



Brigham and Women's Hospital
Founding Member, Mass General Brigham

Management of Ischemic Heart Disease and Lipids

Benjamin M. Scirica, MD MPH
Senior Investigator, TIMI Study Group
Cardiovascular Division, Brigham and Women's Hospital
Associate Professor of Medicine, Harvard Medical School



Benjamin Scirica, MD MPH



- Harvard Medical School
- Residency and Fellowship @ Brigham and Women's Hospital
- MPH @ Harvard School of Public Health
- Associate Professor of Medicine @ Harvard Medical School
 - Clinical focus: Critical Care Cardiology
 - Research focus: Diabetes, Obesity, Care-redesign



Disclosures

Dr. Scirica reports institutional research grants to Brigham and Women's Hospital from Amgen, AstraZeneca, Better Therapeutics, Boehringer Ingelheim, Merck, and NovoNordisk. Consulting fees from AbbVie, Allergan, Amgen AstraZeneca, Bayer, Boehringer Ingelheim, Elsevier Practice Update Cardiology, Hamni, Lexeo, NovoNordisk, and equity in Health [at] Scale.

Key Learning Objectives

- Understand what Stable Ischemic Heart Disease means and its clinical implications
- Review the latest data on lipid-lowering therapies
- Identify key questions regarding coronary revascularization.

What is Ischemic Heart Disease

by any other name...

- Chronic stable angina
- **Chronic coronary syndrome**
- Stable angina pectoris
- Coronary heart disease
- Stable ischemic heart disease
- Stable coronary artery disease
- Non-acute coronary syndrome

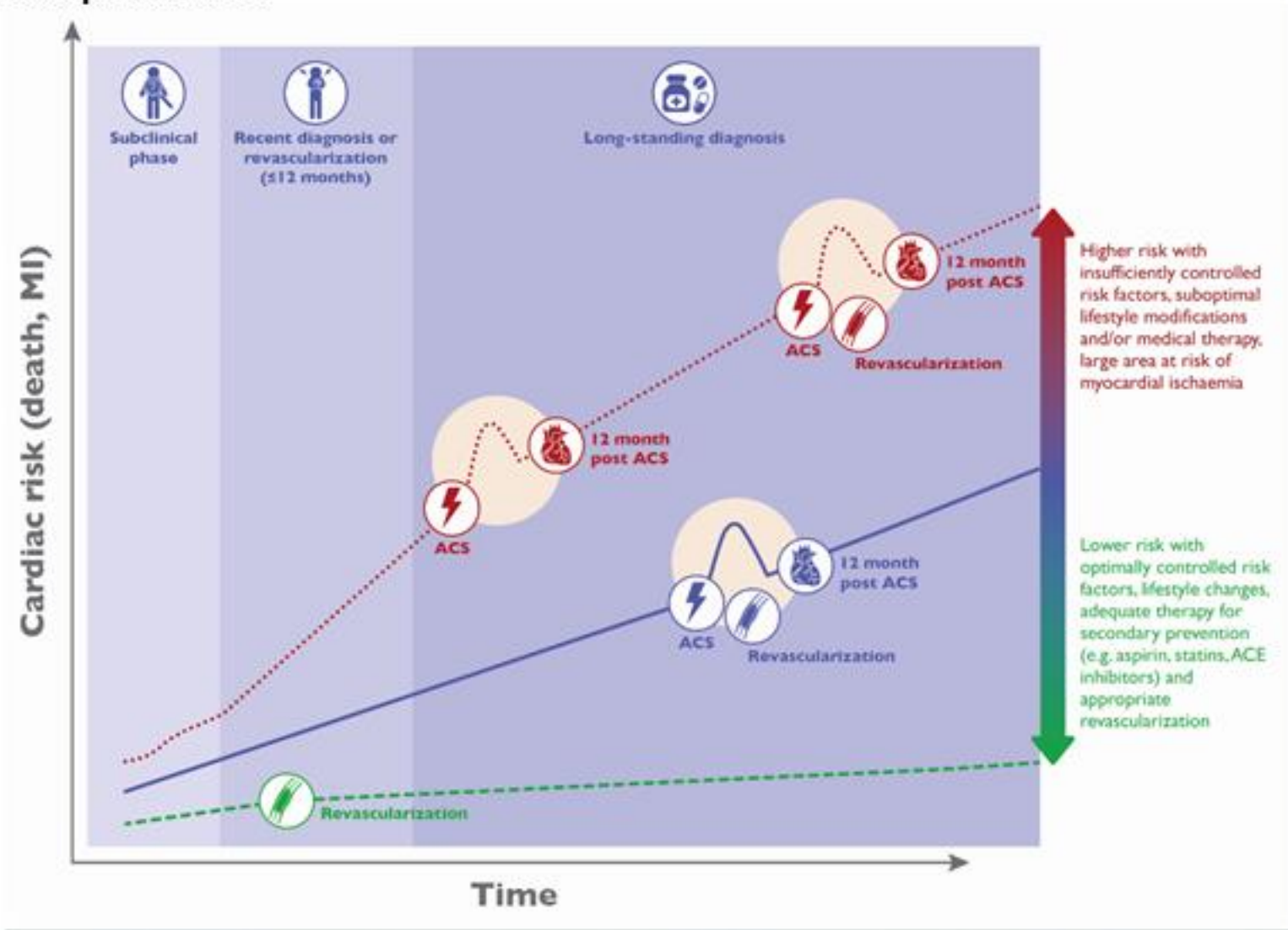
“... angina secondary to stable ischemic heart disease (SIHD) is the most common clinical presentation of cardiovascular disease encountered by general practitioners and cardiologists.”

AHA 2023 CHD Statistics

Population group	Prevalence, CHD, 2017–2020, ≥20 y of age
Both sexes	20 500 000 (7.1%) [95% CI, 6.1%–8.3%]
Males	11 700 000 (8.7%)
Females	8 800 000 (5.8%)
NH White males	9.4%
NH White females	5.9%
NH Black males	6.2%
NH Black females	6.3%
Hispanic males	6.8%
Hispanic females	6.1%
NH Asian males	5.2%
NH Asian females	3.9%
NH American Indian or Alaska Native	...

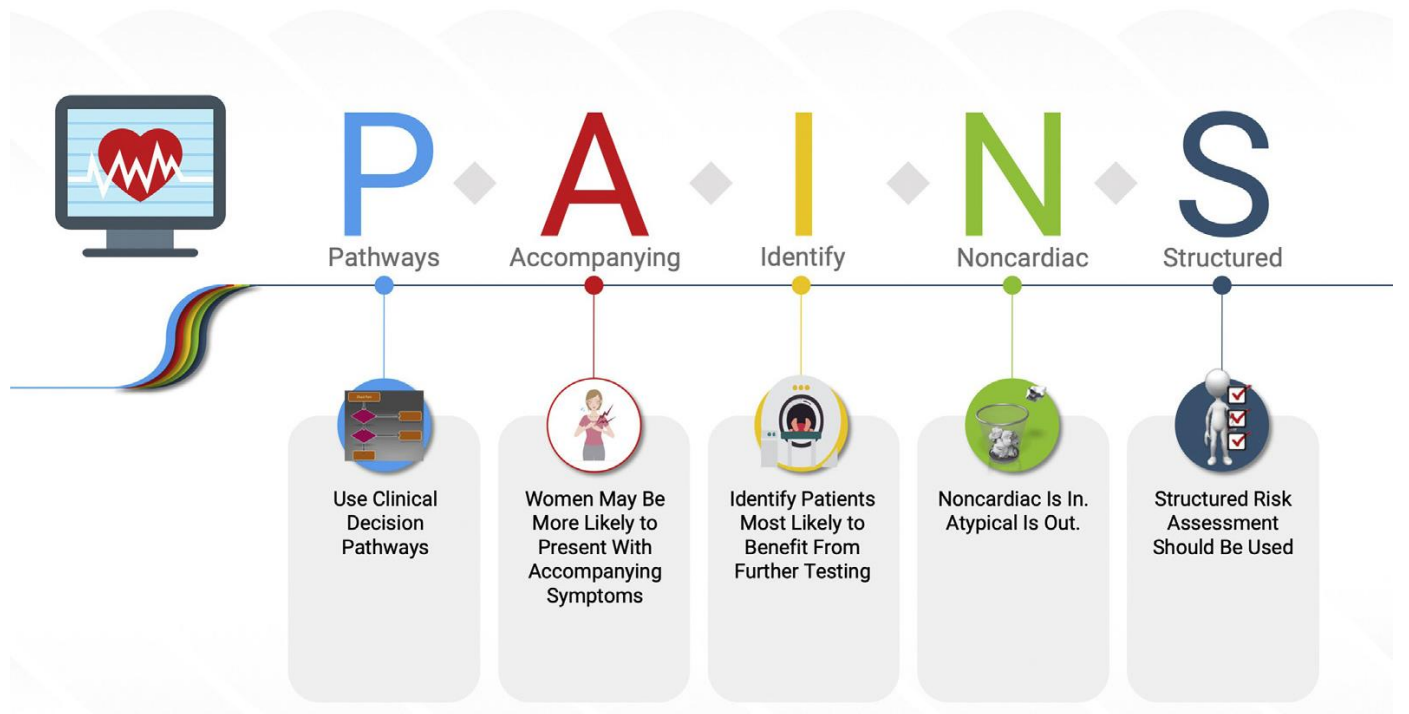
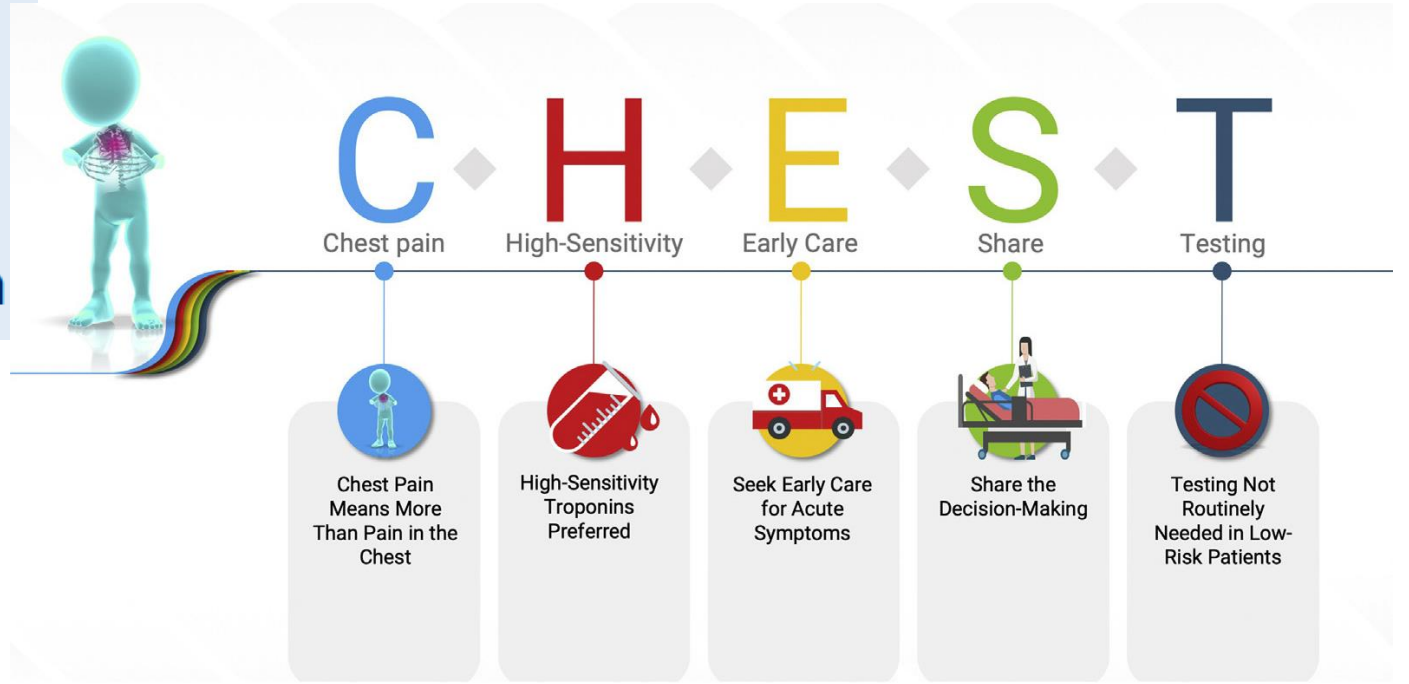
Natural history of chronic coronary syndromes

A dynamic process

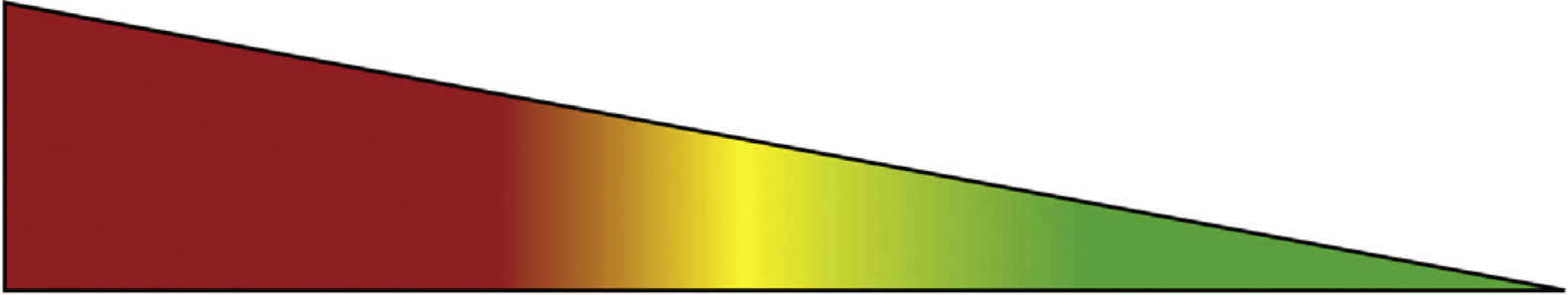


2021 AHA/ACC/ASE/CHEST/SAEM/SCCT/SCMR Guideline for the Evaluation and Diagnosis of Chest Pain

AIM: This clinical practice guideline for the evaluation and diagnosis of chest pain provides recommendations and algorithms for clinicians **to assess and diagnose chest pain in adult patients.**



Index of Suspicion Based on Descriptors



- Central
- Pressure
- Squeezing
- Gripping
- Heaviness
- Tightness
- Exertional/stress-related
- Retrosternal
- Left-sided
- Dull
- Aching
- Stabbing
- Right-sided
- Tearing
- Ripping
- Burning
- Sharp
- Fleeting
- Shifting
- Pleuritic
- Positional

Nomenclature Update

“Noncardiac Is In. Atypical Is Out.”

Noncardiac” should be used if heart disease is not suspected.

“Atypical” is a misleading descriptor of chest pain, and its use is discouraged.



Pre-Test Probability

Light Green – no testing

Green/Orange – testing indicated

Pretest Probabilities of Obstructive CAD in Symptomatic Patients

(A) according to age, sex, and symptoms;

(B) according to age, sex, symptoms, and CAC

Age, y	Chest Pain		Dyspnea	
	Men	Women	Men	Women
30–39	≤4	≤5	0	3
40–49	≤22	≤10	12	3
50–59	≤32	≤13	20	9
60–69	≤44	≤16	27	14
70+	≤52	≤27	32	12

A Pretest probability based on age, sex, and symptoms



B Pretest probability based on age, sex, symptoms, and CAC score⁺



CAC
1–99

CAC
≥100–999

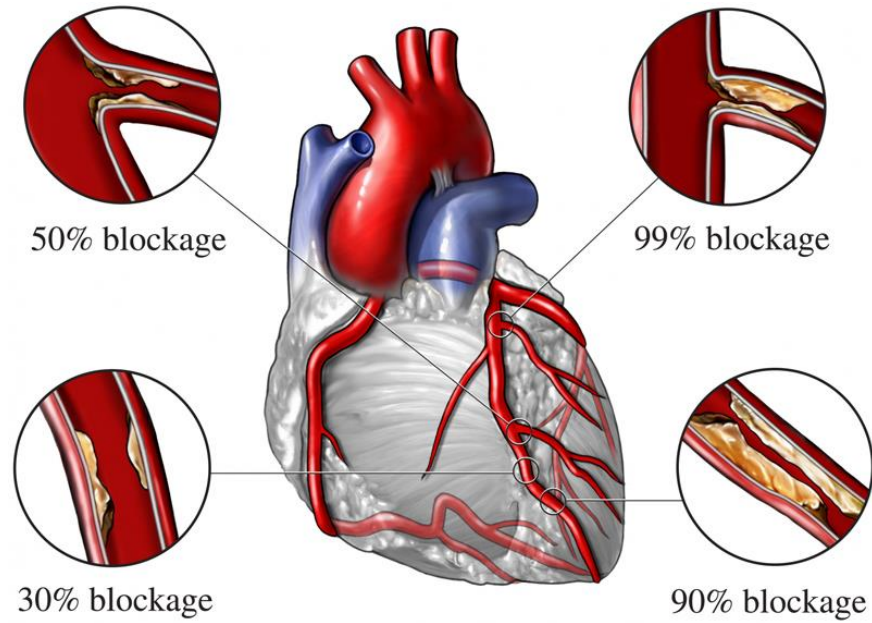
CAC
≥1,000

When to Order What Test

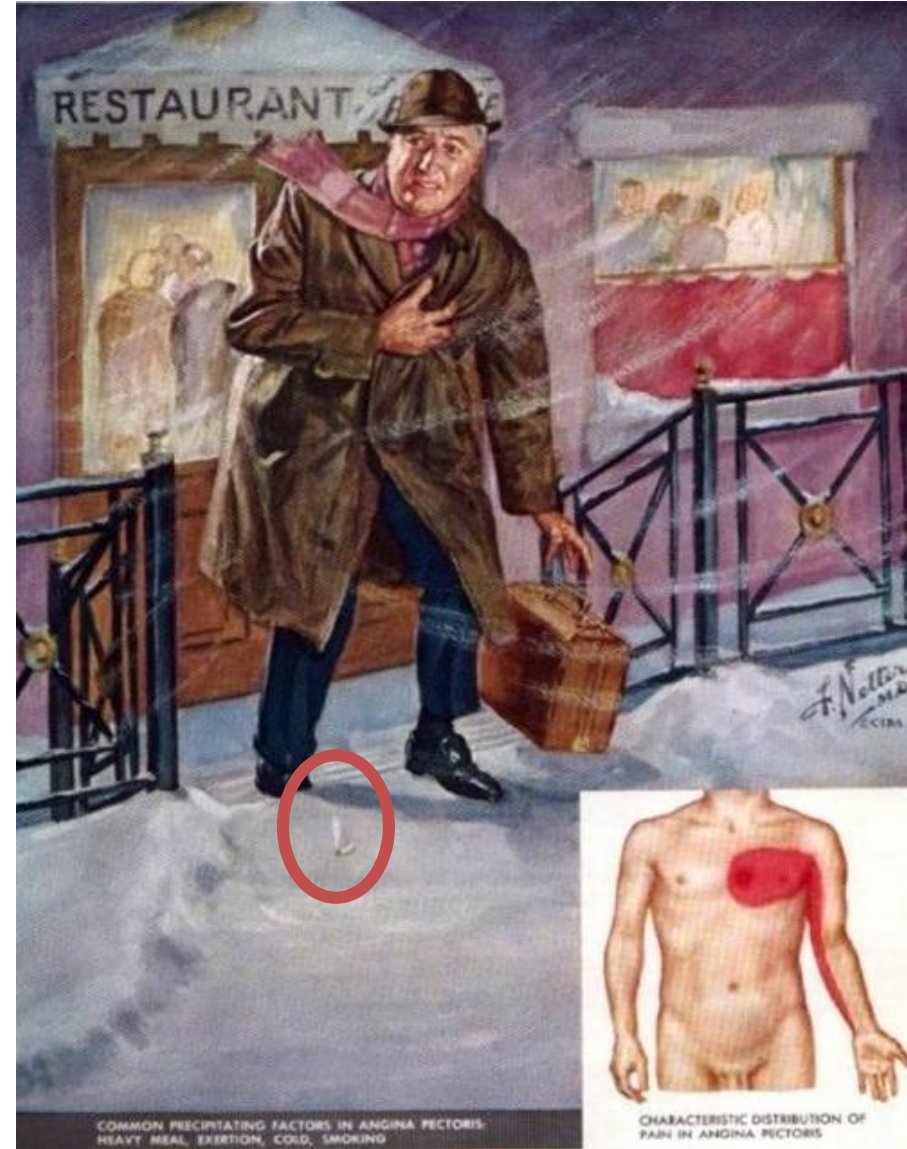
Pretest likelihood of CAD	Low	→	No testing necessary	→	Option for CAC for ASCVD risk stratification
	Intermediate-high	→	Younger patient (<65 y of age)	OR	Less obstructive CAD suspected → CCTA favored
	Intermediate-high	→	Older patient (≥65 y of age)	OR	More obstructive CAD suspected → Stress testing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

Stable Ischemic Heart Disease (Old School)

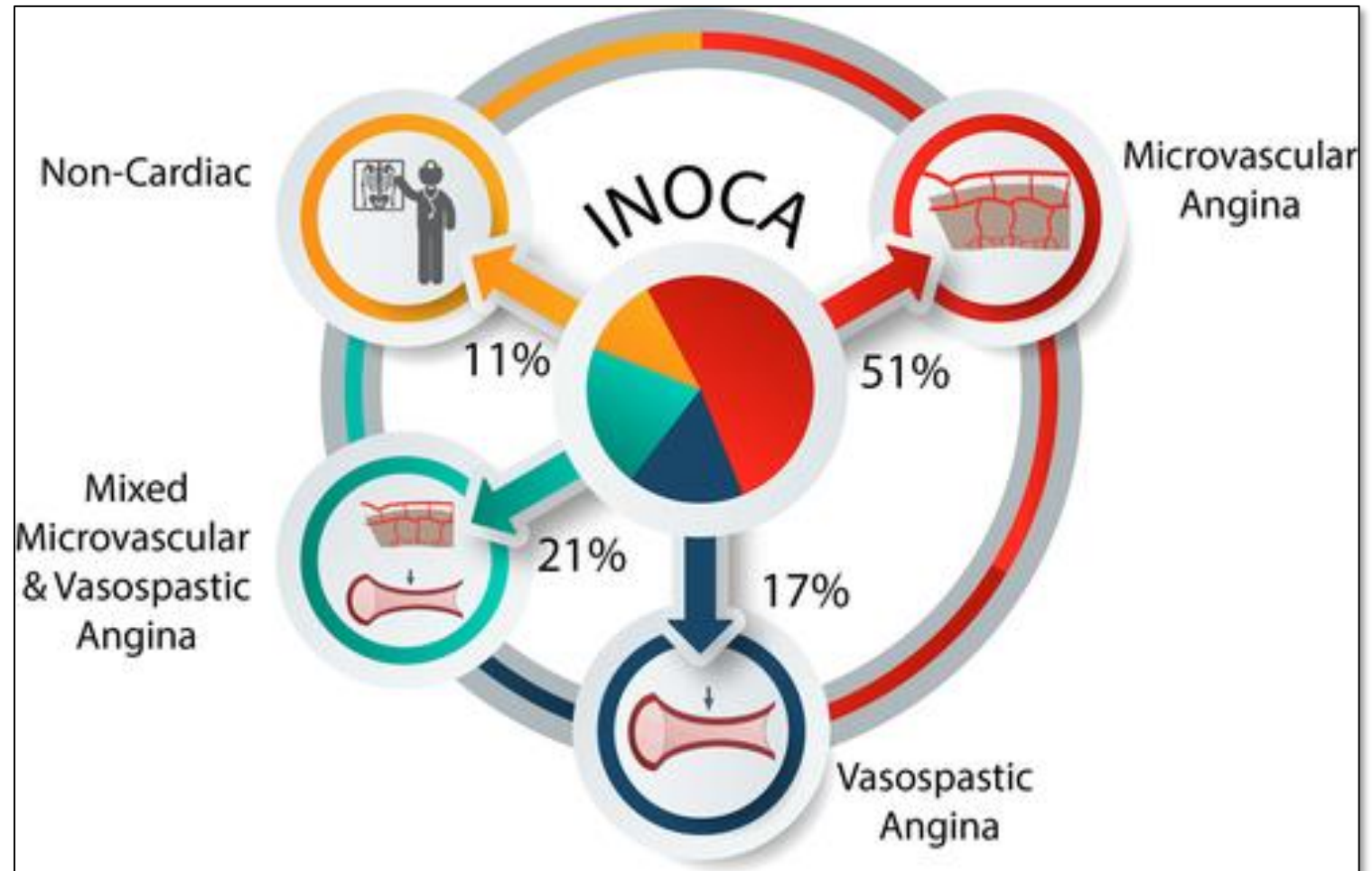
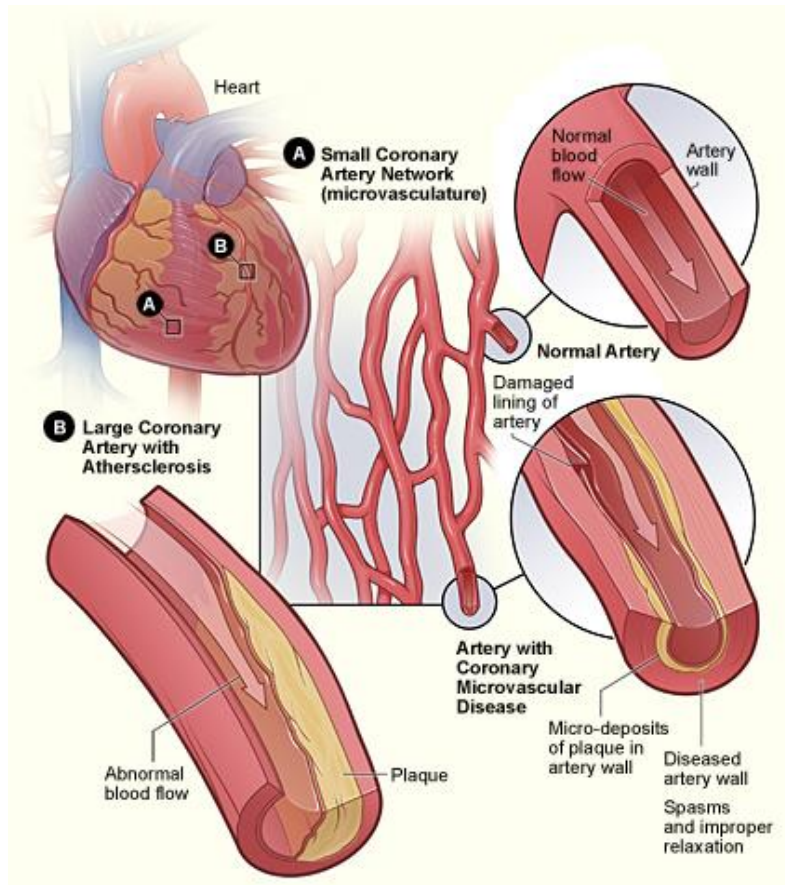


But it's just not that simple



INOCA – A new name for old entity

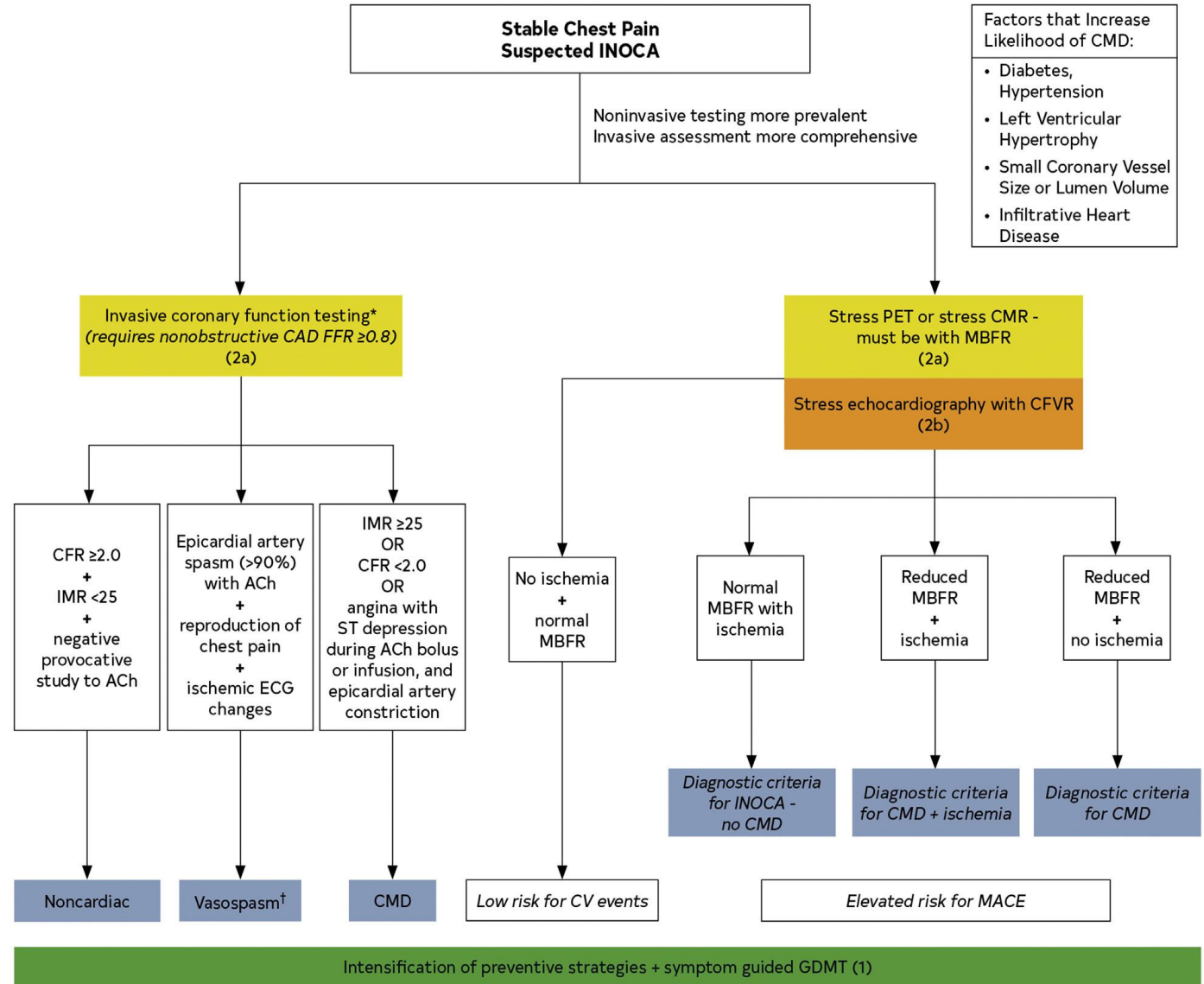
Ischemia with No Obstructive Coronary Artery Disease



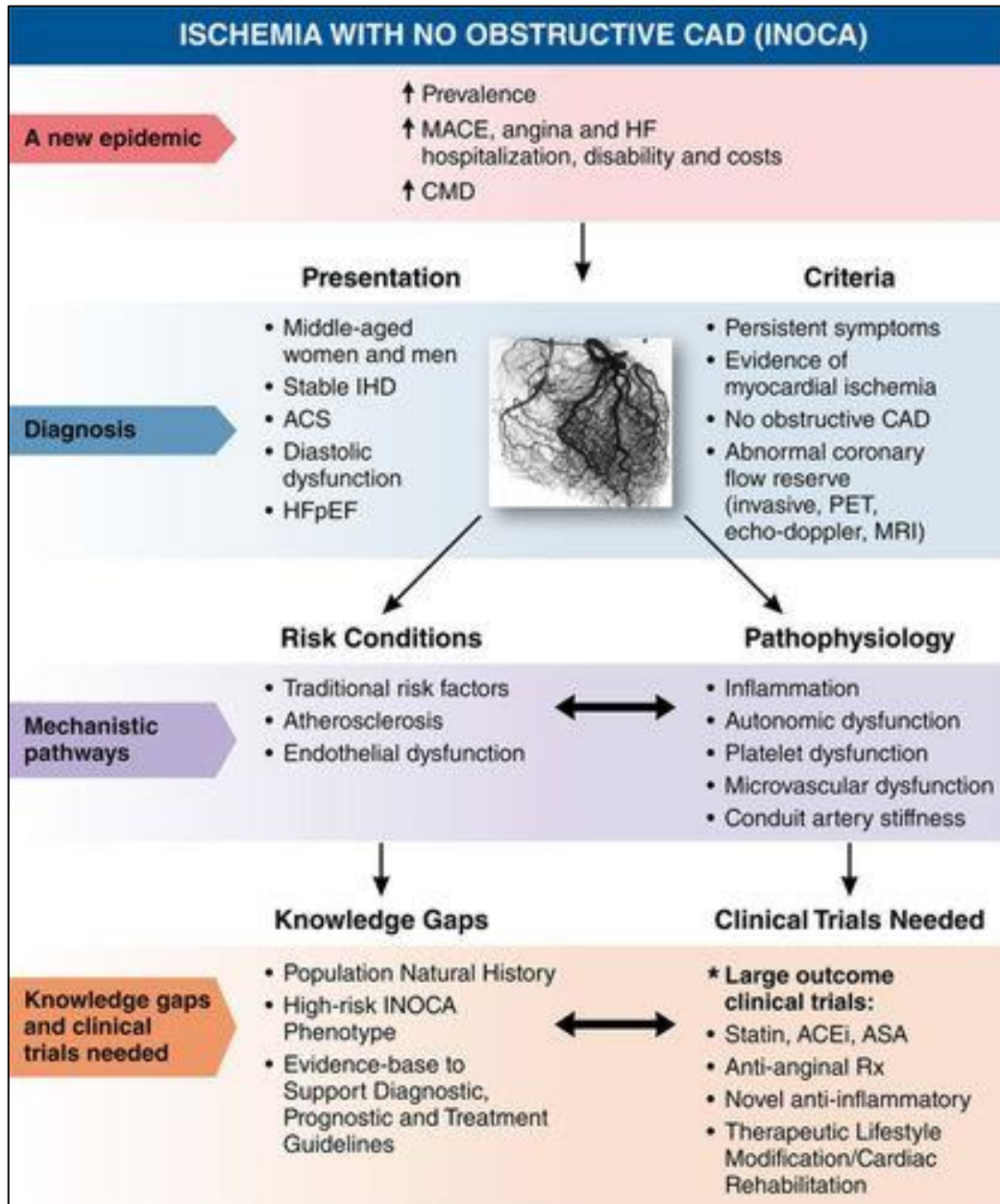
Diagnostic Pathway for Suspected INOCA

In patients with symptoms, don't just stop with a "normal" stress test

Other imaging like **Stress MRI, PET, or Echo**, and even **coronary angiography** can often provide incremental diagnostic information



INOCA – Management



Potential Therapies for CMD	
Pharmacologic	Non-Pharmacologic
<ul style="list-style-type: none"> • Nitrates • Statins • ACE-I • ACE-I + Aldosterone blockade • Calcium antagonists • Low-dose tricyclic antidepressants • Estrogens • PDE-5 inhibitors • Exercise • L-arginine • Ranolazine • Ivabradine • Ranolazine + Ivabradine • Metformin • Rho-kinase inhibitors • Endothelin receptor blockers 	<ul style="list-style-type: none"> • Exercise • Cognitive behavioral therapy • Transcendental meditation • Transcutaneous electrical nerve stimulation

Dual Goals for Management of Stable Ischemic Heart Disease (SIHD)

Prevent MI and Death (Disease Modification)



Improve “Quantity of Life”

Reduce Ischemia & Relieve Anginal Symptoms



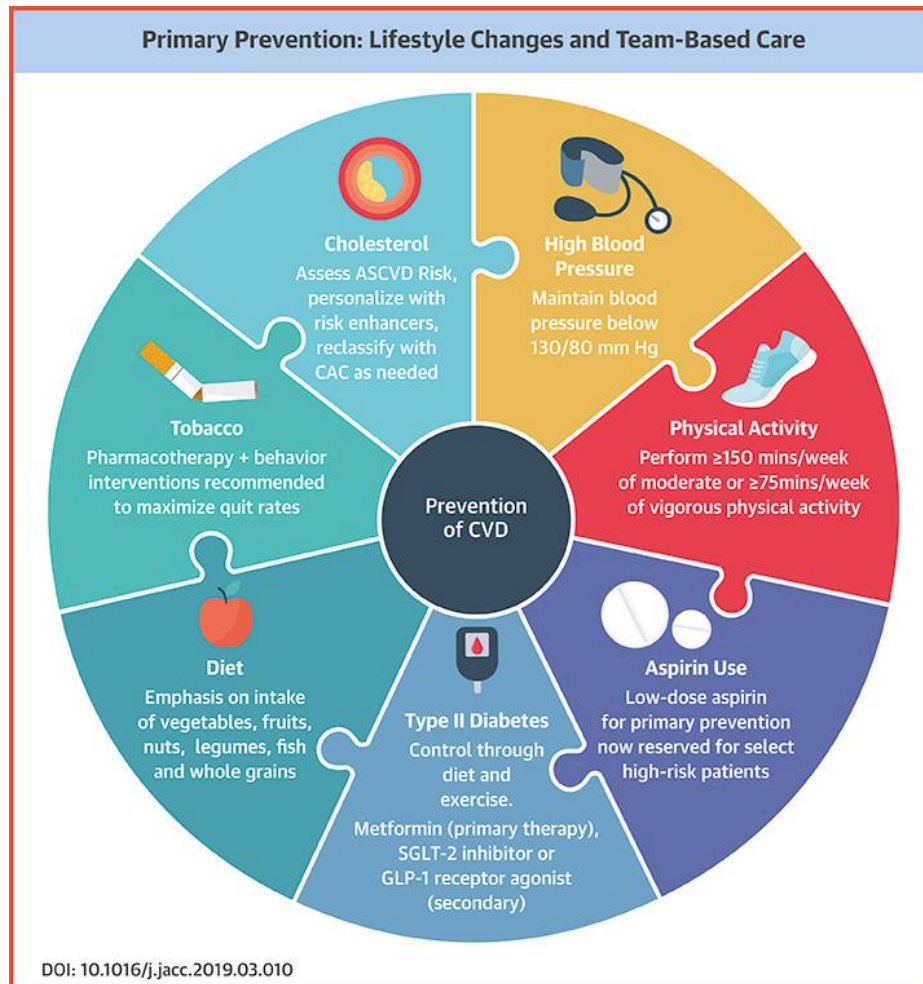
Improve “Quality of Life”

Prevention Goals of Therapy in SIHD

Reduce/stabilize atherosclerotic plaque → ACS/MI/SCD

Primary Prevention

Secondary Prevention



- Antiplatelet Therapy
 - ASA 81 mg; ADP antagonist if recent ACS or stent
- ACEI / ARB (especially if DM, HF, EF <40%, HTN)
- Aggressive Lipid Lowering
- Diabetes Rx with proven CV benefit (GLP1RA and SGLT2i)
- Smoking cessation
- Other Secondary Prevention Measures
 - BP control
 - Weight management *
 - Physical exercise
 - Influenza Vaccine

SECONDARY PREVENTION

ASCVD

High
ASCVD
risk

Initiate
low-dose
aspirin

**IMAGED VASCULAR
DISEASE***

High
ASCVD
risk

Strongly
consider
initiating
low-dose
aspirin

DIABETES

High
ASCVD
risk

Consider
initiating
low-dose
aspirin

Low
ASCVD
risk

Do not
initiate
low-dose
aspirin

**INCREASED
BLEED RISK**

High
ASCVD
risk

Consider
initiating
low-dose
aspirin
and adding a
proton-pump
inhibitor

Low
ASCVD
risk

Do not
initiate
low-dose
aspirin

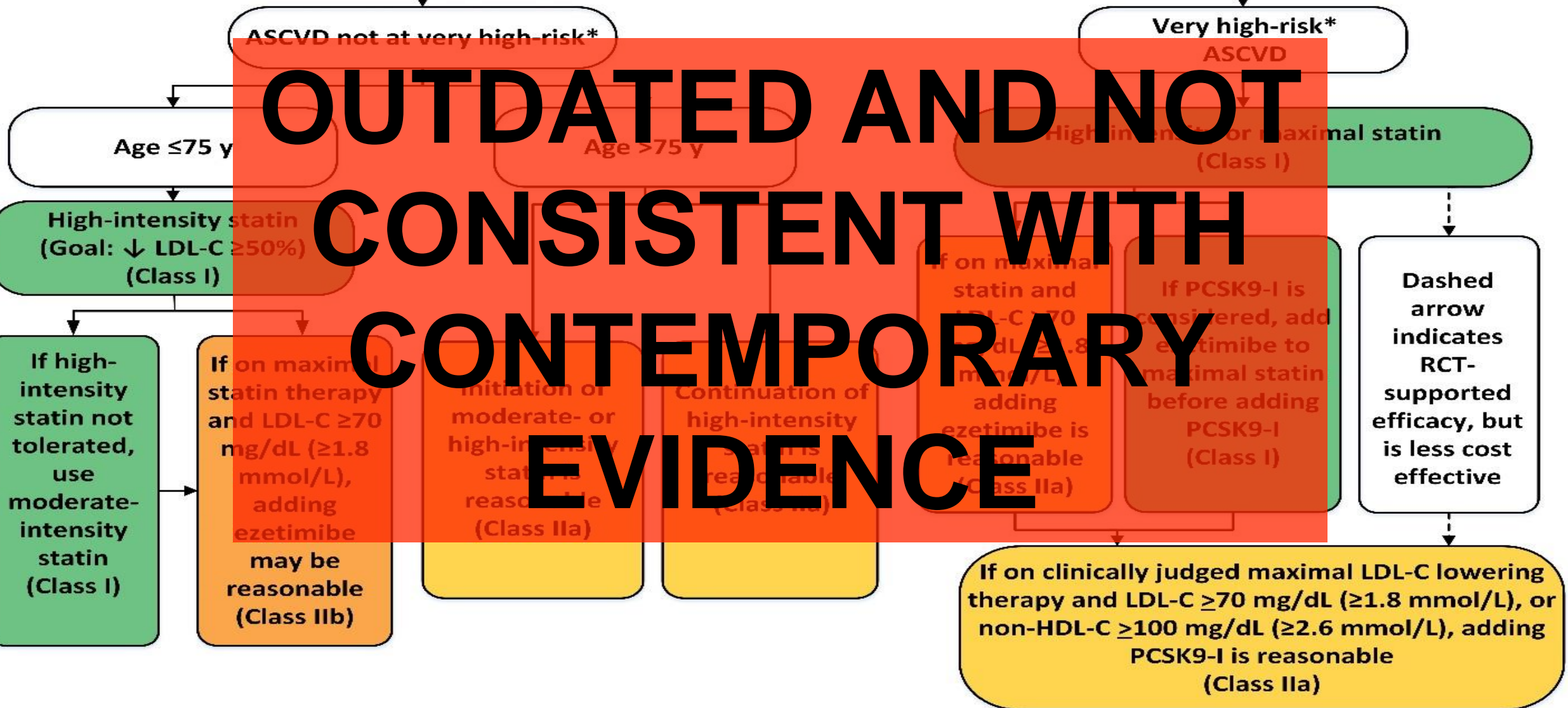
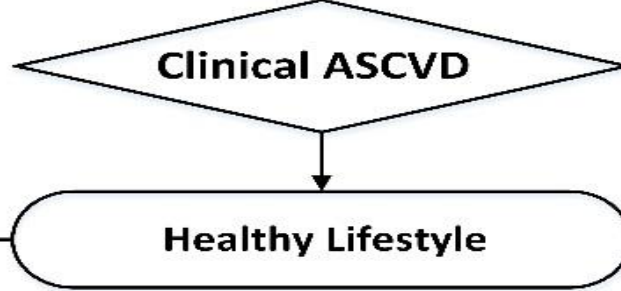
AGE > 70 years

Do not
initiate
low-dose
aspirin

PRIMARY PREVENTION

*Evidence of atherosclerosis on CT scan or vascular ultrasound tests, or an elevated coronary calcium score; ASCVD = atherosclerotic cardiovascular disease.

ACC/AHA Cholesterol Guidelines 2018
Secondary Prevention



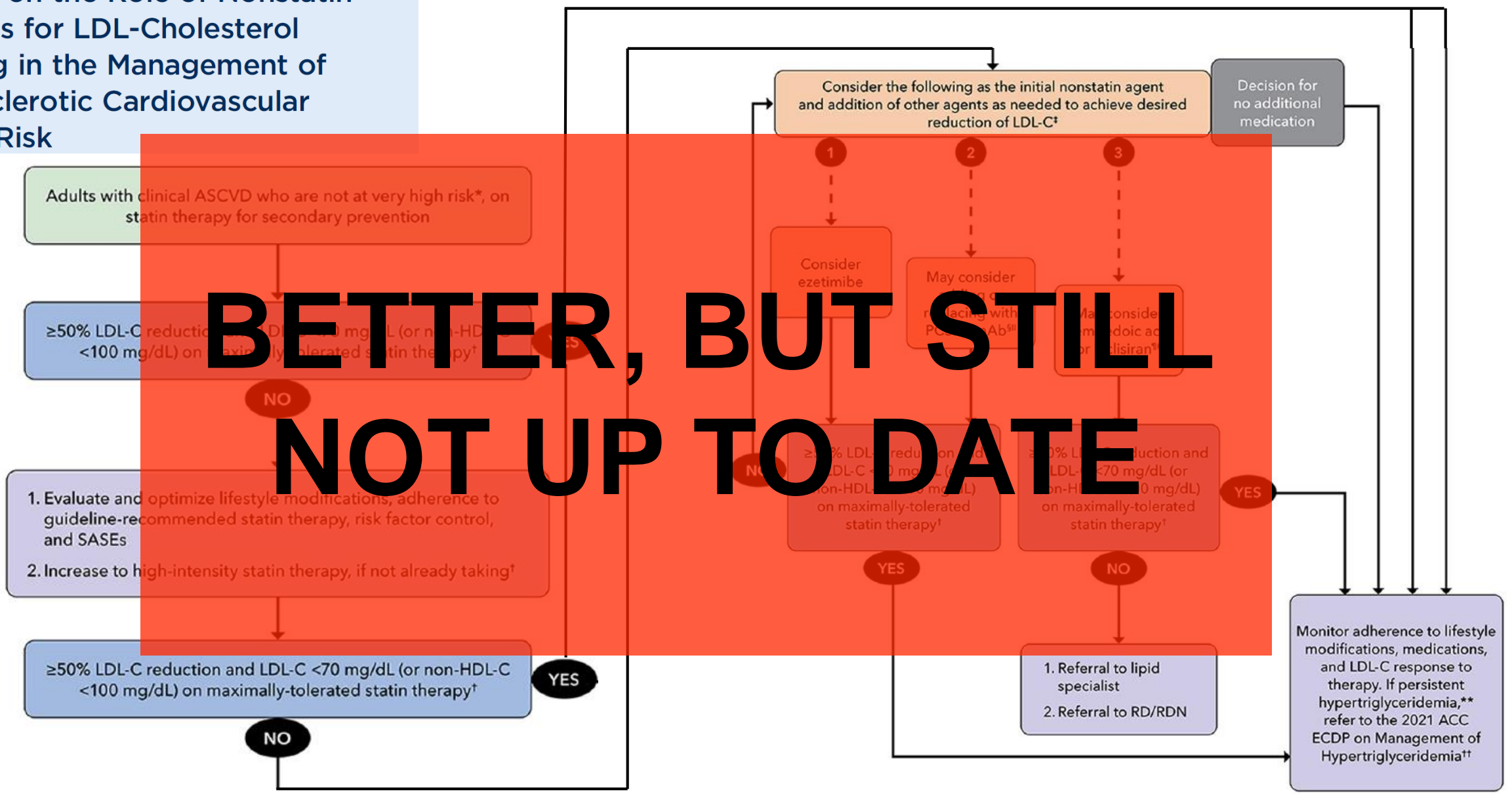
OUTDATED AND NOT CONSISTENT WITH CONTEMPORARY EVIDENCE

Dashed arrow indicates RCT-supported efficacy, but is less cost effective

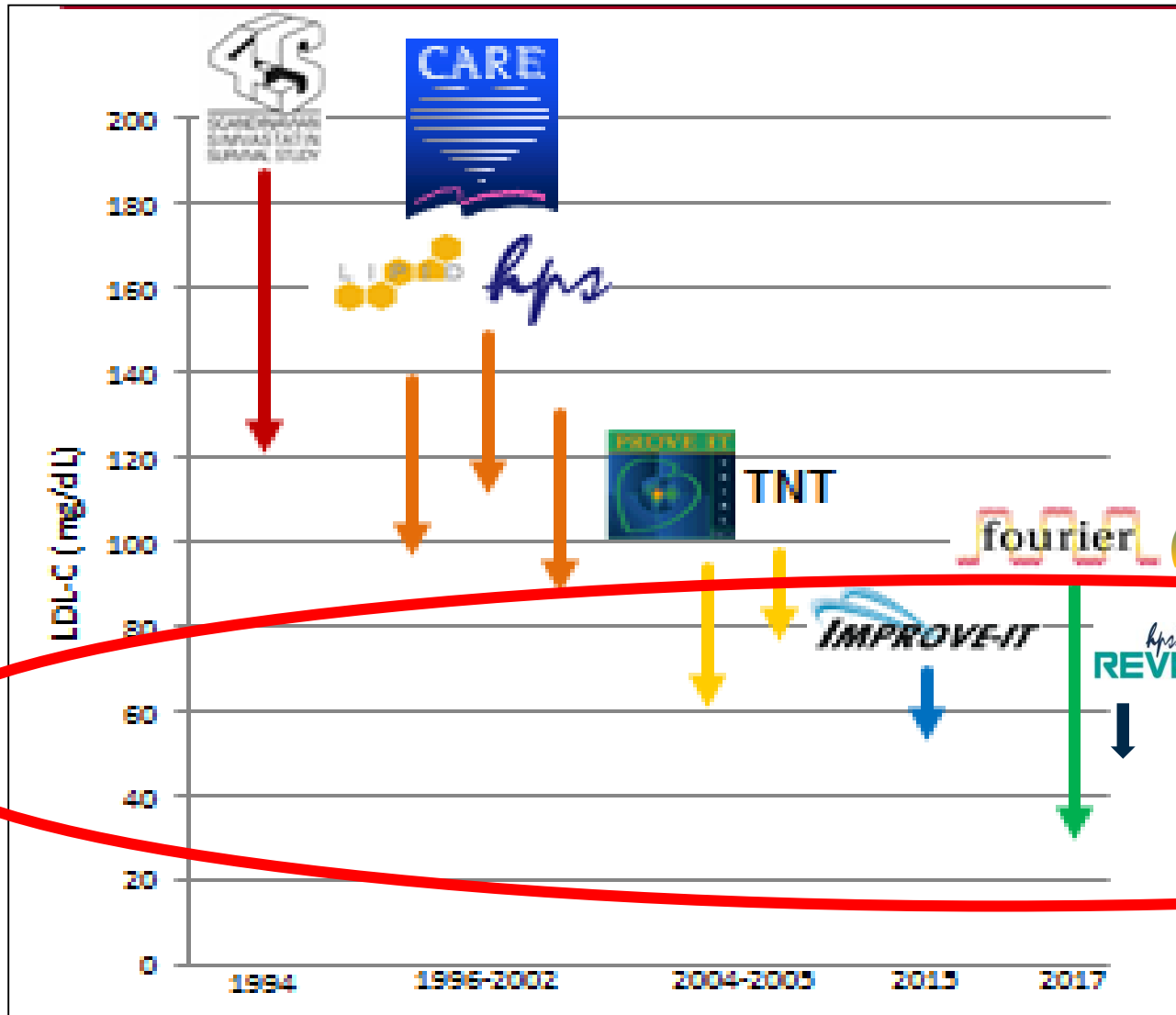
2022 ACC Expert Consensus Decision Pathway on the Role of Nonstatin Therapies for LDL-Cholesterol Lowering in the Management of Atherosclerotic Cardiovascular Disease Risk

ASCVD "Not very high risk" – Goal LDL <70 mg/dl

BETTER, BUT STILL NOT UP TO DATE



LDL-C Levels for Optimal CV Risk Reduction: What We Know Now



High is bad

Average is not good

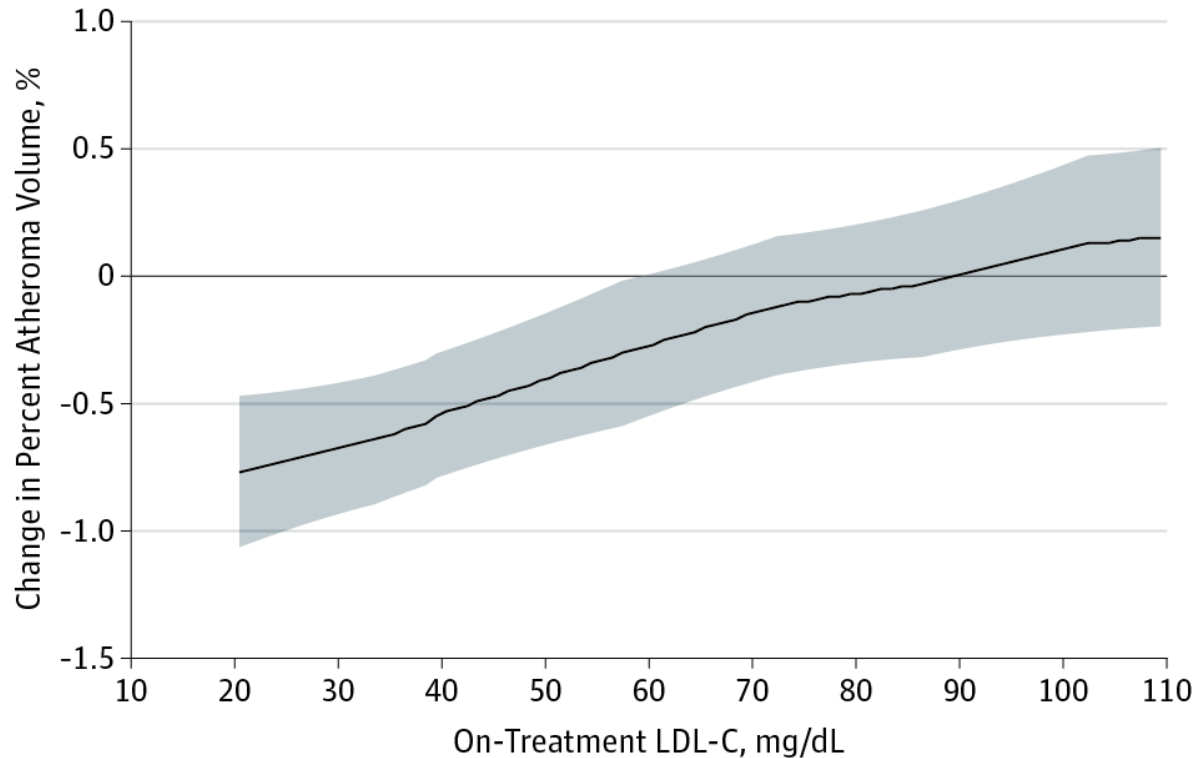
Lower is better

Even lower is even better

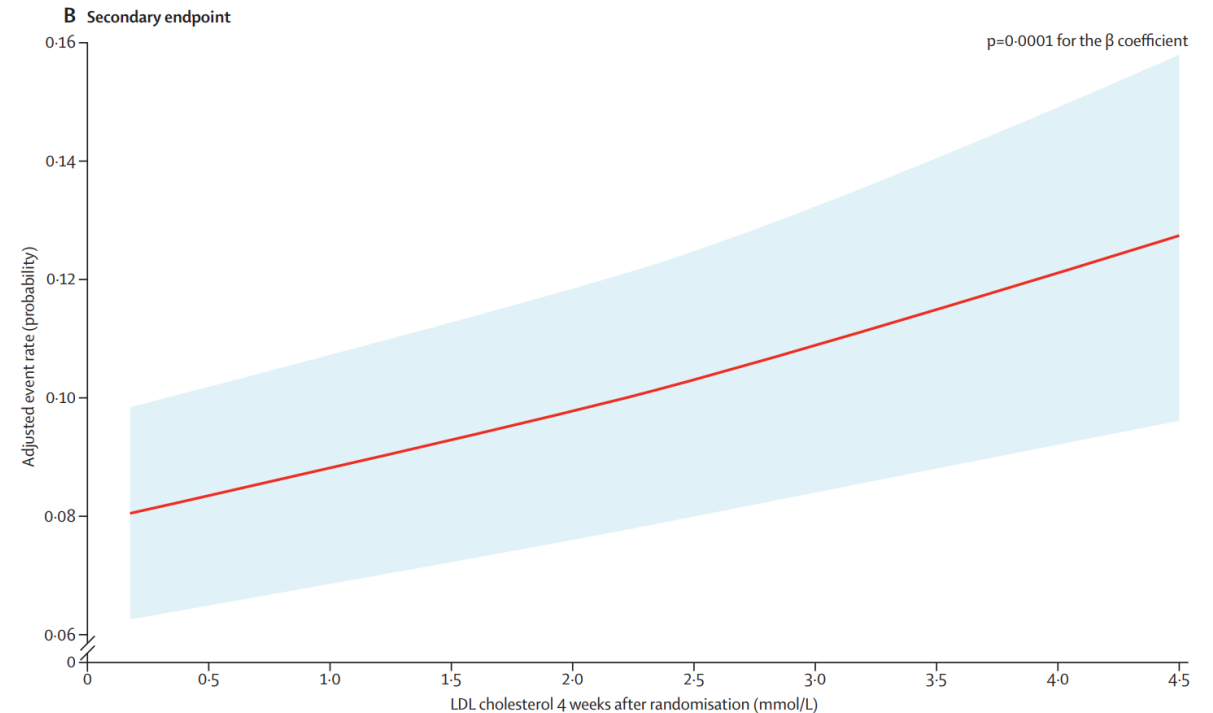
Lowest is best

Achieving Lower LDL-C Modifies Cholesterol Plaques and Clinical Outcomes

Relationship between LDL-C and Percent Atheroma Volume¹



Relationship between LDL-C and Outcomes (CVD, MI, Stroke)²



1. *JAMA* 2016;316(22):2373-2384
2. *Lancet* 2017;390: 1962-71





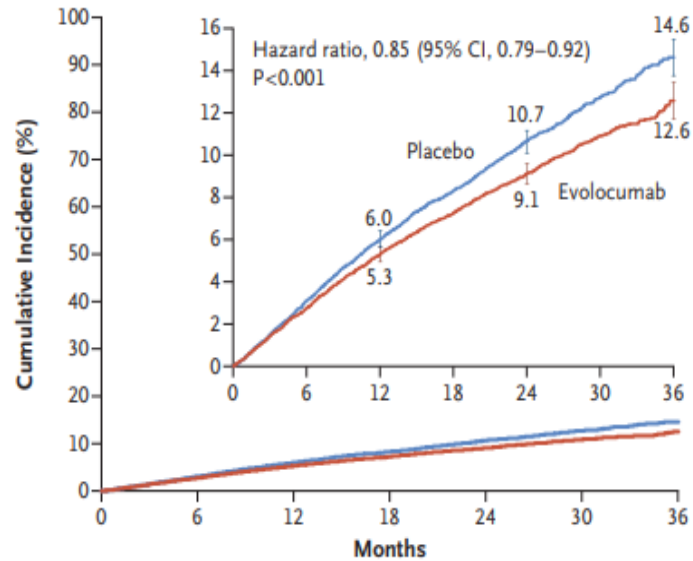
Completed

1 FOURIER¹

Evolocumab (REPATHA®) mAb

Primary Endpoint:

Time to CV death, MI, ischemic stroke, UA hosp, or coronary revascularization



No. at Risk	0	6	12	18	24	30	36
Placebo	13,780	13,278	12,825	11,871	7610	3690	686
Evolocumab	13,784	13,351	12,939	12,070	7771	3746	689

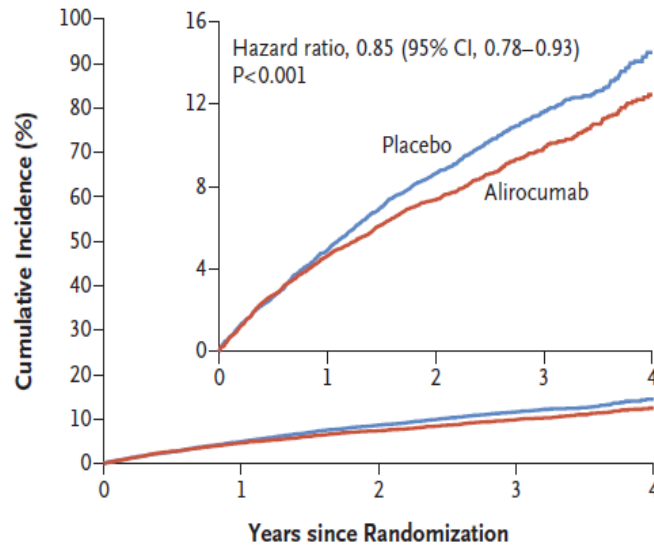
Completed

2 ODYSSEY²

Alirocumab (PRALUENT®) mA

Primary Endpoint:

Time to CHD death, MI, ischemic stroke, or UA hosp



No. at Risk	0	1	2	3	4
Placebo	9462	8805	8201	3471	629
Alirocumab	9462	8846	8345	3574	653

Ongoing

3 VICTORION-2P

Inclisiran (LEQVIO®) siRNA

Primary Endpoint:

Time to CV death, MI, ischemic stroke

Adults with ASCVD

N = 15,000

4 ORION-4

Inclisiran (LEQVIO®) siRNA

Primary Endpoint:

Time to CHD, MI, stroke, UR

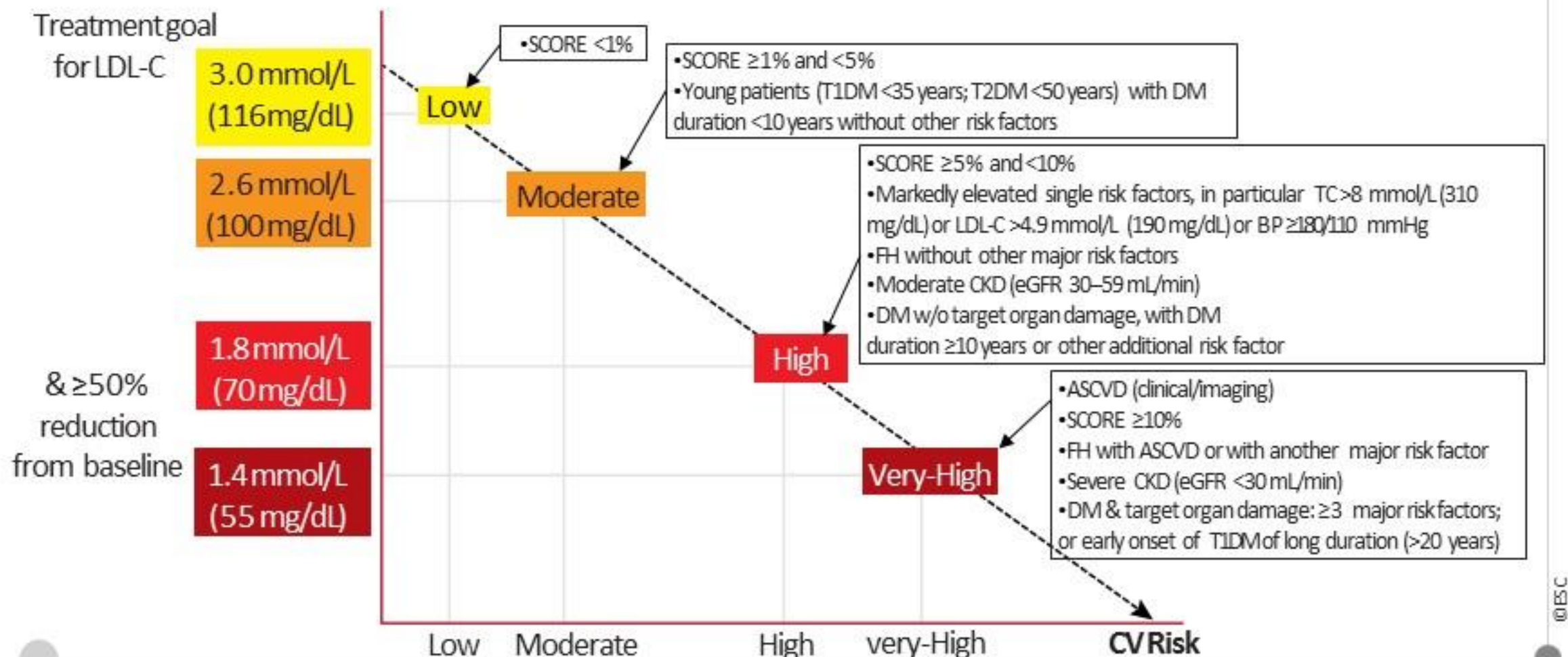
Adults with prior MI, prior stroke, PAD

N = 15,000

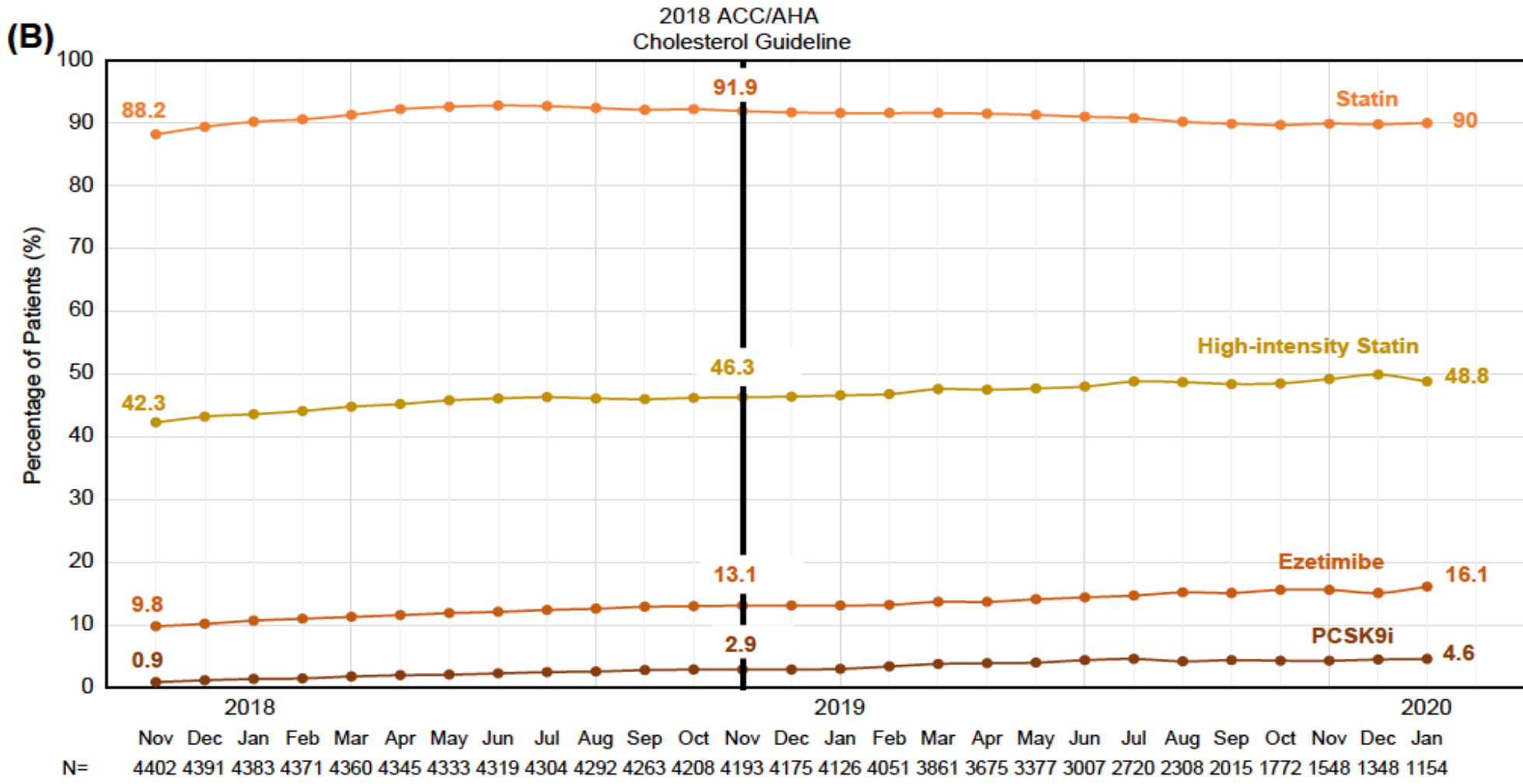
1. Sabatine MS, et al; FOURIER Steering Committee and Investigators. Evolocumab and Clinical Outcomes in Patients with Cardiovascular Disease. N Engl J Med. 2017 May 4;376(18):1713-1722.
 2. Schwartz GG et al. Alirocumab and Cardiovascular Outcomes after Acute Coronary Syndrome. N Engl J Med. 2018 Nov 29;379(22):2097-2107.



Central Illustration Upper panel Treatment goals for low-density lipoprotein cholesterol (LDL-C) across categories of total cardiovascular disease risk



Use of Lipid-Lowering Therapies Over 2 Years in GOULD, a Registry of Patients With Atherosclerotic Cardiovascular Disease in the US



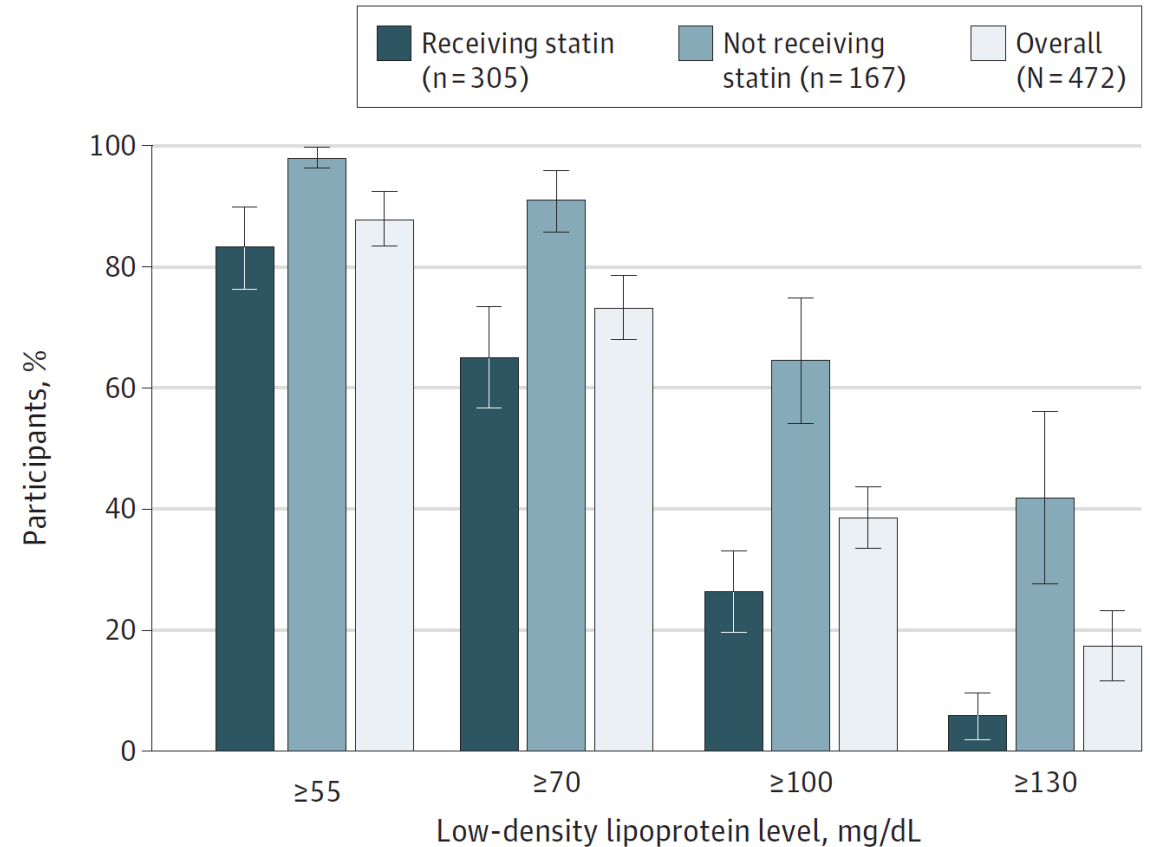
Poor LDL-C Control in the United States

Low-Density Lipoprotein Cholesterol Levels in Adults With Coronary Artery Disease in the US, January 2015 to March 2020

Patients with CAD

- 67.9% on statin
- 6.4% on ezetimibe

	Average LDL (mg/dl)	LDL >70	LDL >55
All CAD	94	74%	88%
Pts on statin	82	65%	83%
Pts on ezetimibe	120	91%	98%



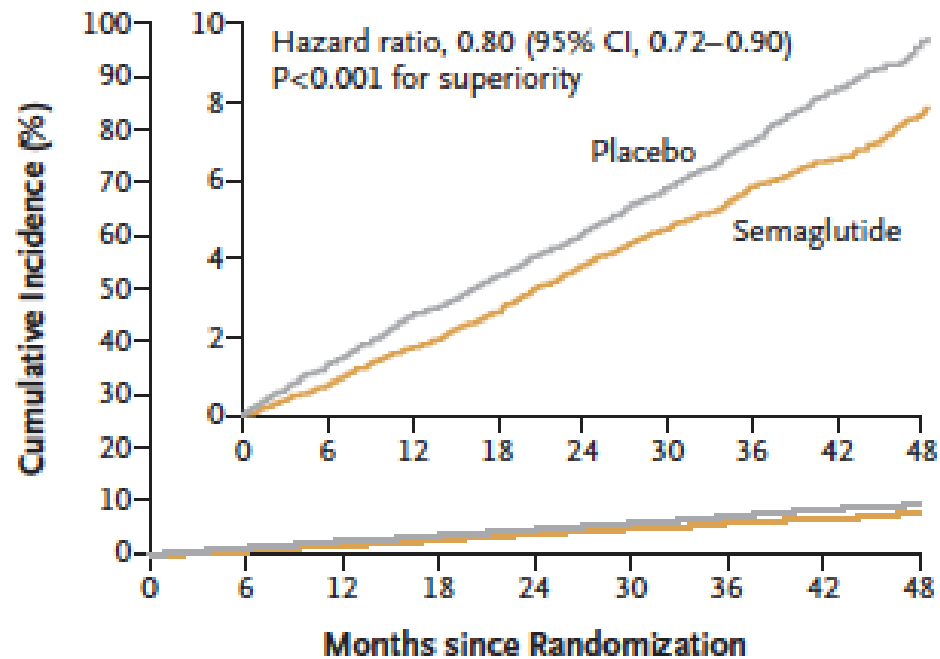
Lipids 2024 - “Lower (LDL) is better)

- Primary prevention: statins (or EZE) -> LDL <100 mg/dl
 - Low-Moderate risk → **LDL <100 mg/dl**
 - High risk → **LDL <70 mg/dl**
- SIHD/ASCVD: statin +/- ezetimibe +/- PCSK9 +/- BDA
 - ASCVD → **LDL <55 mg/dl**
- Statin intolerance: rosuva 2.5 tiw, EZE, early PCSK9
- Check Trig and if >135, add icosapent ethyl 4gm daily
- Check Lp(a) → increased risk and now clinical trials for Lp(a) reduction

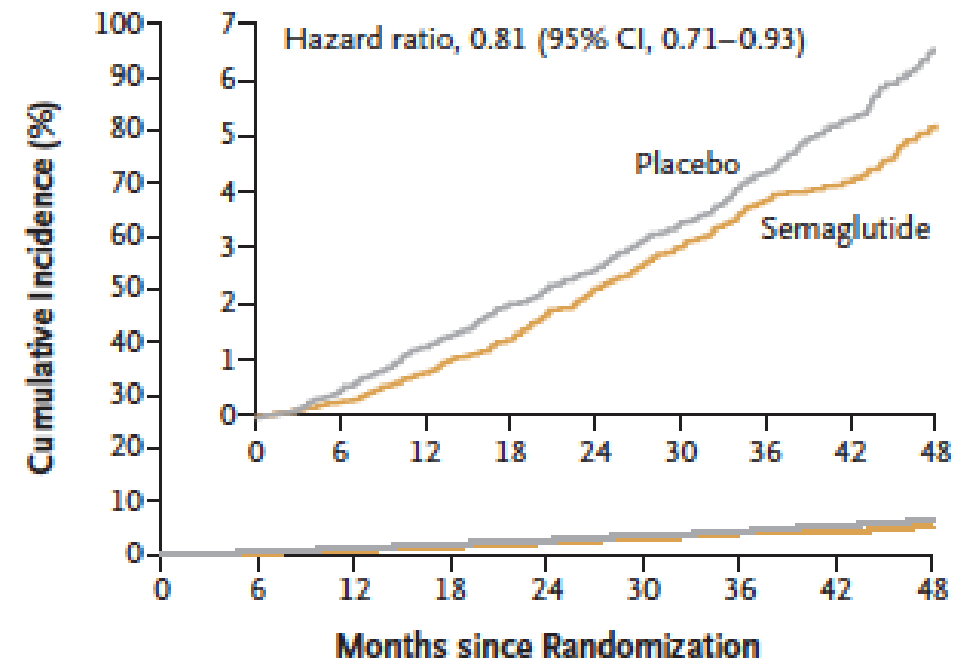
Semaglutide and Cardiovascular Outcomes in Obesity without Diabetes

A. Michael Lincoff, M.D., Kirstine Brown-Frandsen, M.D., Helen M. Colhoun, M.D., John Deanfield, M.D., Scott S. Emerson, M.D., Ph.D., Sille Esbjerg, M.Sc., Søren Hardt-Lindberg, M.D., Ph.D., G. Keees Hovingh, M.D., Ph.D., Steven E. Kahn, M.B., Ch.B., Robert F. Kushner, M.D., Ildiko Lingvay, M.D., M.P.H., Tugce K. Oral, M.D., Marie M. Michelsen, M.D., Ph.D., Jorge Plutzky, M.D., Christoffer W. Tornøe, Ph.D., and Donna H. Ryan, M.D., for the SELECT Trial Investigators*

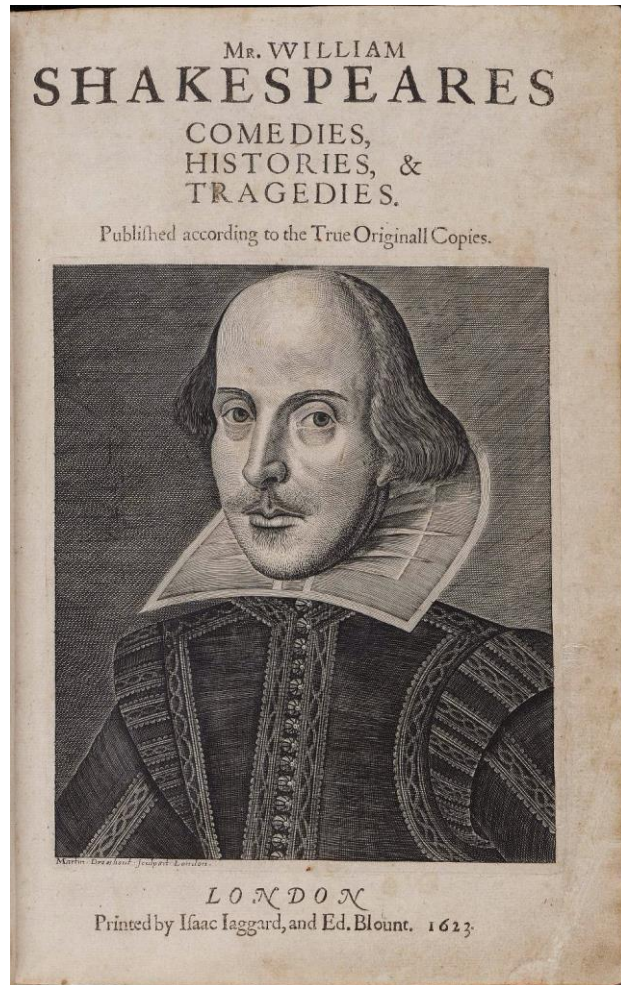
A Primary Cardiovascular Composite End Point



D Death from Any Cause



The Eternal Question in SIHD



***“To cath, or not to cath,
that is the question...”:***

Revascularization - Perception

**Make
patient
live
longer**

Make patient feel better

Revascularization - Reality

**Make patient live
longer**

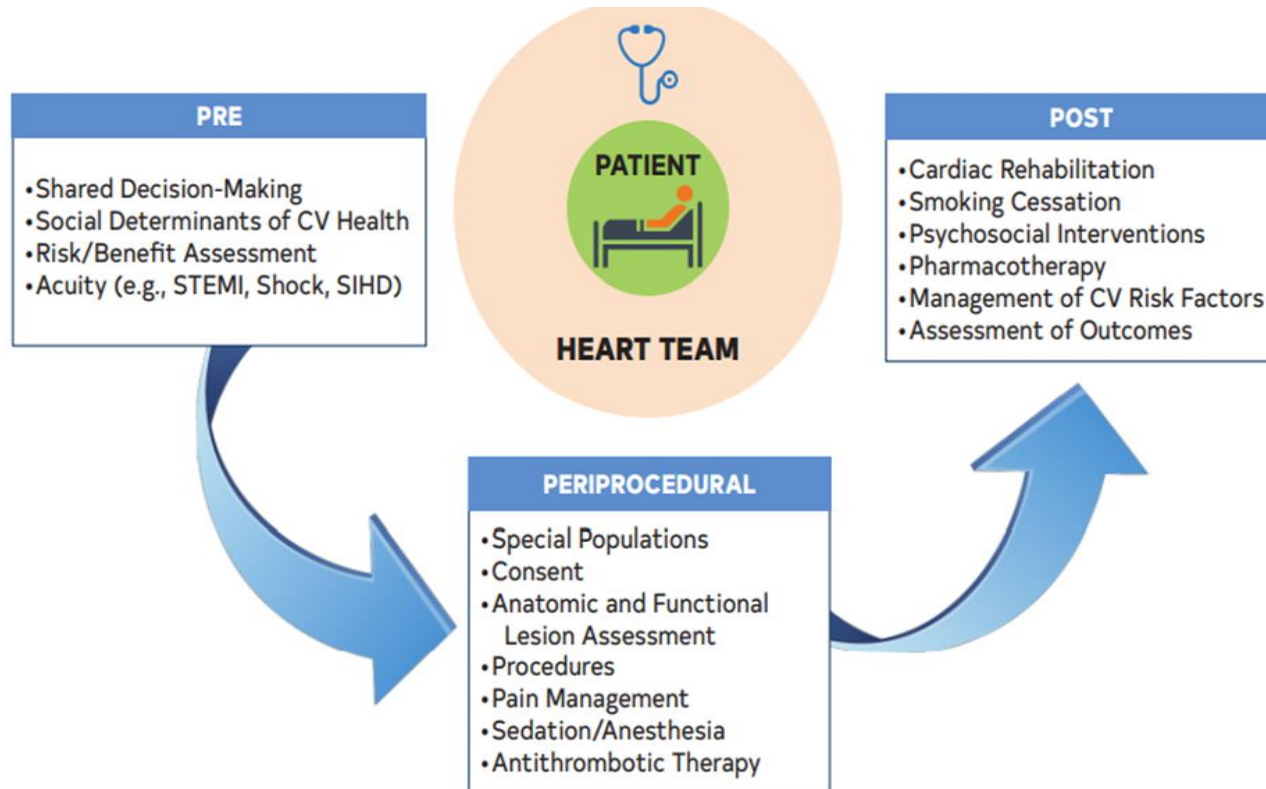
**Make
patient
feel
better**

Key Questions about Revascularization

- Is angina (or anginal equivalent) refractory to medical therapy?
- Is there Left Main Disease?
- How complex is the CAD (eg, SYNTAX score)
- Diabetes?
- LVEF <50%
- Suitability for PCI or CABG
- Patient preference

Patient Centered – Heart Team

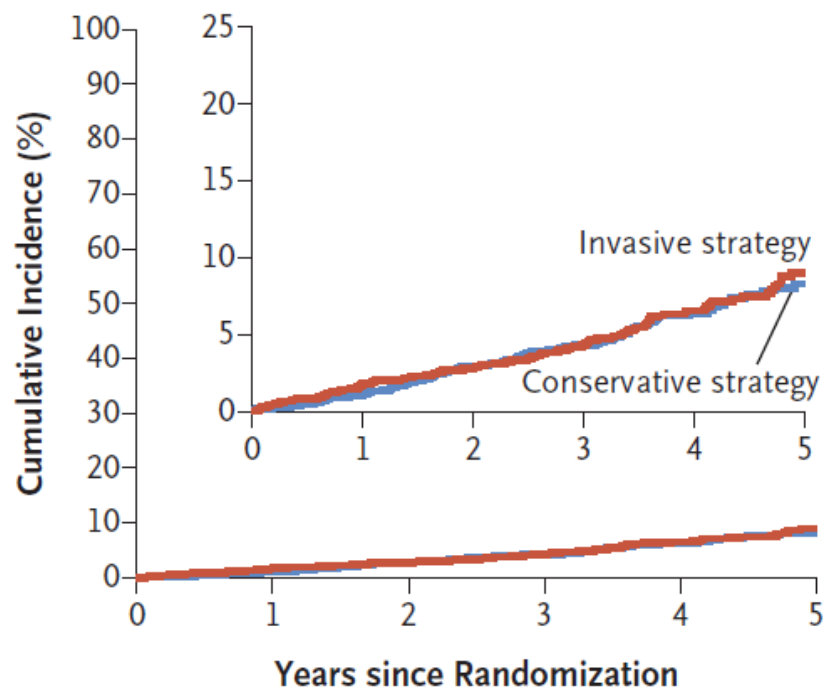
COR	LOE	RECOMMENDATION
1	B-NR	1. In patients for whom the optimal treatment strategy is unclear, a Heart Team approach that includes representatives from interventional cardiology, cardiac surgery, and clinical cardiology is recommended to improve patient outcomes (1-7).



ISCHEMIA Trial



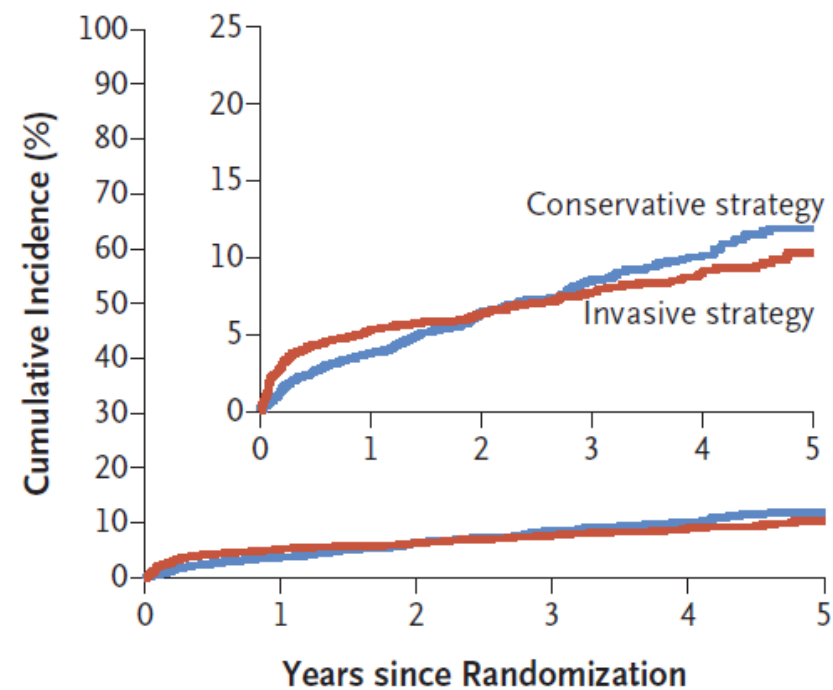
C Death from Any Cause



No. at Risk

Conservative strategy	2591	2548	2065	1445	844	349
Invasive strategy	2588	2518	2061	1431	827	317

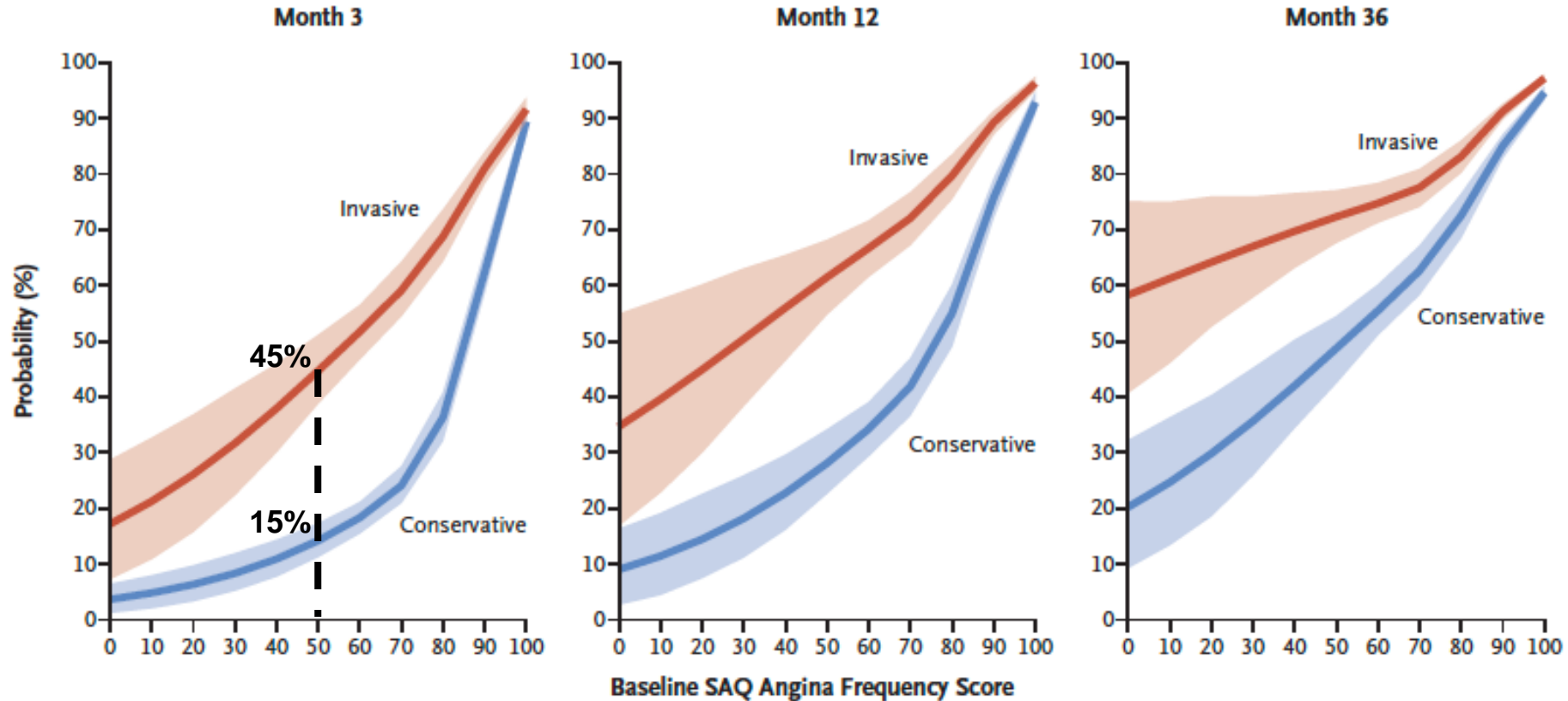
D Myocardial Infarction



No. at Risk

Conservative strategy	2591	2452	1931	1321	747	298
Invasive strategy	2588	2379	1931	1313	742	283

Probability of Being Angina-Free



Summary of “Disease Altering” Interventions in SIHD

- Greatest evidence for life-prolonging or MI-reducing therapy is with optimal medical therapy
- Revascularization is very good for reducing angina and minimizing the need for recurrent coronary interventions.
- But, except in small, high-risk populations, immediate revascularization does not prolong life or reduce the risk of future MI

Key References

- Lawton JS , et al. 2021 ACC/AHA/SCAI Guideline for Coronary Artery Revascularization: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. J Am Coll Cardiol. 2022 Jan, 79 (2) e21–e129
- Gulati D, et al. 2021 AHA/ACC/ASE/CHEST/SAEM/SCCT/SCMR Guideline for the Evaluation and Diagnosis of Chest Pain: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. J Am Coll Cardiol. 2021 Nov, 78 (22) e187–e285\
- Arnett DK , et al. 2019 ACC/AHA Guideline on the Primary Prevention of Cardiovascular Disease: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. J Am Coll Cardiol. 2019 Sep, 74 (10) e177–e232
- Grundy, SM et al. 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Blood Cholesterol: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. J Am Coll Cardiol. 2019 Jun, 73 (24) e285–e350
- Lloyd-Jones D, et al. 2022 ACC Expert Consensus Decision Pathway on the Role of Nonstatin Therapies for LDL-Cholesterol Lowering in the Management of Atherosclerotic Cardiovascular Disease Risk. J Am Coll Cardiol. 2022 Oct, 80 (14) 1366–1418.