CMHC
Cardiometabolic Health Congress

www.cardiometabolichealth.org

Foundations of Cardiometabolic Health Certification Course

Certified Cardiometabolic Health Professional (CCHP)

Coronary Artery Disease

Deepak L. Bhatt, MD, MPH

Executive Director of Interventional Cardiovascular Programs, Brigham and Women's Hospital
Professor of Medicine, Harvard Medical School

BWH BRIGHAM AND WOMEN'S HOSPITAL | Heart & Vascular Center |

HARVARD MEDICAL SCHOOL TEACHING HOSPITAL

Disclosures

Dr. Bhatt discloses the following relationships - Advisory Board: Bayer, Boehringer Ingelheim, Cardax, CellProthera, Cereno Scientific, Elsevier Practice Update Cardiology, Janssen, Level Ex, Medscape Cardiology, Merck, MyoKardia, NirvaMed, Novo Nordisk, PhaseBio, PLx Pharma, Regado Biosciences, Stasys; Board of Directors: Boston VA Research Institute, DRS.LINQ (stock options), Society of Cardiovascular Patient Care, TobeSoft; Chair: Inaugural Chair, American Heart Association Quality Oversight Committee; Data Monitoring Committees: Acesion Pharma, Assistance Publique-Hôpitaux de Paris, Baim Institute for Clinical Research (formerly Harvard Clinical Research Institute, for the PORTICO trial, funded by St. Jude Medical, now Abbott), Boston Scientific (Chair, PEITHO trial), Cleveland Clinic (including for the ExCEED trial, funded by Edwards), Contego Medical (Chair, PERFORMANCE 2), Duke Clinical Research Institute, Mayo Clinic, Mount Sinai School of Medicine (for the ENVISAGE trial, funded by Daiichi Sankyo; for the ABILITY-DM trial, funded by Concept Medical), Novartis, Population Health Research Institute; Rutgers University (for the NIH-funded MINT Trial); Honoraria: American College of Cardiology (Senior Associate Editor, Clinical Trials and News, ACC.org; Chair, ACC Accreditation Oversight Committee), Arnold and Porter law firm (work related to Sanofi/Bristol-Myers Squibb clopidogrel litigation), Baim Institute for Clinical Research (formerly Harvard Clinical Research Institute; RE-DUAL PCI clinical trial steering committee funded by Boehringer Ingelheim; AEGIS-II executive committee funded by CSL Behring), Belvoir Publications (Editor in Chief, Harvard Heart Letter), Canadian Medical and Surgical Knowledge Translation Research Group (clinical trial steering committees), Cowen and Company, Duke Clinical Research Institute (clinical trial steering committees, including for the PRONOUNCE trial, funded by Ferring Pharmaceuticals), HMP Global (Editor in Chief, Journal of Invasive Cardiology), Journal of the American College of Cardiology (Guest Editor; Associate Editor), K2P (Co-Chair, interdisciplinary curriculum), Level Ex, Medtelligence/ReachMD (CME steering committees), MJH Life Sciences, Piper Sandler, Population Health Research Institute (for the COMPASS operations committee, publications committee, steering committee, and USA national co-leader, funded by Bayer), Slack Publications (Chief Medical Editor, Cardiology Today's Intervention), Society of Cardiovascular Patient Care (Secretary/Treasurer), WebMD (CME steering committees); Other: Clinical Cardiology (Deputy Editor), NCDR-ACTION Registry Steering Committee (Chair), VA CART Research and Publications Committee (Chair); Research Funding: Abbott, Afimmune, Aker Biomarine, Amarin, Amgen, AstraZeneca, Bayer, Beren, Boehringer Ingelheim, Bristol-Myers Squibb, Cardax, CellProthera, Cereno Scientific, Chiesi, CSL Behring, Eisai, Ethicon, Faraday Pharmaceuticals, Ferring Pharmaceuticals, Forest Laboratories, Fractyl, Garmin, HLS Therapeutics, Idorsia, Ironwood, Ischemix, Janssen, Javelin, Lexicon, Lilly, Medtronic, Merck, Moderna, MyoKardia, NirvaMed, Novartis, Novo Nordisk, Owkin, Pfizer, PhaseBio, PLx Pharma, Recardio, Regeneron, Reid Hoffman Foundation, Roche, Sanofi, Stasys, Synaptic, The Medicines Company, 89Bio; Royalties: Elsevier (Editor, Cardiovascular Intervention: A Companion to Braunwald's Heart Disease); Site Co-Investigator: Abbott, Biotronik, Boston Scientific, CSI, St. Jude Medical (now Abbott), Philips, Svelte; Trustee: American College of Cardiology; Unfunded Research: FlowCo, Takeda.

This presentation includes off-label and investigational uses of drugs and devices.

CMHC
Cardiometabolic Health Congress

www.cardiometabolichealth.org

Foundations of Cardiometabolic Health Certification Course

Certified Cardiometabolic Health Professional (CCHP)

ACS: Initial Evaluation, Diagnosis, and Treatment

Deepak L. Bhatt, MD, MPH

Executive Director of Interventional Cardiovascular Programs, Brigham and Women's Hospital
Professor of Medicine, Harvard Medical School

BWH BRIGHAM AND WOMEN'S HOSPITAL
| Heart & Vascular Center |

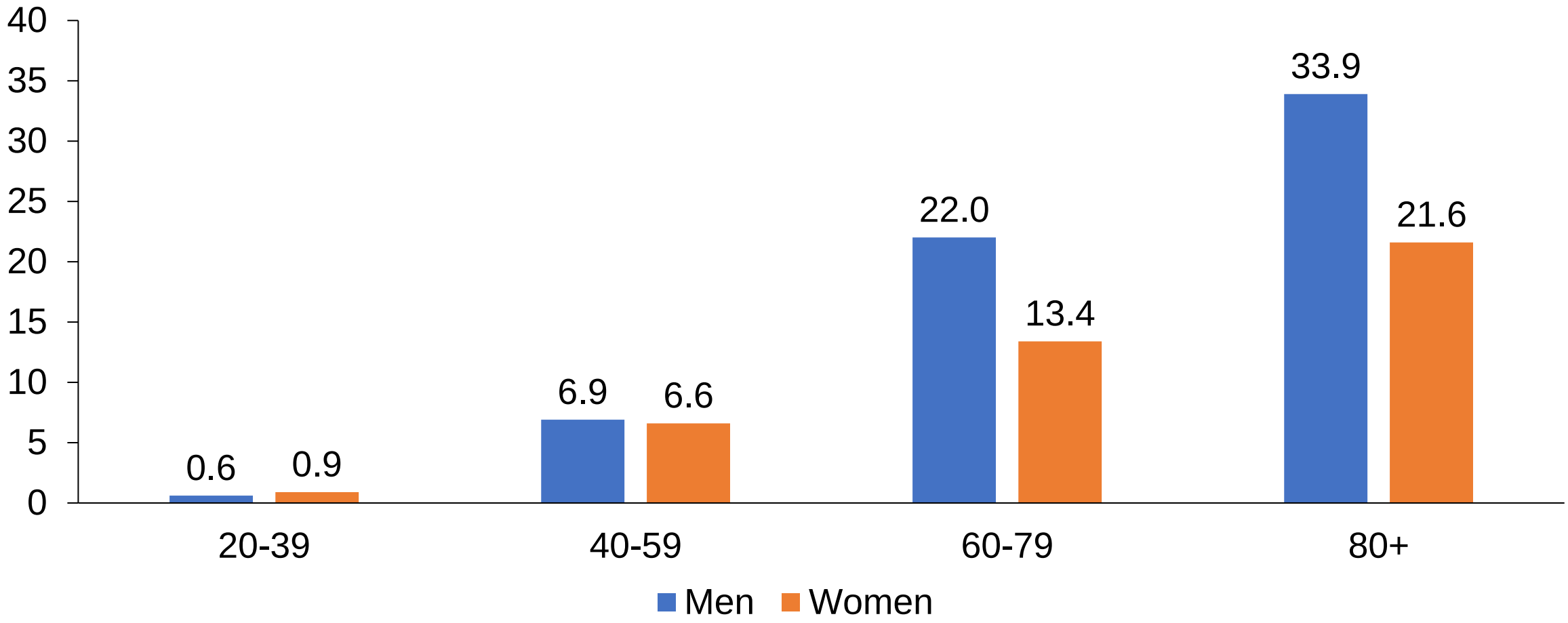
HARVARD MEDICAL SCHOOL TEACHING HOSPITAL

Epidemiology & Burden of Disease

- Coronary artery disease (CAD) is the leading cause of mortality and loss of disability adjusted life years (DALYs) worldwide with nearly 7 million deaths and 129 million DALYs annually
- In the US, an estimated 20.1 million adults aged 20 and older have CAD, and someone has an MI approximately every 40 seconds
- Mortality and incidence differ by country, and in the most recent decades, has fallen in high-income countries; a large portion of this burden falls on low- and middle-income countries

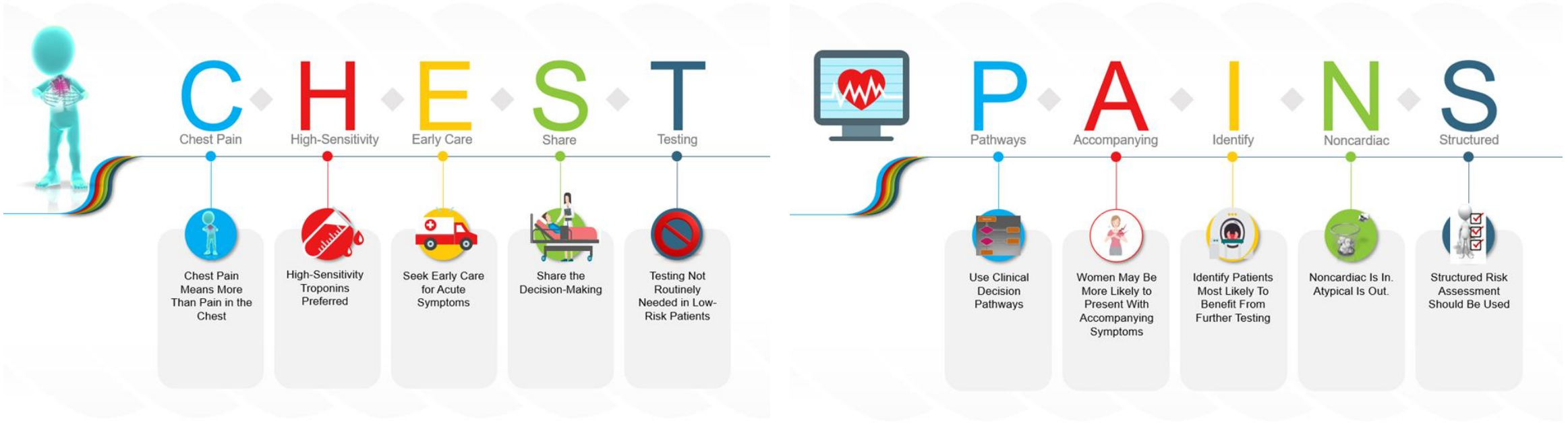
Ralapanawa U, Sivakanesan R. *J Epidemiol Glob Health*. 2021;11:169-177.
Tsao CW, Aday AW, Almarzooq ZI, Alonso A, Beaton AZ, Bittencourt MS, et al. *Circulation*. 2022 Jan 26.

Prevalence of CHD by Age and Sex in the US (2015-2018)



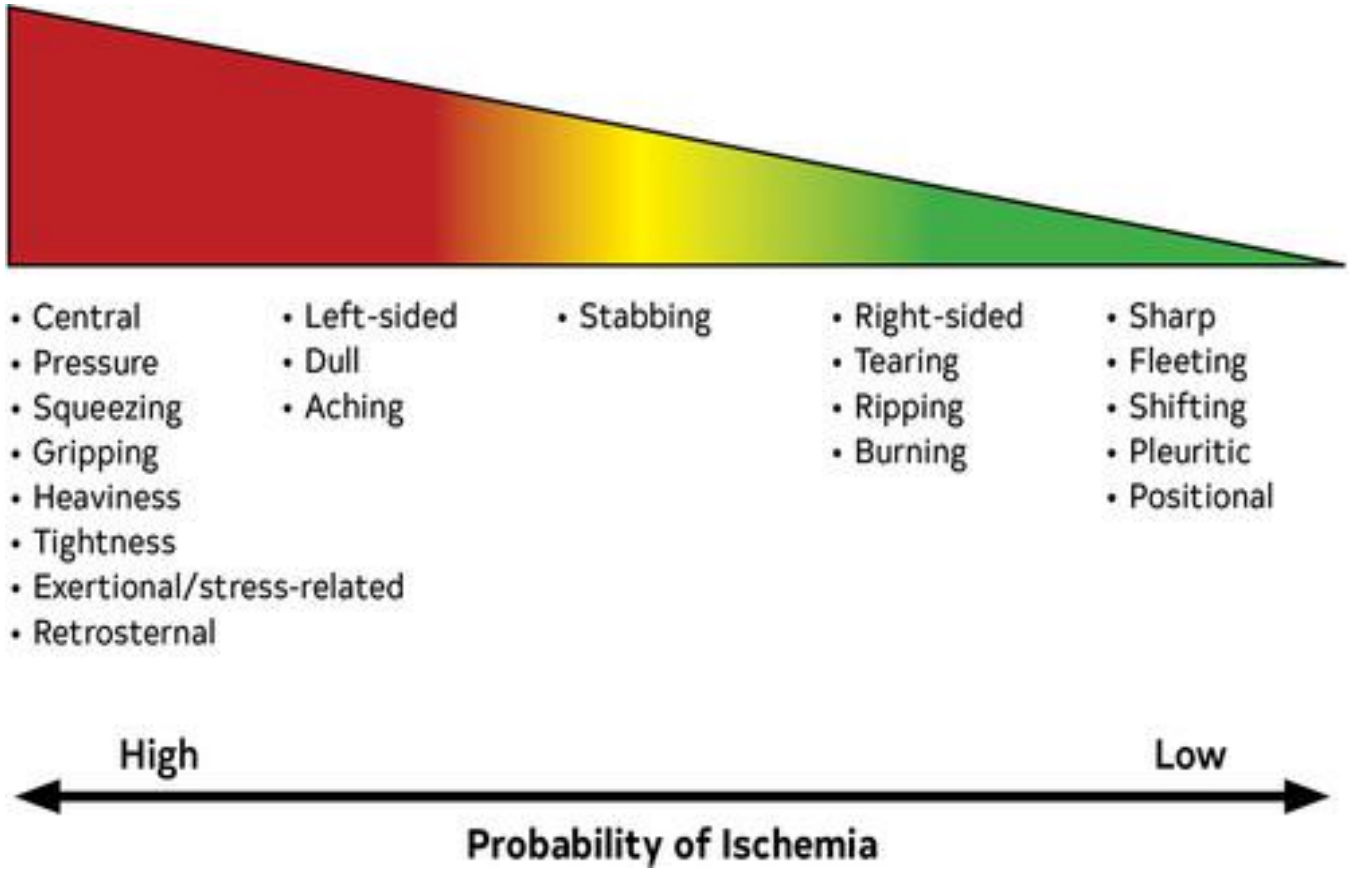
Tsao CW, Aday AW, Almarzooq ZI, Alonso A, Beaton AZ, Bittencourt MS, et al. Circulation. 2022 Jan 26.

Take-Home Messages for the Evaluation and Diagnosis of Chest Pain



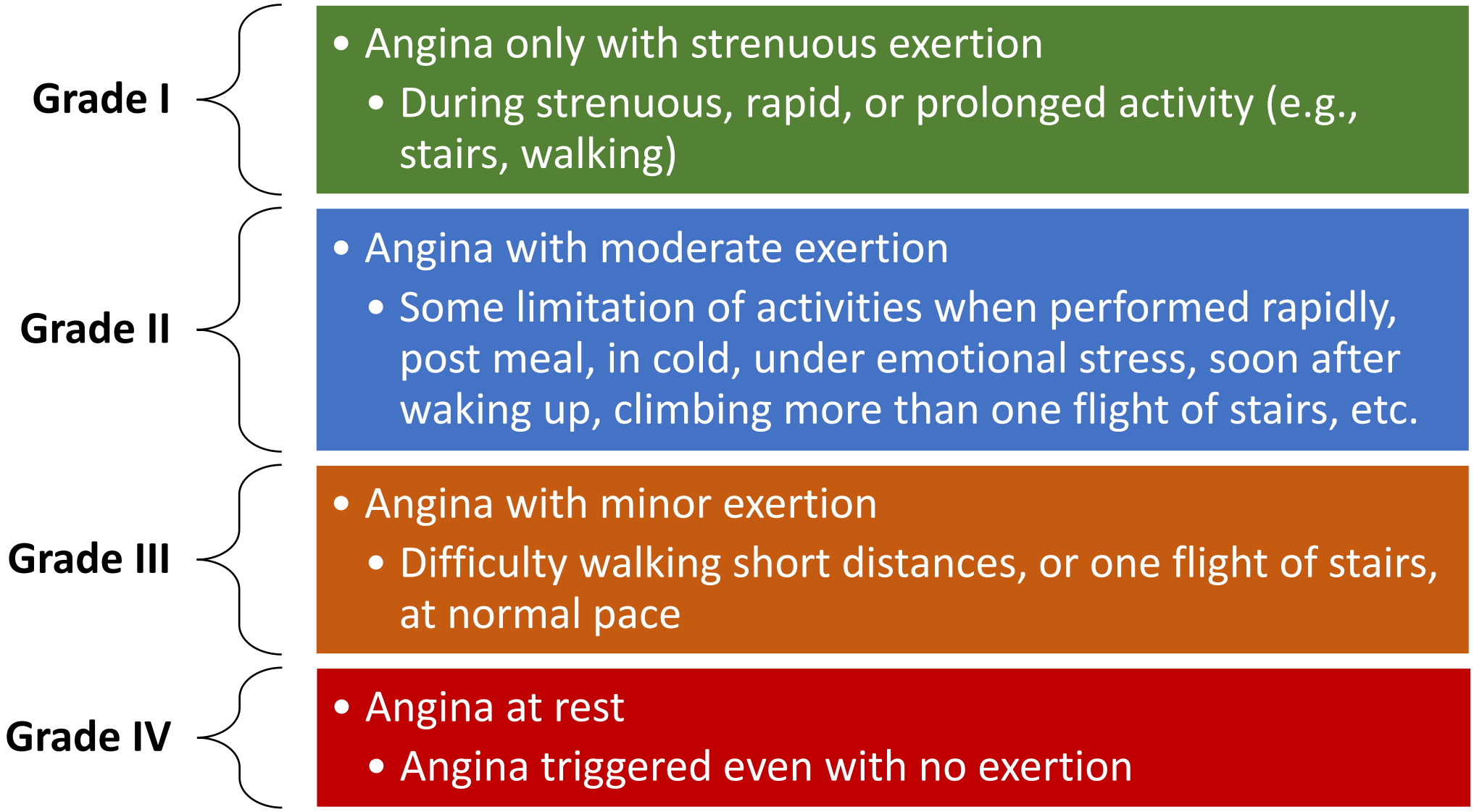
Gulati M, Levy PD, Mukherjee D, Amsterdam E, Bhatt DL, Birtcher KK, et al. Circulation. 2021;144:e368-e454.

Symptoms and Signs: Chest Pain



Gulati M, Levy PD, Mukherjee D, Amsterdam E, Bhatt DL, Birtcher KK, et al. Circulation. 2021;144:e368-e454.

Angina Severity: Canadian Cardiovascular Society



Knuuti J, Wijns W, Saraste A, Capodanno D, Barbato E, Funck-Brenato C, et al. Eur Heart J. 2020;41:407-477.

Commonly Asked Questions about ACS

What Are Acute Coronary Syndromes (ACS)?

- ACS refer to a sudden reduction in blood supply to the heart muscle due to ST-elevation myocardial infarction (STEMI), non-ST-elevation myocardial infarction (NSTEMI), or unstable angina.

How Are ACS Diagnosed?

- In addition to a clinical history that most often includes sudden onset of severe chest discomfort, prompt electrocardiography and high sensitivity troponin measurements are critical to diagnose whether ACS are present and whether a STEMI, NSTEMI, or unstable angina, which further guides the exact therapeutic strategy.

What Causes ACS?

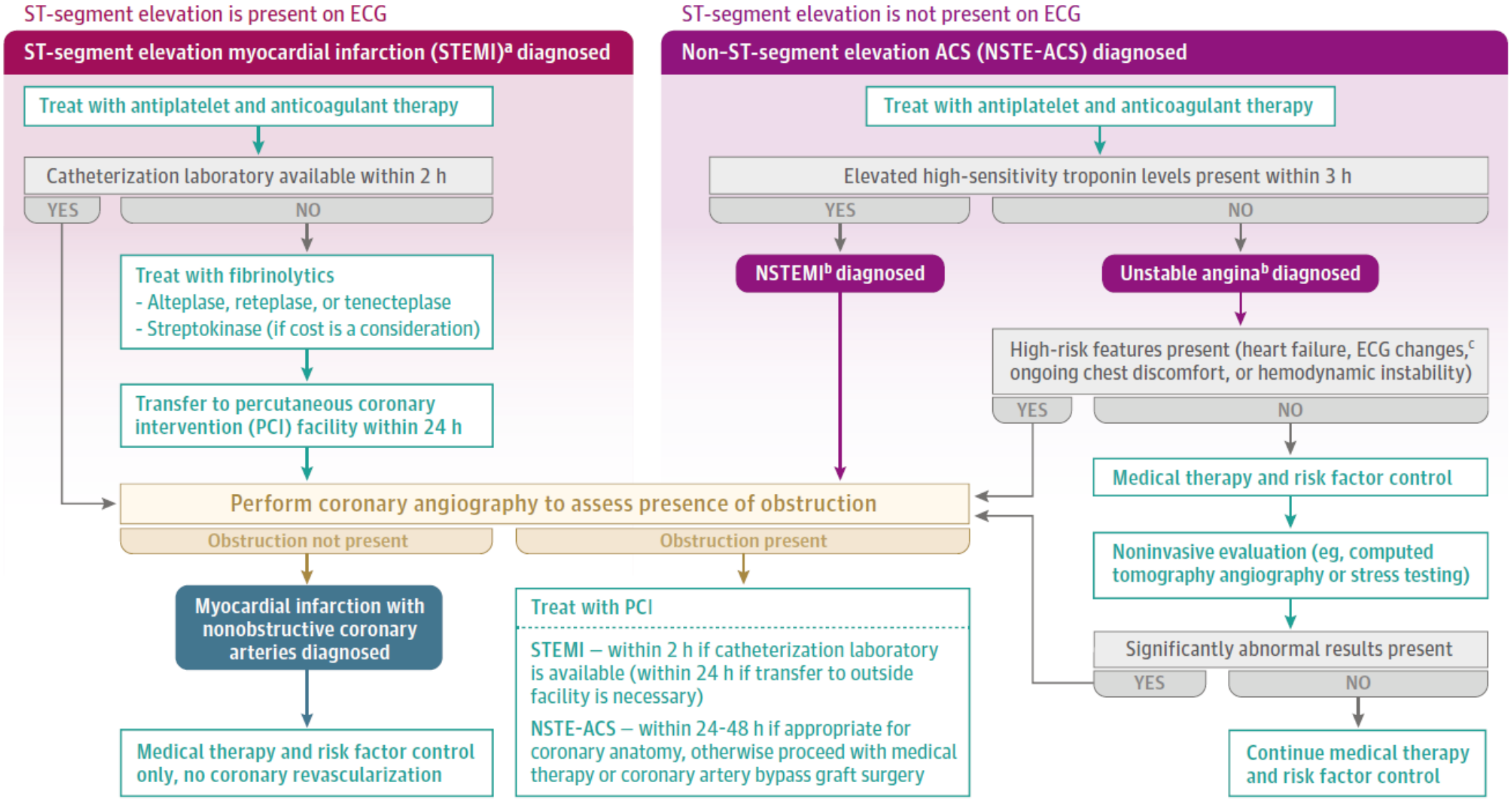
- The most common cause of ACS is rupture of atherosclerotic plaque with thrombus formation. Other less frequent causes include plaque erosion, calcific nodules, coronary spasm, spontaneous coronary artery dissection, coronary embolism, and myocardial infarction with non-obstructive coronary arteries (MINOCA).

Do All Patients With ACS Need a Cardiac Catheterization?

- The majority of patients, such as those with electrocardiographic changes, elevated troponin levels, ongoing chest pain, hypotension, or ventricular arrythmias will need to undergo cardiac catheterization, and based on their coronary anatomy, percutaneous or surgical revascularization. Low risk patients without these features are most often initially managed with medications only and noninvasive testing to risk stratify them.

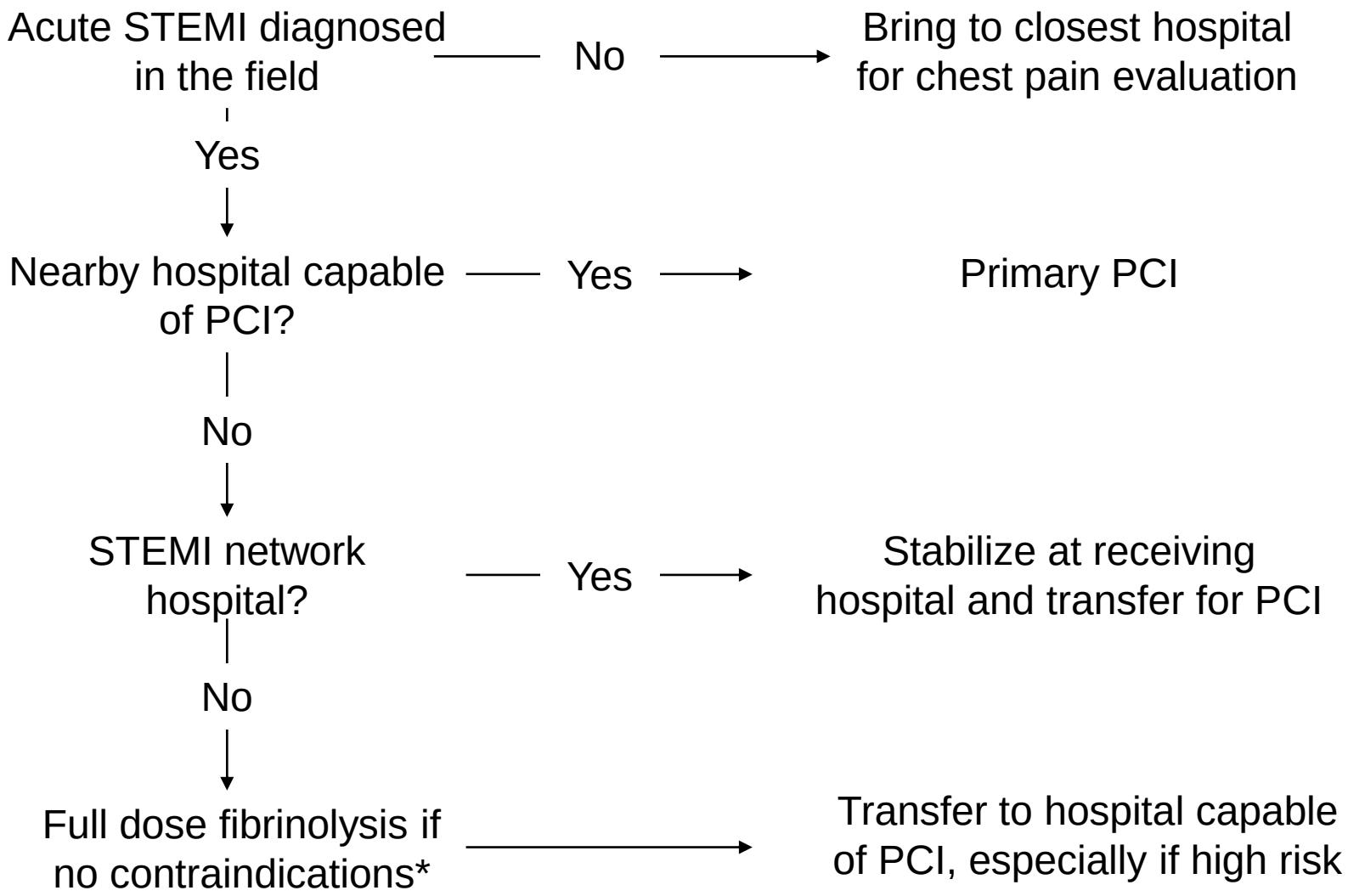
Bhatt DL, Lopes RD, Harrington RA. JAMA. 2022;327:662-675.

Initial Diagnosis and Management of ACS



Bhatt DL, Lopes RD, Harrington RA. JAMA. 2022;327:662-675.

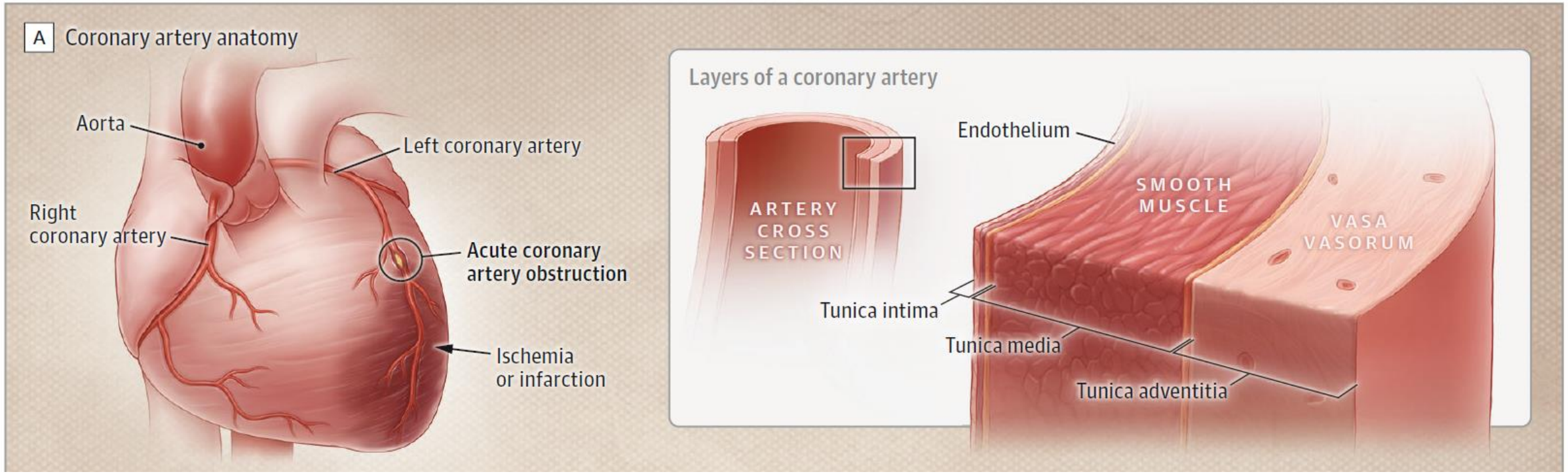
Treatment of STEMI Algorithm



***Consider half-dose agent if 75 years of age or older**

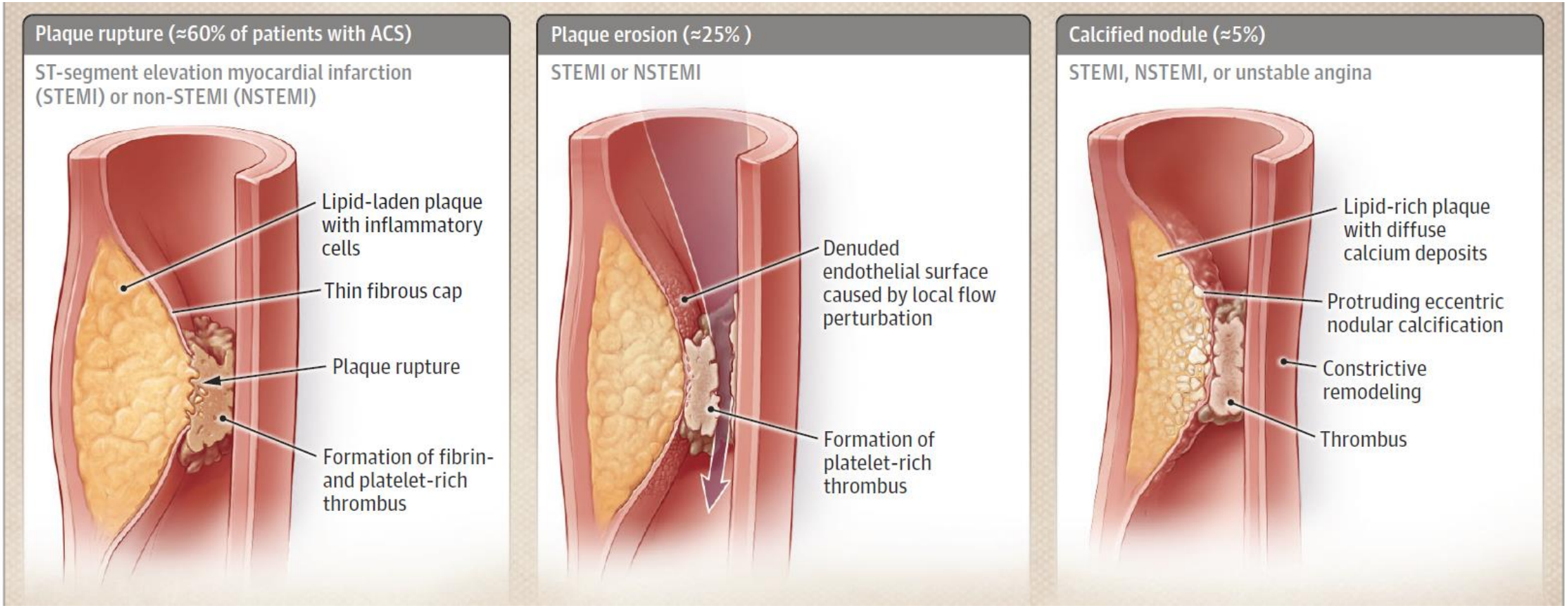
Bhatt DL. N Engl J Med. 2013;368:1446-7.

Plaque Rupture and Etiologies of ACS



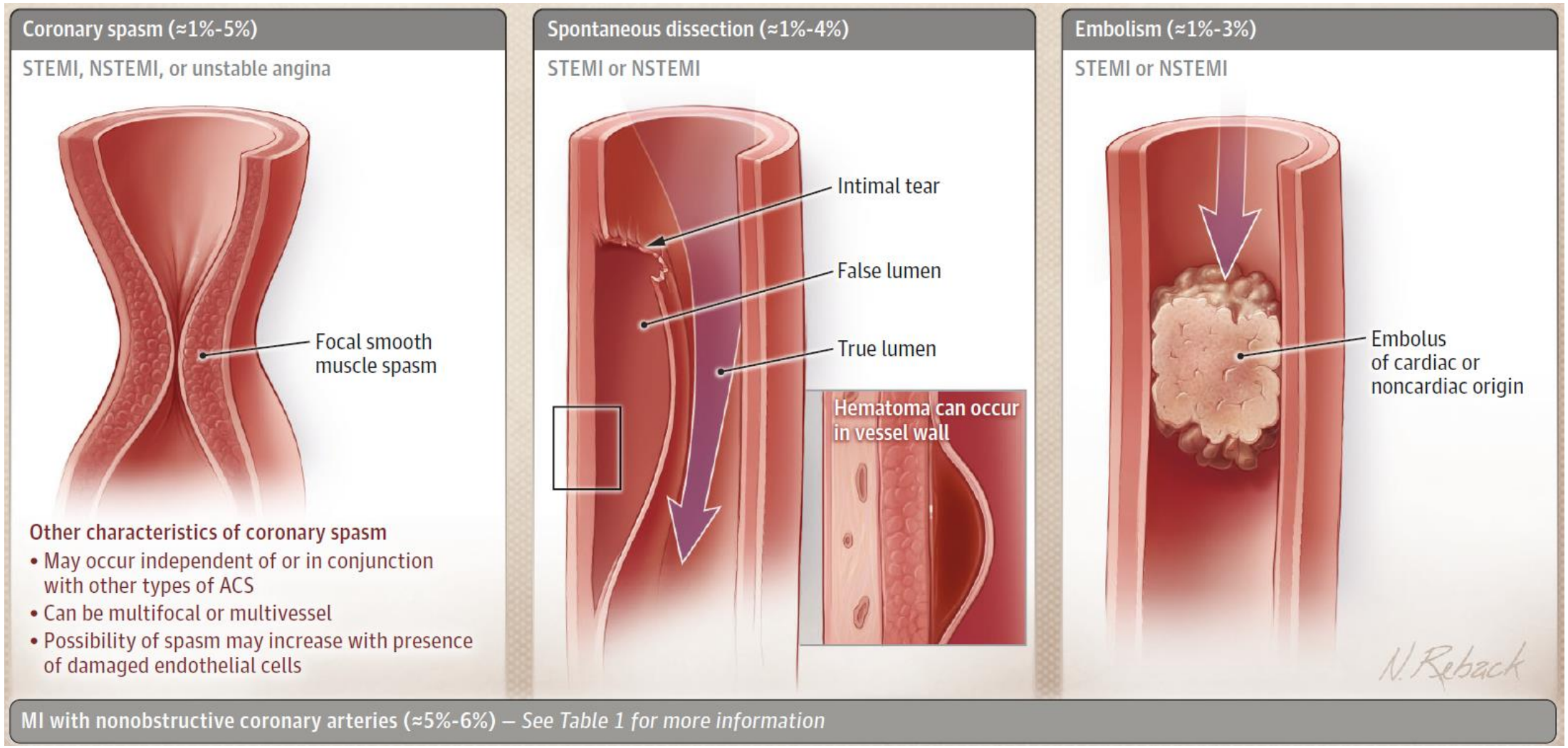
Bhatt DL, Lopes RD, Harrington RA. JAMA. 2022;327:662-675.

Causes of ACS



Bhatt DL, Lopes RD, Harrington RA. JAMA. 2022;327:662-675.

Causes of ACS



Bhatt DL, Lopes RD, Harrington RA. JAMA. 2022;327:662-675.

Etiologies of ACS

Cause	ACS Type	Pathophysiology	Characteristics	% ACS
Plaque rupture	STEMI or NSTEMI	Lipid-laden plaque rupture due to inflammation followed by development of platelet-rich thrombosis	Most common etiology in both sexes	~60%
Plaque erosion	STEMI or NSTEMI	Plaque erosion occurs with local flow perturbation, resulting in a denuded endothelial surface with formation of neutrophil extracellular traps and propagation of thrombus formation	More common in women than men	~25%
Calcific nodule	STEMI, NSTEMI, or UA	A protruding nodular calcification penetrates the lumen surface with subsequent thrombus formation	Patients with CKD and those on dialysis have a higher prevalence of coronary calcific nodules Calcific nodules are associated with a higher rate of requiring repeat coronary revascularization due to growth of the calcified nodule	~5%
Coronary spasm	STEMI, NSTEMI, or UA	Extreme vasoconstriction of an epicardial coronary artery, which causes near or total vessel occlusion and sometimes superimposed thrombosis	In patients with ACS who do not have obstructive CAD on angiography, coronary spasm can be evaluated with provocative testing, such as administering acetylcholine, though typically just treated empirically without such testing	~1-5%
Spontaneous coronary artery dissection (SCAD)	STEMI, NSTEMI,	Obstruction to blood flow due to separation of the medial/adventitial vascular walls associated with intramural hematoma protrusion into the lumen; either in single or multiple arteries; more often affects the middle and distal portions of the artery, most commonly the left anterior descending artery	~90% women (~55% postmenopausal); emotional stress reported in ~50%, physical stress in ~30%; fibromuscular dysplasia, systemic inflammatory disorders, peripartum state, and connective tissue disorders predispose; best to reserve PCI or CABG for refractory symptoms	~1-4%
Coronary artery embolism due to thrombus from elsewhere	STEMI, NSTEMI	Conditions such as AF, left ventricular thrombus, valvular thrombus, or paradoxical emboli from the venous system passing through an atrial or ventricular septal defect are associated with coronary artery embolism, which leads to complete obstruction of an epicardial coronary artery or branch and infarction of the myocardium served by that vessel	Evaluation with transesophageal echocardiography and continuous electrocardiographic monitoring are useful to evaluate for several of the causes	~1-3%
MINOCA	STEMI or NSTEMI	Can occur from a variety of causes, e.g., plaque disruption, epicardial coronary vasospasm, microvascular dysfunction, SCAD, coronary embolism, or coronary thrombosis, which lead to myocardial infarction despite the absence of any severe obstructive coronary artery stenoses, though the specific cause often remains undiagnosed	More prevalent in women (5 times higher odds) and nonwhite patients (1.5 times higher odds); less likely to have traditional cardiovascular risk factors	~5-6%

Bhatt DL, Lopes RD, Harrington RA. JAMA. 2022;327:662-675.

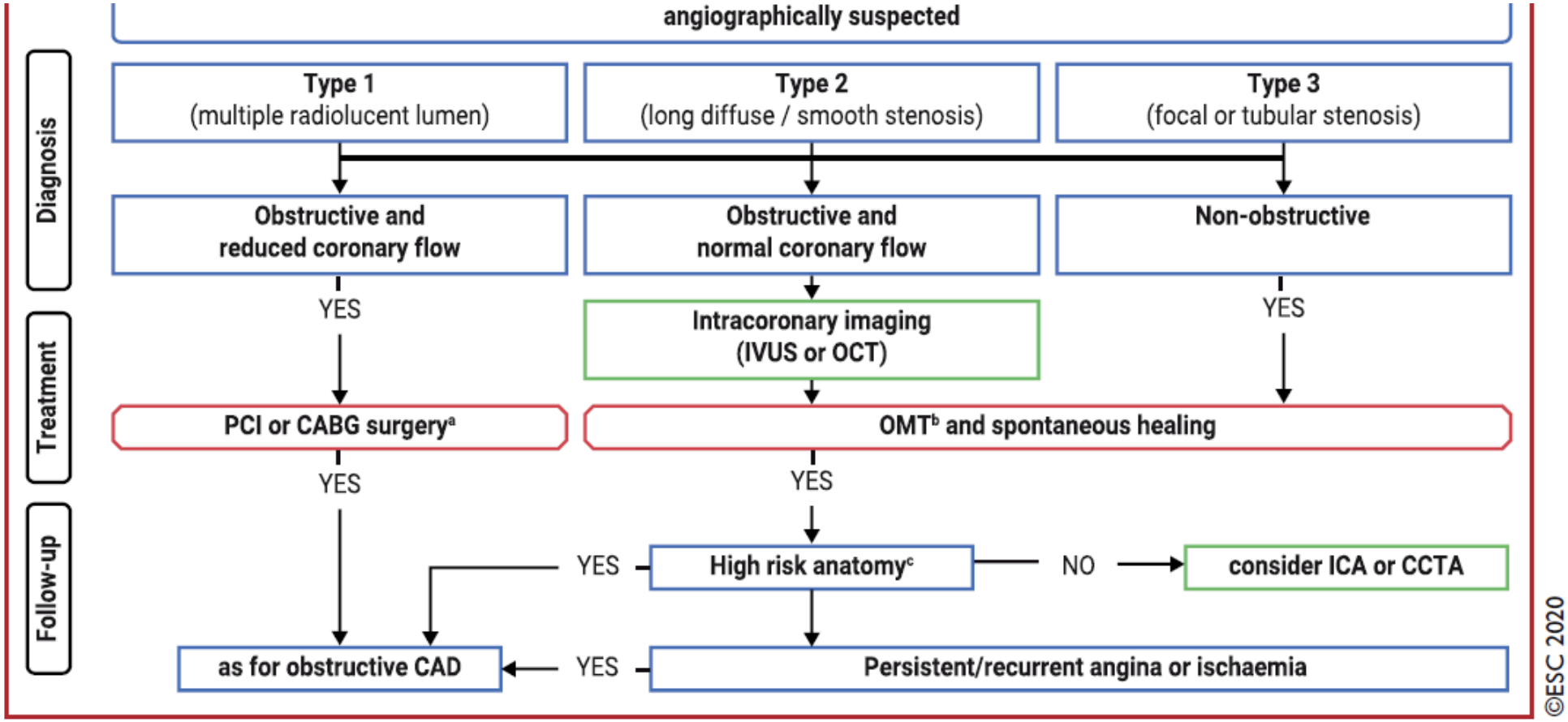
2020 ESC Guidelines for the Management of Acute Coronary Syndromes in Patients Presenting Without Persistent ST-segment Elevation

ESC
European Society of Cardiology

Task Force Members:

Jean-Philippe Collet (Chairperson) (France), **Holger Thiele (Chairperson) (Germany),**
Emanuele Barbato (Italy), Olivier Barthélémy (France), Johann Bauersachs (Germany),
Deepak L. Bhatt (United States of America), Paul Dendale (Belgium), Maria Dorobantu (Romania),
Thor Edvardsen (Norway), Thierry Folliguet (France), Chris P. Gale (United Kingdom), Martine Gilard (France),
Alexander Jobs (Germany), Peter Jüni (Canada), Ekaterini Lambrinou (Cyprus), Basil S. Lewis (Israel),
Julinda Mehilli (Germany), Emanuele Meliga (Italy), Béla Merkely (Hungary), Christian Mueller (Switzerland),
Marco Roffi (Switzerland), Frans H. Rutten (Netherlands), Dirk Sibbing (Germany),
George C. M. Siontis (Switzerland)

Diagnosis & Treatment of Patients with Non-ST-segment Elevation Acute Coronary Syndrome Related to Spontaneous Coronary Artery Dissection



[a]Selection of revascularization strategy for high-risk anatomy according to local expertise. [b]Beta-blocker recommended while benefit of DAPT is questionable. cLeft main or proximal left anterior descendent or circumflex or right coronary artery, multivessel SCAD.

www.escardio.org/guidelines

2020 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation (European Heart Journal 2020 - doi/10.1093/eurheartj/ehaa575)

Recommended Antithrombotic Therapies for ACS

	Which Patients	Dose	Efficacy	Contraindications	Adverse Effects	Duration	Comment
Aspirin	All on presentation	325 mg uncoated aspirin chew and swallow on presentation, followed by 81 mg daily	At 5 weeks, in patients with suspected acute MI, the rate of vascular death was 9.4% with aspirin versus 11.8% with placebo tablets (P <0.00001); non-fatal reinfarction (1.0% vs 2.0%) and non-fatal stroke (0.3% vs 0.6%) also significantly reduced	Aspirin allergy – if time allows, desensitization should be performed in a monitored setting	Major bleeding similar (0.4% with both aspirin and placebo); small absolute excess of minor bleeds compared with placebo (0.6%, p<0.01)	Lifelong, unless major bleeding issues	Aspirin monotherapy remains the most commonly used chronic antiplatelet strategy worldwide
P2Y12 Receptor Antagonist	All patients either after coronary angiography, or if anticipated delay to catheterization of more than 48 hours, on initial presentation	Clopidogrel 600 mg loading dose, followed by 75 mg daily in patients managed medically or undergoing PCI; Prasugrel 60 mg loading dose, followed by 10 mg daily in patients undergoing PCI; Ticagrelor 180 mg loading dose, followed by 90 mg twice daily in patients managed medically or undergoing PCI	Over 12 months, clopidogrel combined with aspirin versus placebo combined with aspirin reduced cardiovascular death, MI, or stroke from 11.4 % to 9.3%, P<0.001; over 15 months, prasugrel plus aspirin versus clopidogrel plus aspirin reduced cardiovascular death, MI, or stroke from 12.1% to 9.9%, P<0.001; over 12 months, ticagrelor plus aspirin versus clopidogrel plus aspirin reduced vascular death, MI, or stroke from 11.7% to 9.8%, P<0.001; vascular death was also reduced from 5.1% to 4.0%, P=0.001)	Active major bleeding Prasugrel should not be used in patients with a history of stroke or transient ischemic attack due to the risk of intracranial hemorrhage Ticagrelor should be used with caution in patients with marked baseline dyspnea; it does not worsen pulmonary function, but may make subsequent assessment of dyspnea more challenging	Significant increases in major bleeding for clopidogrel versus placebo group (3.7% vs 2.7%, P=0.001) Significant increases in major bleeding with prasugrel versus clopidogrel (2.4% vs 1.8%, P=0.03) and in fatal bleeding (0.4% vs 0.1%, P=0.002) Significant increases in major bleeding not related to coronary-artery bypass grafting with ticagrelor vs clopidogrel (4.5% vs. 3.8%, P = 0.03), though similar overall rates of major bleeding (11.6% vs 11.2%, P=0.43)	At least 12 months, and if low bleeding risk and continued high ischemic risk, consider longer duration (if ticagrelor, drop dose to 60 mg twice daily after 12 months)	Assessment of ongoing ischemic and bleeding risks necessary to decide upon DAPT beyond 12 months; usually a bad strategy if at high bleeding risk, such as patients with a history of anemia, thrombocytopenia, or prior bleeding; risk scores might help

Bhatt DL, Lopes RD, Harrington RA. JAMA. 2022;327:662-675.

Recommended Antithrombotic Therapies for ACS

	Which Patients	Dose	Efficacy	Contraindications	Adverse Effects	Duration	Comment
Parenteral Anti-coagulation	All patients on presentation	Unfractionated heparin intravenous bolus and infusion per institutional dosing nomogram; low molecular weight heparin subcutaneously	A meta-analysis of randomized trials showed that short-term (up to 7 days) unfractionated heparin or low molecular weight heparin versus control was associated with a lower rate of death or MI (4.5% versus 7.4%, P=0.0001)	Active major bleeding Known heparin antibodies	No significant increased risk of major bleeding with short term therapy seen in this meta-analysis	Until revascularization in invasively managed patients; until pain free in conservatively managed patients, typically at least 48 hours	For unfractionated heparin, have to use a weight-based nomogram; for low molecular weight heparin, need to be cognizant or kidney function
Oral Anticoagulation	Patients with LV thrombus; atrial fibrillation	Warfarin; NOACs (apixaban, dabigatran, edoxaban, rivaroxaban) preferred for atrial fibrillation if no contraindications	A meta-analysis of randomized trials showed the NOACs were associated with a lower rate of stroke or systemic embolic events than warfarin for atrial fibrillation (3.1% versus 3.8%, P<0.0001) over a median follow-up ranging from 1.8 to 2.8 years	Active major bleeding	NOACs versus warfarin: intracranial bleeding 0.7% versus 1.5% (P<0.0001); gastrointestinal bleeding 2.6% versus 2.0% (P=0.043)	For LV thrombus, at least 3 months, with re-imaging to examine for thrombus persistence to determine the need for continued anticoagulation; potentially lifelong if aneurysm	Controversial exactly what the best regimen is for LV thrombus, with lack of randomized data; for NOACs in impaired kidney function, would carefully follow the label, as dose adjustments are recommended that differ among the agents

Bhatt DL, Lopes RD, Harrington RA. JAMA. 2022;327:662-675.

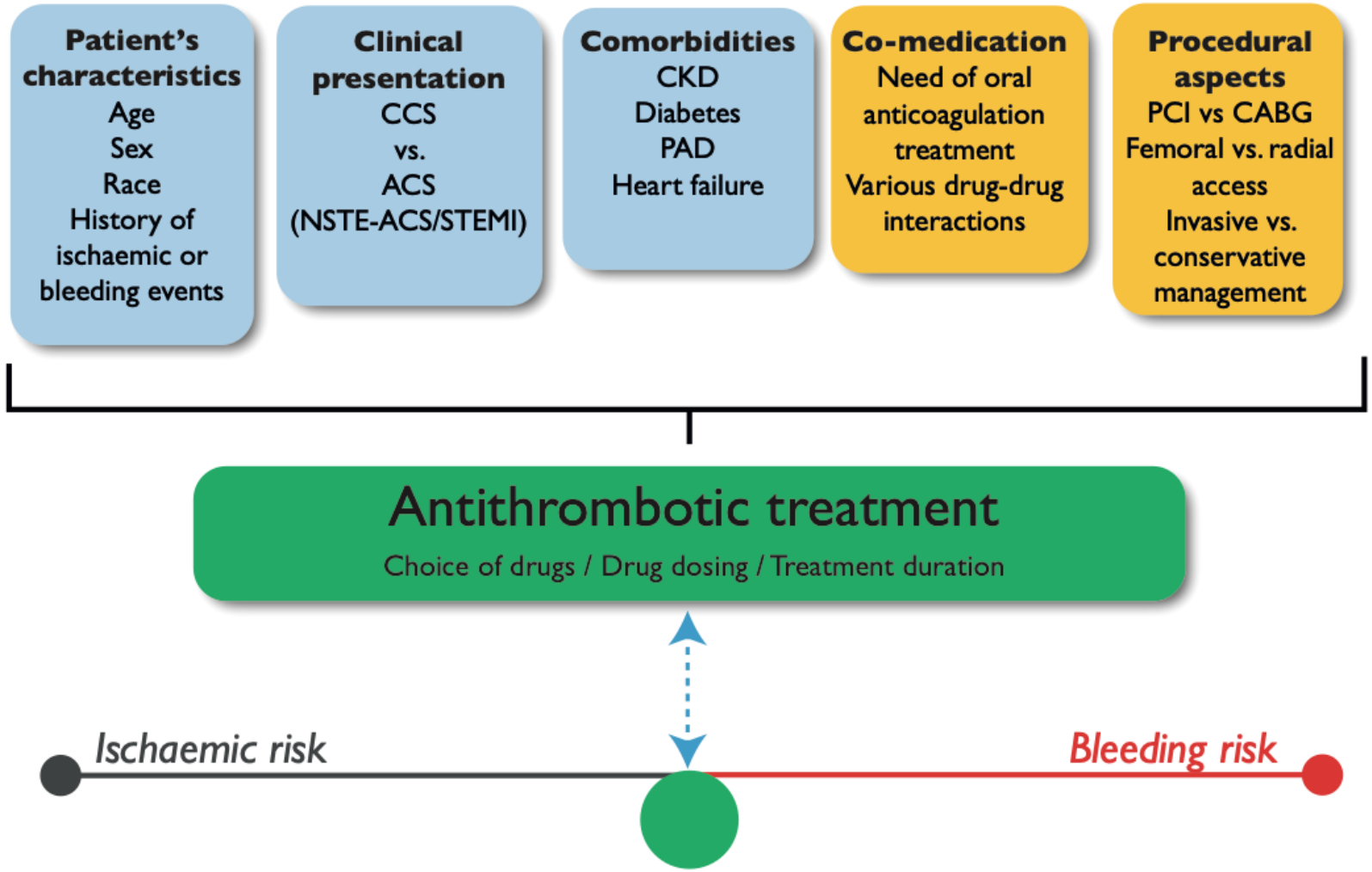


Figure 5

Determinants of antithrombotic treatment in coronary artery disease.

Intrinsic (in blue: patient's characteristics, clinical presentation & comorbidities) and extrinsic (in yellow: co-medication & procedural aspects) variables influencing the choice, dosing, and duration of antithrombotic treatment.

©ESC

2020 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation (European Heart Journal 2020 - doi/10.1093/eurheartj/ehaa575)

Other Recommended Medical Therapies for ACS

	Which Patients	Dose	Efficacy	Contraindications	Adverse Effects	Duration	Comment
High Intensity Statin	All patients on presentation	Maximally tolerated statin dose, such as atorvastatin 40 mg or 80 mg daily or rosuvastatin 20 mg or 40 mg daily	At two years the rate of death, MI, unstable angina requiring rehospitalization, revascularization (performed at least 30 days after randomization), or stroke was reduced from 26.3% with low intensity (pravastatin 40 mg) to 22.4% with high-intensity (atorvastatin 80 mg) statin therapy (P=0.005)	Active liver disease or unexplained, persistent elevations in aminotransferase levels	Elevations in alanine aminotransferase levels more than three times the upper limit of normal were 1.1% with pravastatin group and 3.3% with atorvastatin (P<0.001); discontinuation by the investigators for myalgias or muscle aches or elevations in creatine kinase levels in 2.7% with pravastatin versus 3.3% with atorvastatin (P=0.23)	Lifelong, unless side effects clearly related to drug	If intolerant, switch statins or use lower doses; if that does not work, consider referral to a preventive cardiology clinic
Ezetimibe	In patients already on maximally tolerated statin with LDL-cholesterol ≥ ~50 mg/dL	10 mg daily	When added to statin therapy, ezetimibe versus placebo reduced cardiovascular death, MI, unstable angina requiring rehospitalization, coronary revascularization (performed at least 30 days after randomization), or stroke from 34.7% to 32.7% over 7 years (P=0.016)	Active liver disease	No significant differences in elevations in alanine aminotransferase levels that exceeded three times the upper limit of normal or in muscle-related adverse events	Lifelong	Can also be useful in patients who are truly statin intolerant

Bhatt DL, Lopes RD, Harrington RA. JAMA. 2022;327:662-675.

Other Recommended Medical Therapies for ACS

	Which Patients	Dose	Efficacy	Contraindications	Adverse Effects	Duration	Comment
PCSK9 inhibitor	In patients already on maximally tolerated statin and ezetimibe with LDL-cholesterol ≥ ~70 mg/dL	Alirocumab or evolocumab subcutaneously	Over a median follow-up of 2.8 years, death from CHD, MI, ischemic stroke, or UA requiring hospitalization was reduced from 11.1% to 9.5% (P<0.001); mortality was reduced from 4.1% to 3.5% (P=0.03)	History of a serious hypersensitivity reaction to the drug	Local injection-site reactions were increased from 2.1% to 3.8% (P<0.001)	Lifelong	Effective even at LDL-cholesterol < 100 mg/dL, but cost-effectiveness currently an issue
Icosapent ethyl	Patients with fasting or non-fasting triglycerides ≥ 135 mg/dL, despite maximally tolerated statin dose	2 grams twice a day with meals	Over 6.2 years, icosapent ethyl versus placebo reduced cardiovascular death, MI, stroke, coronary revascularization, or unstable angina from 22.0% to 17.2%, P<0.001; cardiovascular death was reduced from 5.2% to 4.3%, P=0.03	Known hypersensitivity (e.g., anaphylactic reaction) to the drug or its components	Hospitalization for atrial fibrillation or flutter increased from 2.1% to 3.1%, P=0.004; serious bleeding increased from 2.1% to 2.7%, P=0.06)	Lifelong	Unknown if patients with allergies to fish and/or shellfish are at increased risk of allergic reaction; increases risk for hospitalization for AF, especially in patients with a prior history; increases bleeding risk
Beta blockers	Patients with left ventricular dysfunction or significant residual coronary artery disease with angina	Several generic choices	Over a mean of 1.3 years, mortality lower with carvedilol than placebo (12% versus 15%, P=0.03)	Contraindications common class include severe bradycardia, 2nd or 3rd degree heart block, sick sinus syndrome (if no permanent pacemaker), decompensated HF, and cardiogenic shock	Higher rates of side effects with timolol versus placebo: bradycardia (5.0% vs 0.3%, P<0.001); hypotension (3.1% vs 1.6%, P<0.05); cold hands/feet 7.7% vs 0.6%, P<0.001); bronchial obstruction (1.9% vs 0.7%, P<0.05); fatigue (4.8% vs 1.2%, P<0.001)	Lifelong	Benefit in patients with complete revascularization and normal LV function unclear

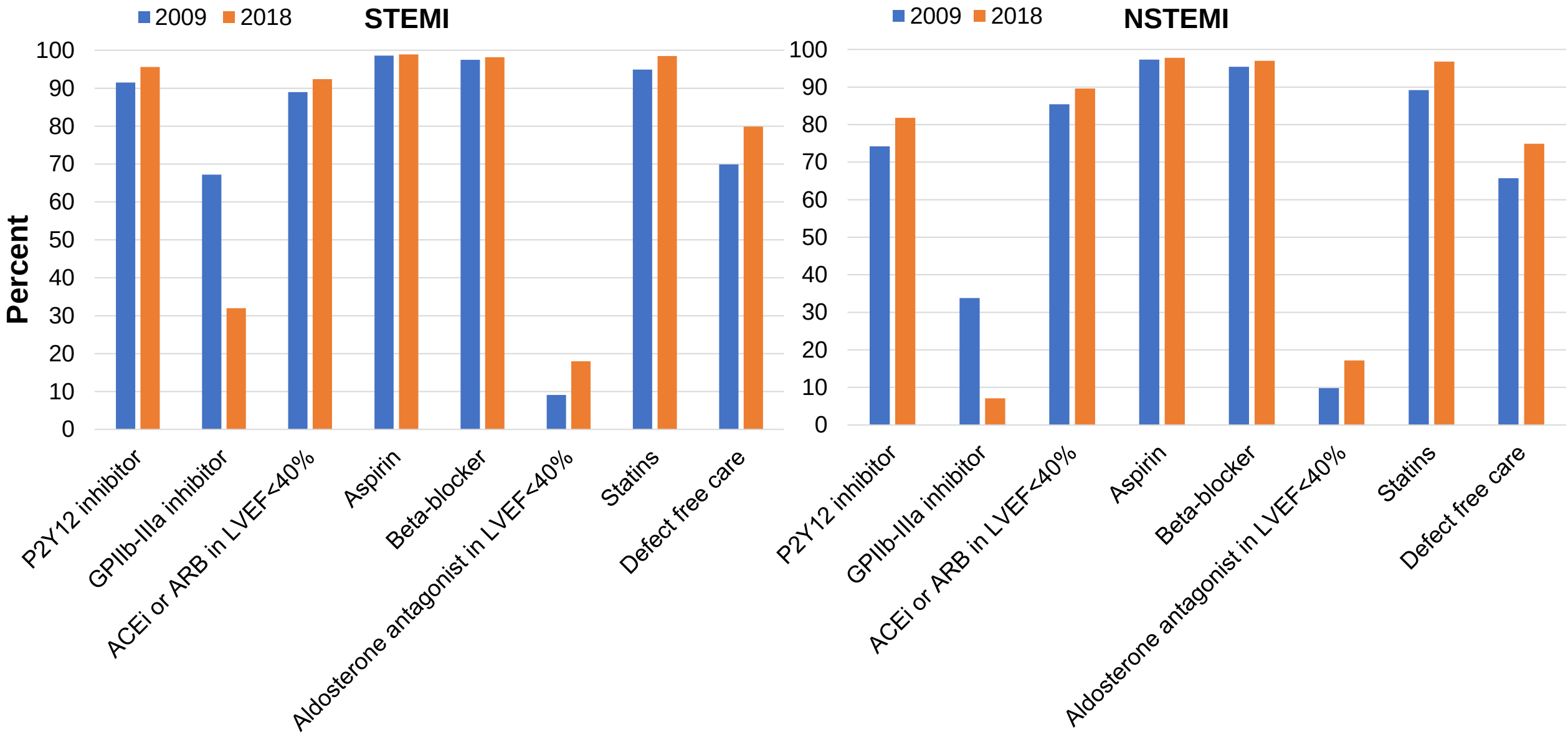
Bhatt DL, Lopes RD, Harrington RA. JAMA. 2022;327:662-675.

Other Recommended Medical Therapies for ACS

	Which Patients	Dose	Efficacy	Contraindications	Adverse Effects	Duration	Comment
ACEi/ARBs	Patients with left ventricular dysfunction or diabetes	Several generic choices	A meta-analysis of randomized trials showed that ACE inhibitors versus control were associated with lower mortality at 30 days (7.1% versus 7.6%, P=0.004)	Contraindications common to the class include a history of angioedema with an ACEi; hereditary or idiopathic angioedema	Increase in hypotension (17.6% versus 9.3%, P=0.01) and kidney dysfunction (1.3% versus 0.6%, P=0.01)	Lifelong	Both ACEi and ARBs provide similar benefit, though ARBs may be a bit better tolerated
Mineralocorticoid Receptor Antagonists	Patients with left ventricular dysfunction	Aldosterone or eplerenone	At a mean follow-up of 24 months, deaths reduced from 46% with placebo to 35% with spironolactone (P<0.001) At a median follow-up of 21 months, cardiovascular death or hospitalization for heart failure was 18.3% with eplerenone versus 25.9% with placebo, P<0.001	Hyperkalemia; with eplerenone specifically, potassium >5.5 mEq/L at initiation; creatinine clearance ≤30 mL/min	Gynecomastia or breast pain in 10% of men with spironolactone versus 1% of men with placebo (P<0.001) Potassium level > 5.5 mmol/L in 11.8% with eplerenone and 7.2% with placebo (P<0.001)	Lifelong	Monitoring of potassium needed, but an underutilized therapy

Bhatt DL, Lopes RD, Harrington RA. JAMA. 2022;327:662-675.

10-Year Trends in MI: Discharge Medications

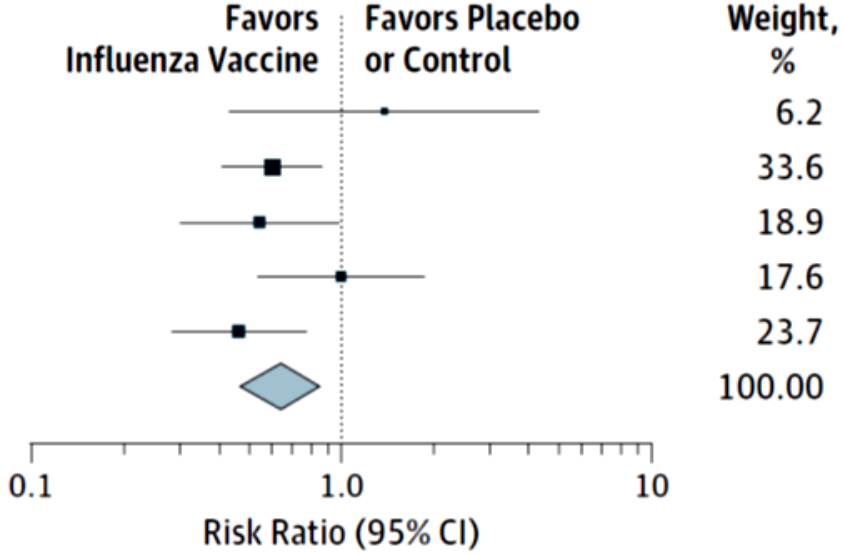


Gandhi S, Garratt KN, Li S, Wang TY, Bhatt DL, Davis LL, Zeitouni M, Kontos MC. Circ Cardiovasc Qual Outcomes. 2022;15:e008112.

Comparing Influenza Vaccine vs Control: MACE

Study	Influenza Vaccine: No. of Events	Influenza Vaccine: Total Participants	Placebo or Control: No. of Events	Placebo or Control: Total Participants	Risk Ratio (95% CI)
Govaert et al,[41] 1994	7	927	5	911	1.38 (0.44-4.32)
FLUVACS,[20, 21] 2004	32	145	54	147	0.60 (0.41-0.87)
FLUCAD,[22, 23] 2008	16	325	30	333	0.55 (0.30-0.98)
De Villiers et al,[42] 2009	20	1620	20	1622	1.00 (0.54-1.85)
Phrommintikul et al,[24] 2011	20	221	42	218	0.47 (0.29-0.77)
Total (95% CI)	95	3238	151	3231	0.64 (0.48-0.86)

Heterogeneity: $\tau^2 = 0.03$; $\chi^2_4 = 5.59$, ($P = .23$); $I^2 = 28\%$
Test for overall effect: $Z = 2.93$ ($P = .003$)

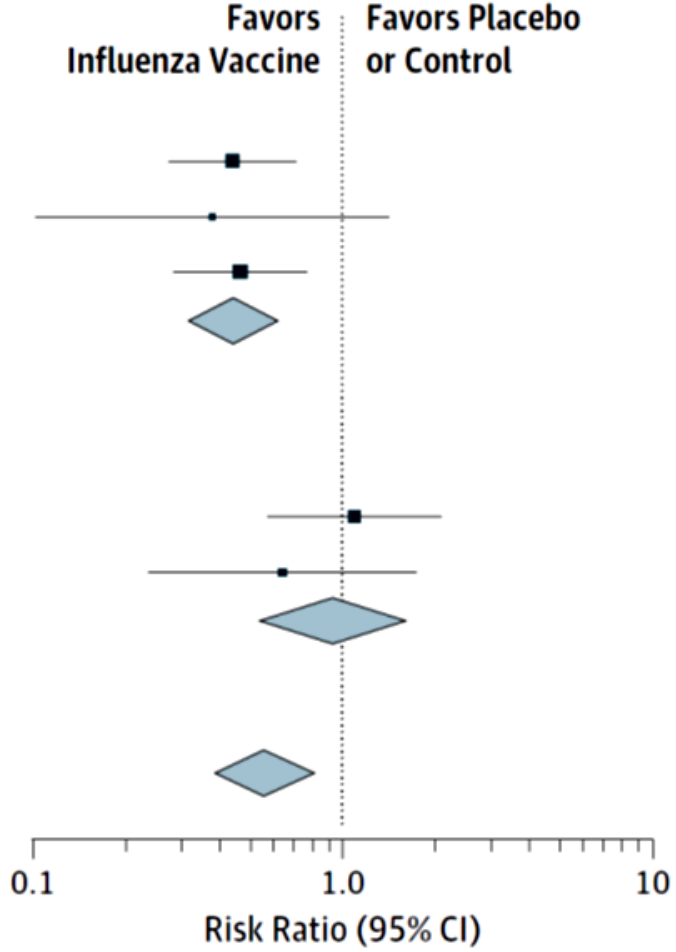


FLUCAD indicates FLU Vaccination Coronary Artery Disease; FLUVACS, FLU Vaccination Acute Coronary Syndromes

Udell JA, Zawi R, Bhatt DL, Keshtar-Jahromi M, Gaughran F, Phrommintikul A, et al. JAMA. 2013;310:1711-1720.

Comparing Influenza Vaccine vs Control: MACE by Timing of ACS

Study	Influenza Vaccine: No. of Events	Influenza Vaccine: Total Participants	Placebo or Control: No. of Events	Placebo or Control: Total Participants	Risk Ratio (95% CI)	Weight, %
Recent ACS						
FLUVACS,[20,21] 2004	18	96	41	97	0.44 (0.28-0.71)	30.6
FLUCAD,[22,23] 2008	3	83	7	74	0.38 (0.10-1.42)	7.1
Phrommintikul et al,[24] 2011	20	221	42	218	0.47 (0.29-0.77)	29.3
Subtotal (95% CI)	41	400	90	389	0.45 (0.32-0.63)	67.0
Heterogeneity: $\tau^2 = 0.00$; $\chi^2_2 = 0.09$, ($P = .96$); $I^2 = 0\%$						
Test for overall effect: $Z = 4.68$ ($P < .001$)						
Stable CAD						
FLUVACS,[20,21] 2004	14	49	13	50	1.10 (0.58-2.09)	21.7
FLUCAD,[22,23] 2008	6	242	10	259	0.64 (0.24-1.74)	11.4
Subtotal (95% CI)	20	291	23	309	0.94 (0.55-1.61)	33.0
Heterogeneity: $\tau^2 = 0.00$; $\chi^2_1 = 0.81$, ($P = .37$); $I^2 = 0\%$						
Test for overall effect: $Z = 0.23$ ($P = .82$)						
Total (95% CI)	61	691	113	698	0.57 (0.39-0.82)	100.00
Heterogeneity: $\tau^2 = 0.06$; $\chi^2_4 = 6.01$, ($P = .20$); $I^2 = 33$						
Test for overall effect: $Z = 3.00$ ($P = .003$)						
Test for subgroup differences: $\chi^2_1 = 5.11$, ($P = .02$); $I^2 = 80.4\%$						



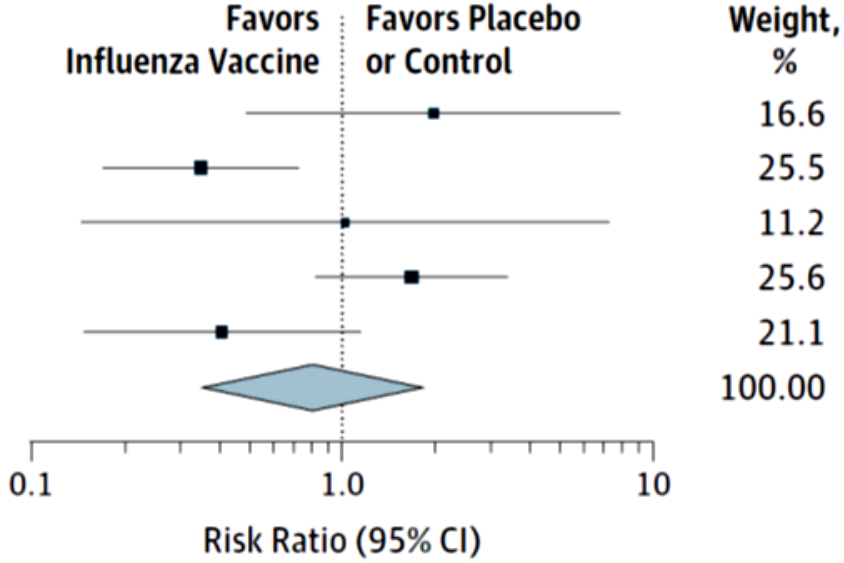
FLUCAD indicates FLU Vaccination Coronary Artery Disease; FLUVACS, FLU Vaccination Acute Coronary Syndromes

Udell JA, Zawi R, Bhatt DL, Keshtar-Jahromi M, Gaughran F, Phrommintikul A, et al. JAMA. 2013;310:1711-1720.

Comparing Influenza Vaccine vs Control: CV Mortality

Study	Influenza Vaccine: No. of Events	Influenza Vaccine: Total Participants	Placebo or Control: No. of Events	Placebo or Control: Total Participants	Risk Ratio (95% CI)	Weight, %
Govaert,[41] 1994	6	927	3	911	1.97 (0.49-7.84)	16.6
FLUVACS,[20, 21] 2004	9	145	26	147	0.35 (0.17-0.72)	25.5
FLUCAD,[22, 23] 2008	2	325	2	333	1.02 (0.15-7.23)	11.2
De Villiers et al,[42] 2009	20	1620	12	1622	1.67 (0.82-3.40)	25.6
Phrommintikul et al,[24] 2011	5	221	12	218	0.41 (0.15-1.15)	21.1
Total (95% CI)	42	3238	55	3231	0.81 (0.36-1.83)	100.00

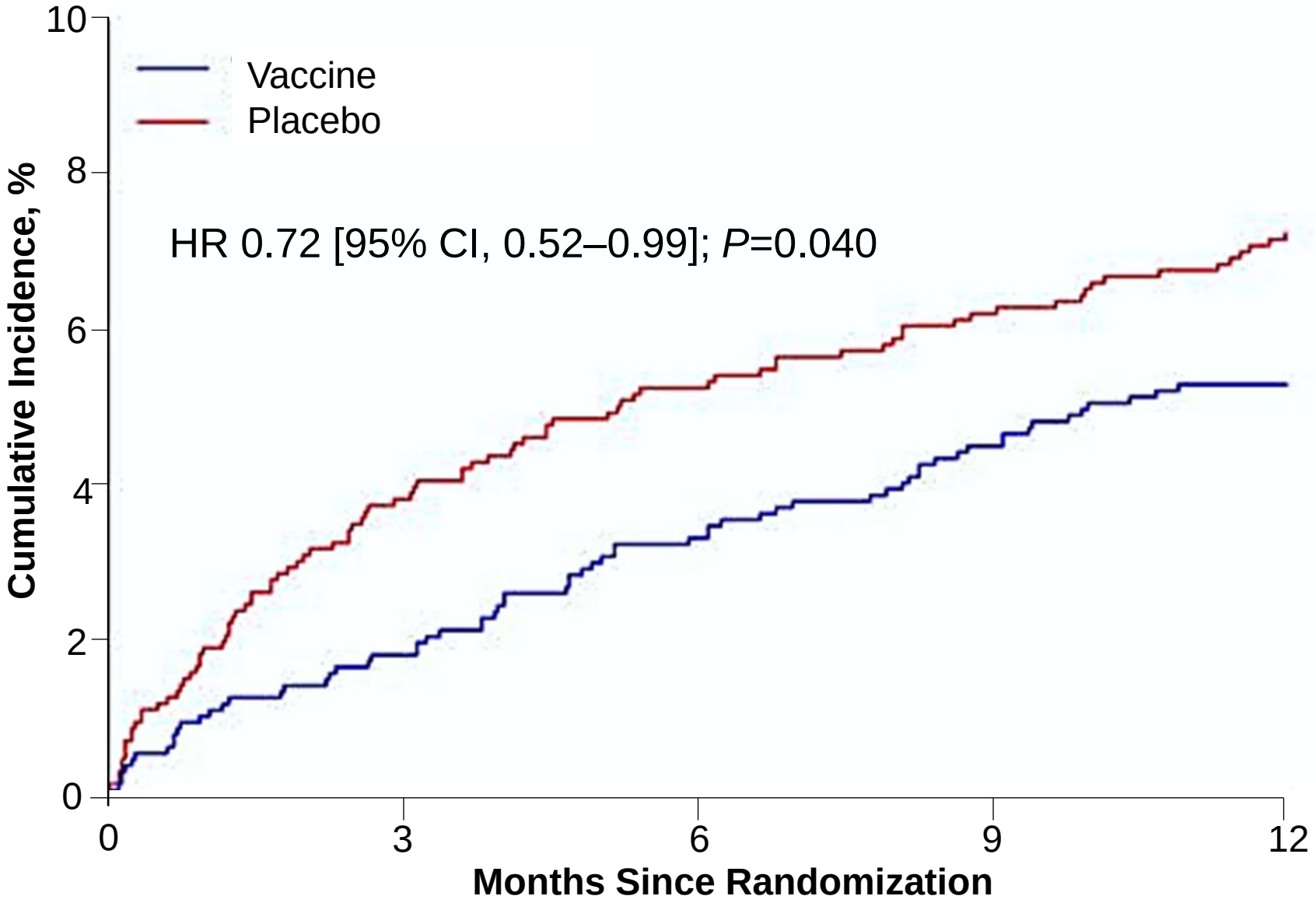
Heterogeneity: $\tau^2 = 0.54$; $\chi^2_4 = 12.36$, ($P = .01$); $I^2 = 68\%$
Test for overall effect: $Z = 0.50$ ($P = .61$)



FLUCAD indicates FLU Vaccination Coronary Artery Disease; FLUVACS, FLU Vaccination Acute Coronary Syndromes

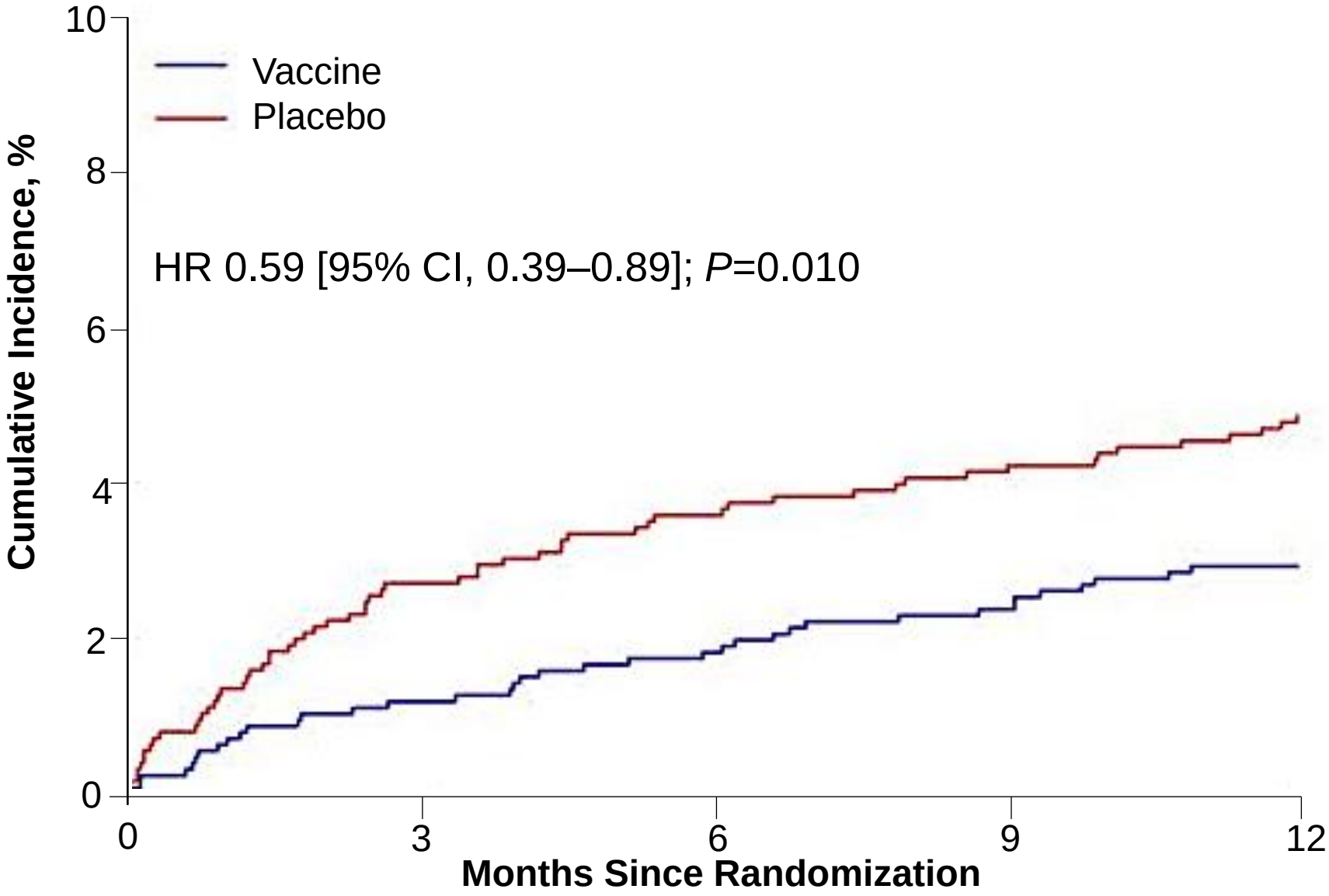
Udell JA, Zawi R, Bhatt DL, Keshtar-Jahromi M, Gaughran F, Phrommintikul A, et al. JAMA. 2013;310:1711-1720.

Influenza Vaccine vs Placebo: Composite of All-Cause Death, MI, or Stent Thrombosis in Time-to-Event Analysis



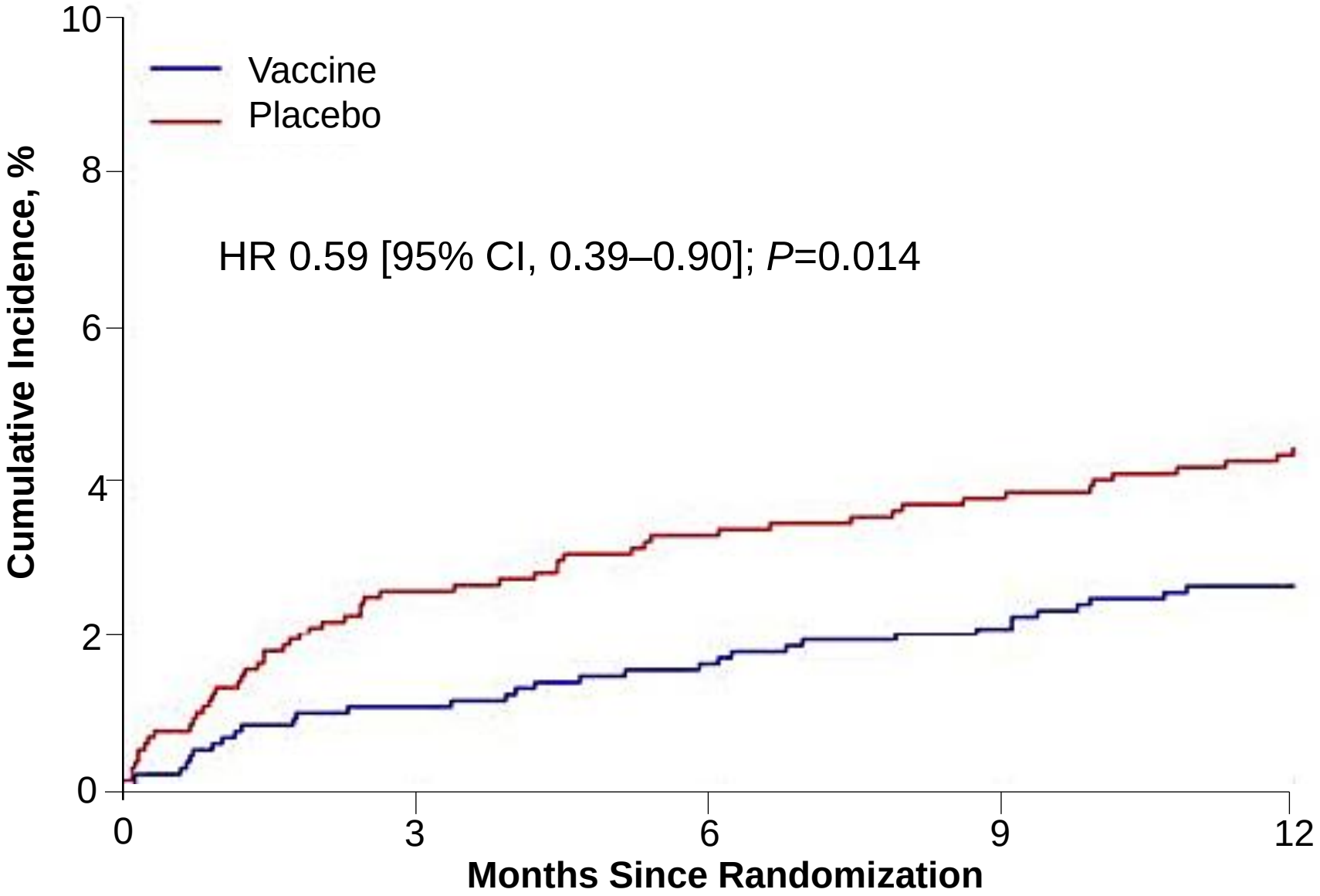
Fröbert O, Götberg M, Erlinge D, Akhtar Z, Christiansen EH, MacIntyre CR, et al. Circulation. 2021;144:1476–1484.

Influenza Vaccine vs Placebo: All-Cause Death



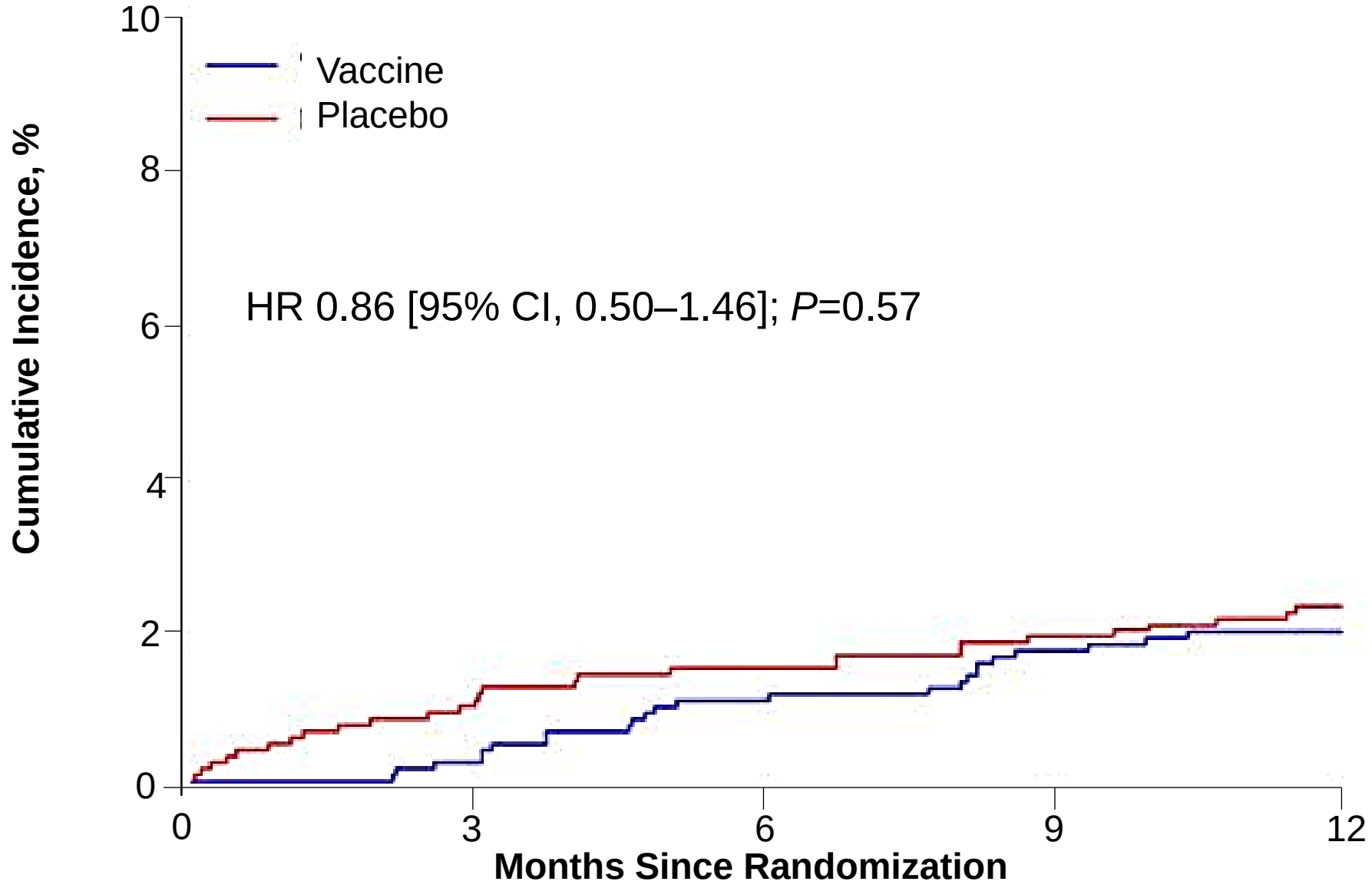
Fröbert O, Götberg M, Erlinge D, Akhtar Z, Christiansen EH, MacIntyre CR, et al. Circulation. 2021;144:1476–1484.

Influenza Vaccine vs Placebo: CV Death



Fröbert O, Götberg M, Erlinge D, Akhtar Z, Christiansen EH, MacIntyre CR, et al. Circulation. 2021;144:1476–1484.

Influenza Vaccine vs Placebo: Myocardial Infarction



Fröbert O, Götberg M, Erlinge D, Akhtar Z, Christiansen EH, MacIntyre CR, et al. Circulation. 2021;144:1476–1484.

CMHC Cardiometabolic Health Congress

www.cardiometabolichealth.org

Foundations of Cardiometabolic Health Certification Course

Certified Cardiometabolic Health Professional (CCHP)

Stable CAD: Testing and Evaluation

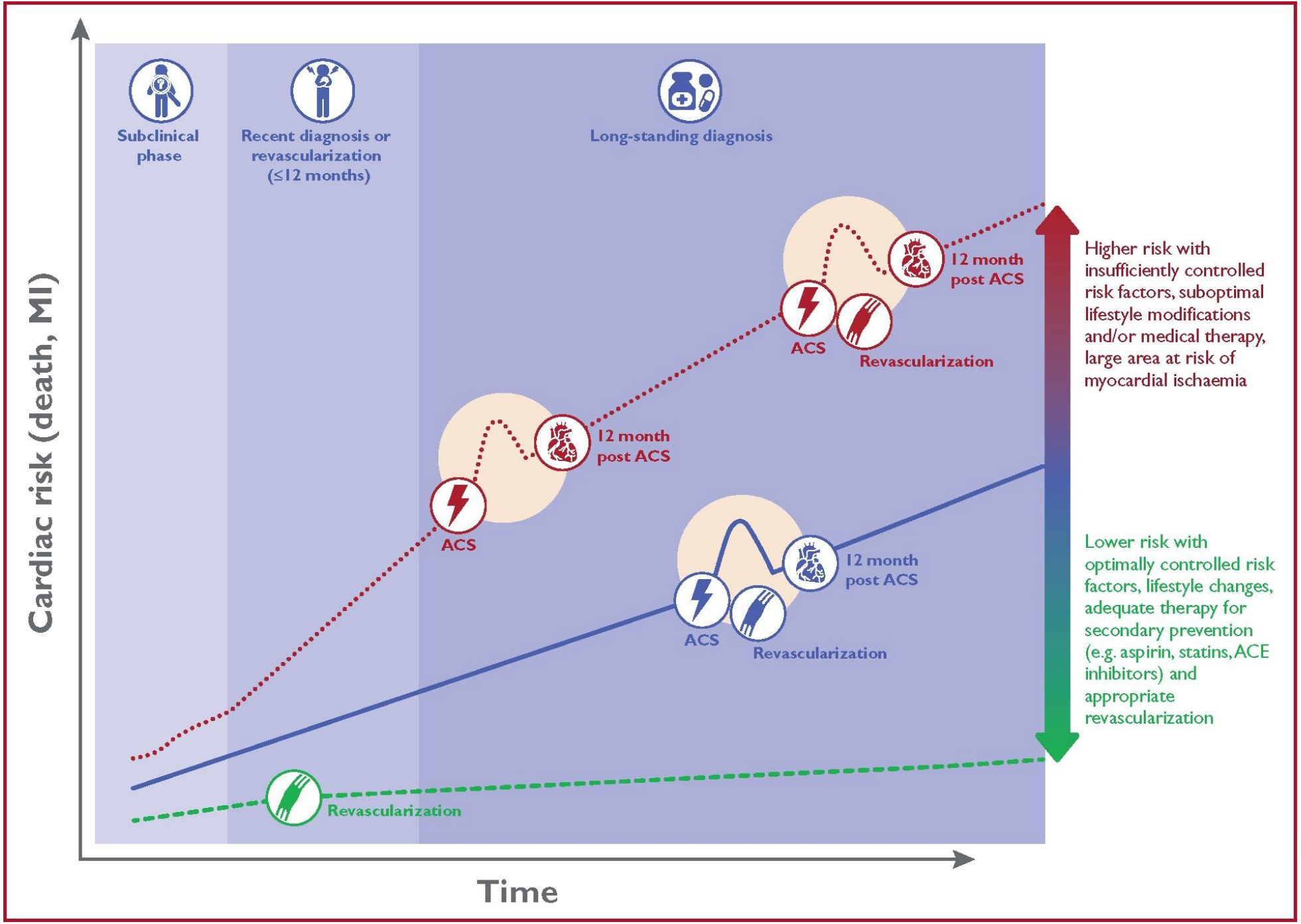
Deepak L. Bhatt, MD, MPH

Executive Director of Interventional Cardiovascular Programs, Brigham and Women's Hospital
Professor of Medicine, Harvard Medical School

BWH BRIGHAM AND WOMEN'S HOSPITAL | Heart & Vascular Center |

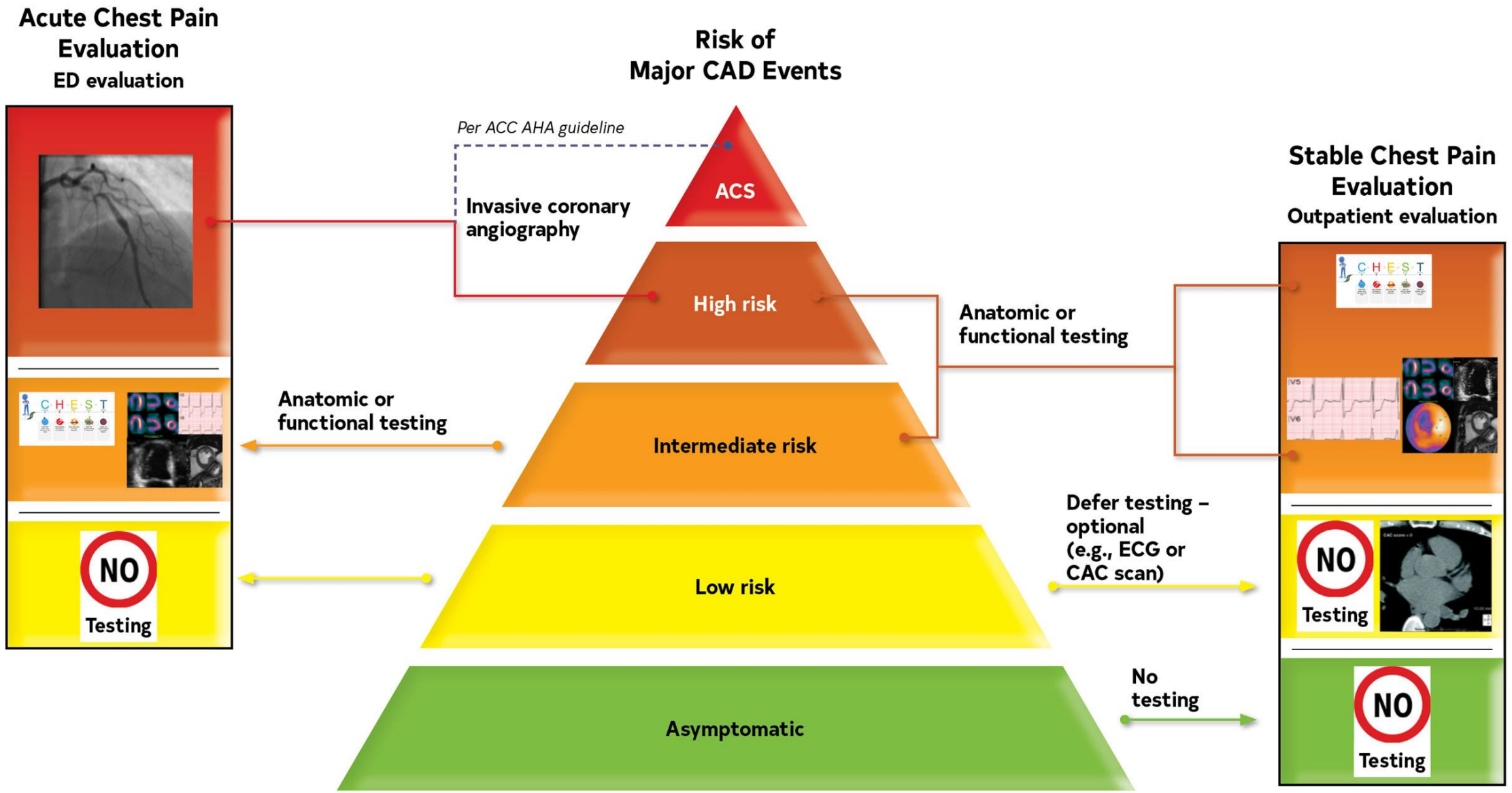
HARVARD MEDICAL SCHOOL TEACHING HOSPITAL

Natural History



Knuuti J, Wijns W, Saraste A, Capodanno D, Barbato E, Funck-Brenato C, et al. Eur Heart J. 2020;41:407-477.

Cardiac Testing



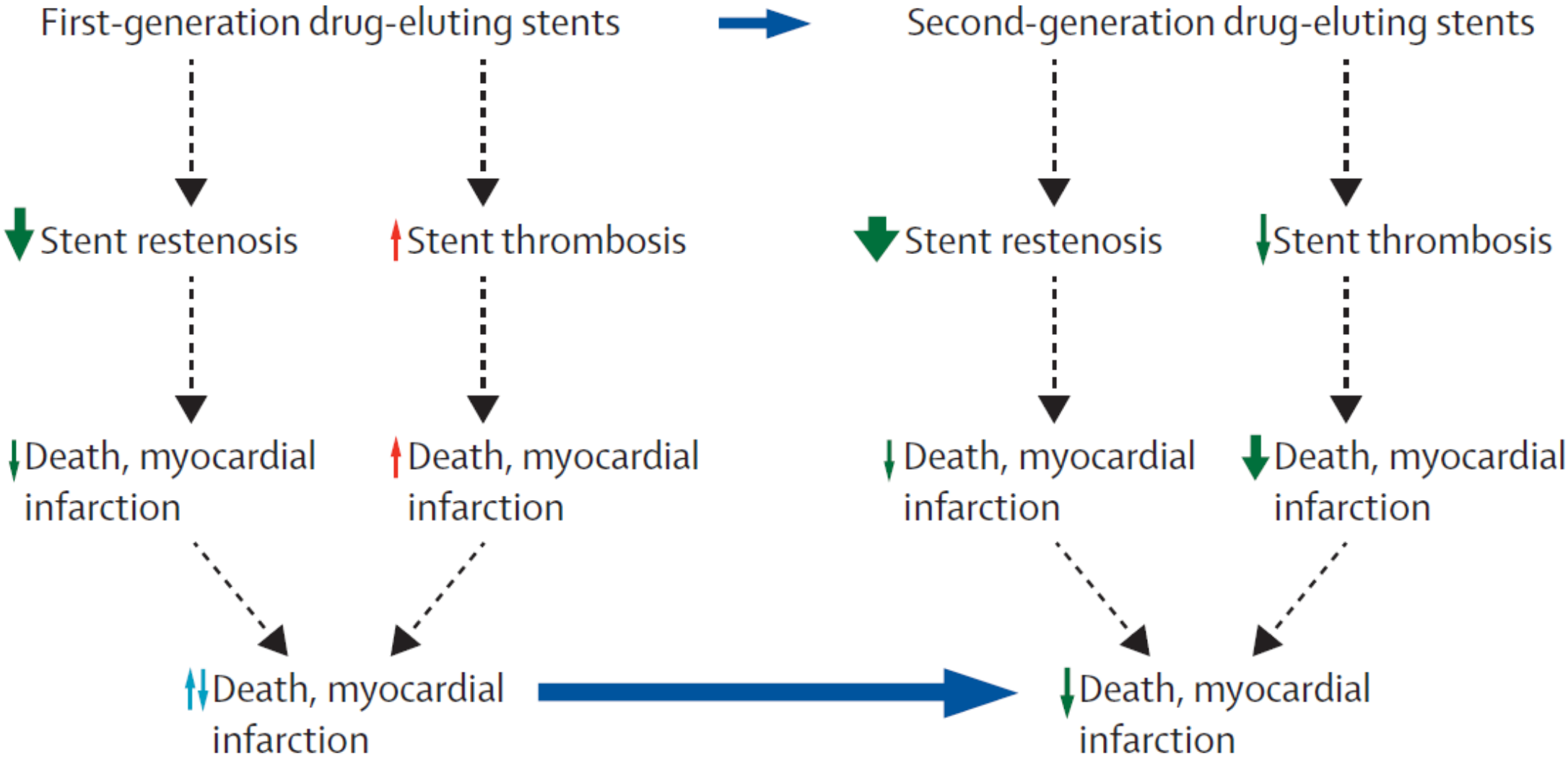
Gulati M, Levy PD, Mukherjee D, Amsterdam E, Bhatt DL, Birtcher KK, et al. Circulation. 2021;144:e368-e454.

Timing of PCI Based on Clinical Syndrome

Stable Angina	NSTEMI or Unstable Angina	STEMI
• ~20% treated with PCI • Severe stenosis on angiogram • PCI elective: after patient begins maximally tolerated medical therapy, if substantial symptoms and ischemia persist • PCI improves angina and reduces future need for urgent revascularization in severe single-vessel disease; advantages and disadvantages vs CABG in multivessel disease and in left-main disease • If no PCI: antianginal medications, which may require dose escalation with time; when medications are no longer effective there may be a need for elective or urgent revascularization	• ~50% treated with PCI • Ulcerated lesion on angiogram • PCI urgent: 24-48 hours (within 24 ideal) • PCI emergent: if ongoing symptoms or dynamic ECG changes • PCI reduces the composite of death or myocardial infarction • If no PCI, stress test prior to discharge, and if significant ischemia, coronary angiography and revascularization based on coronary anatomy	• ~90% treated with PCI • Occlusive lesion on angiogram • Emergent: within 90-120 minutes (within 60 ideal) • PCI reduces death • If no PCI, treatment with fibrinolytics, with prompt transfer for probable PCI

Bhatt DL. JAMA. 2018;319:2127-8.

Second Generation Drug-Eluting Stents and Decreased Risk of MI and CV Death: Theoretical Framework

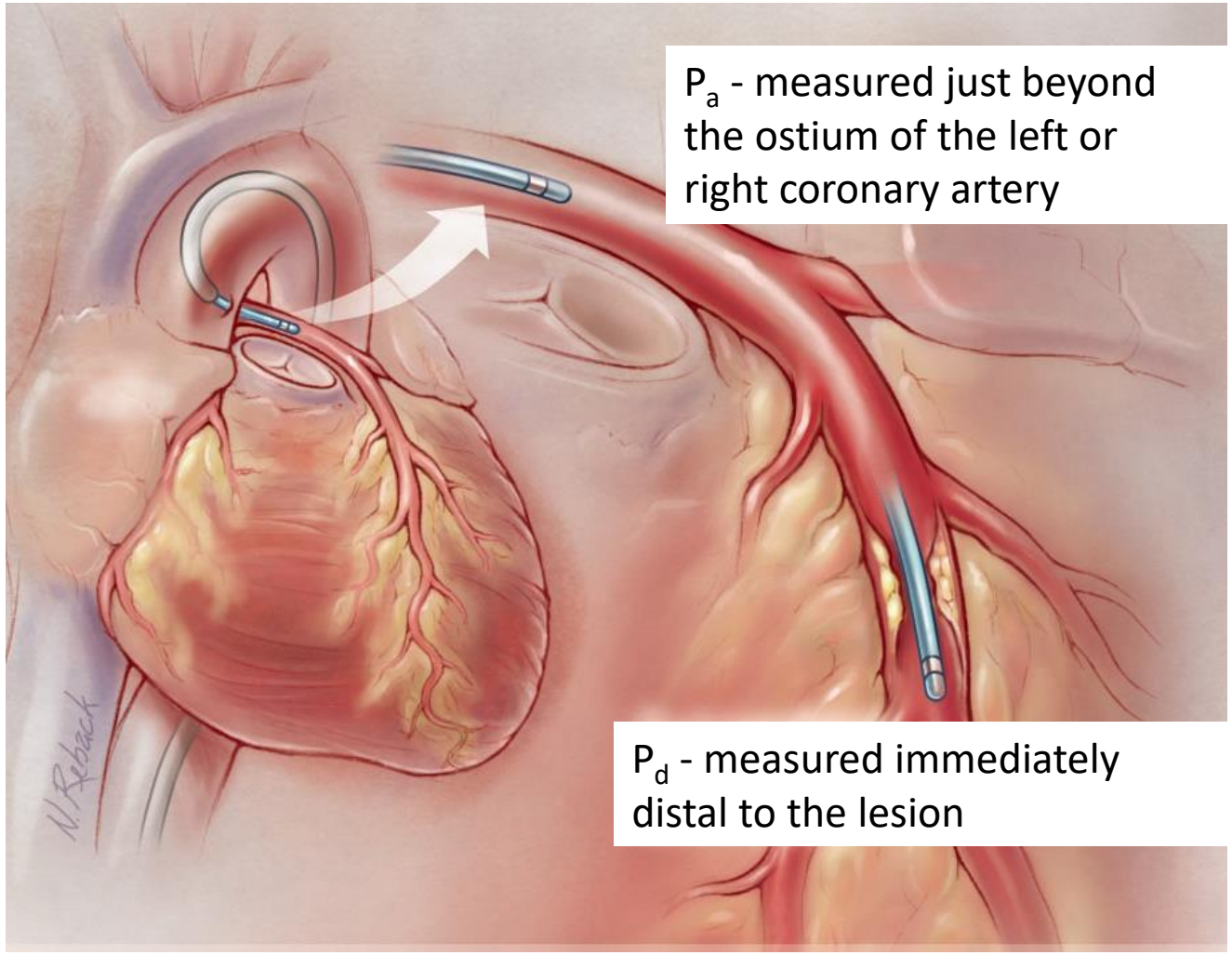


Bhatt DL. Lancet. 2012;380:1453-5.

Fractional Flow Reserve Measurement for the Physiological Assessment of Coronary Artery Stenosis Severity

- Adding FFR to angiography aids understanding of angiographically ambiguous lesions
- A wire equipped with a pressure sensor measures intracoronary pressure proximal and distal to the lesion
- FFR = ratio of P_d to P_a
- A value of 1.0 is considered normal flow
- The instantaneous wave-free ratio value for ischemia is ≤ 0.89
- An FFR ≤ 0.80 can diagnose myocardial ischemia either at rest or after vasodilator

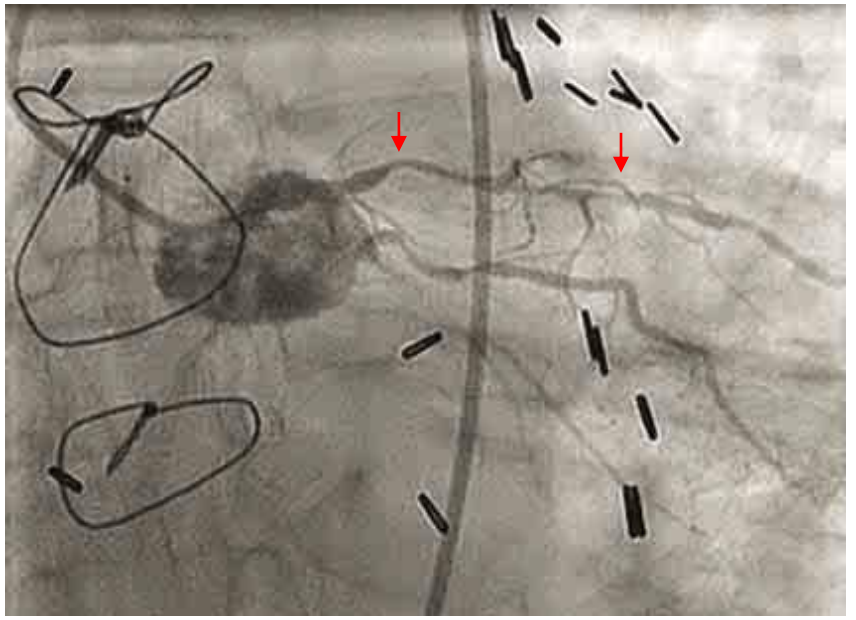
$$\frac{Pd}{Pa} = \frac{75}{100} = 0.75$$



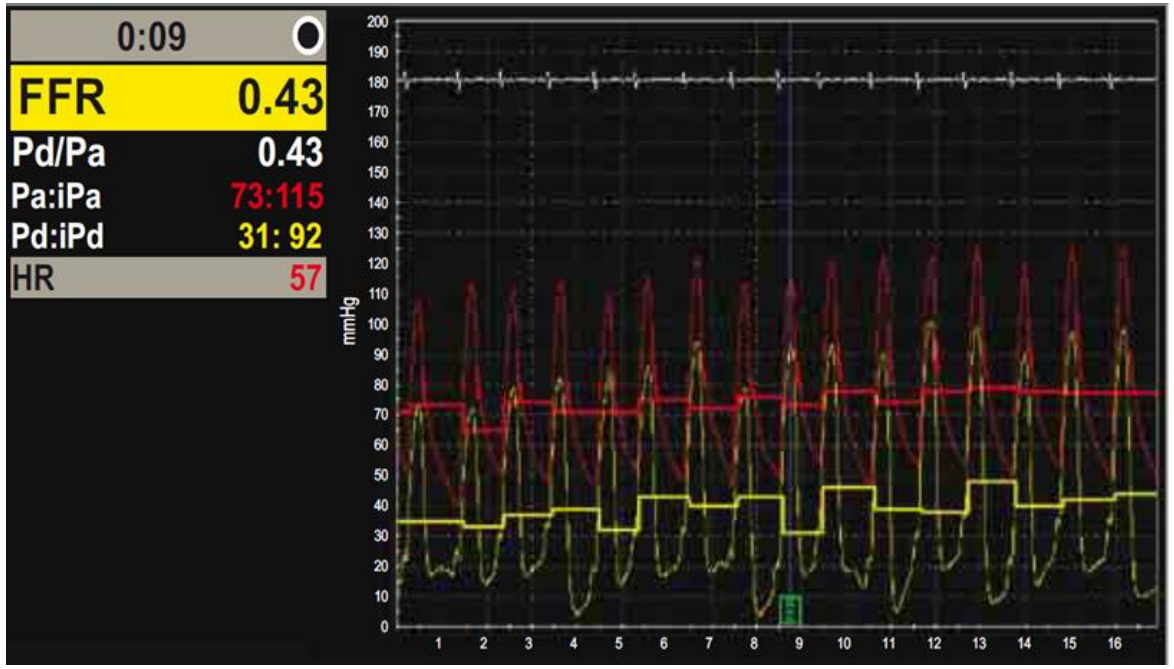
Bhatt DL. JAMA. 2018;320:1275-1276.

FFR Example

- This patient received a 2.5 × 23-mm everolimus-eluting stent initially placed in the distal lesion, as it was more hemodynamically significant
- AFFR with adenosine was repeated after this
- procedure for the proximal lesion, revealing a nadir value of 0.78
- The patient received an overlapping 2.75 × 18-mm everolimus-eluting stent in the proximal lesion
- With stents in both lesions, the repeated FFR value with adenosine was 0.93
- >0.95 is ideal post stent placement, but the residual proximal disease in this patient can be treated medically



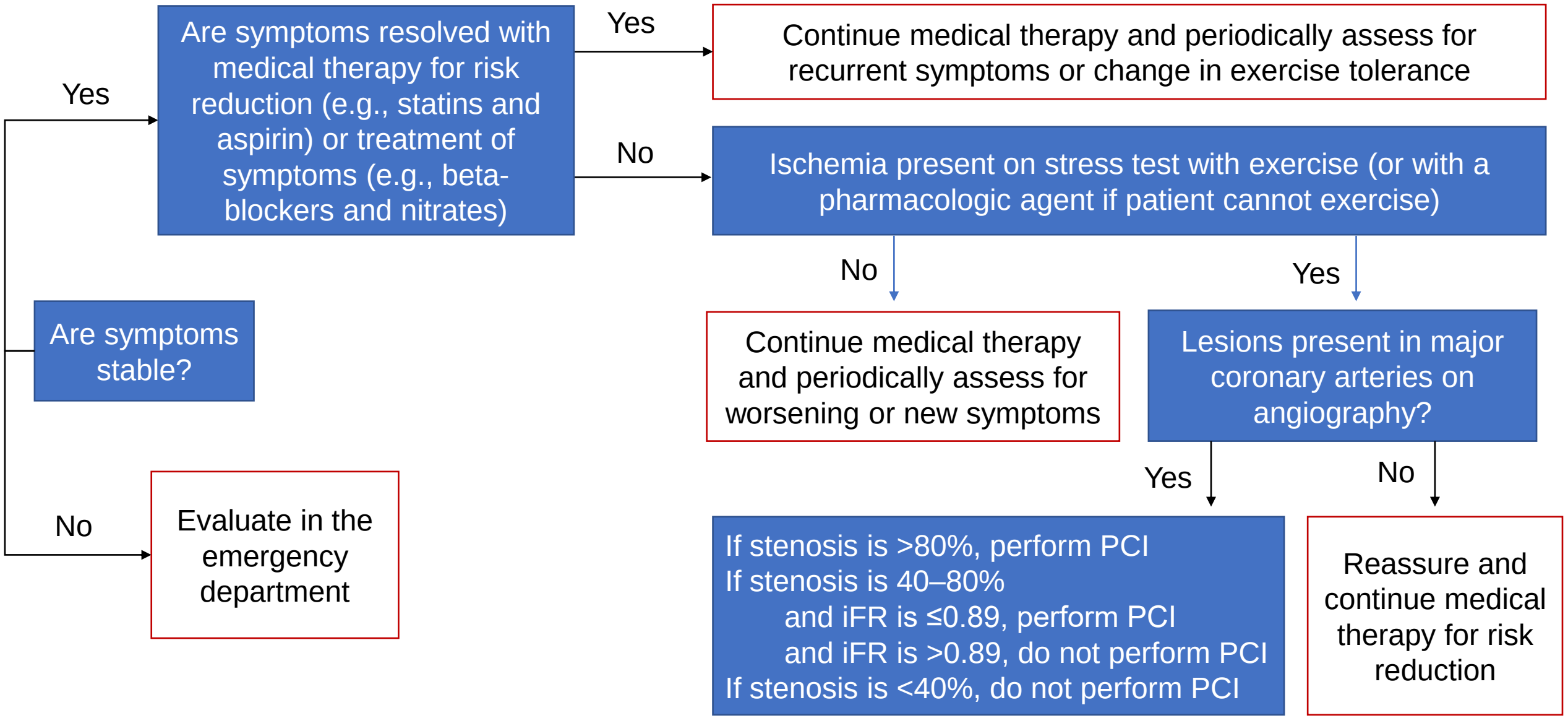
2 serial lesions of intermediate severity



FFR measurement post induction of maximal hyperemia

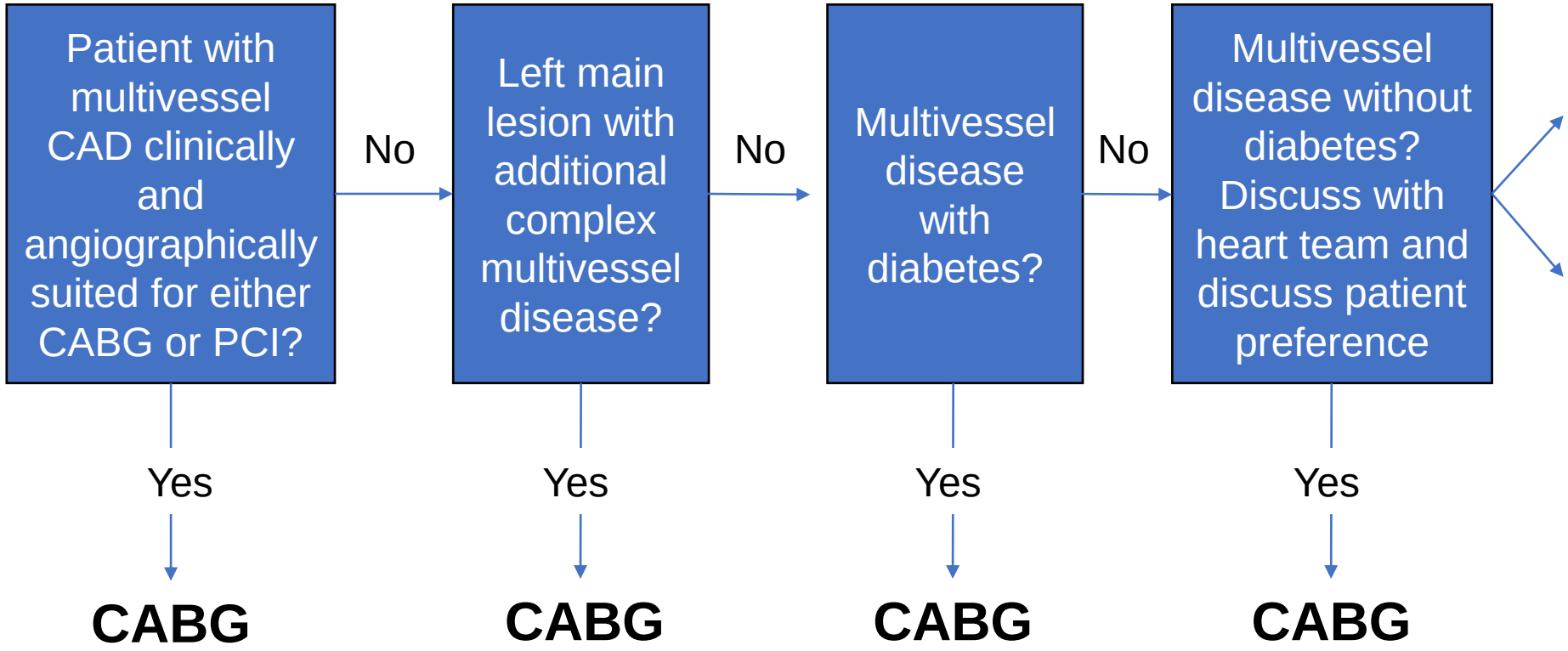
Kumbhani DJ, Bhatt DL. JAMA Cardiol. 2016;1:359-360.

Stable Coronary Disease: Evaluation



Bhatt DL. N Engl J Med. 2017;376:1879-1881.

CABG for Patients with Diabetes and Multivessel Disease



Favors CABG:

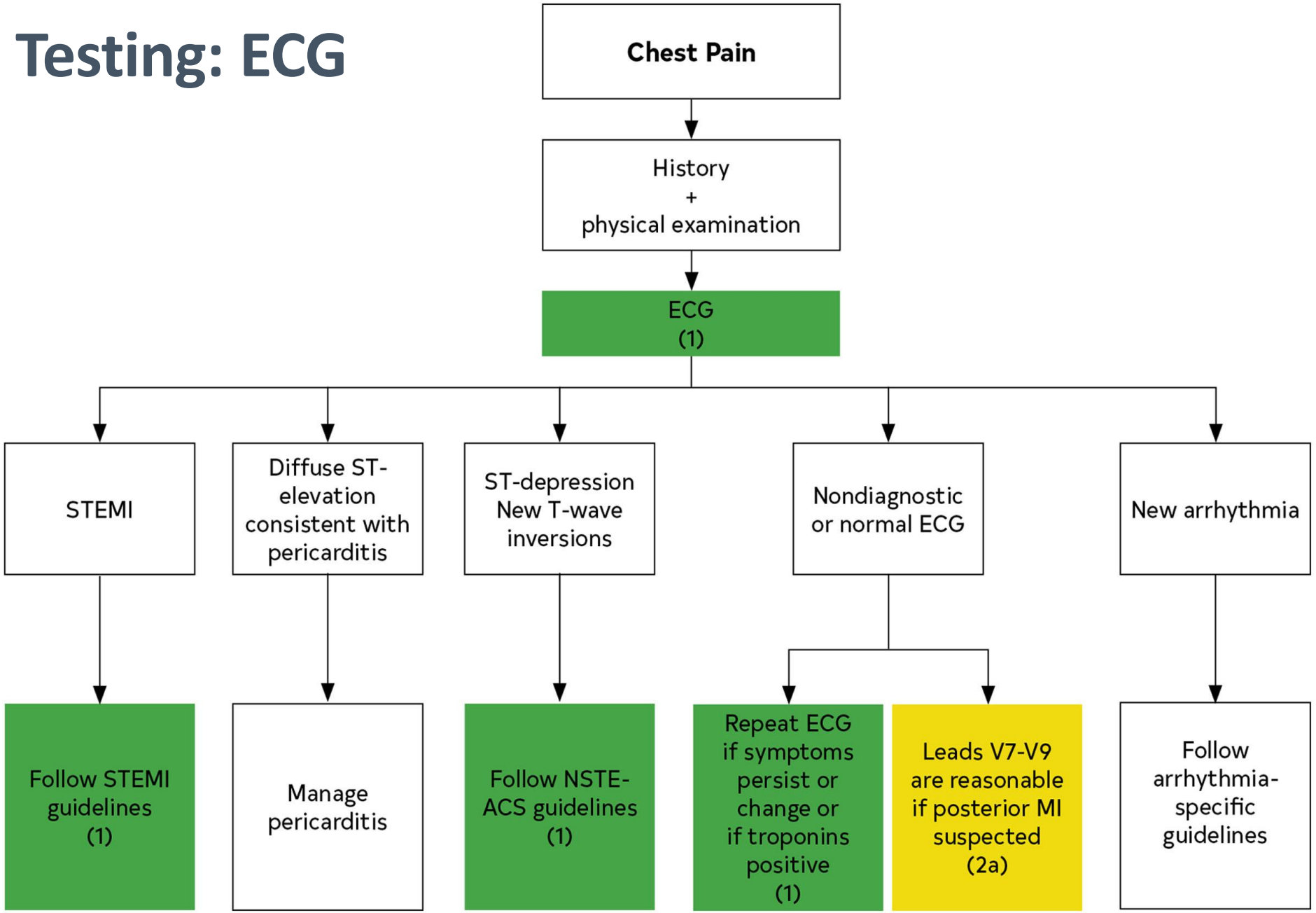
Patient with high lesion complexity due to lower incidence of repeat revascularization and lower burden of residual angina

Favors PCI:

Patient with high stroke risk or advanced age due to less arrythmia, bleeding, and wound complications as well as faster recovery time

Bhatt DL. Lancet. 2018;391:913-914.

Testing: ECG



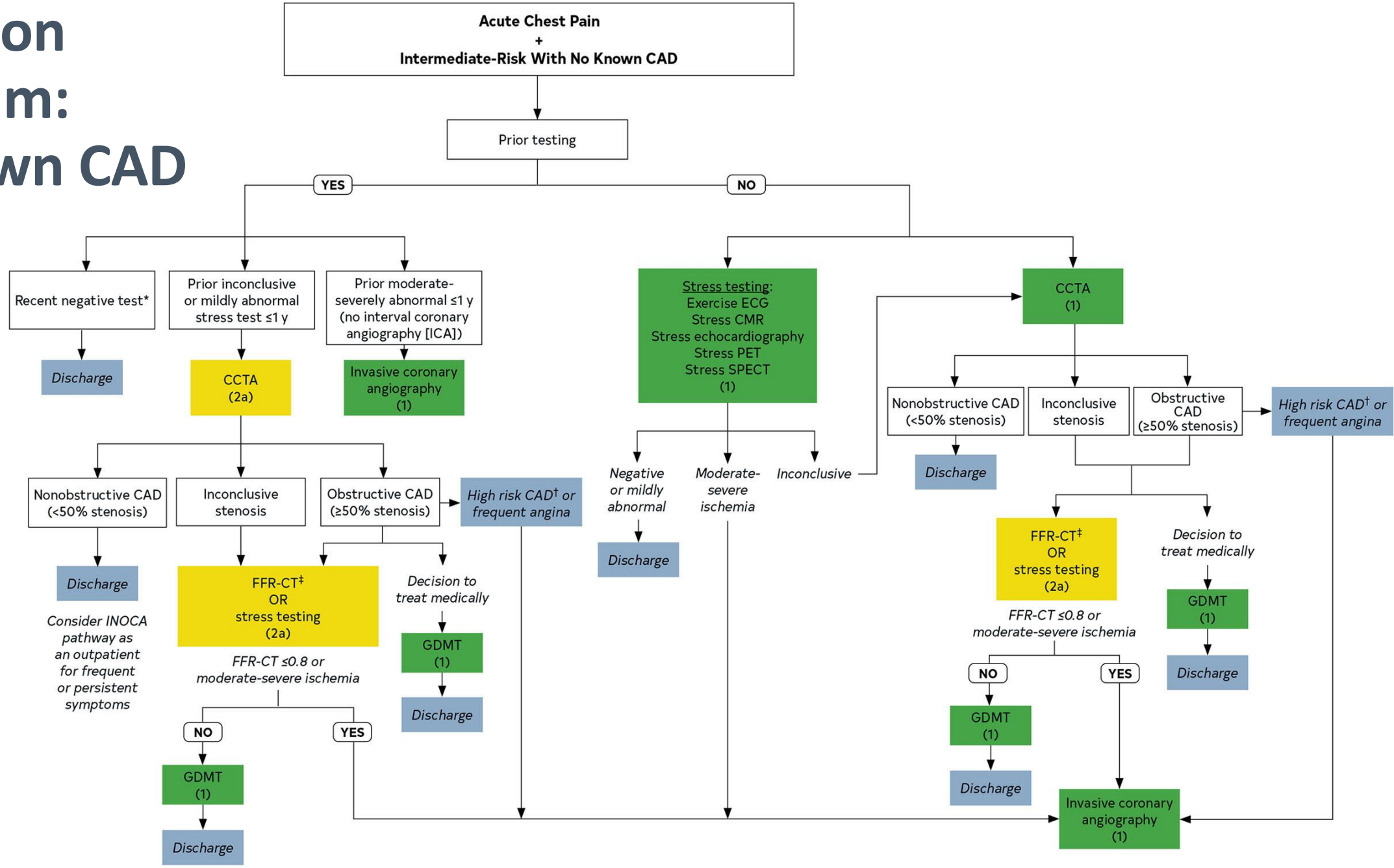
Gulati M, Levy PD, Mukherjee D, Amsterdam E, Bhatt DL, Birtcher KK, et al. Circulation. 2021;144:e368-e454.

Testing: Biochemical Tests

- Full blood count (including hemoglobin), lipid profile (including LDL-C), creatinine measurement
- If evaluation suggests ACS, repeated measure of troponin with high-sensitivity or ultrasensitive are recommended to rule out myocardial injury
- If clinical suspicion of thyroid disorder, assessment of thyroid function is recommended
- Screening for T2DM in patients with suspected and established chronic coronary syndromes should be implemented with HbA1c and fasting glucose measurements

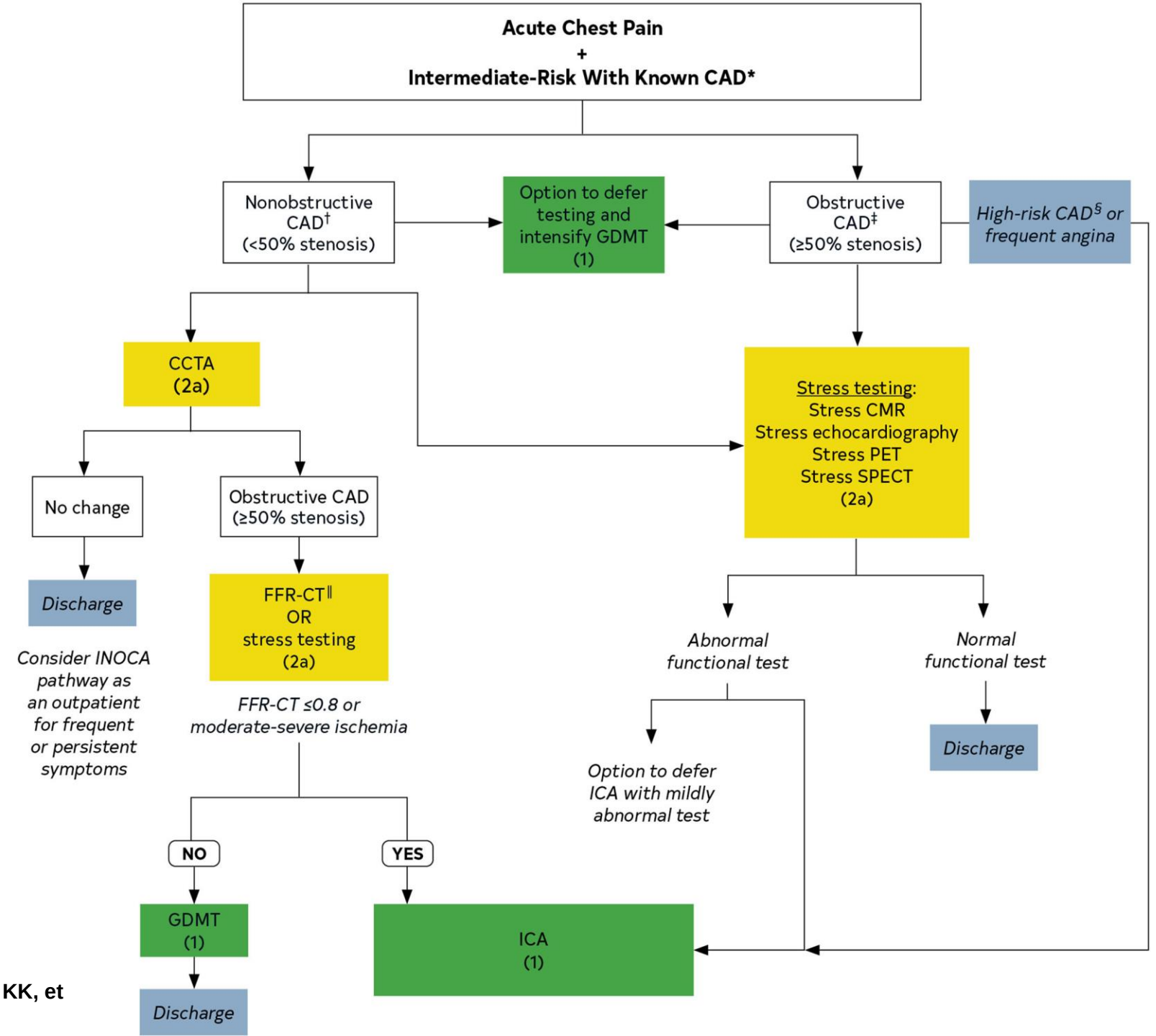
Knuuti J, Wijns W, Saraste A, Capodanno D, Barbato E, Funck-Brenato C, et al. Eur Heart J. 2020;41:407-477.

Evaluation Algorithm: No Known CAD



Gulati M, Levy PD, Mukherjee D, Amsterdam E, Bhatt DL, Birtcher KK, et al. Circulation. 2021;144:e368-e454.

Evaluation Algorithm: Known CAD



Gulati M, Levy PD, Mukherjee D, Amsterdam E, Bhatt DL, Birtcher KK, et al. Circulation. 2021;144:e368-e454.

Testing: Choosing the Right Test

Pretest likelihood of CAD						
	Low →	No testing necessary →	Option for CAC for ASCVD risk stratification			
	Intermediate-high →	Younger patient (<65 y of age)	OR	Less obstructive CAD suspected →	CCTA favored	
	Intermediate-high →	Older patient (≥65 y of age)	OR	More obstructive CAD suspected →	Stress testing favored	

Stress testing information	ETT	Stress echocardiography	SPECT MPI	PET MPI	Stress CMR MPI
Patient capable of exercise	✓	✓	✓		
Pharmacologic stress indicated		✓	✓	✓	✓
Quantitative flow				✓	✓
LV dysfunction/scar		✓	✓	✓	✓

CCTA = coronary computed tomography angiography; ETT = exercise tolerance test; SPECT = single-photon emission computed tomography; CMR = cardiovascular magnetic resonance

Gulati M, Levy PD, Mukherjee D, Amsterdam E, Bhatt DL, Birtcher KK, et al. Circulation. 2021;144:e368-e454.

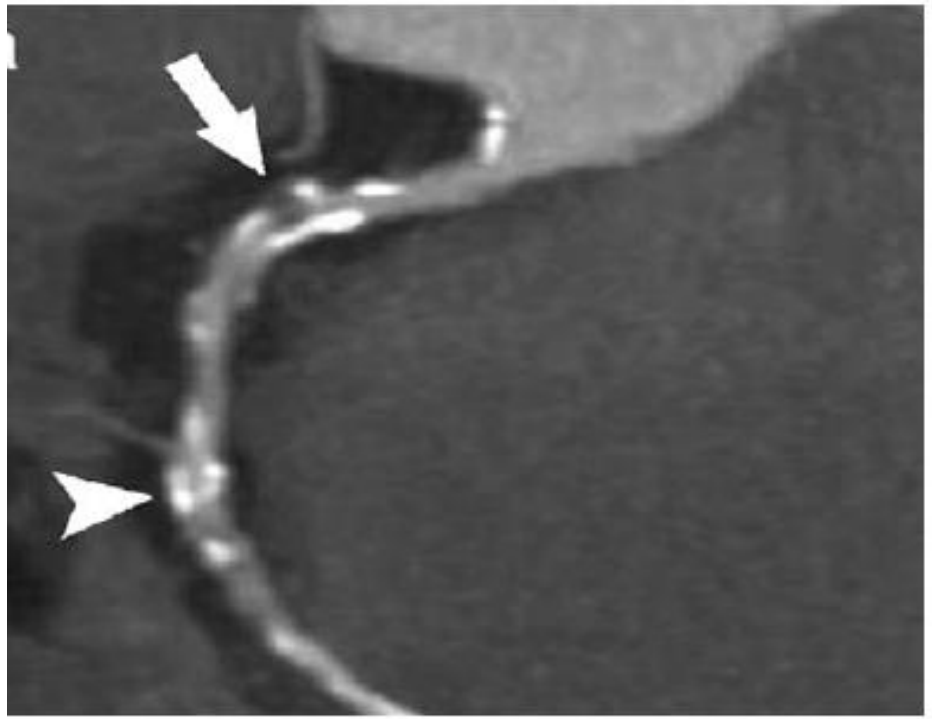
Testing: Choosing the Right Test

	Favors use of CCTA	Favors use of stress imaging
Goal	• Rule out obstructive CAD • Detect nonobstructive CAD	• Ischemia-guided management
Availability and expertise	• High-quality imaging and expert interpretation routinely available	• High-quality imaging and expert interpretation routinely available
Likelihood of obstructive CAD	• Age <65 y	• Age ≥65 y
Prior test results	• Prior functional study inconclusive	• Prior CCTA inconclusive
Other compelling indications	• Anomalous coronary arteries • Require evaluation of aorta or pulmonary arteries	• Suspect scar (especially if PET or stress CMR available) • Suspect coronary microvascular dysfunction (when PET or CMR available)

Gulati M, Levy PD, Mukherjee D, Amsterdam E, Bhatt DL, Birtcher KK, et al. Circulation. 2021;144:e368-e454.

Testing: Coronary CTA

- Coronary CTA allows for visualization of the coronary artery lumen and wall using intravenous contrast agent
- High accuracy for detection of coronary stenoses; however, stenoses 50-90% may not be functionally significant
- Non-invasive or invasive functional testing is recommended for further evaluation of angiographic stenosis detected by coronary CTA or invasive angiography

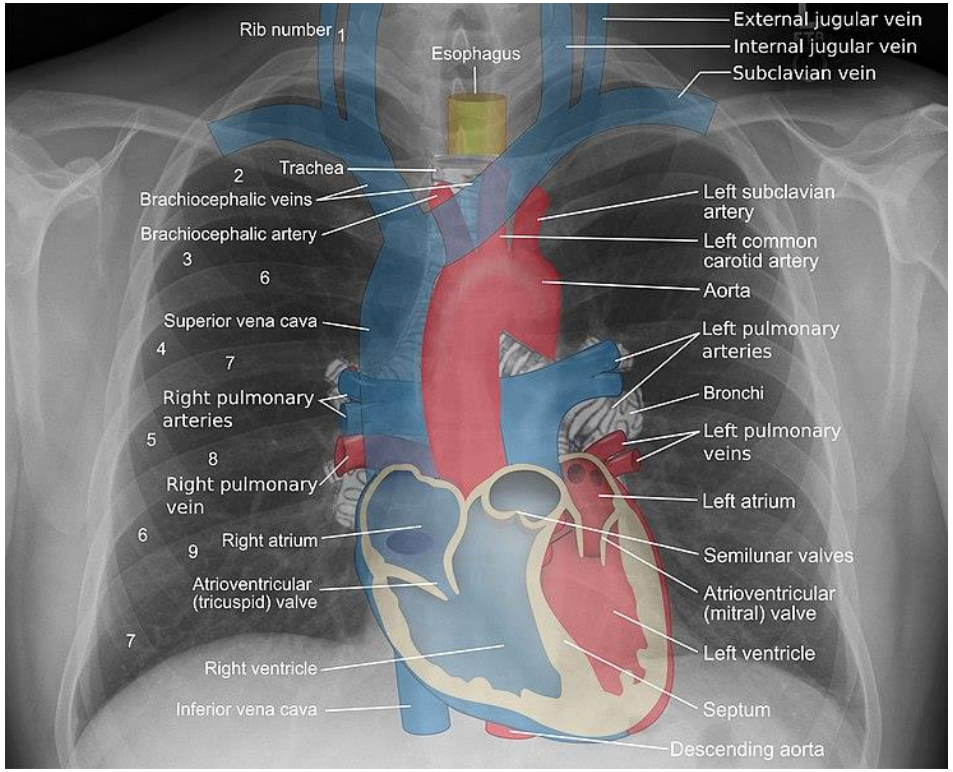


CC BY 2.5, https://commons.wikimedia.org/w/index.php?curid=1694485

Knuuti J, Wijns W, Saraste A, Capodanno D, Barbato E, Funck-Brenato C, et al. Eur Heart J. 2020;41:407-477.

Testing: Chest X-Ray

- Recommended for patients with atypical presentation, signs and symptoms of HF, or suspicion of pulmonary disease



Mikael Häggström, M.D. - Author info - Reusing images- Conflicts of interest: None Mikael Häggström Using source images by ZooFari, Stillwaterising and Gray's Anatomy creators, CC BY-SA 3.0, via Wikimedia Commons

Knuuti J, Wijns W, Saraste A, Capodanno D, Barbato E, Funck-Brenato C, et al. Eur Heart J. 2020;41:407-477.

CMHC Cardiometabolic Health Congress

www.cardiometabolichealth.org

Foundations of Cardiometabolic Health Certification Course

Certified Cardiometabolic Health Professional (CCHP)

The Treatment of CAD

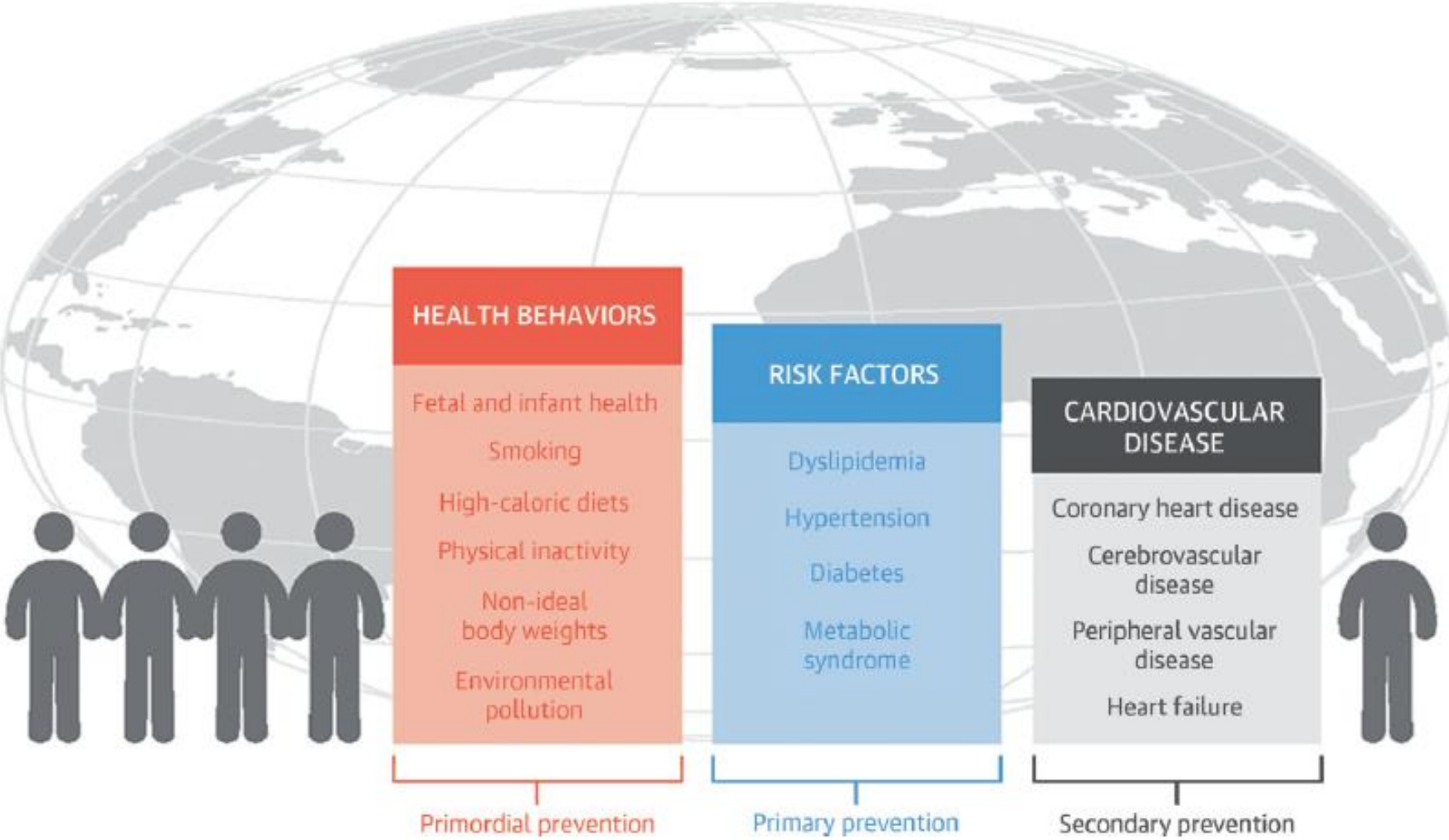
Deepak L. Bhatt, MD, MPH

Executive Director of Interventional Cardiovascular Programs, Brigham and Women's Hospital
Professor of Medicine, Harvard Medical School

BWH BRIGHAM AND WOMEN'S HOSPITAL | Heart & Vascular Center |

HARVARD MEDICAL SCHOOL TEACHING HOSPITAL

Primordial, Primary, Secondary Prevention



Vaduganathan M, Venkataramini AS, Bhatt DL. J Am Coll Cardiol. 2015;66:1535-1537

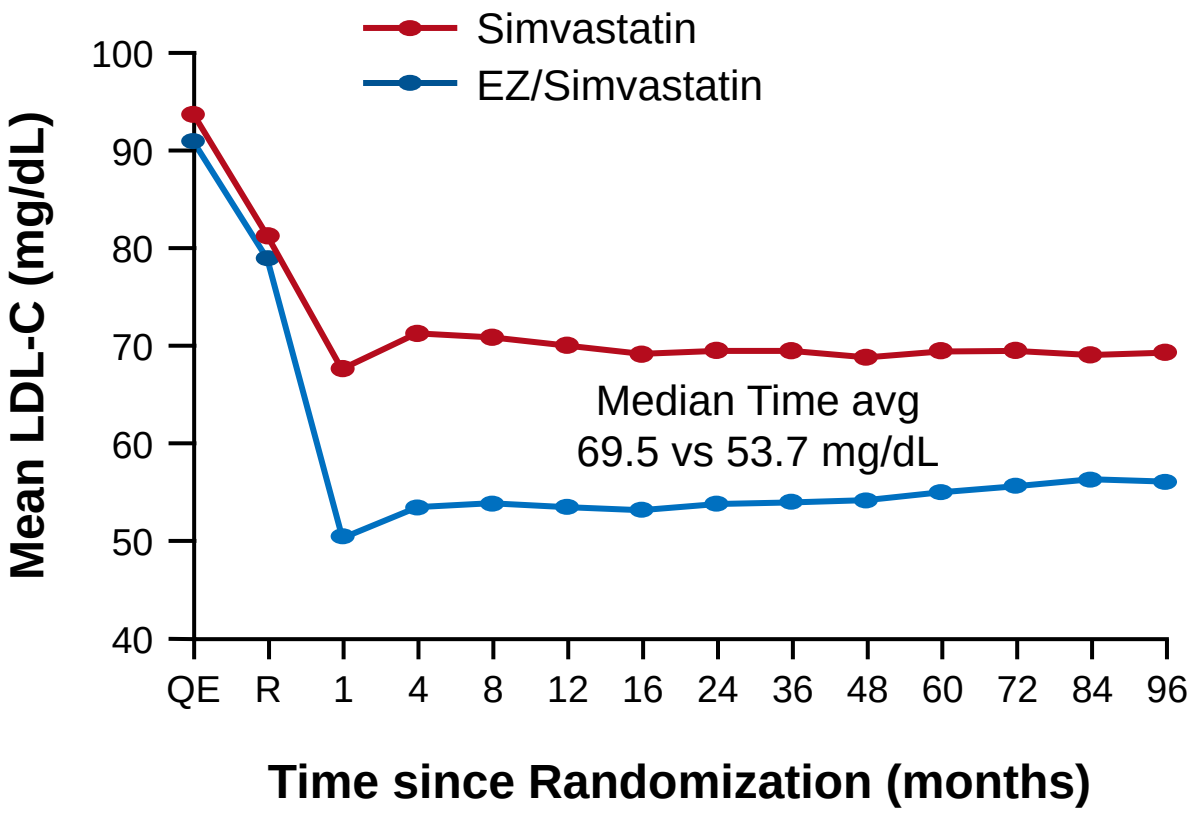
Lifestyle Management

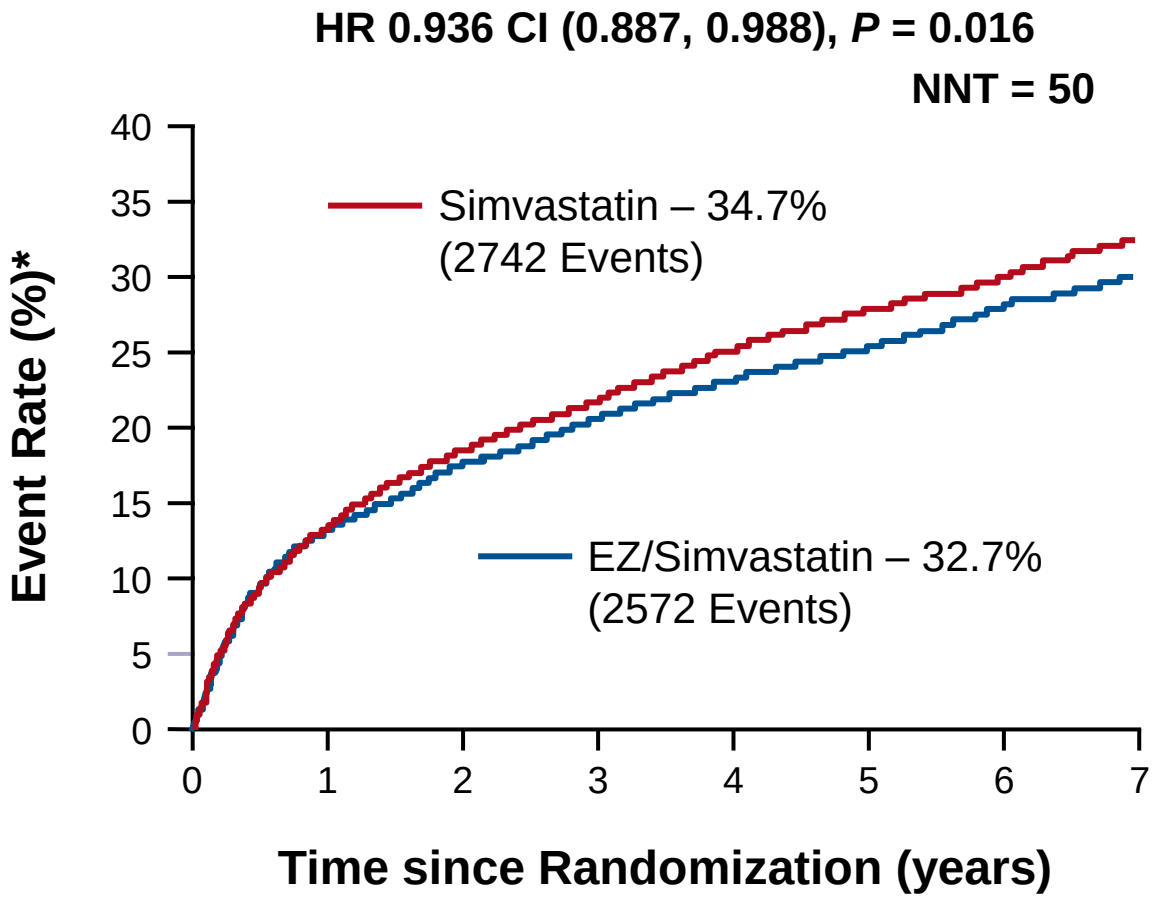
- **Healthy diet**
  - Recommend diet high in vegetables, fruits, and whole grains; saturated fat should be less than 10% of intake; alcohol should be limited (<100 grams/week)
- **Healthy weight**
  - Obtain and maintain a healthy weight, or reduce weight through recommended energy intake and increased physical activity
- **Smoking cessation**
  - Provide patients with strategies to help them quit
- **Physical activity**
  - 30-60 minutes of moderate physical activity most days, irregular activity still beneficial
- **Cardiac rehabilitation**
  - Exercised-based cardiac rehab reduces cardiovascular mortality; currently underutilized for chronic coronary syndromes
- **Psychosocial factors**
  - Patients with heart disease are at 2-fold risk of mood and anxiety disorders; assessment for these factors is recommended, and clinical trials have shown that psychological interventions and pharmacological interventions show benefit for these factors as well as cardiac mortality
- **Environmental factors**
  - Air pollutants increases cardiovascular risk, and environmental noise increases risk of CVD

Knuuti J, Wijns W, Saraste A, Capodanno D, Barbato E, Funck-Brenato C, et al. Eur Heart J. 2020;41:407-477.

IMPROVE-IT: Primary Results

18,144 ACS patients randomized to simvastatin alone or ezetimibe (EZ)/simvastatin, 6-year median follow up

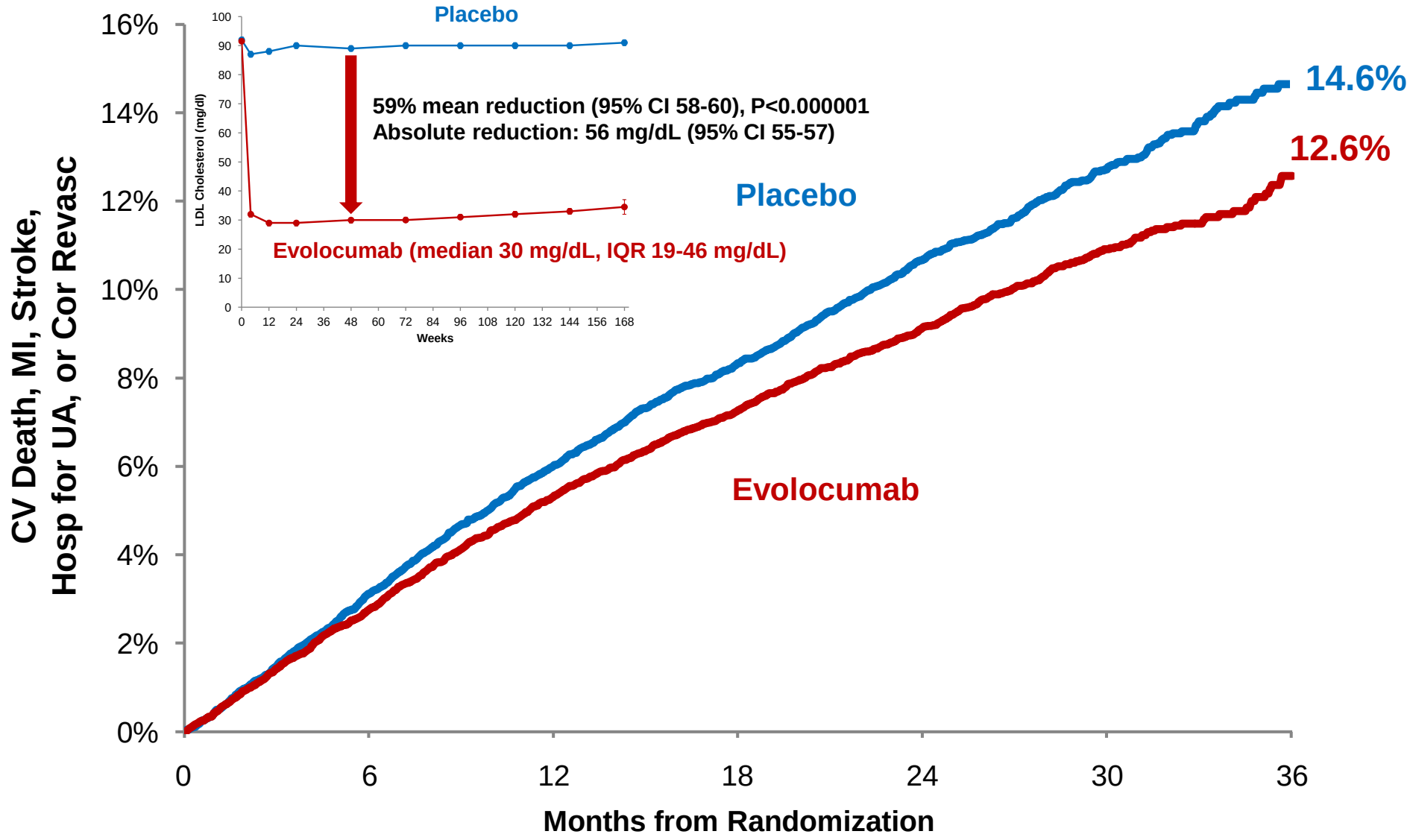




*Primary endpoint (cardiovascular death, MI, UA, coronary revascularization, or stroke).

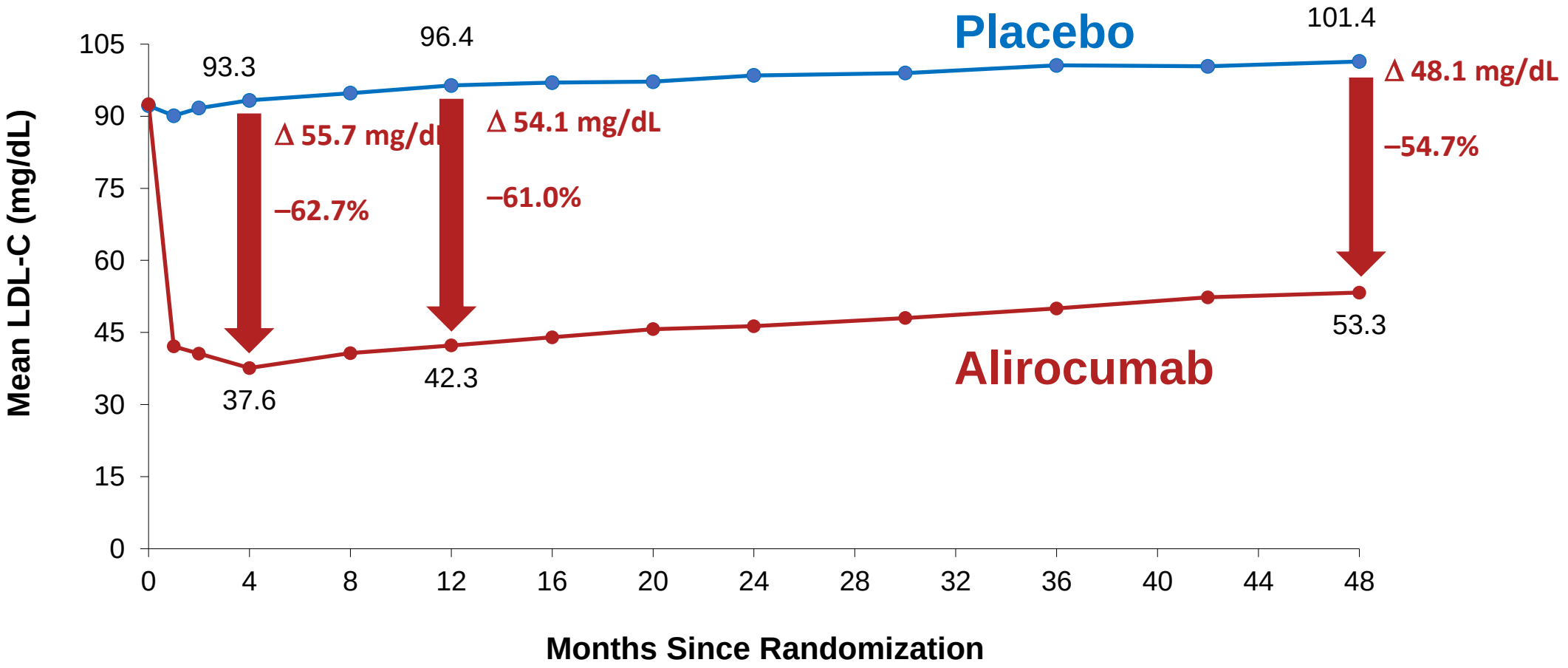
Cannon CP, Blazing MA, Giugliano RP, et al…. Braunwald E, Califf RM. *N Engl J Med.* 2015;372:2387–2397.

FOURIER



Sabatine MS, Giugliano RP, Keech AC, Honarpour N, Wiviott SD, Murphy SA, et al. N Engl J Med. 2017;376:1713-22.

ODYSSEY OUTCOMES:
LDL-C On-Treatment Analysis

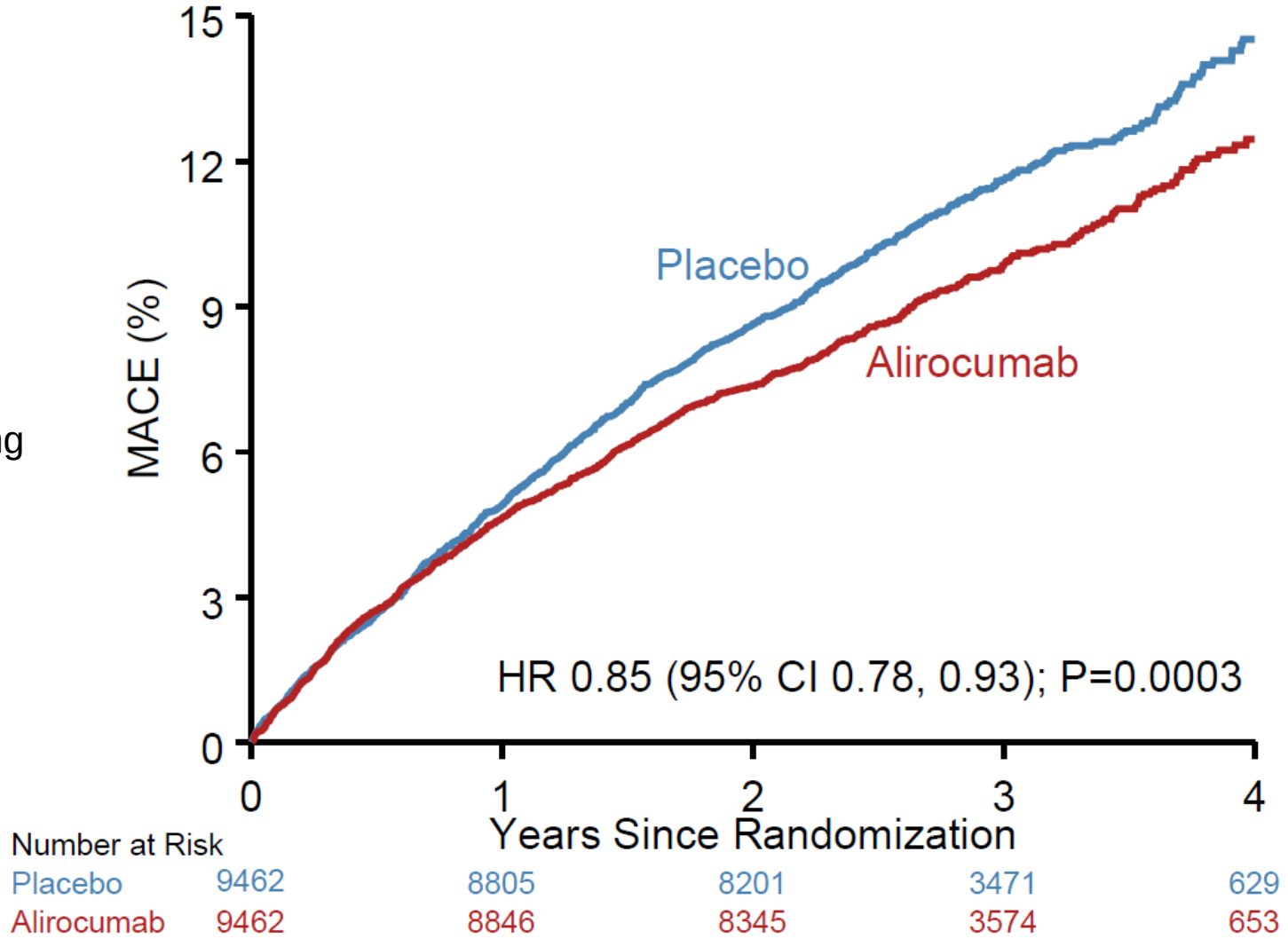


Excludes LDL-C values after premature treatment discontinuation or blinded switch to placebo. Approximately 75% of months of active treatment were at the 75 mg dose.

Schwartz GG, Steg PG, Szarek M, Bhatt DL, Bittner VA, Diaz R, et al. N Engl J Med. 2018;379:2097-2107.

Primary Efficacy Endpoint: MACE

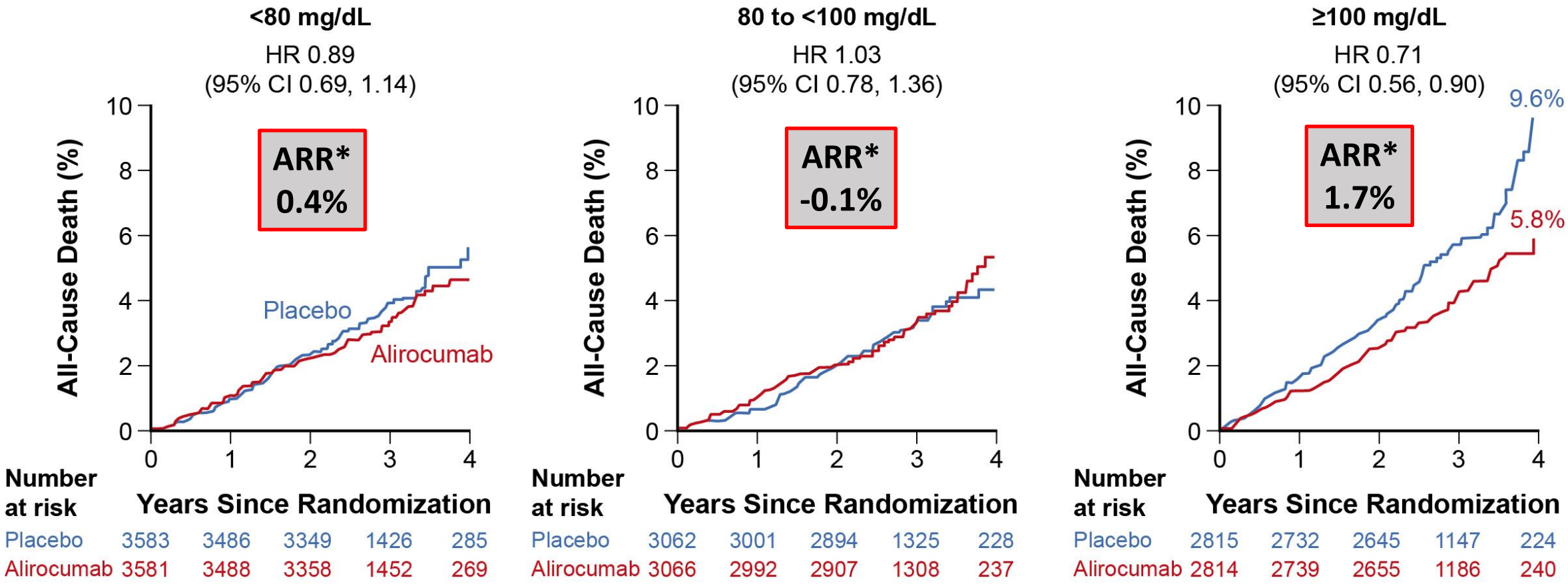
MACE: CHD death, non-fatal MI, ischemic stroke, or unstable angina requiring hospitalization



NNT 49 for 4 years

Schwartz GG, Steg PG, Szarek M, Bhatt DL, Bittner VA, Diaz R, et al. N Engl J Med. 2018;379:2097-2107.

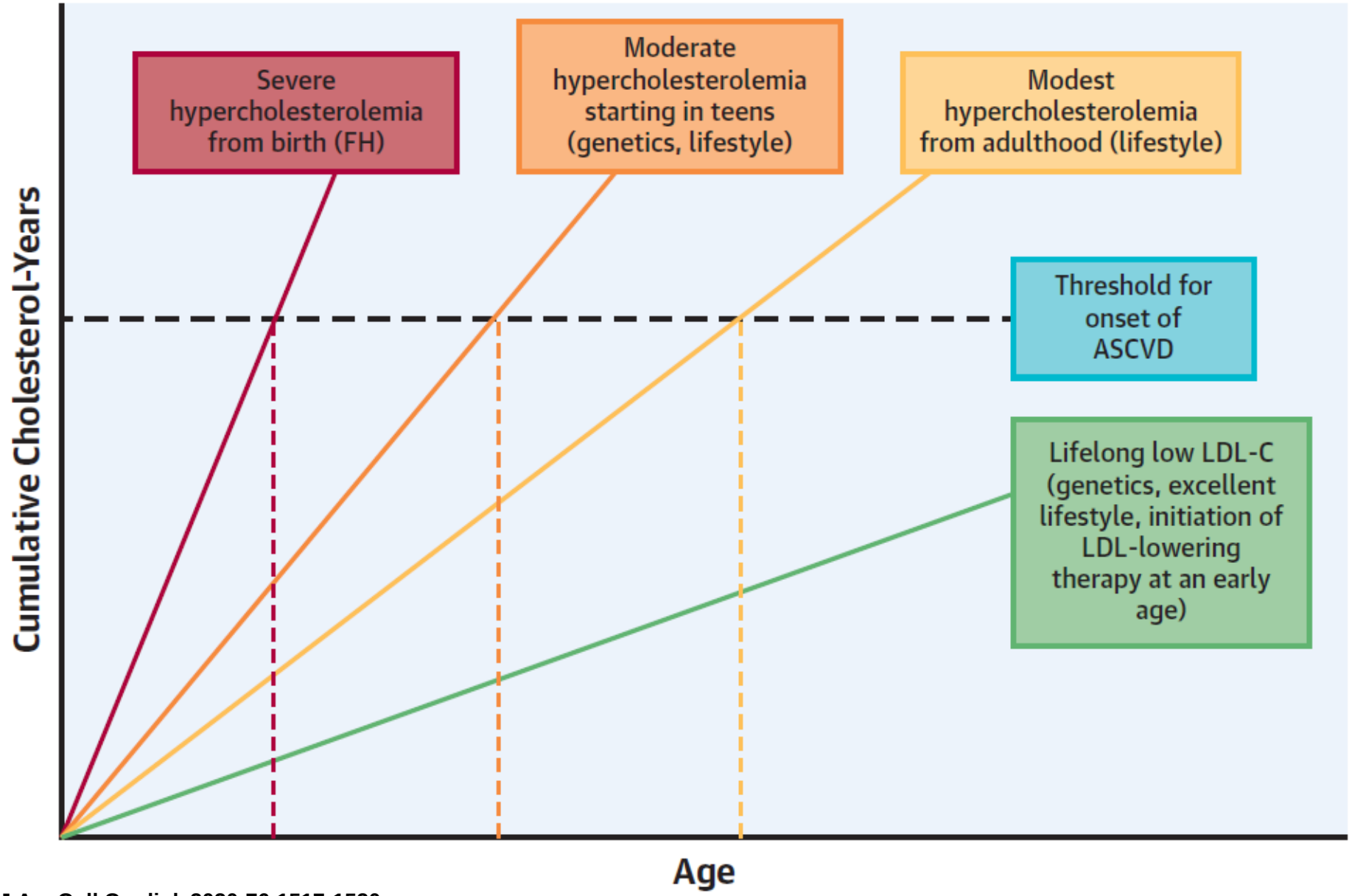
All-cause Death in 3 Predefined Categories of Baseline LDL-C



*Absolute risk reduction: Interaction P=0.005
Post hoc analysis

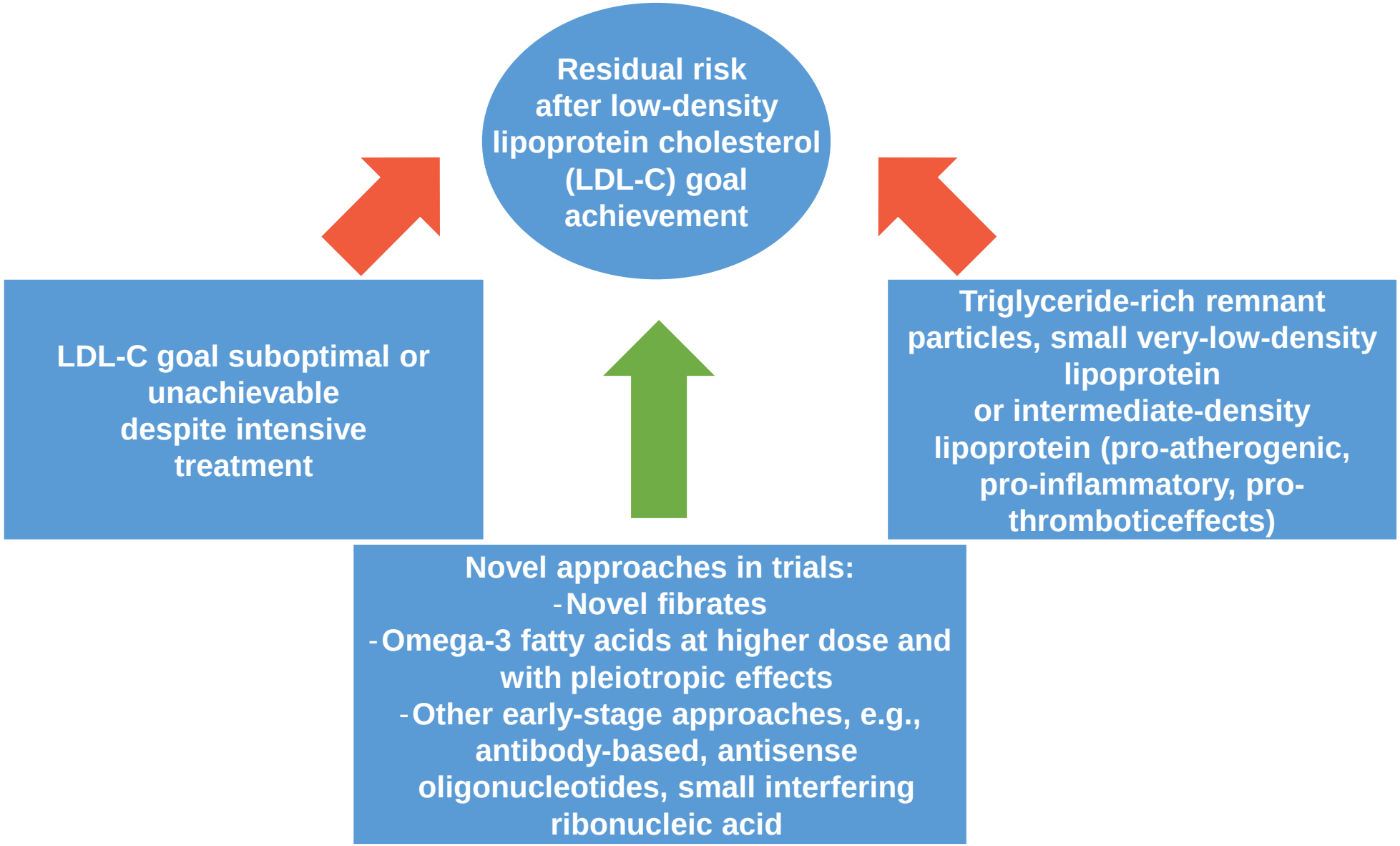
Steg PG, Szarek M, Bhatt DL, Bittner VA, Brégeault MF, Dalby AJ, Diaz R, et al. Circulation 2019;140:103-112.

“Cholesterol-Years” for CV Risk Prediction and Treatment



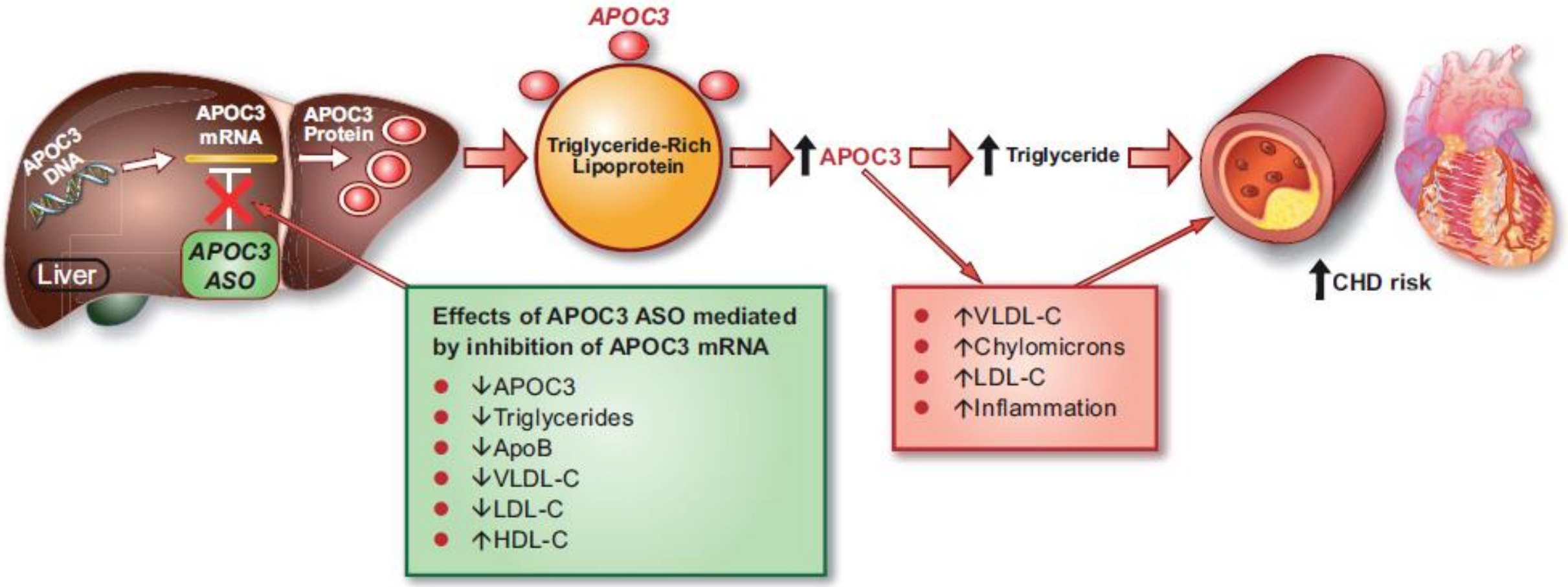
Shapiro MD, Bhatt DL. J Am Coll Cardiol. 2020;76:1517-1520.

Promising Therapies for Hypertriglyceridemia



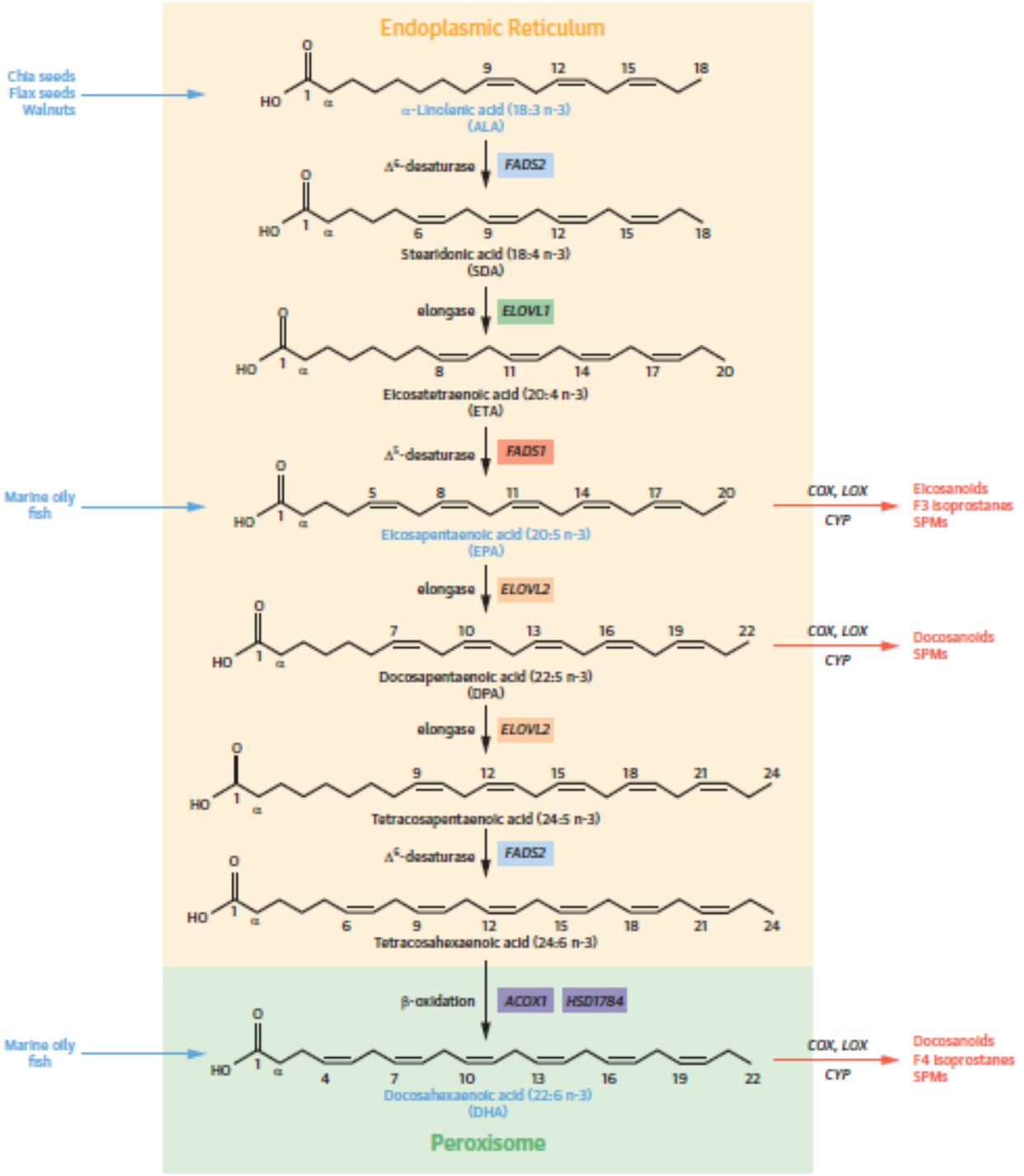
Ganda OP, Bhatt DL, Mason RP, Miller M, Boden WE. J Am Coll Cardiol. 2018;72:330-343.

Targeting RNA to Lower Triglycerides:
Long Strides from Short Molecules



Qamar A, Libby P, Bhatt DL. Eur Heart J. 2019; 40:2797-2800.

A Revolution in Omega-3 Fatty Acid Research



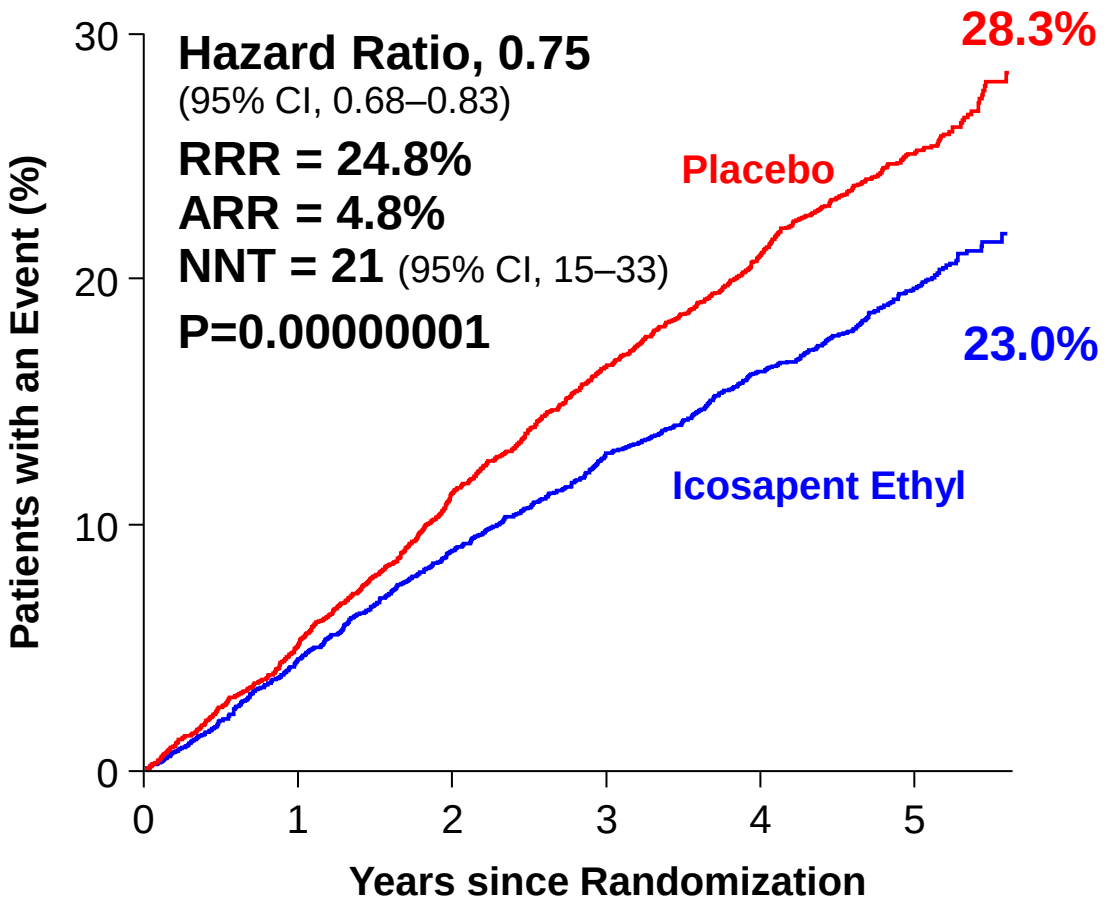
Bhatt DL, Budoff MJ, Mason RP. J Am Coll Cardiol. 2020;76:2098-2101.

Primary and Key Secondary Composite Endpoints

reduce-it

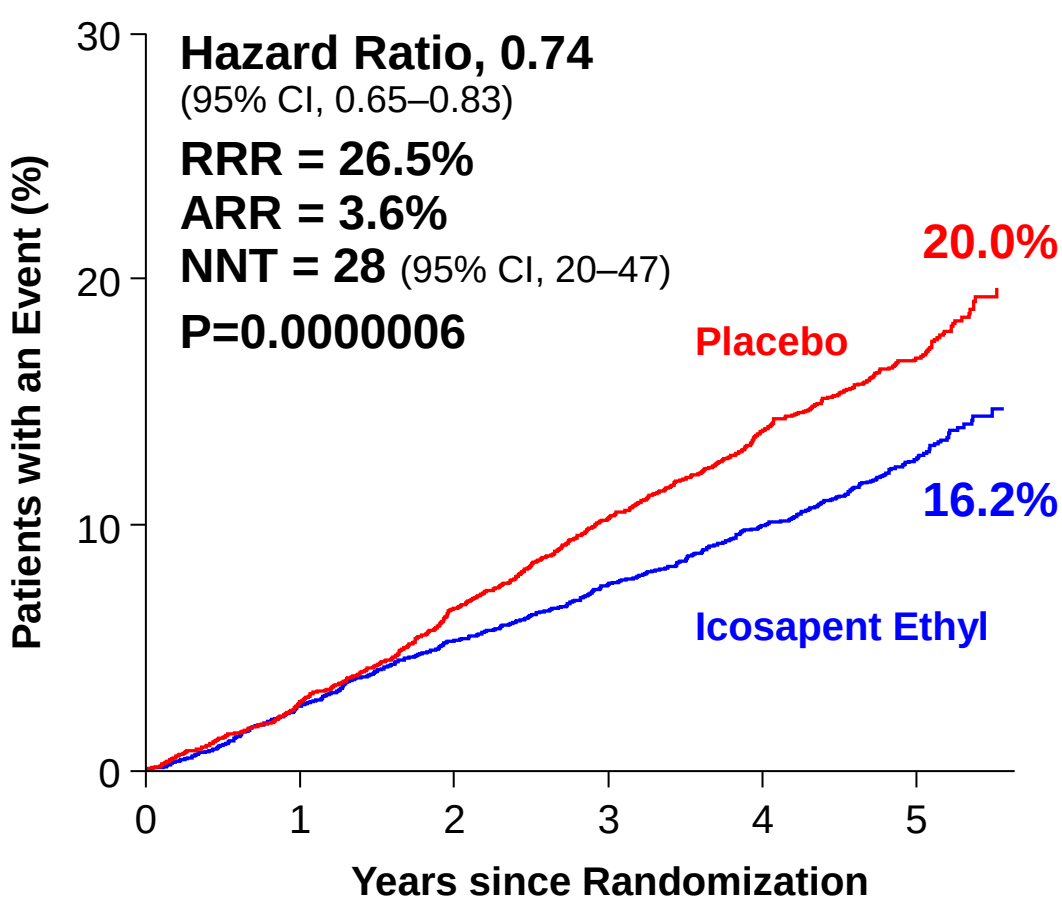
Primary Composite Endpoint:

CV Death, MI, Stroke, Coronary Revasc, Unstable Angina



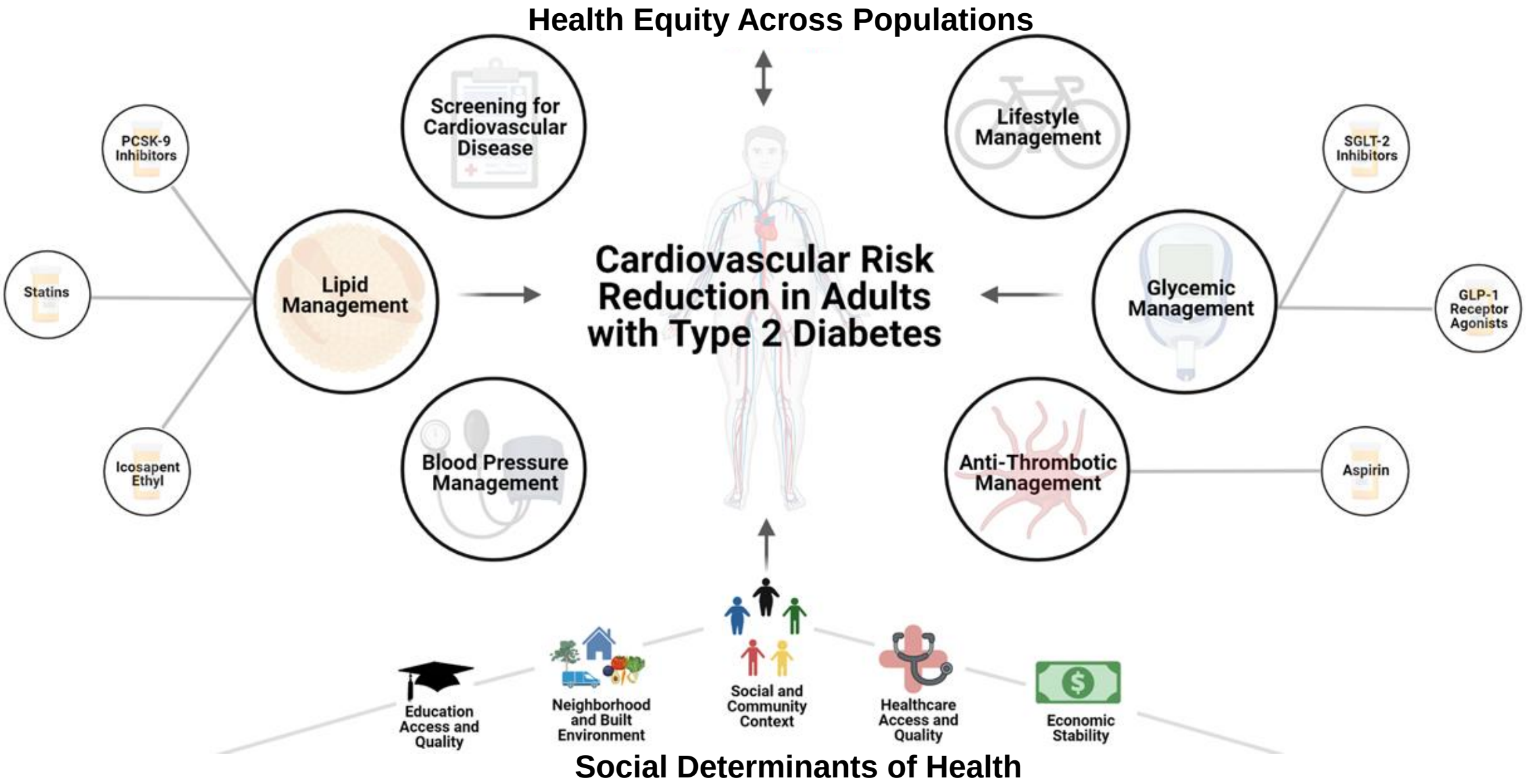
Key Secondary Composite Endpoint:

CV Death, MI, Stroke



Bhatt DL, Steg PG, Miller M, et al. N Engl J Med. 2019; 380:11-22. Bhatt DL. AHA 2018, Chicago.

Cardiovascular Risk Reduction:T2DM



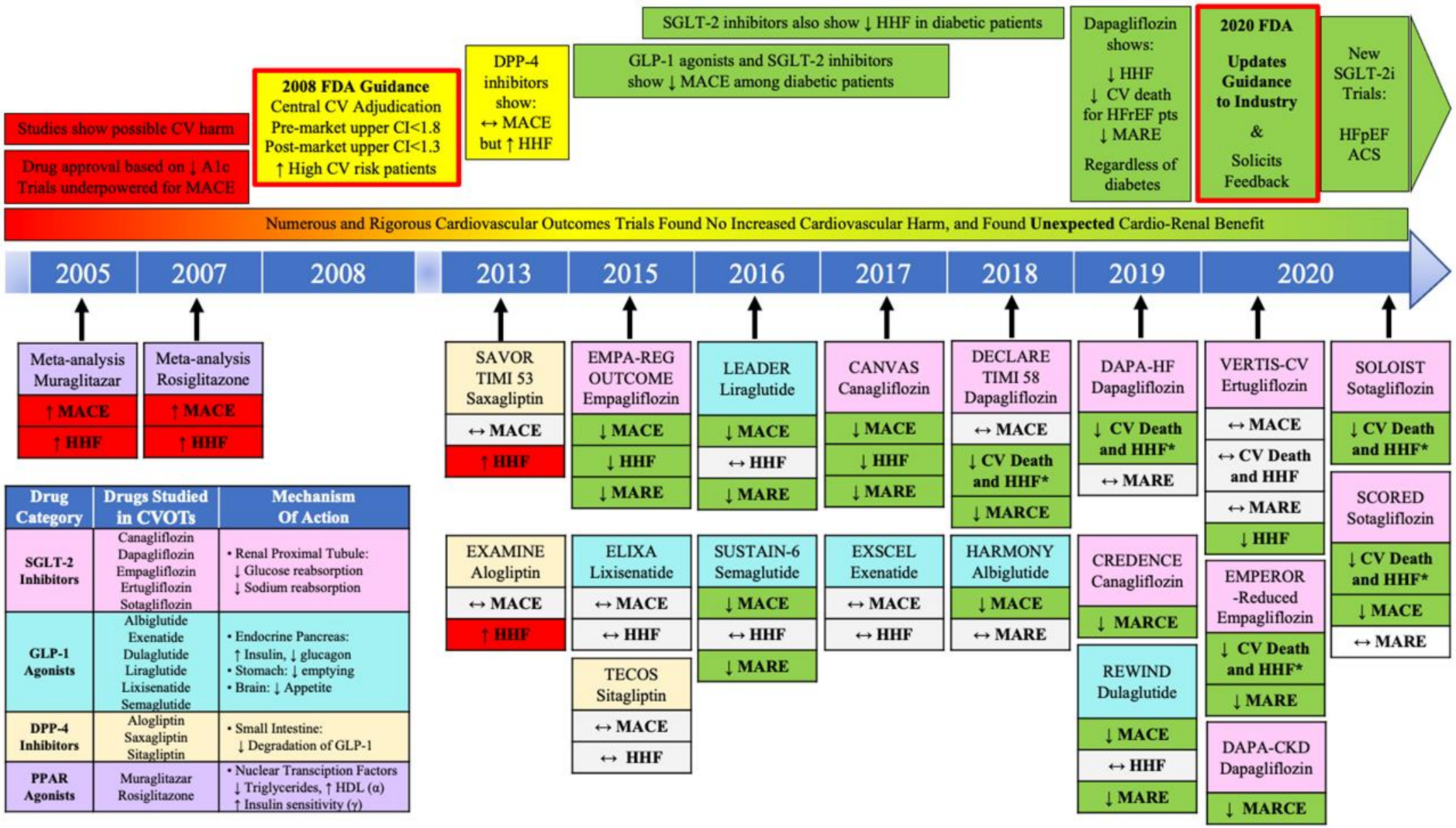
Joseph JJ, Deedwania P, Acharya T, Aguilar D, Bhatt DL, Chyun DA, et al. Circulation. 2022;144:00–00.

CAD and T2DM

- >34.2 million Americans have diabetes; 90-95% of this population is type 2
- Cardiovascular disease is the leading cause of morbidity and mortality in patients with diabetes (type 1 and type 2)

Joseph JJ, Deedwania P, Acharya T, Aguilar D, Bhatt DL, Chyun DA, et al. Circulation. 2022;144:00–00.

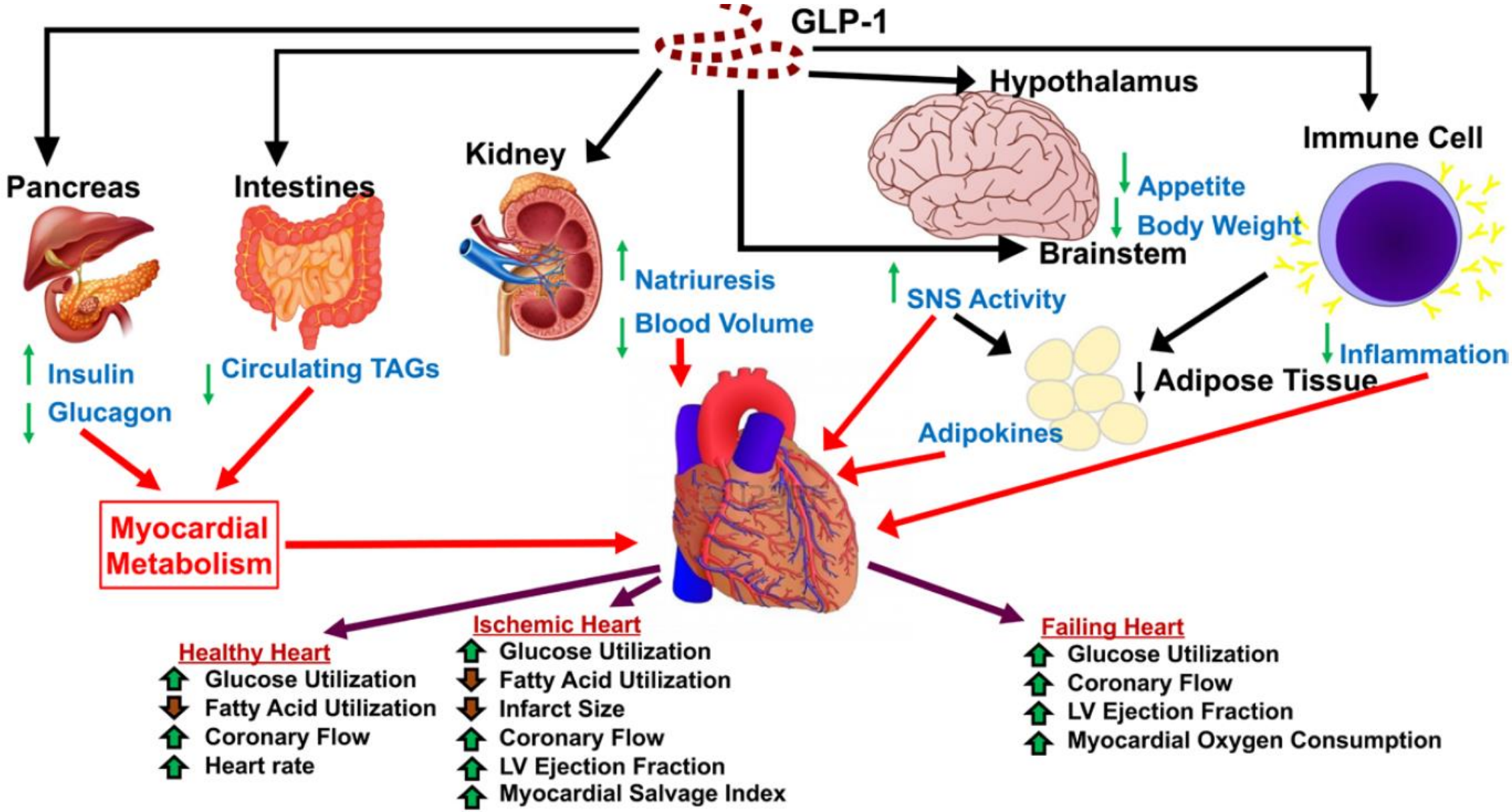
Noninsulin Diabetes Drug Development



Drug Category	Drugs Studied in CVOTs	Mechanism Of Action
SGLT-2 Inhibitors	Canagliflozin Dapagliflozin Empagliflozin Ertugliflozin Sotagliflozin	• Renal Proximal Tubule: ↓ Glucose reabsorption ↓ Sodium reabsorption
GLP-1 Agonists	Albiglutide Exenatide Dulaglutide Liraglutide Lixisenatide Semaglutide	• Endocrine Pancreas: ↑ Insulin, ↓ glucagon • Stomach: ↓ emptying • Brain: ↓ Appetite
DPP-4 Inhibitors	Alogliptin Saxagliptin Sitagliptin	• Small Intestine: ↓ Degradation of GLP-1
PPAR Agonists	Muraglitazar Rosiglitazone	• Nuclear Transciption Factors ↓ Triglycerides, ↑ HDL (α) ↑ Insulin sensitivity (γ)

Ferro EG, Elshazly MB, Bhatt DL. Cardiol Clin. 2021;39:335-351.

Potential Indirect CV Effects of GLP-1R Agonists



Joseph JJ, Deedwania P, Acharya T, Aguilar D, Bhatt DL, Chyun DA, et al. Circulation. 2022;144:00–00.

Management of Stable CAD in Patients with T2DM: Antithrombotics

T2DM is a generalized prothrombotic state caused by altered coagulation and altered platelet function

Aspirin alone

- Lowest risk of bleeding but high residual platelet reactivity increases CV risk

Clopidogrel alone

- Decreased CV risk without meaningfully increased bleeding risk vs aspirin alone

Aspirin+clopidogrel/ticagrelor

- Decreased CV risk with increased risk of bleeding; targets patients with additional risk factor and low bleeding risk

Aspirin+low dose rivaroxaban

- Decreased CV risk with increased bleeding risk; targets the aberrant coagulation with T2DM

Arnold SV, Bhatt DL, Barsness GW, Beatty AL, Deedwania PC, Inzucchi SE, et al. Circulation. 2020;141:e779–e806

Management of Stable CAD in Patients with T2DM: Blood Pressure

Coexisting hypertension increases risk of MI, stroke, and all-cause mortality

Target BP

- <140/90 mm Hg in most patients; consider <130/80 mm Hg if additional risk factors for stroke or microvascular complications

ACEi/ARB

- First-line therapy because of decreased CV risk with CAD

Long-acting thiazide diuretic

- Good CV risk reduction; slight increase in glucose

CCBs

- Good CV risk reduction and effective antianginal

Aldosterone antagonists

- Particularly effective in patients with prior MI or LV dysfunction

Beta-blockers

- Do not reduce mortality in uncomplicated patients with stable CAD; vasodilating β-blocker for less adverse metabolic impact

Arnold SV, Bhatt DL, Barsness GW, Beatty AL, Deedwania PC, Inzucchi SE, et al. Circulation. 2020;141:e779–e806

Management of Stable CAD in Patients with T2DM: Lipids

Atherogenic lipid anomalies include hypertriglyceridemia, low HDL-C, and small, dense LDL particles

High-intensity statins

- Cornerstone of lipid therapy and secondary prevention

Ezetimibe and PCSK9 inhibitors

- Additional CV risk reduction when LDL is >70 mg/dL despite maximally tolerated statins

Niacin

- Not recommended

Fibrates

- Recommended when triglycerides are very high (eg, >500 mg/dL) to reduce the risk of pancreatitis

Icosapent Ethyl

- Consider for further CV risk reduction when triglycerides remain elevated (>135 mg/dL) despite maximally tolerated statin

Arnold SV, Bhatt DL, Barsness GW, Beatty AL, Deedwania PC, Inzucchi SE, et al. Circulation. 2020;141:e779–e806

Management of Stable CAD in Patients with T2DM: Glycemic Control

Hyperglycemia increases CV risk, but impact of glucose-lowering therapies on outcomes is complex, and therapy needs to be individualized.

Glycemic target

<7.0% if young and healthy (life expectancy >10-20 y); depends on preferences and capacity

<8.0% or 8.5% for older patients with comorbidities or at high risk for hypoglycemia; depends on preferences, capacity, and types of treatment used

Arnold SV, Bhatt DL, Barsness GW, Beatty AL, Deedwania PC, Inzucchi SE, et al. Circulation. 2020;141:e779–e806

Management of Stable CAD in Patients with T2DM: Glucose-Lowering Medications

Metformin	CV benefit possible (low-quality evidence)
	No associated weight gain or hypoglycemia
SGLT2is	CV benefit; reduction in MACEs and HF hospitalizations
	Associated with weight loss, no hypoglycemia, lower BP, and less progression of CKD
GLP-1 RAs	CV benefit; reduction in MACEs (some inconsistency among drugs)
	Associated with weight loss and no hypoglycemia
Thiazolidinediones	CV benefit likely (not HF)
	No hypoglycemia; associated with weight gain, edema, risk of HF, and bone fractures
DPP4 inhibitors	Neutral on CV outcomes
	No associated weight gain or hypoglycemia
Insulin and sulfonylureas	Likely neutral on CV outcomes
	Associated with weight gain and hypoglycemia

Arnold SV, Bhatt DL, Barsness GW, Beatty AL, Deedwania PC, Inzucchi SE, et al. Circulation. 2020;141:e779–e806

Management of Stable Angina in Patients with CAD: Medical Therapy

No antianginal medications reduce morbidity or mortality in stable CAD and have similar impact on reducing angina

Beta-blockers	CCBs	Long-acting nitrates	Ranolazine
• Preference for vasodilating ones with less adverse metabolic effects	• Avoid non-dihydropyridines in patients with LV dysfunction or with beta-blockers	• Long-term use can cause endothelial dysfunction	• No hemodynamic effects • Moderate HbA1c reduction

Arnold SV, Bhatt DL, Barsness GW, Beatty AL, Deedwania PC, Inzucchi SE, et al. Circulation. 2020;141:e779–e806

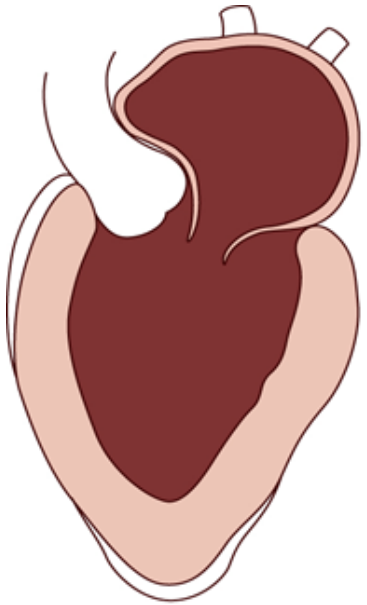
Management of Stable Angina in Patients with CAD: Revascularization

Both surgical and percutaneous revascularization outcomes are impaired in the setting of T2DM, with increased risk of both procedural complications and recurrent ischemic events

Multivessel CAD, left main disease, complex coronary artery			
CABG is associated with lower MACEs compared to PCI	Use of internal mammary artery to anterior wall is an important driver of benefit of CABG	Typically achieve more complete revascularization with CABG vs PCI	Newest-generation drug-eluting stents have narrowed the gap between CABG and PCI

Arnold SV, Bhatt DL, Barsness GW, Beatty AL, Deedwania PC, Inzucchi SE, et al. Circulation. 2020;141:e779–e806

The Evolution of SGLT2i in HF Management



Diabetes **Diabetes and No Diabetes**

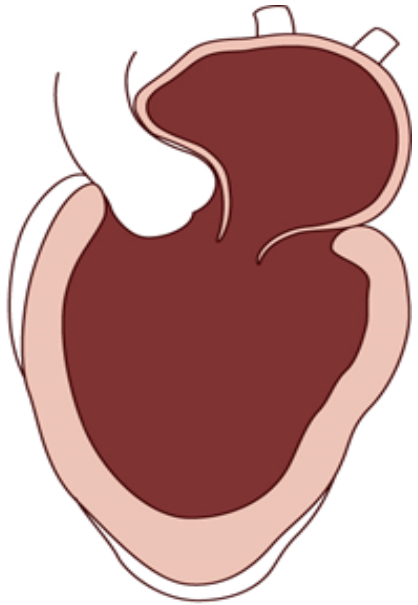
Window of opportunity for treatment

Pre-clinical (subclinical) stage of the disease | **Clinical stage of the disease** | **Detectable cardiac involvement**

0 years **10 years** **18-20 years**

- CANVAS Program
- CREDENCE
- DAPA-CKD
- DECLARE-TIMI 58
- EMPA-REG OUTCOME
- VERTIS CV
- SCORED

- DAPA-HF
- *DELIVER HFpEF*
- EMPEROR-Preserved
- EMPEROR-Reduced
- SOLOIST-WHF



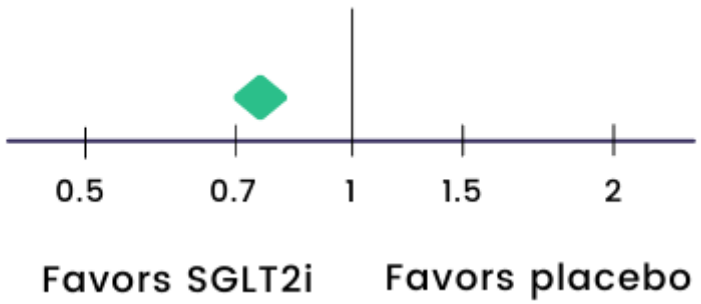
Normal Ventricular Function

Advanced Heart Failure

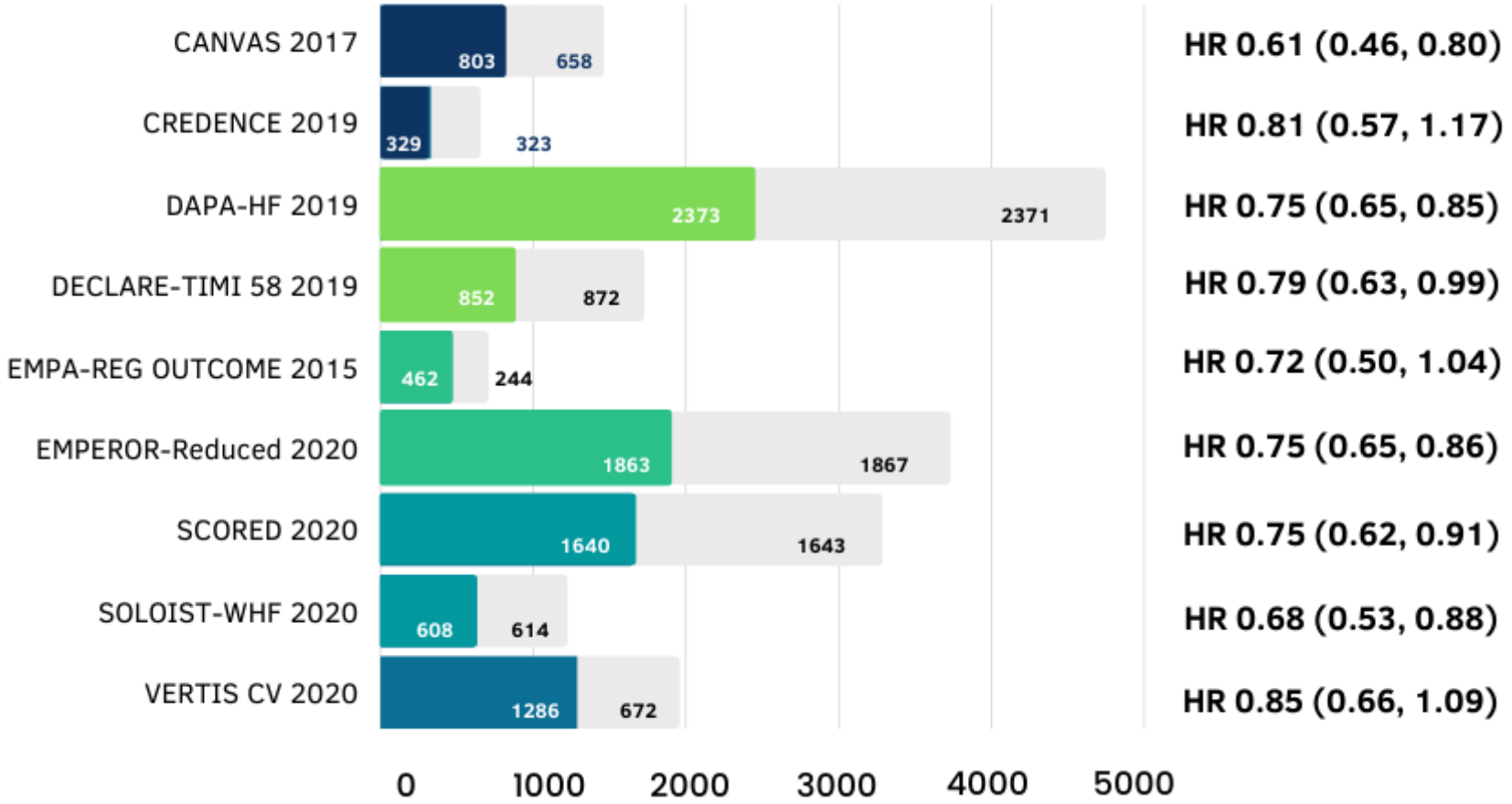
Adapted from Bhatt DL, Verma S, Braunwald E. Cell Metabolism. 2019;30:847-849.

Effect of SGLT2is on CV Death and HF Hospitalizations in Patients with HF

Cardiovascular mortality or hospitalizations for HF



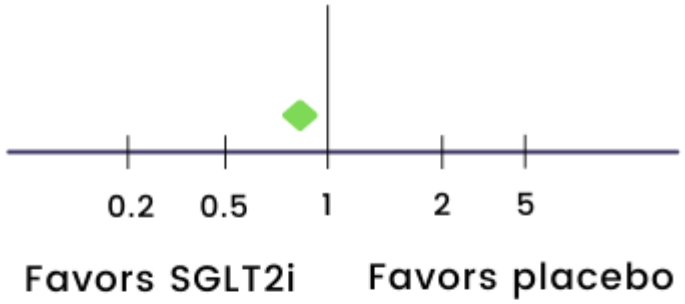
HR 0.75; 95% CI 0.70-0.80



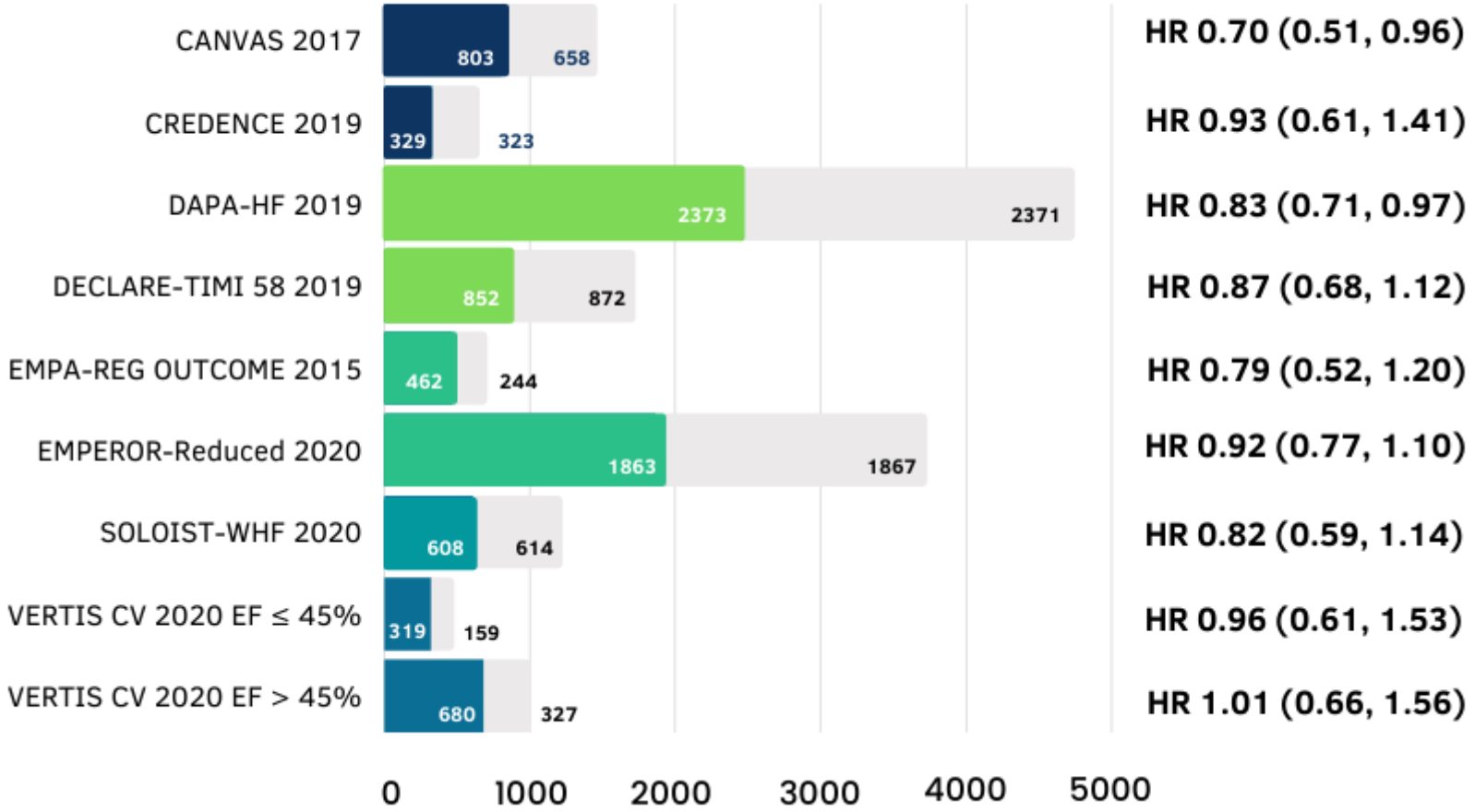
Cardoso R, Graffunder FP, Ternes CMP, Fernandes A, Rocha AV, Fernandes G, Bhatt DL. EClinicalMedicine. 2021;36:100933.

Effect of SGLT2is on All-Cause Mortality in Patients with HF

All-cause mortality



HR 0.86; 95% CI 0.79-0.94

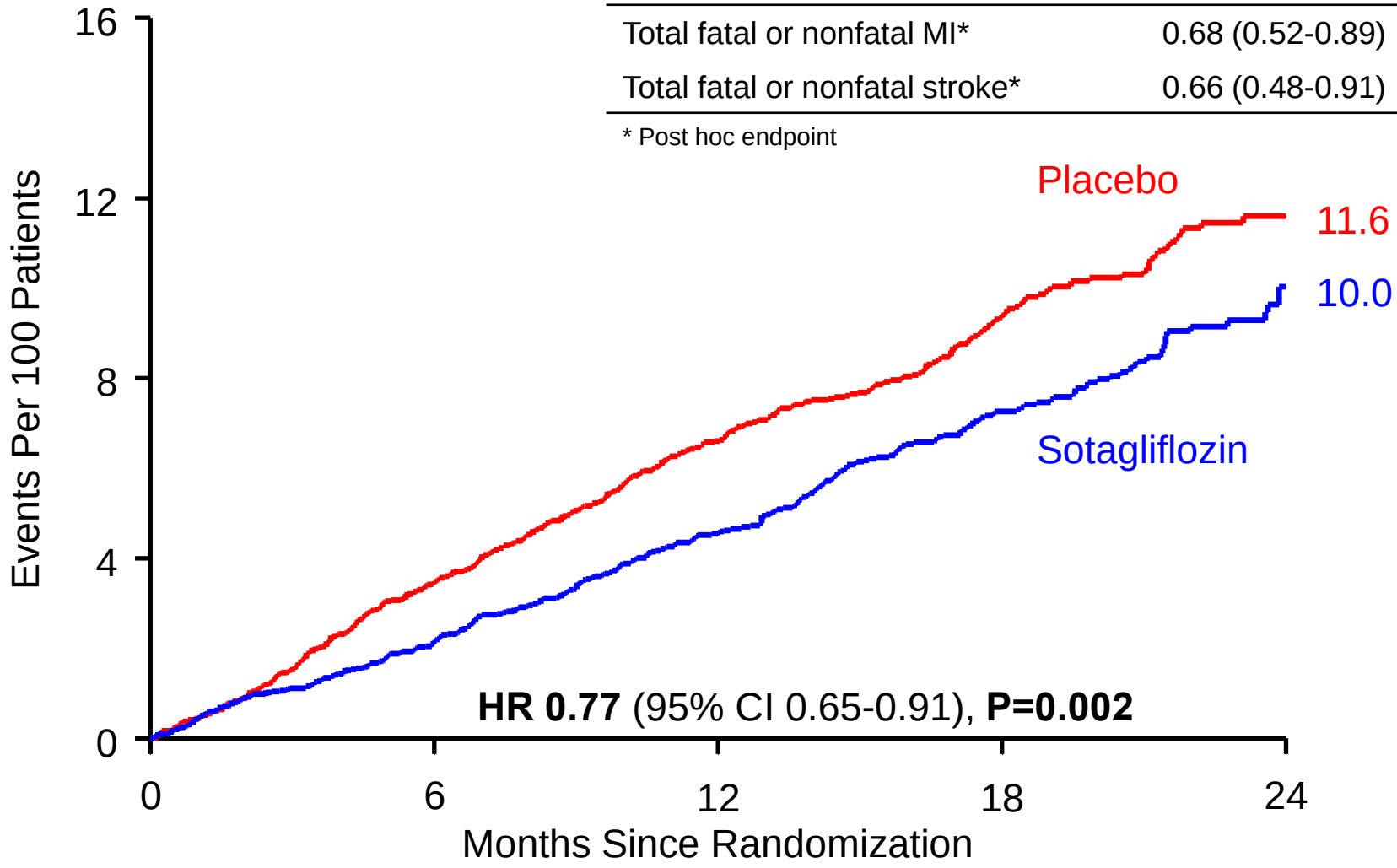


Cardoso R, Graffunder FP, Ternes CMP, Fernandes A, Rocha AV, Fernandes G, Bhatt DL. EClinicalMedicine. 2021;36:100933.

Total CV Death, Non-Fatal MI, or Non-Fatal Stroke

Endpoint	HR (95% CI)	P-value
Total fatal or nonfatal MI*	0.68 (0.52-0.89)	0.004
Total fatal or nonfatal stroke*	0.66 (0.48-0.91)	0.012

* Post hoc endpoint

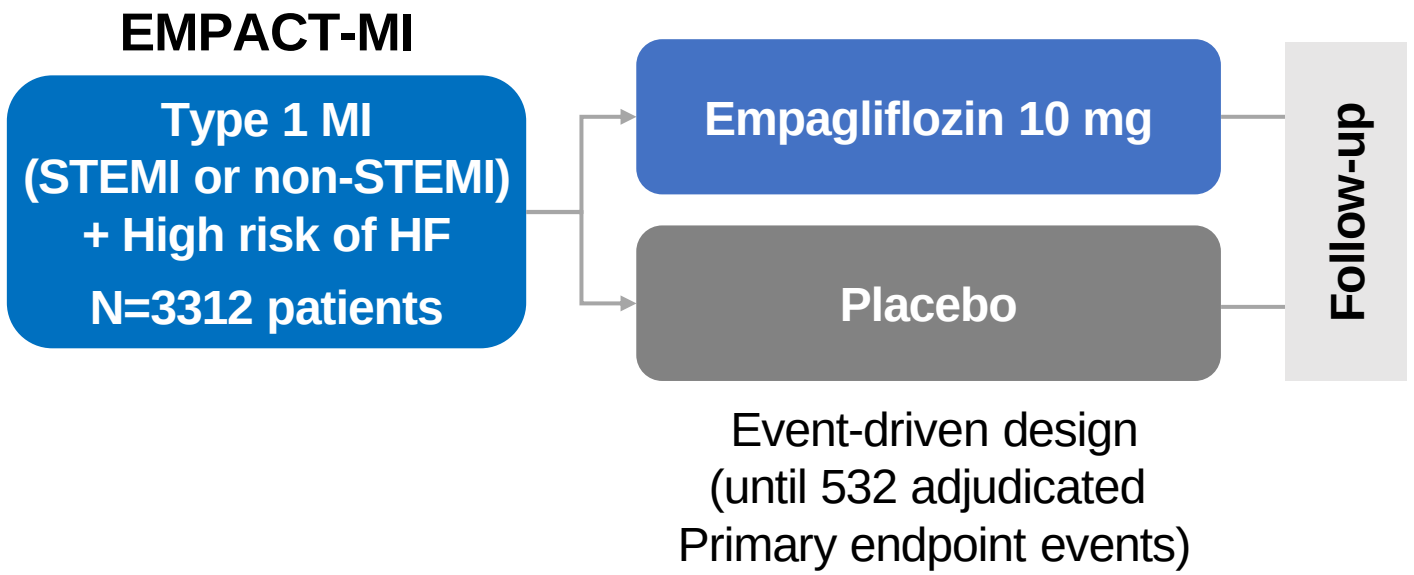


Bhatt DL, Szarek M, Pitt B, Cannon CP, Leiter LA, McGuire DK, Lewis JB, et al. N Engl J Med. 2021; 384:129-139. Bhatt DL. AHA 2020, virtual.

EMPACT MI: Evaluate the Effect of Empagliflozin on HHF and Mortality in Patients With MI

Aim: Assess the safety and efficacy of empagliflozin for prevention of HHF and all-cause mortality

Population: Patients hospitalized for acute myocardial infarction, with high risk of HF and mortality



PRIMARY ENDPOINT

- **Composite of time to first heart failure hospitalization or all-cause mortality**

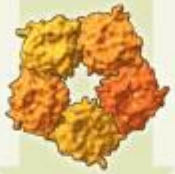
SELECT SECONDARY ENDPOINTS

- **HHF or death**
- **All-cause hospitalizations or death**
- **CV hospitalizations or death**
- **MI hospitalization or death**

STEMI, ST-elevation myocardial infarction

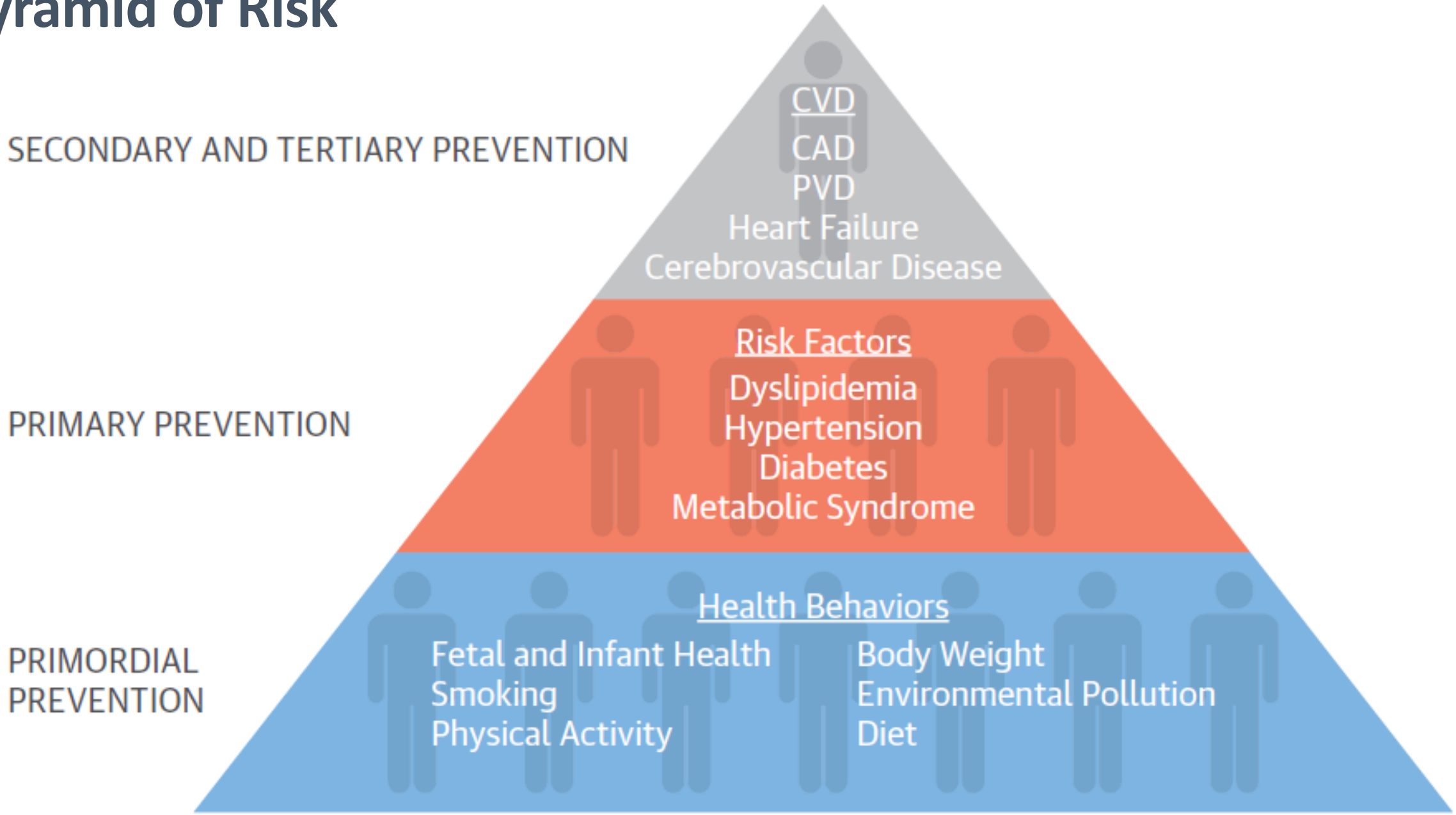
ClinicalTrials.gov NCT04509674, accessed April 12, 2021.

Redefining Residual Risk in the Current Era

Biological Issue	Residual Cholesterol Risk	Residual Inflammatory Risk	Residual Thrombotic Risk	Residual Triglyceride Risk	Residual Lp(a) Risk	Residual Diabetes Risk
						
Critical Biomarker	LDL-C ≥100 mg/dL	hsCRP ≥2mg/L	No simple biomarker	TG ≥150mg/dL	Lp(a) ≥50mg/dL	HbA1c Fasting glucose
Potential Intervention	Targeted LDL/Apo B Reduction	Targeted Inflammation Reduction	Targeted Antithrombotic Reduction	Targeted Triglyceride Reduction	Targeted Lp(a) Reduction	SGLT2 Inhibitors GLP-1 Agonists
Randomized Trial Evidence	IMPROVE-IT FOURIER SPIRE ODYSSEY	CANTOS COLCOT *LoDoCo2* *OASIS-9*	PEGASUS COMPASS THEMIS	REDUCE-IT *PROMINENT*	Planned	EMPA-REG CANVAS DECLARE CREDENCE LEADER SUSTAIN-6 REWIND

Lawler PR, Libby P, Bhatt DL, Godoy LC, Luscher TF, Bonow RO, Verma S, Ridker PM. Eur Heart J. 2021;42:113-131.

Pyramid of Risk



Hong KN, Fuster V, Rosenson RS, Rosendorff C, Bhatt DL. J Am Coll Cardiol. 2017;70:2171-2185.

BRIGHAM AND WOMEN'S HOSPITAL

Heart & Vascular Center

Thank You!

Deepak L. Bhatt, MD, MPH
Executive Director,
Interventional Cardiovascular Programs,
BWH Heart & Vascular Center;
Professor of Medicine,
Harvard Medical School
Email: DLBhattMD@post.Harvard.edu
Twitter: @DLBhattMD

HARVARD MEDICAL SCHOOL
TEACHING HOSPITAL