US prices is projected to be of high value compared with standard of care.[18]
Cost Value Statement: Intermediate Value	B-NR	3. In patients with CCD and type 2 diabetes, addition of an SGLT2 inhibitor at US prices is projected to be of intermediate value compared with standard of care.[18]
1	A	4. In patients with CCD and heart failure with LVEF ≤40%, use of an SGLT2 inhibitor is recommended to reduce the risk of cardiovascular death and heart failure hospitalization[19-22] and to improve QOL,[23,24] irrespective of diabetes status.*
Cost Value Statement: Intermediate Value	B-NR	5. In patients with CCD and heart failure with LVEF ≤40%, addition of an SGLT2 inhibitor to GDMT, irrespective of diabetes status, is projected to be of intermediate value at US prices.[25,26]
2a	B-R	6. In patients with CCD and heart failure with LVEF >40%, use of an SGLT2 inhibitor can be beneficial in decreasing heart failure hospitalizations[27,28] and to improve QOL,[4,29] irrespective of diabetes status.
Cost Value Statement: Intermediate Value	B-NR	7. In patients with CCD and heart failure with LVEF >40%, addition of an SGLT2 inhibitor to GDMT, irrespective of diabetes status, is projected to be of uncertain value at US prices.[30]

*Modified from the 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure.[31]

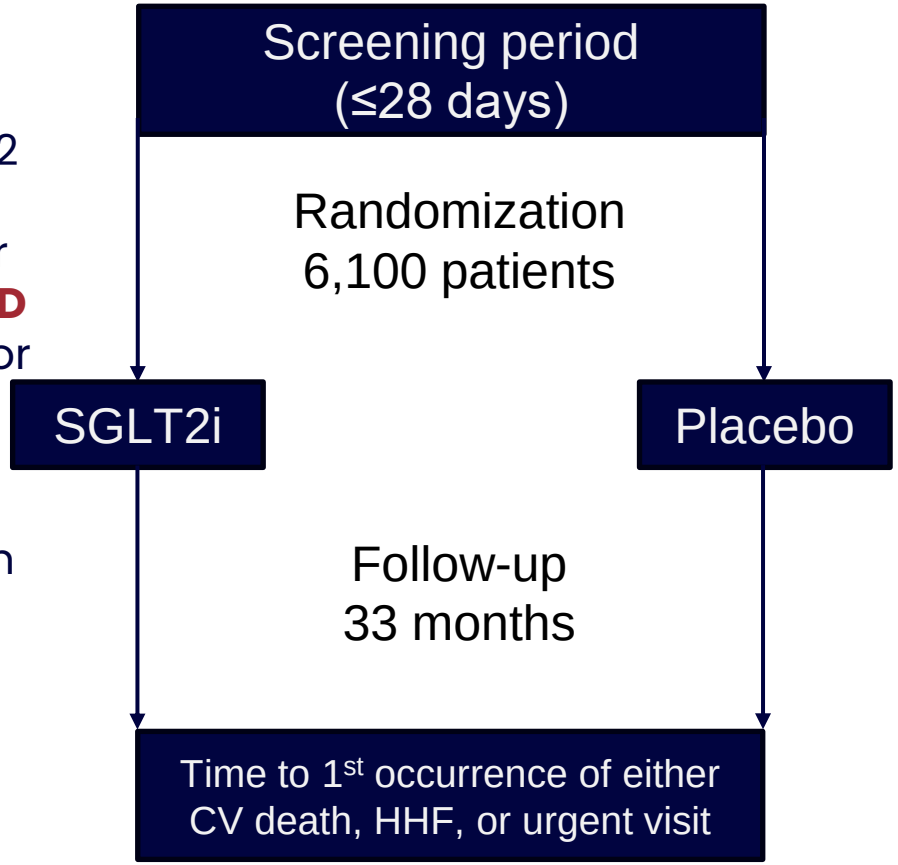
In patients with CCD and type 2 diabetes, **SGLT2 inhibitors** significantly reduce the risk of MACE, with additional benefits in terms of weight loss and progression of kidney disease.

SGLT2i in CCD



EMPEROR-PRESERVED Trial

Among patients with HF with preserved ejection fraction, SGLT2 inhibitors reduced the risk of HF hospitalization or cardiovascular death in the **EMPEROR-PRESERVED** trial and the risk of worsening HF or cardiovascular death in the **DELIVER** trial with the primary endpoints driven by significant reductions in HF hospitalization in both trials.



DELIVER Trial

2023 AHA Guideline for SGLT2i Indications

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*Modified from the 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure.[31]

Medical Therapy for Relief of Angina

Recommendations for Medical Therapy for Relief of Angina
Referenced studies that support the recommendations are summarized in the Online Data Supplement.

COR	LOE	RECOMMENDATIONS
1	B-R	1. In patients with CCD and angina, antianginal therapy with either a beta blocker, CCB, or long-acting nitrate is recommended for relief of angina or equivalent symptoms.*[1-3]
1	B-R	2. In patients with CCD and angina who remain symptomatic after initial treatment, addition of a second antianginal agent from a different therapeutic class (beta blockers, CCB, long-acting nitrates) is recommended for relief of angina or equivalent symptoms.*[3-6]
1	B-R	3. In patients with CCD, ranolazine is recommended in patients who remain symptomatic despite treatment with beta blockers, CCB, or long-acting nitrate therapies.*[7,8]
1	B-NR	4. In patients with CCD, sublingual nitroglycerin or nitroglycerin spray is recommended for immediate short-term relief of angina or equivalent symptoms.*[9,10]
3: Harm	B-R	5. In patients with CCD and normal LV function, the addition of ivabradine to standard anti-anginal therapy is potentially harmful.*[11]

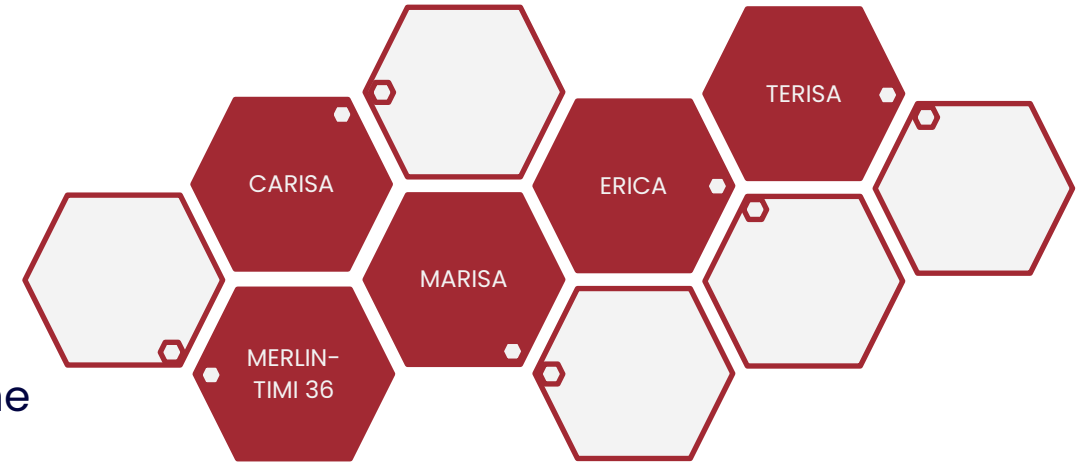
*Modified from the 2012 ACC/AHA Multisociety Guideline for the Diagnosis and Management of Patients With SIHD.[12]

Ranolazine in CCD

Two randomized, placebo-controlled studies showed that the addition of ranolazine on the background of standard anti-anginal therapy improved anginal outcomes.

In the **CARISA trial**, 823 patients with CCD were randomized to placebo or 1 of 2 doses of ranolazine. After 12 weeks of therapy, **ranolazine improved exercise capacity and more effectively relieved angina compared with placebo**.

In the **ERICA trial**, 565 patients with CCD and persistent symptoms despite a maximally tolerated dose of amlodipine were randomized to ranolazine or placebo. After 6 weeks, patients randomized to ranolazine **had significantly fewer anginal episodes and less nitroglycerin consumption**.



Medical Therapy for Relief of Angina

Recommendations for Medical Therapy for Relief of Angina
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COR	LOE	RECOMMENDATIONS
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*Modified from the 2012 ACC/AHA Multisociety Guideline for the Diagnosis and Management of Patients With SIHD.[12]

THANKS