Preamble:

The International CARDIO Alliance to Improve Disease Outcomes (iCARDIO Alliance: https://icardioalliance.org) aims to bring together leading cardiovascular societies around the globe as partner organizations to improve the quality of cardiovascular care, from prevention and diagnosis to treatment and follow-up. The goal of these global implementation guidelines is to achieve global representation on writing panels and to produce concise and practical guidelines applicable to all cardiovascular care worldwide.(1) In addition to clinical practice guidelines developed by other medical associations, the recommendations by iCARDIO Alliance take into account resource availability on at least 3 economic levels (with no economic consideration; resources somewhat limited; resources severely limited). They are written by a team including world-renowned experts with a maximum of 50% of the writing task force representing Europe and North America and 50% or more from the rest of the world. The peer review team is also made up of global experts further enriching these documents and leading to a final phase of public review open to all. Furthermore, we implement a public review process for all our guideline documents. In this way, the viewpoints of many persons with lived experience are embedded within this global implementation guideline process. All guideline documents are published in several journals and open access. Through this innovative approach iCARDIO Alliance hopes to enhance guideline dissemination and implementation on a global scale.

The public review phase the iCARDIO Global Implementation Guidelines on Ischemic Heart Disease Management 2026 right now and will last until February 28, 2026. All comments must be submitted via the dedicated comment form which can be downloaded from the Global Cardiology website as well as from the iCARDIO Alliance website (Home - iCARDIO Alliance). Please use page, line, and/or table and recommendation numbers for reference in your commentaries as appropriate. Comments received will be taken into consideration, but will not be published. Anonymous comments will be disregarded.

The deadline for receiving comments is February 28, 2026.
To submit your comments please use the comment form and send it to: public.review@icardio.org

Draft Document for Public Consultation:

iCARDIO ALLIANCE GLOBAL IMPLEMENTATION GUIDELINES ON ISCHEMIC HEART DISEASE MANAGEMENT 2026

CONCEPTS

Ischemic heart disease (IHD) remains the leading cause of morbidity and mortality worldwide. Coronary artery disease (CAD) encompasses any pathological process capable of compromising myocardial perfusion and although numerous etiologies exist, including vasculitis, spontaneous coronary artery dissection, and coronary embolism, the majority of CAD is attributable to coronary atherosclerosis, which constitutes the focus of this document. For practical purposes, CAD is considered present when any degree of atherosclerotic involvement exceeds zero percent stenosis, recognizing that even minimal coronary atherosclerosis represents a systemic disease process with prognostic implications.

Chronic Ischemic Heart Disease (CIHD) represents the traditional designation for the stable manifestations of coronary atherosclerosis, emphasizing myocardial ischemia resulting from an imbalance between oxygen supply and demand. In 2019, the European Society of Cardiology introduced the concept of Chronic Coronary Syndromes (CCS)(2), while the American Heart Association and American College of Cardiology, in their 2023 guidelines, adopted the term Chronic Coronary Disease (CCD).(3) Despite subtle semantic differences, these terms are largely synonymous, all referring to the chronic, stabilized phases of coronary atherosclerosis as distinct from acute coronary syndromes; throughout this document, we have chosen to use CIHD.

While this document addresses CIHD, a critical question is when the acute phase transitions to the “chronic” phase. The acute coronary syndromes are characterized by plaque rupture or erosion, acute thrombus formation, and dynamic

coronary obstruction, with immediate priorities centered on urgent or emergent reperfusion. The transition to the chronic phase occurs when the acute thrombotic process has resolved and the patient enters a period of relative pathophysiological stability, by convention, at 12 months following an acute coronary syndrome, reflecting the observation that recurrent ischemic event rates plateau after approximately one year. However, the chronic phase is not synonymous with low risk, as the atherosclerotic process continues and previously stable plaques may become vulnerable.

In CIHD, the focus shifts to adequate identification, risk stratification and long-term secondary prevention and, when indicated, coronary revascularization. Among the pillars of secondary prevention, antithrombotic therapy merits particular attention due to its complexity and evolving evidence base. Its selection, intensity, duration, and adaptations represent nuanced clinical decisions that are influenced by the balance between ischemic risk reduction and bleeding risks, concomitant indications, and time passed since the acute event, and sometimes occurs earlier than the conventional 12 months. This document addresses the assessment and management of patients with CIHD, including the diagnosis and risk stratification, pharmacological therapy, revascularization, specific clinical conditions, special populations, and long-term follow-up.

GRADING AND RECOMMENDATIONS

Recommendations are classified based on available evidence and consensus regarding benefit and harm: These categories are intended to guide clinicians globally, with flexibility to apply recommendations according to local resources, clinical judgment, and patient needs. Based on the available evidence and consensus among the committee members regarding the risks and benefits of interventions, the recommendations were classified as Strongly Recommend (SR), Recommend (R), Suggest (Su), and Do Not Do (DND).

Table 1: Grading and Recommendation

No.	DEFINITION	LEVEL OF RECOMMENDATION
1-01	Evidence or consensus that a specific diagnostic test or treatment is effective, beneficial and valuable.	**Strongly Recommend (SR)**
1-02	Majority of evidence or opinions support the benefits or effectiveness.	**Recommend (R)**
1-03	Usefulness or effectiveness is less clearly supported by evidence or opinion.	**Suggest (Su)**
1-04	Evidence or consensus suggests that it is ineffective and, in some cases, may even be harmful.	**Do not do (DND)**

BURDEN OF ISCHEMIC HEART DISEASE

Ischemic heart disease (IHD)—also referred to as coronary artery disease—remains the leading global cause of death and disability. It is responsible for approximately 9 million deaths annually and affects an estimated 126 million people worldwide, accounting for about 1.72% of the global population.(4–6) This translates to a prevalence rate of approximately 1,655 cases per 100,000 people, with trends consistently showing IHD as the dominant non-communicable cause of mortality for over two decades.(4,7,8) IHD has also an important socioeconomic burden.(9) It is associated with an increased risk of disability, and a 1.5-fold greater risk of unemployment.(10) It is currently the leading contributor to disability-adjusted life years (DALYs) worldwide due to non-communicable diseases.(6,8,11) By

2030, global prevalence is projected to exceed 1,845 per 100,000, with forecasts suggesting a rise to 1,917 per 100,000 in certain regions.(5)

This escalation is driven by the rising prevalence of cardiovascular risk factors (12–14), but also due to aging of populations. The United Nations projected that the population over age 65 will increase from 1 in 11 in 2019 to 1 in 6 by 2050(15), substantially increasing the clinical and economic burden on healthcare systems. The financial impact of IHD is both direct and indirect. In high-income countries, healthcare expenditures for IHD approach 1–1.5% of GDP, while in low- and middle-income countries, up to 10% of health budgets are spent on cardiovascular disease care, with devastating consequences for household economics.(9,16) While IHD poses a significant global challenge, its burden varies widely by region. Eastern Europe bears a particularly heavy cardiovascular burden(17), where socioeconomic and healthcare limitations amplify lifestyle-related risk factors. In contrast, some regions in Asia and Africa are seeing evolving patterns marked by underdiagnosis, increasing exposure to risk factors and undertreatment, resulting in an emerging epidemic.(16,18–20)

Also, in IHD, sex disparities remain evident, with men experiencing a higher IHD prevalence (1,786 per 100,000) than women (1,522 per 100,000), though postmenopausal incidence in women rises sharply.(5) Beyond these epidemiological trends, the burden of chronic IHD (CIHD) represents a particularly pressing challenge for healthcare systems. This burden arises from two main sources: the growing population of patients who survive an acute coronary syndrome (ACS) event and subsequently transition into chronic coronary disease (CCD) or chronic coronary syndrome (CCS) stage; and second, those who present de novo with CIHD without a preceding acute event.

ASSESSMENT OF ISCHEMIC HEART DISEASE

The assessment of suspected CIHD involves a comprehensive evaluation of clinical features, biomarkers, electrocardiogram, imaging and invasive approach in selected cases. Proper evaluation allows risk stratification, and directs further investigations, to improve symptoms, quality of life and cardiovascular outcomes.(3,21)

(a) Clinical Presentation

The typical symptom of IHD is chest pain, but only 10% to 25% of patients undergoing functional or anatomical testing in contemporary cohorts, experience classic angina.(22,23) Most individuals present with nonspecific symptoms, such as chest discomfort rather than pain, throat, arm, jaw discomfort, nausea, exertional dyspnea, diaphoresis or fatigue. Classic angina is defined as substernal pressure triggered by exertion or emotional stress that improves with rest or nitroglycerin. Women frequently report non-classical symptoms such as jaw pain, epigastric discomfort, nausea, or unexplained fatigue — leading to under recognition and delayed diagnosis.(24) Risk scores (such as SCORE2, Pooled Cohort Equation, PREVENT) often underestimate cardiovascular risk in women. In older people, IHD may present with non-anginal symptoms, including syncope, delirium, or breathlessness.

Table 2: Initial Clinical Assessment Recommendations

No.	Guideline Statement	Level of Recommendation
2-01	Assess the cardiovascular risk factors, medical history, and symptom characteristics in all individuals with symptoms of suspected myocardial ischemic origin.	**SR**

2-02	Assess the characteristics, duration, and associated features in all patients with chest pain or chest discomfort.	**SR**
2-03	Consider IHD in women who present with chest pain or other symptoms such as jaw pain, epigastric discomfort, nausea, or unexplained fatigue.	**SR**
2-04	Consider ACS in older people with acute dyspnea, syncope or acute delirium	**SR**

ACS (Acute Coronary Syndrome), IHD (Ischemic Heart Disease), SR (Strong Recommendation)

a) Biomarkers

High-sensitivity cardiac troponin assays allow rapid exclusion or confirmation of myocardial injury and should be used to evaluate patients with suspected ACS. Creatine Kinase MB fraction (CK-MB) may be useful in the suspicion of recurrent myocardial infarction in patients with recent myocardial infarction. This includes post-procedural (percutaneous coronary intervention or coronary artery bypass graft surgery) myocardial infarction.(25) Myoglobin is no longer recommended for diagnostic purposes. Lipid profile, hemoglobin, creatinine, microalbuminuria and glycemic indices (fasting glucose and HbA1c) should be part of the routine blood workup in suspected IHD. Lipoprotein(a), which should be checked in adults once in a lifetime, is currently a marker that may help to identify patients at high risk of early-onset or severe atherosclerosis.(26) Markers of inflammation, such as hs-CRP, are associated with worse prognosis and may guide intensification of lipid-lowering therapy or consideration of anti-inflammatory treatment. Natriuretic peptides are useful for the prognosis in patients with IHD and well as those with suspected heart failure.(27)

Table 3: Biomarker Recommendations

No.	Guideline Statement	Level of Recommendation
3-01	Request in all individuals with suspected IHD: full blood count (including hemoglobin), serum creatinine with estimated GFR, microalbuminuria, lipid profile including LDL-C, and glycemic status with HbA1c and/or fasting plasma glucose.	**SR**
3-02	Request thyroid function in patients with suspected CIHD.	**SR**
3-03	Request lipoprotein(a) (at least once) in patients with suspected CIHD	**SR**
3-04	Request high-sensitivity C-reactive protein to further stratify the risk in those with CIHD.	**Su**
3-05	Measure the troponin in all patients with suspected ACS, and repeat if the first value is non-diagnostic	**SR**

ACS (Acute Coronary Syndrome), CIHD (Chronic Ischemic Heart Disease), HbA1c (Hemoglobin A1c), GFR (Glomerular filtration rate), LDL-C (Low-Density Lipoprotein Cholesterol), R (Recommendation), SR (Strong Recommendation), Su (Suggestion)

b) Rest and Exercise ECG

A resting 12-lead ECG is fundamental in the evaluation of IHD and should be performed promptly within the first 10 minutes after the first medical contact in all patients with acute chest pain.(28) ST-segment elevation or depression, Q

waves, conduction abnormalities or complex ventricular arrhythmias may indicate ongoing ischemia or previous myocardial infarction. In patients with persistent symptoms and a nondiagnostic ECG, serial ECGs and/or posterior leads (V7–V9), and/or right precordial leads may improve diagnostic yield when posterior myocardial infarction is suspected.(29) Exercise ECG is less sensitive and less specific for diagnosis but remains valuable for evaluating functional capacity and stratifying event risk.(30) Its accuracy is reduced with baseline ECG abnormalities or concurrent use of digitalis (ST-T abnormalities or left bundle branch block).

Table 4: ECG & Exercise ECG Recommendations

No.	Guideline Statement	Level of Recommendation
4-01	Perform a 12-lead ECG in all individuals with suspected IHD	**SR**
4-02	In patients with acute chest pain, a resting 12-lead ECG should be acquired and reviewed for STEMI within 10 minutes after first medical contact.	**SR**
4-03	In patients with chest pain and a nondiagnostic initial ECG, serial 12-lead ECGs should be performed when clinical suspicion of ACS is high, symptoms are persistent, or the clinical condition deteriorates.	**SR**
4-04	Consider exercise ECG in selected patients without chest pain and no ACS, to assess exercise tolerance, symptoms, arrhythmias, blood pressure response, and event risk, when the information is likely to change the diagnostic or treatment plan.	**R**
4-05	Do not order an exercise ECG to rule out obstructive CAD in patients in whom ACS is suspected	**DND**
4-06	Do not order an exercise ECG to rule out obstructive CAD in low-intermediate risk patients if CCTA or functional imaging tests are available	**DND**
4-07	Exercise ECG is not recommended for diagnostic purposes in patients with ≥0.1 mV ST-segment depression on resting ECG, left bundle branch block, ventricular pacing or who are being treated with digitalis.	**DND**
Resources severely limited	*Use exercise ECG as a risk stratification exam if CCTA or functional imaging tests are unavailable.*	
Resources severely limited	*In patients at intermediate or high pre-test probability for CAD, optimal medical therapy should be provided to address modifiable risk factors, if functional or anatomic imaging tests are not available or where financial resources are restricted.*	

CAD (Coronary Artery Disease), CCTA (Coronary Computed Tomography Angiography), DND (Do Not Do), ECG (Electrocardiogram), R (Recommendation), SR (Strong Recommendation), STEMI (ST-Elevation Myocardial Infarction)

c) Non-Invasive Cardiac Imaging

Both anatomic and functional imaging play a fundamental role in the diagnosis of IHD. CCTA identifies coronary stenoses and atherosclerotic plaque and is recommended for evaluating patients at low to intermediate risk. The SCOT-HEART trial confirmed the prognostic value of CCTA in CIHD(31), which can be complemented by non-invasive fractional flow reserve (FFR) evaluated by CCTA further to assess the hemodynamic significance of intermediate

stenoses. Stress imaging (e.g., echocardiography, PET/SPECT, CMR) provides key data on myocardial perfusion, wall motion, and ischemia burden. All can be useful to detecting ischemia with non-obstructed coronary arteries (INOCA), but does not define the underlying endotype (e.g., microvascular vs vasospastic), when obstructive CAD has been ruled out. Test choice should consider availability, local expertise, pre-test probability, and patient characteristics.

Table 5: Non-Invasive Imaging Recommendations

No.	Guideline Statement	Level of Recommendation
5-01	Order a transthoracic echocardiogram to assess LVEF, identify regional wall motion abnormalities, detect non-coronary cardiac disease, and refine risk stratification.	**SR**
5-02	Request chest radiography in patients with chest pain to evaluate for other potential cardiac, pulmonary, and thoracic causes of symptoms. or to rule out pulmonary causes of chest pain.	**SR**
5-03	For low and intermediate risk patients with stable chest pain and no known CAD, CCTA (including FFR) is effective for diagnosis, risk stratification, and guiding treatment decisions.	**SR**
5-04	For intermediate and high-risk patients with stable chest pain and no known CAD, stress imaging (echocardiography, PET/SPECT MPI, or CMR) is effective for the diagnosis of myocardial ischemia and risk assessment.	**SR**
5-05	Perform a functional imaging exam to assess myocardial ischemia if CCTA has shown CAD of uncertain functional significance or when it is not diagnostic.	**SR**

CAD (Coronary Artery Disease), CCTA (Coronary Computed Tomography Angiography), CMR (Cardiac Magnetic Resonance), FFR (Fractional Flow Reserve), LVEF (Left Ventricular Ejection Fraction), PET (Positron Emission Tomography), SPECT MPI (Single Photon Emission Computed Tomography Myocardial Perfusion Imaging), SR (Strong Recommendation)

d) Invasive Assessment of CIHD

In CIHD, invasive coronary angiography (ICA) is still the gold standard for coronary anatomy evaluation and is indicated in:

a) High pre-test probability of obstructive CAD;
b) High-risk patients with findings of poor prognosis:
- Severe left ventricular dysfunction
- Low-threshold angina or equivalent / Duke Treadmill score<-10
- Complex ventricular arrhythmia

c) High-risk patients after imaging testing
- significant ischemia in imaging methods
  i. ≥3 of 16 segments with stress-induced hypokinesia or akinesia in stress echocardiography
  ii. area of ischemia ≥10% of the LV myocardium in stress SPECT or PET
  iii. ≥2 of 16 segments with stress perfusion defects or ≥3 dobutamine-induced dysfunctional segments in stress CMR

- CT showing left main disease with ≥50% stenosis, three-vessel disease with ≥70% stenosis, or two-vessel disease including the proximal LAD with ≥70% stenosis, or one-vessel disease of the proximal LAD with ≥70% stenosis and FFR-CT ≤0.8.

d) Persistent symptoms related to CIHD despite optimal medical treatment (section 5);

e) Patients with inconclusive yet suspicious non-invasive tests.

In CIHD context, physiological lesion assessment using fractional flow reserve (FFR) or instantaneous wave-free ratio (iFR) helps in the guidance of revascularization decisions and may lead to outcomes improvement.(32,33) In symptomatic patients with CIHD and non-obstructive coronary arteries, ANOCA/INOCA, coronary functional tests (e.g., coronary flow reserve, index of microvascular resistance, acetylcholine provocation) performed by experienced operators are essential to identify microvascular and/or vasospastic mechanisms.

Table 6: Invasive Assessment Recommendations

No.	Guideline Statement	Level of Recommendation
6-01	Perform invasive coronary angiography with physiological lesion assessment to confirm or exclude the diagnosis of obstructive CAD in individuals with high pre-test probability, severe or unstable symptoms uncontrolled by pharmacologic therapy, or high event risk based on clinical evaluation.	**SR**
6-02	Perform invasive coronary function testing in selected symptomatic patients with documented or suspected ANOCA/INOCA.	**R**
Resources severely limited	*Restrict invasive coronary angiography to high-risk or refractory cases.*	

ANOCA (Angina with No Obstructive Coronary Artery disease), CAD (Coronary Artery Disease), INOCA (Ischemia with No Obstructive Coronary Artery disease), R (Recommendation), SR (Strong Recommendation), Su (Suggestion)

TREATMENT OF CHRONIC ISCHEMIC HEART DISEASE

The management of CIHD relies upon multifaceted modification of risk factors, pharmacotherapy, and revascularization where indicated. A stepwise evidence-based approach is critical to maximize prognosis, manage symptoms, and avoid disease progression.

LIFESTYLE MODIFICATION AND PREVENTIVE STRATEGIES

In addition to disease modifying medication, lifestyle interventions included in cardiac rehabilitation programs are the cornerstone of CIHD care. These programs include organized regimens of diet, physical activity, smoking cessation programs, and psychosocial support (to address depression, stress, social isolation…) which reduce cardiovascular events and improve quality of life. Diets rich in vegetables, fruits, legumes, nuts, whole grains, and lean protein, such as the Mediterranean diet (which also includes fish and olive oil), has been shown to provide consistent cardiovascular benefit.(34,35) Low sodium intake was associated with lower risk of events in patients with CIHD(36), particularly those with hypertension.(37) Physical activity of 150–300 minutes/week at moderate intensity or 75–150 minutes/week at vigorous intensity is associated with a substantial reduction in mortality. Smoking cessation reduces the risk of premature death by over one-third. Alcohol consumption should be stopped or restricted to maximally recommended

thresholds for males and females. Behavioral interventions, included in cardiac rehabilitation programs, are critical to sustaining lifestyle change. Mobile health tools and structured education may improve adherence and outcomes. Influenza vaccination should be recommended to all patients with CIHD.(38–40)

Table 7: Lifestyle Recommendations

No.	Guideline Statement	Level of Recommendation
7-01	Refer all patients with CIHD to a multidisciplinary exercise-based cardiac rehabilitation program to improve cardiovascular risk profile and reduce cardiovascular mortality.	**SR**
7-02	Aerobic physical activity of at least 150–300 min per week of moderate intensity or 75–150 min per week of high intensity and reduction in sedentary time.	**SR**
7-03	Following a diet emphasizing vegetables, fruits, legumes, nuts, whole grains, and lean protein (e.g. Mediterranean diet), and low sodium intake	**SR**
7-04	Maintaining and achieving healthy weight (BMI 18.5–24.9 kg/m²; for Asians 18.5-22.9 kg/m²) and target appropriate waist circumference (<94 cm for men, <80 cm for women, for Asian men <90 cm and <80 cm for Asian women).	**SR**
7-05	Refer smoker for smoking cessation in specialized services	**SR**
7-06	Assess the psychosocial status to direct psychological interventions	**SR**
7-07	Prescribe influenza vaccination to all CIHD patients	**SR**
Resources severely limited	*Refer patients with IHD to structured follow-up programs to assess the adherence to all measures that improve cardiovascular risk profile*	
Resources severely limited	*Encourage and reinforce at every visit, active lifestyle, healthy nutrition, and smoking cessation (when applicable) through brief physician advice and basic counseling,*	

BMI (Body Mass Index), CIHD (Chronic Ischemic Heart Disease), SR (Strong Recommendation)

RISK FACTOR MANAGEMENT

a) Diabetes Mellitus

Patients with IHD and type 2 diabetes mellitus are at elevated risk for recurrent cardiovascular events. Treatment should include agents with demonstrated cardiovascular benefit, particularly SGLT2 inhibitors and GLP-1 receptor agonists (41–43) alongside glycemic control. SGLT2 inhibitors and GLP-1 receptor agonists reduce the risk of cardiovascular events, hospitalizations with heart failure, and progression of renal dysfunction, independent of glycemic targets.(44)

b) Lipid Management

An LDL-C goal <1.4 mmol/L (55 mg/dL) and at least a 50% reduction from baseline are recommended in patients with established IHD. High-intensity statin therapy is the first-line treatment, with or without ezetimibe, where available and accessible.(45,46) The addition of PCSK9 inhibitors should be considered if targets are unmet (47,48) based on further

risk reduction with these drugs. Bempedoic acid can also be considered in this context. Icosapent ethyl (2 grams twice daily) may be used in patients with IHD and hypertriglyceridemia (>150 mg/dL).(49) For statin-intolerant patients bempedoic acid (preferably with ezetimibe to achieve LDL-C goal) should be considered.(50)

c) Hypertension

Blood pressure targets are generally set at <130/80 mmHg for most patients with IHD. First-line agents include angiotensin converting enzyme inhibitors (ACE-I) or angiotensin receptor blockers (ARB), often combined with dihydropyridine calcium channel blockers or thiazide/thiazide-like diuretics in single-pill combination should be preferred to improve adherence. Beta-blockers can be important in patients with prior myocardial infarction with incomplete revascularization or in those with heart failure with reduced ejection fraction.

d) Inflammation

Inflammation plays a central role in atherogenesis and cardiovascular events. Targeting residual inflammatory risk, several clinical trials have explored therapies that reduce inflammatory activity independent of lipid-lowering. Canakinumab, a monoclonal antibody against interleukin-1β, demonstrated reduced cardiovascular events in the CANTOS trial but has not been commercialized for this indication.(51) Low-dose colchicine reduced cardiovascular events in trials such as COLCOT and LoDoCo2 (52,53), making it a feasible anti-inflammatory option in secondary prevention, despite the absence of benefits in the CLEAR trial post-MI.(54)

Table 8: Risk Factor Management Recommendations

No.	Guideline Statement	Level of Recommendation
8-01	Use SGLT2 inhibitors with proven CV benefits in patients with CIHD associated with T2DM or HF to reduce CV events.	**SR**
8-02	Use GLP-1 receptor agonists with proven CV benefit in obese patients with T2DM and CIHD to reduce CV events	**SR**
8-03	Consider semaglutide in CIHD patients without T2DM with BMI≥27 kg/m²	**R**
8-04	Prescribe lipid-lowering treatment in CIHD patients, with LDL-C goal of <1.4 mmol/L (55 mg/dL) and a ≥50% reduction	**SR**
Resources severely limited	*Prescribe the most potent and affordable available statin, at the maximally tolerated dosage*	
8-05	Use a high-intensity lipid lowering treatment with high-intensity statin with or without ezetimibe in all patients with CIHD.	**SR**
8-06	Prescribe bempedoic acid preferably with ezetimibe in all patients with CIHD intolerant to statins	**SR**
8-07	Prescribe PCSK9 inhibitor in patients who do not achieve their goal on a maximum tolerated dose of statin and ezetimibe, combination	**SR**
8-08	Prescribe bempedoic acid in patients who do not achieve their goal on a maximum tolerated dose of statin and ezetimibe, combination	**Su**
8-09	Prescribe icosapent ethyl (2 grams twice daily) is recommended in patients with CIHD and hypertriglyceridemia	**R**

8-10	Prescribe ACE-I (or ARB) in patients with CIHD, with concomitant elevated blood pressure, diabetes, or heart failure.	**SR**
8-11	Consider low-dose colchicine in patients with CIHD	**Su**

ACE-I (Angiotensin-Converting Enzyme Inhibitor), ARB (Angiotensin Receptor Blocker), BMI (Body Mass Index), CIHD (Chronic Ischemic Heart Disease), CV (Cardiovascular), GLP-1 (Glucagon-Like Peptide-1), HbA1c (Hemoglobin A1c), HF (Heart Failure), IHD (Ischemic Heart Disease), LDL-C (Low-Density Lipoprotein Cholesterol), PCSK9 (Proprotein Convertase Subtilisin/Kexin Type 9), R (Recommendation), SGLT2 (Sodium–Glucose Cotransporter-2), SR (Strong Recommendation), Su (Suggestion), T2DM (Type 2 Diabetes Mellitus

ANTIANGINAL AND ANTITHROMBOTIC STRATEGY

The primary goals of pharmacologic therapy in IHD are symptom improvement, improvement of quality of life, and prevention of adverse cardiovascular events.

a) Antianginal Therapy

The conventional approach to antianginal therapy has followed a hierarchical, stepwise model using first-line agents (beta-blockers, CCBs) and second-line drugs (long-acting nitrates, nicorandil, ranolazine, ivabradine, trimetazidine). However, we emphasize that medical therapy in CIHD should be individualized based on patient-specific factors, and adaptative according to aspects such as the hemodynamic profile (blood pressure, heart rate), comorbidities (notably heart failure or atrial fibrillation), concomitant medications (considering drug interactions), the underlying pathophysiology of ischemia and patient preferences.(55) Local drug availability should also be considered. The use of fixed-dose combinations is encouraged to improve adherence and clinical outcomes.

b) Antithrombotic Therapy

Antiplatelet therapy with low-dose aspirin (75–100 mg daily) or clopidogrel (75 mg) is recommended for all IHD patients without an indication for oral anticoagulation.(56) Standard dual antiplatelet therapy (DAPT) regimens with aspirin and a P2Y12 inhibitor (ticagrelor, prasugrel, or clopidogrel) should be given for 12 months after myocardial infarction, but can be shorter or longer, depending on bleeding vs. ischemic risk. In CIHD the recommended DAPT duration is 1–3 months for high bleeding risk, 6 months for standard risk, and ≥12 months for high ischemic risk.(21,57) Extended DAPT beyond 12 months using aspirin with clopidogrel, ticagrelor, or rivaroxaban (2.5 mg twice daily) should be considered in high ischemic risk patients without elevated bleeding risk. De-escalation therapies should be considered in patients at high bleeding and low ischemic risk. These include switching from ticagrelor or prasugrel to clopidogrel, also the reduction of prasugrel from 10 mg to 5 mg, or ticagrelor 90 mg twice daily after 1-3 months and continuation for 12-15 months as monotherapy without aspirin.

Table 9: Antianginal Therapy Recommendations

No.	Guideline Statement	Level of Recommendation
9-01	Prescribe short-acting nitrates for immediate relief of angina.	**SR**
9-02	Prescribe beta-blockers and/or CCBs to control symptoms as the initial treatment of CIHD in patients without contraindications	**SR**
9-03	Prescribe long-acting nitrates, nicorandil, ivabradine, and metabolic agents, such as ranolazine or trimetazidine, when clinically appropriate	**R**
9-04	Do not prescribe ivabradine with verapamil or diltiazem in patients with CIHD	**DND**

CCB (Calcium Channel Blockers), CIHD (Chronic Ischemic Heart Disease), DND (Do Not Do), R (Recommendation), SR (Strong Recommendation)

Table 10: Antithrombotic Therapy Recommendations

No.	Guideline Statement	Level of Recommendation
10-01	Prescribe a single antiplatelet agent (low-dose aspirin or clopidogrel) in CIHD patients, unless on therapeutic anticoagulation for another indication	**SR**
Resources severely limited	*Prescribe low-dose aspirin to all CIHD patients, unless on therapeutic anticoagulation for another indication*	
10-02	Prescribe rivaroxaban (2.5 mg twice daily) in addition to low-dose aspirin in selected stable high-risk CIHD patients (in patients who had ACS, consider this >1 year after ACS)	**R**
10-03	Prescribe low-dose aspirin and clopidogrel for 6 months as the default antithrombotic strategy after PCI-stenting in CIHD patients without indication for oral anticoagulation (e.g. atrial fibrillation)	**SR**
10-04	Discontinue DAPT in 1–3 months after PCI, and continue single antiplatelet therapy in CCS patients at high bleeding risk, but not at high ischemic risk.	**SR**
Post ACS patients (12 months after ACS)		
10-05	Prescribe low-dose aspirin or clopidogrel (single antiplatelet therapy) as the default strategy after 12 months of the ACS event	**SR**
10-06	Discontinue antiplatelet therapy and maintain oral anticoagulation in patients with indication for oral anticoagulation (e.g. atrial fibrillation)	**SR**
10-07	Prescribe dual antithrombotic therapy in patients with high ischemic risk and without high bleeding risk: a) Low-dose aspirin and clopidogrel 75 mg b) Low-dose aspirin and prasugrel 10 mg (or 5 mg if increased ≥75 years or body weight <60 kg) c) Low-dose aspirin and ticagrelor 60 mg twice daily d) Low-dose aspirin and rivaroxaban 2.5 mg twice daily	**R**
10-08	Prescribe ticagrelor 90 mg twice daily (single antiplatelet therapy) after 12 months of the ACS event in patients with high ischemic risk and without high bleeding risk	**Su**
10-09	Do not prescribe prasugrel in patients with prior stroke	**DND**

ACS (Acute Coronary Syndrome), CCS (Chronic Coronary Syndrome), CRT (Cardiac Resynchronization Therapy), DAPT (Dual Antiplatelet Therapy), DND (Do Not Do), PCI (Percutaneous Coronary Intervention), R (Recommendation), SR (Strong Recommendation), Su (Suggestion)

REVASCULARIZATION: PERCUTANEOUS CORONARY INTERVENTION (PCI) AND CORONARY ARTERY BYPASS GRAFTING (CABG) SURGERY.

Revascularization may be required for symptom relief, for prognostic improvement, or both. The decision between medical therapy alone, PCI, or CABG should be based on symptom burden, ischemia burden and/or anatomical complexity of coronary lesions, as well as individual risk factors such as frailty or patients' preferences. PCI is preferred in single- or two-vessel disease without diabetes. In contrast, CABG provides better outcomes in patients with diabetes, multivessel disease, and/or high SYNTAX scores.(58–60) CABG has also shown long-term improvement of survival compared to optimal medical therapy in patients with multivessel disease and Left Ventricular Ejection Fraction (LVEF) ≤35%.(61) Functional lesion assessment using FFR or iFR along with intravascular imaging are useful in the selection of lesion and PCI optimization.(62–64) A Heart Team approach is recommended for complex cases.

Table 11: Revascularization Recommendations

No.	Guideline Statement	Level of Recommendation
11-01	Perform myocardial revascularization of functionally significant lesions to improve symptoms and/or prognosis in CIHD patients with persistent angina or anginal equivalents, despite optimal medical treatment, or significant ischemia	**SR**
11-02	Discuss in Heart Team complex obstructive coronary disease cases in whom revascularization is being considered	**SR**
11-03	Calculate the STS score (https://acsdriskcalc.research.sts.org/) or EuroSCORE II (https://www.euroscore.org/) to estimate the risk of procedural mortality and/or 30-day mortality after CABG.	**SR**
11-04	Calculate the SYNTAX score (https://syntaxscore.org/) in patients with multivessel obstructive CAD to aid in the choice between PCI and CABG.	**SR**
11-05	Prefer CABG over PCI* in myocardial revascularization if: a) LMD with multivessel disease and low surgical risk b) MVD and diabetes c) MVD and LVEF≤35%	**SR**
11-06	Prefer PCI over CABG in myocardial revascularization if: a) LMD with SYNTAX score ≤22 b) MVD without diabetes, where PCI can provide similar revascularization completeness as CABG	**R**

CABG (Coronary Artery Bypass Grafting), CAD (Coronary Artery Disease), CIHD (Chronic Ischemic Heart Disease), LMD (Left Main Disease), LVEF (Left Ventricular Ejection Fraction), MVD (Multivessel Disease), PCI (Percutaneous Coronary Intervention), R (Recommendation), SR (Strong Recommendation), STS (Society of Thoracic Surgeons), SYNTAX (Synergy Between PCI With Taxus and Cardiac Surgery): * Assuming acceptable surgical risk and availability of expertise.

SPECIFIC CLINICAL CONDITIONS IN ISCHEMIC HEART DISEASE

a) Heart Failure and CIHD

Heart failure (HF) resulting from IHD is a leading cause of morbidity and mortality, responsible for approximately 50% of all HF cases in industrialized countries. Contributing mechanisms include prior myocardial infarction resulting in loss of viable tissue, as well as chronic ischemia leading to hibernating myocardium. Echocardiographic classification based on LVEF distinguishes HF with reduced EF (HFrEF <40%), with mildly reduced EF (HFmrEF 40–49%, also termed “mid-range”), and HF with preserved EF (HFpEF ≥50%). Clinical evaluation includes assessment of symptoms, measurement of biomarkers (e.g., natriuretic peptides), imaging including echocardiography and may include other modalities such as PET/SPECT, CMR, coronary CTA, or invasive coronary angiography. Further guidance on HF management is available in disease-specific guidelines.(65,66)

Table 12: Recommendations for Patients with Heart Failure and CIHD.

No.	Guideline Statement	Level of Recommendation
12-01	Measure BNP or NT-proBNP or MR-proANP, in patients with suspected HF and CIHD to exclude or confirm HF.	**SR**
12-02	Enroll patients with ischemic HF in a multidisciplinary HF management program	**SR**

12-03	Prescribe ACE-I/ARNI, MRA, SGLT2 inhibitor, and HF-specific beta-blocker (bisoprolol, carvedilol, nebivolol or sustained-release metoprolol succinate) to patients with HFrEF.	**SR**
12-04	Prescribe SGLT2 inhibitor (dapagliflozin or empagliflozin) to patients with HFmrEF or HFpEF	**SR**
12-05	Prescribe MRA to patients with HFmrEF or HFpEF	**R** (fineronone) **Su** (spironolactone)
12-06	An ARB is recommended in symptomatic patients with HFrEF unable to tolerate an ACE-I or ARNI	**SR**
12-07	Replace ACE-I or ARB by ARNI in symptomatic HFrEF patients	**SR**
12-08	Prescribe ivabradine to patients with HFrEF (LVEF≤35%) and NYHA class II to III who are receiving GDMT, including maximally tolerated beta-blockers, and have sinus rhythm with a heart rate≥70 bpm	**SR**
12-09	Use diuretics in patients with HF and signs of congestion to alleviate symptoms	**SR**
12-10	Use ICD in patients with symptomatic ischemic HF (NYHA II–III), LVEF ≤35% despite ≥3 months of optimized GDMT, if expected to survive >1 year with good functional status.	**SR**
12-11	Use ICD therapy in patients who are at least 40 days post-MI, have an LVEF ≤ 30%, and have a prognosis of more than 1 year of survival.	**SR**
12-12	Use CRT in patients with symptomatic HF, sinus rhythm, LVEF ≤35% despite GDMT, and QRS duration ≥150 ms with LBBB QRS morphology.	**SR**
12-13	Consider advanced therapies (mechanical circulatory support, heart transplantation) in eligible patients with end-stage heart failure refractory to other treatments.	**R**

ACE-I (Angiotensin-Converting Enzyme Inhibitor), ARB (Angiotensin Receptor Blocker), ARNI (Angiotensin Receptor–Neprilysin Inhibitor), CRT (Cardiac Resynchronization Therapy), GDMT (Guideline-Directed Medical Therapy), HF (Heart Failure), HFmrEF (Heart Failure with Mildly Reduced Ejection Fraction), HFpEF (Heart Failure with Preserved Ejection Fraction), HFrEF (Heart Failure with Reduced Ejection Fraction), ICD (Implantable Cardioverter Defibrillator), LBBB (Left Bundle Branch Block), LVEF (Left Ventricular Ejection Fraction), MRA (Mineralocorticoid Receptor Antagonist), NYHA (New York Heart Association), R (Recommendation), SR (Strong Recommendation), SGLT2 (Sodium–Glucose Cotransporter-2), Su (Suggestion)

b) Ischemia with Non-Obstructive Coronary Arteries (INOCA)

Ischemia with Non-Obstructive Coronary Arteries (INOCA) includes microvascular angina (MVA) and vasospastic angina (VSA). These syndromes are more prevalent in women, associated with significant symptoms and an unfavorable prognosis.(67,68) Pathophysiology involves coronary microvascular dysfunction and/or epicardial coronary artery spasm. Diagnosis requires invasive coronary functional testing or non-invasive stress imaging with coronary flow reserve assessment, which can be assessed using stress CMR, PET and stress echo.

Table 13: Recommendations for INOCA

No.	Guideline Statement	Level of Recommendation
13-01	Control all modifiable cardiovascular risk factors	**SR**
13-02	Perform invasive coronary functional testing in selected persistently symptomatic patients with suspected ANOCA/INOCA	**SR**

13-03	Perform non-invasive testing in persistently symptomatic patients with documented or suspected ANOCA/INOCA, using available imaging modalities to assist in diagnosis (Stress CMR, Stress PET, Stress Echocardiography, Doppler of LAD)	**R**
13-04	Perform a resting 12-lead ECG and ambulatory ECG recording in patients with suspected vasospastic angina.	**R**
13-05	In patients with suspected vasospastic angina and repetitive episodes of rest angina associated with ST-segment changes, invasive coronary angiography is recommended.	**R**
13-06	Prescribe calcium channel blockers for isolated vasospastic angina	**SR**
13-07	Nitrates should be considered to prevent recurrent episodes in vasospastic angina.	**R**
13-08	Avoid beta-blockers in patients with vasospastic angina	**DND**
13-09	Prescribe combination therapy with nitrates, calcium channel blockers, and/or other antianginal drugs in patients with overlapping types of INOCA	**R**
13-10	Prescribe antianginal medications to reduce ischemia in microvascular angina with reduced coronary flow reserve,	**R**
13-11	Prescribe ACE-I in patients with endothelial dysfunction-related angina	**R**

ACE-I (Angiotensin-Converting Enzyme Inhibitors), ANOCA (Angina with Non-Obstructive Coronary Arteries), CAD (Coronary Artery Disease), ECG (Electrocardiogram), INOCA (Ischemia with Non-Obstructive Coronary Arteries), LAD (Left anterior descending artery), R (Recommendation), SR (Strong Recommendation), Su (Suggestion).

c. Refractory Angina

Refractory angina is characterized by persistent chest pain lasting longer than three months, caused by myocardial ischemia that does not respond adequately to optimal medical therapy or revascularization. It may result from obstructive coronary artery disease or INOCA. Emerging treatment strategies from small trials and/or registries include enhanced external counterpulsation (EECP), coronary sinus reducer devices, and spinal cord stimulation (69–72), available in limited specialized centers.

Table 14: Recommendations for Refractory Angina

No.	Guideline Statement	Level of Recommendation
14-01	Perform invasive coronary functional testing in patients with refractory angina.	**SR**
14-02	Use EECP in selected patients with refractory angina after failure of medical therapy	**Su**
14-03	Use coronary sinus reducer in selected patients with debilitating angina and obstructive CAD with reversible ischemia in the left coronary artery territory, refractory to optimal strategies.	**Su**
14-04	Use spinal cord stimulation in selected patients with refractory angina after failure of medical therapy.	**Su**

CAD (Coronary Artery Disease), EECP (enhanced external counterpulsation), SR (Strong Recommendation), Su (Suggestion)

OTHER SPECIFIC CONDITIONS

a) Atrial Fibrillation

AF frequently coexists with coronary disease, complicating symptom interpretation and increasing thromboembolic risk. Coronary artery stenosis exceeding 50% luminal obstruction attributes 1 point to the CHAD2S2-VA score and adds to the thromboembolic risk. Rate or rhythm control strategies should be individualized based on LVEF, symptoms, and comorbidities. Anticoagulation is essential for stroke prevention, and single antiplatelet therapy should be discontinued if anticoagulation is initiated.(73)

b) Chronic Kidney Disease

CKD patients are at high risk of both ischemic and bleeding events. PCI should not be withheld solely due to contrast-induced nephropathy risk. Hydration and procedural planning are important to minimize nephrotoxicity. The volume of contrast material should be minimized in ICA for diagnosis or intervention purposes. The risks associated with an early invasive strategy were highlighted in the ISCHEMIA-CKD study. Patients with advanced kidney disease and moderate or severe ischemia on stress testing, undergoing early invasive strategy, showed an increased risk of stroke and death or initiation of dialysis, without improving the risk of death or myocardial infarction.(74)

c) Cancer

Cancer therapies may increase cardiovascular risk. A multidisciplinary cardio-oncology approach is essential to balance cancer treatment with IHD management, particularly in cases of cardiotoxicity or thrombotic risk.(75)

d) HIV

Individuals living with HIV have an increased risk of cardiovascular disease, partially due to antiretroviral therapy impact on lipid profiles. When prescribing statins, clinicians should choose agents with minimal drug interactions, acknowledging that protease inhibitors have strong interference with cytochromes, i.e. CYP3A4. Simvastatin and lovastatin are contraindicated in this setting. Pitavastatin showed favorable results in the primary prevention setting (76), but atorvastatin or rosuvastatin may be used at the maximum dose allowed and tolerated by the protease inhibitors regimen, along with ezetimibe if required to achieve and maximize LDL-C goals. When antiplatelet therapy with P2Y12 inhibitors is required, prasugrel, differently from clopidogrel and ticagrelor, does not have relevant interactions with protease inhibitors.

e) High Bleeding Risk

Validated bleeding risk scores (e.g., PRECISE-DAPT, ARC-HBR) should guide antithrombotic therapy. In high-risk patients, DAPT duration may need to be shortened. A proton pump inhibitor (PPI) should be considered to reduce gastrointestinal bleeding risk.

Table 15: Recommendations for Other Specific Conditions

No.	Guideline Statement	Level of Recommendation
15-01	Prescribe a DOAC instead of VKA in patients with CIHD with a long-term indication for OAC, unless contraindicated (mechanical valvular prosthesis and rheumatic mitral stenosis).	**SR**
15-02	Promote hydration in patients with obstructive coronary disease and CKD to minimize contrast-induced nephropathy during PCI.	**SR**
15-03	Discuss the cases of CIHD and cancer in a multidisciplinary team including cardiology and oncology expertise due to complexity in the management of these patients	**SR**
15-04	Prescribe potent statin with less interaction with antiretroviral drugs in HIV patients	**SR**
15-05	Prescribe proton pump inhibitor in CIHD patients at increased GI bleeding risk treated with single antiplatelet therapy#	**R**
15-06	Prescribe proton pump inhibitor in CIHD patients at increased GI bleeding risk treated with combined antithrombotic drugs#	**SR**

Consider the following risk factors to prescribe proton pump inhibitors on a individual basis: history of gastrointestinal ulcer/haemorrhage, chronic non-steroidal anti-inflammatory drug/corticosteroid use, age ≥65 years, Dyspepsia, Gastro-oesophageal reflux disease, Helicobacter pylori infection, Chronic alcohol use; CAD (Coronary Artery Disease), CIHD (Chronic Ischemic Heart Disease), CKD (Chronic Kidney Disease), DOAC (Direct Oral Anticoagulant), GI (Gastrointestinal), HIV (Human Immunodeficiency Virus), OAC (Oral Anticoagulation), PCI (Percutaneous Coronary Intervention), SR (Strong Recommendation), VKA (Vitamin K Antagonist)

SPECIAL CONSIDERATIONS IN CHRONIC ISCHEMIC HEART DISEASE

Certain populations require individualized assessment and therapy in the management of CIHD. Women and older/frail adults often have diagnostic delays, suboptimal treatment patterns, and increased procedural risks. This section provides guidance to optimize care in these groups.

a) Women: Addressing Under Recognition, Delayed Diagnosis and Undertreatment

Despite significant advancements in cardiovascular medicine, women with CIHD continue to be underdiagnosed and undertreated. Cardiovascular disease remains the leading cause of death among women worldwide, yet gender-based disparities persist in both diagnosis and treatment of the disease.(77) These gaps arise not only from biological differences but also from systematic biases in clinical evaluation. The clinical presentation of CIHD in women more frequently diverges from the classical pattern of exertional chest pressure seen in men. Women commonly report breathlessness, fatigue, epigastric discomfort, or pain radiating to the neck or jaw.(21,78–80) Emotional stress, more than physical exertion, is a frequent trigger. The symptoms experienced by women are often misattributed to anxiety, gastrointestinal disorders, or musculoskeletal pain, leading to diagnostic delays and late initiation of treatment. The more frequent absence of obstructive CAD must not be mistaken for the absence of CIHD. Treatment disparities include lower use of evidence-based medications such as antiplatelets, statins, beta-blockers, and ACE-I.(81) Women are also less likely to be referred to cardiac rehabilitation programs. Differences in body composition and drug metabolism may further impact treatment effectiveness and side effect profiles. Addressing these disparities requires a tailored, sex-specific approach. Comprehensive symptom assessment should routinely include non-classic features. When non-

obstructive findings are present, functional testing may help uncover microvascular disease. Personalized risk assessment must integrate female-specific risk factors to optimize outcomes and close the care gap.

Table 16: Recommendations for Women with IHD

No.	Guideline Statement	Level of Recommendation
16-01	Consider CIHD in women who present with chest pain or other symptoms such as jaw pain, epigastric discomfort, nausea, palpitations, or unexplained fatigue.	**SR**
16-02	Prescribe optimal medical therapy for CIHD in both women and men.	**SR**
16-03	If obstructive CAD is not present, consider non-invasive or invasive imaging and/or coronary function testing to detect ANOCA /INOCA	**R**
16-04	Avoid systemic post-menopausal hormone therapy in women with CIHD, due to the absence of cardiovascular benefit and an increased risk of venous thromboembolism	**DND**

ANOCA (Angina with No Obstructive Coronary Artery disease), CIHD (Chronic Ischemic Heart Disease), IHD (Ischemic Heart Disease), INOCA (Ischemia with No Obstructive Coronary Artery disease), R (Recommendation), SR (Strong Recommendation), Su (Suggestion), DND (Do Not Do)

b) Older People and Frail Patients

The ongoing demographic shift toward an aging population has significantly influenced cardiovascular care. Adults aged 75 and older now represent the most rapidly expanding group among those living with chronic coronary syndromes. Managing ischemic heart disease (IHD) in this population presents unique challenges due to a higher burden of comorbidities, diminished physiological reserves, and increased vulnerability to risks associated with both diagnostic evaluations and therapeutic procedures. Frailty—marked by reduced strength, endurance, and physiological function—commonly coexists with cardiovascular disease and affects over 25% of patients with established IHD.(82) (83) Older adults often present with non-classic or atypical manifestations of myocardial ischemia. Rather than typical angina, symptoms may include dyspnea, fatigue, confusion, delirium, or functional decline. Silent ischemia is also more prevalent, particularly in individuals with diabetes or prior infarction. Cognitive impairment may limit symptom reporting and affect adherence, further complicating assessment. A key principle in managing older patients is individualized care, guided by life expectancy, comorbidities, procedural risk, and patient preferences. Frailty assessment tools and comprehensive geriatric assessment (CGA) can inform decision-making, particularly regarding revascularization. CGA evaluates medical, functional, cognitive, nutritional, and social domains, and has been shown to improve prognostication and care planning. Despite these complexities, older adults with IHD can benefit from medical therapy and revascularization—provided risks are carefully weighed and management aligns with patient-centered goals.

Older patients have increased bleeding risk, especially during dual antiplatelet therapy (DAPT). Shorter DAPT durations (1–3 months) may be preferred when ischemic risk is low and bleeding risk is high. Clopidogrel might be chosen over more potent agents in these circumstances.(21,57) Use of proton pump inhibitors (PPIs) is recommended during DAPT to reduce gastrointestinal bleeding.

Table 17: Recommendations for Older People and Frail Patients

No.	Guideline Statement	Level of Recommendation
17-01	Monitor drug side effects, intolerance, drug-drug interactions, overdosing, and procedural complications in all patients with CIHD, and more strictly in older people.	**SR**
17-02	Consider all diagnostic and treatment decisions (including revascularization) based on symptoms, extent of ischemia, frailty, life expectancy, comorbidities, and patient preferences	**R**
17-03	Acknowledge the procedural risks to guide shared decision-making, particularly in older people with complex coronary disease in whom revascularization is being considered	**SR**

CIHD (Chronic Ischemic Heart Disease), R (Recommendation), SR (Strong Recommendation)

c) Follow-Up of Patients with Chronic Ischemic Heart Disease

Long-term follow-up plays a crucial role in the management of patients with CIHD, supporting sustained risk reduction, treatment adherence, and the early detection of clinical deterioration. A structured, personalized approach to follow-up enhances clinical outcomes, promotes quality of life, and helps optimize healthcare resource utilization.

The primary goals of follow-up in patients with CIHD are**:**

- Evaluate new symptoms onset, or symptoms progression.
- Detect complications or recurrence of ischemic events.
- Ensure adherence to pharmacologic therapy and lifestyle modifications.
- Reinforce secondary prevention, including cardiovascular risk factor control.

Maintaining all treatment goals, particularly the use of antiplatelet drugs, smoking cessation, recommended LDL-C and blood pressure levels, is associated with better outcomes.(84) Follow-up should begin soon after the index event or diagnosis, typically within 6–8 weeks and continue at intervals tailored to the patient's clinical stability and overall risk profile. Those who have recently undergone revascularization, experience ongoing symptoms, or present with complex comorbidities may require more frequent and intensive monitoring. Each follow-up visit should include a detailed clinical history and physical examination, complemented by review of medications, symptom status, lifestyle adherence, and psychological well-being. Serial ECGs and biomarker assessments may be indicated in specific contexts. Further diagnostic testing is warranted when symptoms change, or with clinical suspicion of disease progression or new ischemia. A multidisciplinary approach involving primary care, cardiology, rehabilitation, and allied health professionals improves continuity and outcomes. Communication between care levels is essential for managing transitions post-discharge and for tailoring care to the patient's context. The use of electronic health records, structured care plans, and patient education tools enhances patient engagement, particularly in those with polypharmacy. Shared decision making should be utilized to improve treatment adherence and patient empowerment. Cardiac rehabilitation should be strongly encouraged, as it improves exercise tolerance, medication adherence, psychosocial health, and survival. Despite these benefits, referral rates remain suboptimal — particularly among women, minorities, and older people. Patients should be periodically reassessed for ongoing needs for antianginal therapy, intensity of antithrombotic therapy, and possible de-escalation of pharmacologic regimens in light of evolving risk-benefit considerations.

Table 18: Recommendations about CIHD patients follow-up.

No.	Guideline Statement	Level of Recommendation
18-01	Schedule periodic visits (e.g., annual) to a general practitioner or cardiovascular healthcare professional, evaluate cardiovascular risk factor control and assess changes in risk status, disease status, and comorbidities, regardless of symptoms.	**SR**
18-02	Schedule the first follow-up appointment within 4–6 weeks after diagnosis or treatment modification, with subsequent visits every 3–6 months during the first year, and annual visits thereafter if stable.	**SR**
18-03	Provide a structured and individualized follow-up to all patients with CIHD to optimize long-term outcomes.	**SR**
18-04	Assess regularly the symptoms, lifestyle, medication adherence, and clinical status to guide ongoing therapy.	**SR**
18-05	Control the cardiovascular risk factors (blood pressure, LDL-C, glycemic status including HbA1c, adherence to smoking cessation, and optimize weight management) during follow-up, using evidence-based treatments and targets	**SR**
18-06	Refer patients with CIHD to multidisciplinary cardiac rehabilitation is recommended to support secondary prevention and quality of life.	**SR**
18-07	Use digital tools, remote monitoring, or telehealth in selected patients to support long-term adherence.	**R**

CIHD (Chronic Ischemic Heart Disease), HbA1c (Hemoglobin A1c), LDL-C (Low-Density Lipoprotein Cholesterol), R (Recommendation), SR (Strong Recommendation)

Older patients have increased bleeding risk, especially during dual antiplatelet therapy (DAPT). Shorter DAPT durations (1–3 months) may be preferred when ischemic risk is low and bleeding risk is high. Clopidogrel might be chosen over more potent agents in these circumstances.(21,57) Use of proton pump inhibitors (PPIs) is recommended during DAPT to reduce gastrointestinal bleeding.

CONCLUSION

These global guidelines from the iCardio Alliance provide comprehensive, resource adaptive recommendations for the assessment, diagnosis, treatment, and follow up of CIHD. These guidelines emphasize equity and patient-centered care across diverse healthcare settings. Application of guideline directed care globally has the potential to improve the outcomes of those living with this form of cardiovascular disease.

REFERENCES

1. Pinto FJ, Anker SD, Abraham WT, Atherton JJ, Butler J, Chopra V, et al. The Global Implementation Guidelines Initiative: how to optimize cardio-renal-metabolic care worldwide. Global Cardiology. 2025 Apr 16;3(1).

2. Knuuti J, Wijns W, Achenbach S, Agewall S, Barbato E, Bax JJ, et al. 2019 ESC guidelines for the diagnosis and management of chronic coronary syndromes. Eur Heart J. 2020;41(3):407–77.

3. Virani SS, Newby LK, Arnold S V., Bittner V, Brewer LC, Demeter SH, et al. 2023 AHA/ACC/ACCP/ASPC/NLA/PCNA Guideline for the Management of Patients With Chronic Coronary Disease. J Am Coll Cardiol. 2023 Aug;82(9):833–955.

4. Vaduganathan M, Mensah GA, Turco JV, Fuster V, Roth GA. The Global Burden of Cardiovascular Diseases and Risk. J Am Coll Cardiol. 2022 Dec;80(25):2361–71.

5. Khan MA, Hashim MJ, Mustafa H, Baniyas MY, Al Suwaidi SKBM, AlKatheeri R, et al. Global Epidemiology of Ischemic Heart Disease: Results from the Global Burden of Disease Study. Cureus [Internet]. 2020 Jul 23;47(2):747–58. Available from: https://www.cureus.com/articles/36728-global-epidemiology-of-ischemic-heart-disease-results-from-the-global-burden-of-disease-study

6. Liang P, Zhang S, Yan M, Huang H, Kang J, Li Y, et al. Trends and predictive research on the global burden of ischemic heart disease from 1990 to 2021: an analysis of the Global Burden of Disease study 2021. Front Public Health. 2025 Sep 19;13.

7. Zhou X, Ruan W, Jie H, Liu H, Wang T, Li J, et al. Global Trends in Ischemic Heart Disease Mortality from 1990 to 2021 and 2036 Projections: Insights from GBD 2021 Data. Glob Heart. 2025 Oct 10;20(1):92.

8. Shi H, Xia Y, Cheng Y, Liang P, Cheng M, Zhang B, et al. Global burden of ischaemic heart disease from 2022 to 2050: projections of incidence, prevalence, deaths, and disability-adjusted life years. Eur Heart J Qual Care Clin Outcomes. 2025 Jun 23;11(4):355–66.

9. Rittiphairoj T, Bulstra C, Ruampatana C, Stavridou M, Grewal S, Reddy CL, et al. The economic burden of ischaemic heart diseases on health systems: a systematic review. BMJ Glob Health. 2025 Feb 12;10(2):e015043.

10. Jespersen L, Abildstrøm SZ, Hvelplund A, Galatius S, Madsen JK, Pedersen F, et al. Symptoms of angina pectoris increase the probability of disability pension and premature exit from the workforce even in the absence of obstructive coronary artery disease. Eur Heart J. 2013 Nov;34(42):3294–303.

11. Vos T, Lim SS, Abbafati C, Abbas KM, Abbasi M, Abbasifard M, et al. Global burden of 369 diseases and injuries in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. The Lancet. 2020 Oct;396(10258):1204–22.

12. Ferrari AJ, Santomauro DF, Aali A, Abate YH, Abbafati C, Abbastabar H, et al. Global incidence, prevalence, years lived with disability (YLDs), disability-adjusted life-years (DALYs), and healthy life expectancy (HALE) for 371 diseases and injuries in 204 countries and territories and 811 subnational locations, 1990–2021: a systematic analysis for the Global Burden of Disease Study 2021. The Lancet. 2024 May;403(10440):2133–61.

13. Yang H, Ma Q, Han L, Liu H. A global prediction of cardiovascular disease from 2020 to 2030. Front Cardiovasc Med. 2025 Aug 11;12.

14. Bhupathiraju SN, Hu FB. Epidemiology of Obesity and Diabetes and Their Cardiovascular Complications. Circ Res. 2016 May 27;118(11):1723–35.

15. United Nations. Department of Economic and Social Affairs. World Social Report 2023: Leaving no one behind in an ageing world. 2023.

16. Gheorghe A, Griffiths U, Murphy A, Legido-Quigley H, Lamptey P, Perel P. The economic burden of cardiovascular disease and hypertension in low- and middle-income countries: a systematic review. BMC Public Health [Internet]. 2018 Dec 6;18(1):975. Available from: https://bmcpublichealth.biomedcentral.com/articles/10.1186/s12889-018-5806-x

17. Cenko E, Manfrini O, Fabin N, Dorobantu M, Kedev S, Milicic D, et al. Clinical determinants of ischemic heart disease in Eastern Europe. The Lancet Regional Health - Europe. 2023 Oct;33:100698.

18. Gouda HN, Charlson F, Sorsdahl K, others. Burden of non-communicable diseases in sub-Saharan Africa, 1990–2017: results from the Global Burden of Disease Study 2017. Lancet Glob Health. 2019;7:e1375–e1387.

19. Prabhakaran D, Jeemon P, Sharma M, Roth GA, Johnson C, Harikrishnan S, et al. The changing patterns of cardiovascular diseases and their risk factors in the states of India: the Global Burden of Disease Study 1990–2016. Lancet Glob Health. 2018 Dec;6(12):e1339–51.

20. Zubaid M, Rashed W, Alsheikh-Ali AA, Garadah T, Alrawahi N, Ridha M, et al. Disparity in ST-segment Elevation Myocardial Infarction Practices and Outcomes in Arabian Gulf Countries (Gulf COAST Registry). Heart Views. 2017;18(2):41–6.

21. Vrints C, Andreotti F, Koskinas KC, Rossello X, Adamo M, Ainslie J, et al. 2024 ESC Guidelines for the management of chronic coronary syndromes. Eur Heart J. 2024 Sep 29;45(36):3415–537.

22. Douglas PS, Hoffmann U, Patel MR, Mark DB, Al-Khalidi HR, Cavanaugh B, et al. Outcomes of Anatomical versus Functional Testing for Coronary Artery Disease. New England Journal of Medicine. 2015 Apr 2;372(14):1291–300.

23. Douglas PS, Nanna MG, Kelsey MD, Yow E, Mark DB, Patel MR, et al. Comparison of an Initial Risk-Based Testing Strategy vs Usual Testing in Stable Symptomatic Patients With Suspected Coronary Artery Disease: The PRECISE Randomized Clinical Trial. JAMA Cardiol. 2023 Oct 1;8(10):904–14.

24. Kaur G, Oliveira-Gomes D De, Rivera FB, Gulati M. Chest Pain in Women: Considerations From the 2021 AHA/ACC Chest Pain Guideline. Curr Probl Cardiol. 2023 Jul;48(7):101697.

25. Spitzer E, McFadden E, Vranckx P, Garcia-Garcia HM, Seltzer JH, Held C, et al. Critical Appraisal of Contemporary Clinical Endpoint Definitions in Coronary Intervention Trials: A Guidance Document. JACC Cardiovasc Interv. 2019 May 13;12(9):805–19.

26. Kronenberg F, Mora S, Stroes ESG, Ference BA, Arsenault BJ, Berglund L, et al. Lipoprotein(a) in atherosclerotic cardiovascular disease and aortic stenosis: a European Atherosclerosis Society consensus statement. Eur Heart J. 2022 Oct 14;43(39):3925–46.

27. Morrow DA, de Lemos JA, Blazing MA, Sabatine MS, Murphy SA, Jarolim P, et al. Prognostic value of serial B-type natriuretic peptide testing during follow-up of patients with unstable coronary artery disease. JAMA. 2005 Dec 14;294(22):2866–71.

28. Gulati M, Levy PD, Mukherjee D, Amsterdam E, Bhatt DL, Birtcher KK, et al. 2021 AHA/ACC/ASE/CHEST/SAEM/SCCT/SCMR Guideline for the Evaluation and Diagnosis of Chest Pain: Executive Summary. J Am Coll Cardiol. 2021 Nov;78(22):2218–61.

29. van der Ende MY, Siland JE, Snieder H, van der Harst P, Rienstra M. Population-based values and abnormalities of the electrocardiogram in the general Dutch population: The <scp>LifeLines</scp> Cohort Study. Clin Cardiol. 2017 Oct 12;40(10):865–72.

30. Mark DB, Shaw L, Harrell FE, Hlatky MA, Lee KL, Bengtson JR, et al. Prognostic Value of a Treadmill Exercise Score in Outpatients with Suspected Coronary Artery Disease. New England Journal of Medicine. 1991 Sep 19;325(12):849–53.

31. Coronary CT Angiography and 5-Year Risk of Myocardial Infarction. New England Journal of Medicine. 2018 Sep 6;379(10):924–33.

32. Xaplanteris P, Fournier S, Pijls NHJ, Fearon WF, Barbato E, Tonino PAL, et al. Five-Year Outcomes with PCI Guided by Fractional Flow Reserve. New England Journal of Medicine. 2018 Jul 19;379(3):250–9.

33. Götberg M, Christiansen EH, Gudmundsdottir IJ, Sandhall L, Danielewicz M, Jakobsen L, et al. Instantaneous Wave-free Ratio versus Fractional Flow Reserve to Guide PCI. New England Journal of Medicine. 2017 May 11;376(19):1813–23.

34. Delgado-Lista J, Alcala-Diaz JF, Torres-Peña JD, Quintana-Navarro GM, Fuentes F, Garcia-Rios A, et al. Long-term secondary prevention of cardiovascular disease with a Mediterranean diet and a low-fat diet (CORDIOPREV): a randomised controlled trial. The Lancet. 2022 May;399(10338):1876–85.

35. Laffond A, Rivera-Picón C, Rodríguez-Muñoz PM, Juárez-Vela R, Ruiz de Viñaspre-Hernández R, Navas-Echazarreta N, et al. Mediterranean Diet for Primary and Secondary Prevention of Cardiovascular Disease and Mortality: An Updated Systematic Review. Nutrients. 2023 Jul 28;15(15):3356.

36. O'Donnell MJ, Yusuf S, Mente A, Gao P, Mann JF, Teo K, et al. Urinary Sodium and Potassium Excretion and Risk of Cardiovascular Events. JAMA. 2011 Nov 23;306(20).

37. Sacks FM, Svetkey LP, Vollmer WM, Appel LJ, Bray GA, Harsha D, et al. Effects on Blood Pressure of Reduced Dietary Sodium and the Dietary Approaches to Stop Hypertension (DASH) Diet. New England Journal of Medicine. 2001 Jan 4;344(1):3–10.

38. Rodrigues BS, Alves M, Duarte GS, Costa J, Pinto FJ, Caldeira D. The impact of influenza vaccination in patients with cardiovascular disease: An overview of systematic reviews. Trends Cardiovasc Med. 2021 Jul;31(5):315–20.

39. Caldeira D, Ferreira JJ, Costa J. Influenza vaccination and prevention of cardiovascular disease mortality. The Lancet. 2018;391(10119).

40. Fröbert O, Götberg M, Erlinge D, Akhtar Z, Christiansen EH, MacIntyre CR, et al. Influenza Vaccination After Myocardial Infarction: A Randomized, Double-Blind, Placebo-Controlled, Multicenter Trial. Circulation. 2021 Nov 2;144(18):1476–84.

41. Zinman B, Wanner C, Lachin JM, Fitchett D, Bluhmki E, Hantel S, et al. Empagliflozin, Cardiovascular Outcomes, and Mortality in Type 2 Diabetes. New England Journal of Medicine. 2015 Nov 26;373(22):2117–28.

42. Marso SP, Daniels GH, Brown-Frandsen K, Kristensen P, Mann JFE, Nauck MA, et al. Liraglutide and Cardiovascular Outcomes in Type 2 Diabetes. New England Journal of Medicine. 2016 Jul 28;375(4):311–22.

43. Lincoff AM, Brown-Frandsen K, Colhoun HM, Deanfield J, Emerson SS, Esbjerg S, et al. Semaglutide and Cardiovascular Outcomes in Obesity without Diabetes. New England Journal of Medicine. 2023 Dec 14;389(24):2221–32.

44. Cosentino F, Grant PJ, Aboyans V, Bailey CJ, Ceriello A, Delgado V, et al. 2019 ESC Guidelines on diabetes, pre-diabetes, and cardiovascular diseases developed in collaboration with the EASD. Eur Heart J. 2020 Jan 7;41(2):255–323.

45. Cholesterol Treatment Trialists' (CTT) Collaboration. Efficacy and safety of more intensive lowering of LDL cholesterol: a meta-analysis of data from 170 000 participants in 26 randomised trials. The Lancet. 2010 Nov;376(9753):1670–81.

46. Cannon CP, Blazing MA, Giugliano RP, McCagg A, White JA, Theroux P, et al. Ezetimibe Added to Statin Therapy after Acute Coronary Syndromes. New England Journal of Medicine. 2015 Jun 18;372(25):2387–97.

47. Sabatine MS, Giugliano RP, Keech AC, Honarpour N, Wiviott SD, Murphy SA, et al. Evolocumab and Clinical Outcomes in Patients with Cardiovascular Disease. New England Journal of Medicine. 2017 May 4;376(18):1713–22.

48. Schwartz GG, Steg PG, Szarek M, Bhatt DL, Bittner VA, Diaz R, et al. Alirocumab and Cardiovascular Outcomes after Acute Coronary Syndrome. New England Journal of Medicine. 2018 Nov 29;379(22):2097–107.

49. Bhatt DL, Steg PG, Miller M, Brinton EA, Jacobson TA, Ketchum SB, et al. Cardiovascular Risk Reduction with Icosapent Ethyl for Hypertriglyceridemia. New England Journal of Medicine. 2019 Jan 3;380(1):11–22.

50. Nissen SE, Lincoff AM, Brennan D, Ray KK, Mason D, Kastelein JJP, et al. Bempedoic Acid and Cardiovascular Outcomes in Statin-Intolerant Patients. New England Journal of Medicine. 2023 Apr 13;388(15):1353–64.

51. Ridker PM, Everett BM, Thuren T, MacFadyen JG, Chang WH, Ballantyne C, et al. Antiinflammatory Therapy with Canakinumab for Atherosclerotic Disease. New England Journal of Medicine. 2017 Sep 21;377(12):1119–31.

52. Tardif JC, Kouz S, Waters DD, Bertrand OF, Diaz R, Maggioni AP, et al. Efficacy and Safety of Low-Dose Colchicine after Myocardial Infarction. New England Journal of Medicine. 2019 Dec 26;381(26):2497–505.

53. Nidorf SM, Fiolet ATL, Mosterd A, Eikelboom JW, Schut A, Opstal TSJ, et al. Colchicine in Patients with Chronic Coronary Disease. New England Journal of Medicine. 2020 Nov 5;383(19):1838–47.

54. Jolly SS, d'Entremont MA, Lee SF, Mian R, Tyrwhitt J, Kedev S, et al. Colchicine in Acute Myocardial Infarction. New England Journal of Medicine. 2025 Feb 13;392(7):633–42.

55. Ferrari R, Gowdak LHW, Padilla F, Quek DKL, Ray S, Rosano G, et al. The European Society of Cardiology 2024 Guidelines on Chronic Coronary Syndromes: A Critical Appraisal. J Clin Med. 2025 Feb 11;14(4):1161.

56. Collaboration AT. Collaborative meta-analysis of randomised trials of antiplatelet therapy for prevention of death, myocardial infarction, and stroke in high risk patients. BMJ. 2002 Jan 12;324(7329):71–86.

57. Byrne RA, Rossello X, Coughlan JJ, Barbato E, Berry C, Chieffo A, et al. 2023 ESC Guidelines for the management of acute coronary syndromes. Eur Heart J. 2023 Oct 12;44(38):3720–826.

58. Farkouh ME, Domanski M, Sleeper LA, Siami FS, Dangas G, Mack M, et al. Strategies for Multivessel Revascularization in Patients with Diabetes. New England Journal of Medicine. 2012 Dec 20;367(25):2375–84.

59. Velazquez EJ, Lee KL, Jones RH, Al-Khalidi HR, Hill JA, Panza JA, et al. Coronary-Artery Bypass Surgery in Patients with Ischemic Cardiomyopathy. New England Journal of Medicine. 2016 Apr 21;374(16):1511–20.

60. Mohr FW, Morice MC, Kappetein AP, Feldman TE, Ståhle E, Colombo A, et al. Coronary artery bypass graft surgery versus percutaneous coronary intervention in patients with three-vessel disease and left main coronary disease: 5-year follow-up of the randomised, clinical SYNTAX trial. The Lancet. 2013 Feb;381(9867):629–38.

61. Velazquez EJ, Lee KL, Jones RH, Al-Khalidi HR, Hill JA, Panza JA, et al. Coronary-Artery Bypass Surgery in Patients with Ischemic Cardiomyopathy. N Engl J Med. 2016 Apr 21;374(16):1511–20.

62. De Bruyne B, Pijls NHJ, Kalesan B, Barbato E, Tonino PAL, Piroth Z, et al. Fractional Flow Reserve–Guided PCI versus Medical Therapy in Stable Coronary Disease. New England Journal of Medicine. 2012 Sep 13;367(11):991–1001.

63. Lee JM, Choi KH, Song Y Bin, Lee JY, Lee SJ, Lee SY, et al. Intravascular Imaging–Guided or Angiography-Guided Complex PCI. New England Journal of Medicine. 2023 May 4;388(18):1668–79.

64. Ali ZA, Landmesser U, Maehara A, Matsumura M, Shlofmitz RA, Guagliumi G, et al. Optical Coherence Tomography–Guided versus Angiography-Guided PCI. New England Journal of Medicine. 2023 Oct 19;389(16):1466–76.

65. ICARDIO-Alliance WTF. Draft Document for Public Consultation: iCARDIO Alliance Global Implementation Guidelines on Heart Failure 2025. Global Cardiology. 2024 Dec 30;2(4).

66. Chopra V, Khan MS, Abdelhamid M, Abraham WT, Amir O, Anker SD, et al. iCARDIO Alliance Global Implementation Guidelines on Heart Failure 2025. Heart Lung Circ. 2025 Jul;34(7):e55–82.

67. Ong P, Camici PG, Beltrame JF, Crea F, Shimokawa H, Sechtem U, et al. International standardization of diagnostic criteria for microvascular angina. Int J Cardiol. 2018 Jan;250:16–20.

68. Beltrame JF, Crea F, Kaski JC, Ogawa H, Ong P, Sechtem U, et al. The Who, What, Why, When, How and Where of Vasospastic Angina. Circulation Journal. 2016;80(2):289–98.

69. Gallone G, Baldetti L, Tzanis G, Gramegna M, Latib A, Colombo A, et al. Refractory Angina: From Pathophysiology to New Therapeutic Nonpharmacological Technologies. JACC Cardiovasc Interv [Internet]. 2020 Jan 13;13(1):1–19. Available from: http://www.ncbi.nlm.nih.gov/pubmed/31918927

70. Amin AM, Khan U, Khlidj Y, Katamesh BE, Elbenawi H, Ewis A, et al. Efficacy and safety of coronary sinus reducer for refractory angina: a systematic review and meta-analysis of randomized controlled trials. Coron Artery Dis. 2024 Oct 31;

71. Caceres J, Atal P, Arora R, Yee D. Enhanced external counterpulsation: A unique treatment for the "No-Option" refractory angina patient. J Clin Pharm Ther. 2021 Apr 7;46(2):295–303.

72. Imran TF, Malapero R, Qavi AH, Hasan Z, de la Torre B, Patel YR, et al. Efficacy of spinal cord stimulation as an adjunct therapy for chronic refractory angina pectoris. Int J Cardiol. 2017 Jan;227:535–42.

73. Van Gelder IC, Rienstra M, Bunting K V, Casado-Arroyo R, Caso V, Crijns HJGM, et al. 2024 ESC Guidelines for the management of atrial fibrillation developed in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS). Eur Heart J. 2024 Sep 29;45(36):3314–414.

74. Bangalore S, Maron DJ, O'Brien SM, Fleg JL, Kretov EI, Briguori C, et al. Management of Coronary Disease in Patients with Advanced Kidney Disease. New England Journal of Medicine. 2020 Apr 23;382(17):1608–18.

75. Lyon AR, López-Fernández T, Couch LS, Asteggiano R, Aznar MC, Bergler-Klein J, et al. 2022 ESC Guidelines on cardio-oncology developed in collaboration with the European Hematology Association (EHA), the European Society for Therapeutic Radiology and Oncology (ESTRO) and the International Cardio-Oncology Society (IC-OS). Eur Heart J. 2022 Nov 1;43(41):4229–361.

76. Grinspoon SK, Fitch K V., Zanni M V., Fichtenbaum CJ, Umbleja T, Aberg JA, et al. Pitavastatin to Prevent Cardiovascular Disease in HIV Infection. New England Journal of Medicine. 2023 Aug 24;389(8):687–99.

77. Vogel B, Acevedo M, Appelman Y, Bairey Merz CN, Chieffo A, Figtree GA, et al. The Lancet women and cardiovascular disease Commission: reducing the global burden by 2030. The Lancet. 2021 Jun;397(10292):2385–438.

78. Hemal K, Pagidipati NJ, Coles A, Dolor RJ, Mark DB, Pellikka PA, et al. Sex Differences in Demographics, Risk Factors, Presentation, and Noninvasive Testing in Stable Outpatients With Suspected Coronary Artery Disease. JACC Cardiovasc Imaging. 2016 Apr;9(4):337–46.

79. Shaw LJ, Bairey Merz CN, Pepine CJ, Reis SE, Bittner V, Kelsey SF, et al. Insights From the NHLBI-Sponsored Women's Ischemia Syndrome Evaluation (WISE) Study. J Am Coll Cardiol. 2006 Feb;47(3):S4–20.

80. Mehta LS, Beckie TM, DeVon HA, Grines CL, Krumholz HM, Johnson MN, et al. Acute Myocardial Infarction in Women. Circulation. 2016 Mar;133(9):916–47.

81. Gulati M, Shaw LJ, Bairey Merz CN. Myocardial Ischemia in Women: Lessons From the NHLBI WISE Study. Clin Cardiol. 2012 Mar 2;35(3):141–8.

82. Afilalo J, Alexander KP, Mack MJ, Maurer MS, Green P, Allen LA, et al. Frailty Assessment in the Cardiovascular Care of Older Adults. J Am Coll Cardiol. 2014 Mar;63(8):747–62.

83. Fried LP, Tangen CM, Walston J, Newman AB, Hirsch C, Gottdiener J, et al. Frailty in Older Adults: Evidence for a Phenotype. J Gerontol A Biol Sci Med Sci. 2001 Mar 1;56(3):M146–57.

84. Maron DJ, Newman JD, Anthopolos R, Lu Y, Stevens S, Boden WE, et al. Guideline-Directed Medical Therapy and Outcomes in the ISCHEMIA Trial. J Am Coll Cardiol. 2025 Apr;85(12):1317–31.