CARDI·OH

Ohio Cardiovascular and Diabetes Health Collaborative

School of Medicine
Case Western Reserve University

In partnership with:

The Ohio State University College of Medicine

College of Medicine and Life Sciences, The University of Toledo

Ohio University Heritage College of Osteopathic Medicine

Northeast Ohio Medical University

University of Cincinnati Family and Community Medicine

Boonshoft School of Medicine, Wright State University

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Ohio Colleges of Medicine Government Resource Center

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Project ECHO®

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Cardi-OH ECHO

What's New in Cardiovascular Prevention? A Series of Case-Based Discussions

November 3, 2022

Cardi-OH ECHO Team and Presenters

FACILITATOR

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Case Western Reserve University

DIDACTIC PRESENTER

Ian J. Neeland, MD
Case Western Reserve University

LEAD DISCUSSANT

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CASE PRESENTER

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(case presented by Dr. Rao)

Disclosure Statements

- The following speakers have a relevant financial interest or affiliation with one or more organizations that could be perceived as a real or apparent conflict of interest in the context of the subject of their presentation:
  - Marilee Clemons, PharmD; Danette Conklin, PhD; Kathleen Dungan, MD, MPH; Adam T. Perzynski, PhD; Goutham Rao, MD; Christopher A. Taylor, PhD, RDN, LD, FAND*
- The remaining speakers have no financial relationships with any commercial interest related to the content of this activity:
  - Karen Bailey, MS, RDN, LD, CDCES; Kristen Berg, PhD; Elizabeth Beverly, PhD; Ian Neeland, MD; James Werner, PhD, MSSA; Jackson Wright, MD, PhD
- The following members of the planning committee DO NOT have any disclosures/financial relationships from any ineligible companies:
  - Shari Bolen, MD; Richard Cornachione; Carolyn Henceroth; Gillian Irwin; Michael Konstan, MD; Elizabeth Littman; Devin O'Neill; Steven Ostrolencki; Ann Nevar; Claire Rollins; Catherine Sullivan

* These financial relationships are outside the presented work.
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Person-Centered Language Recommendations

The ADA and the APA recommend language that emphasizes inclusivity and respect:

- **Gender**: Gender is a social construct and social identity; use term "gender" when referring to people as a social group. Sex refers to biological sex assignment; use term "assigned sex" when referring to the biological distinction.
- **Race**: Race is a social construct that is used broadly to categorize people based on physical characteristics, behaviors, and geographic location. Race is not a proxy for biology or genetics. Examining health access, quality, and outcome data by allows the healthcare system to assist in addressing the factors contributing to inequity.
- **Sexual Orientation**: Use the term "sexual orientation" rather than "sexual preference" or "sexual identity." People choose partners regardless of their sexual orientation; however, sexual orientation is not a choice.
- **Disability**: The nature of a disability should be indicated when it is relevant. Disability language should maintain the integrity of the individual. Language should convey the expressed preference of the person with the disability.
- **Socioeconomic Status**: When reporting SES, provide detailed information about a person's income, education, and occupation/employment. Avoid using pejorative and generalizing terms, such as "the homeless" or "poor."
- **Violent Language**: Avoid sayings like 'killing it,' 'pull the trigger,' 'take a stab at it,' 'off the reservation,' etc.

Flanagin A et al., 2021, JAMA; Dickinson JK et al., Diabetes Care, 2017; American Psychological Association, 2021; ODM, 2021.

Methods for Assessing Cardiovascular Risk

Ian J. Neeland, MD, FAHA, FACC

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Director, Translational Science Unit
Co-Director, Center for Integrated and Novel Approaches in Vascular-Metabolic Disease (CINEMA)
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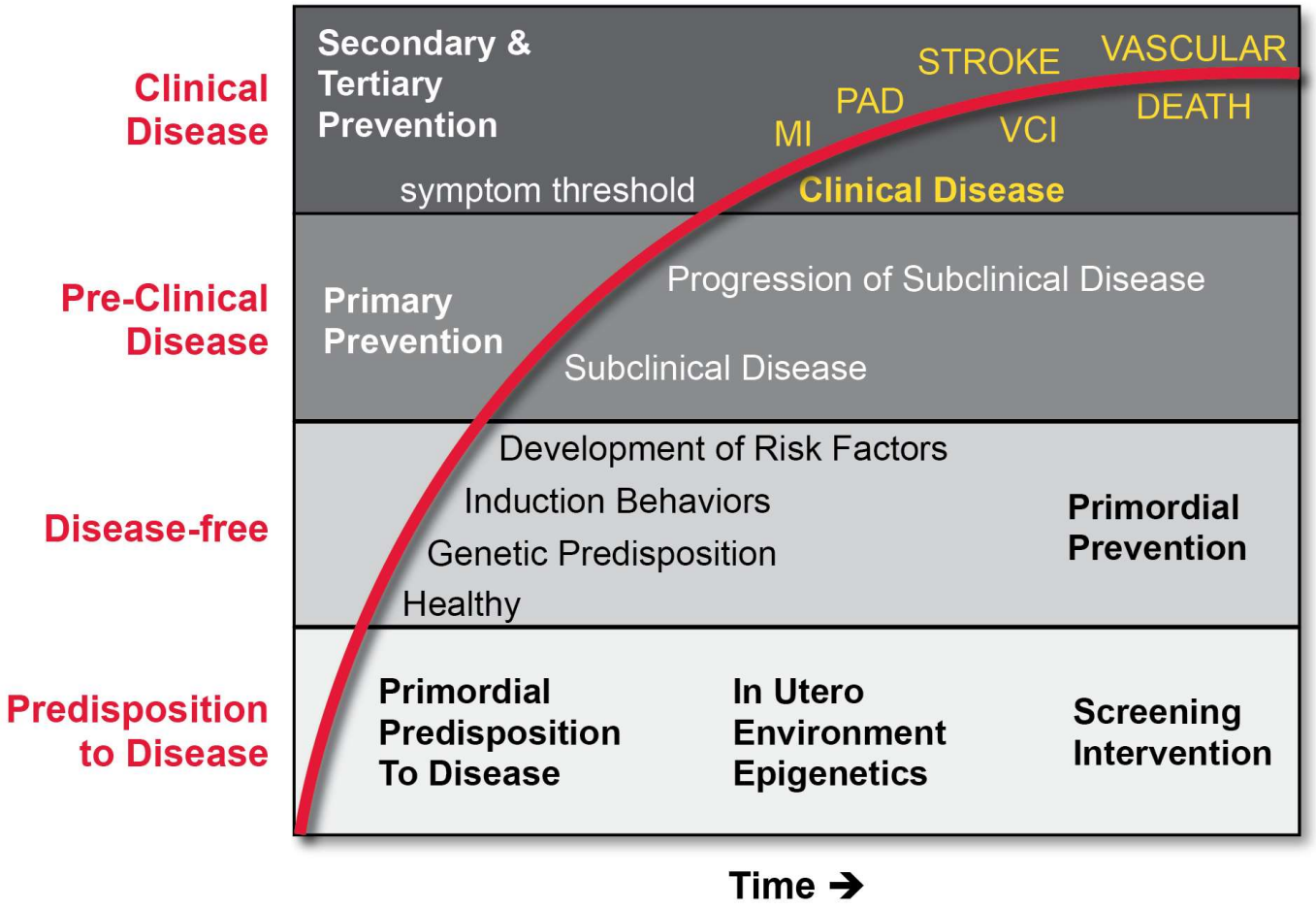
The Cardiovascular Risk "Timeline"



Traditional ASCVD Risk Factors

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Non-Modifiable

Age
- Men ≥ 45 years old
- Women ≥ 55 years old

Sex

Race

Family History

Modifiable

High Cholesterol

Smoking

High Blood Pressure

Diabetes

Obesity

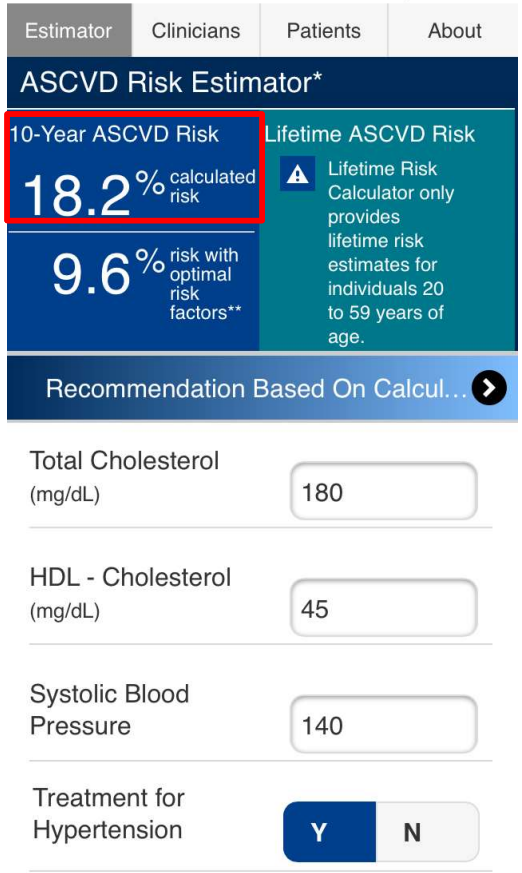
Alcohol

Physical Inactivity

Pooled Cohort Equations Risk Calculator

10-year risk of MI, Stroke, or CV death

- Age
- Sex
- Race (Black/White)
- Total Cholesterol
- HDL Cholesterol
- Systolic BP
- Hypertension
- Diabetes
- Current smoking



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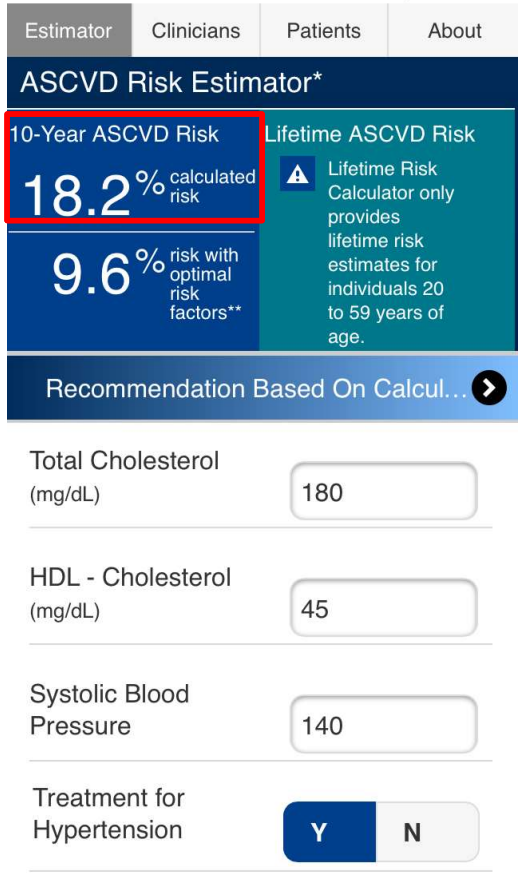

PCE may overestimate risk in some and underestimate risk in others

Additional tests to refine risk assessment

- Recognizing the imprecision of CVD risk prediction and the uncertainty clinicians and patients may encounter regarding the potential benefits of drug therapy for an individual patient at borderline or intermediate 10-year ASCVD risk, additional testing is reasonable.
- In general, identification of subclinical atherosclerosis rather than use of serum biomarkers is preferred, because of the extensive body of evidence demonstrating the superior utility of atherosclerosis disease assessment, particularly with CAC measurement, over any serum biomarker for the prediction of future ASCVD events.
- Other modalities for assessing subclinical atherosclerosis, including carotid intima-media thickness and carotid plaque burden assessment, are weaker predictors of overall ASCVD events compared with the CAC score.

Lloyd-Jones DM, et al. Use of Risk Assessment Tools to Guide Decision-Making in the Primary Prevention of Atherosclerotic Cardiovascular Disease: A Special Report From the American Heart Association and American College of Cardiology. 2018

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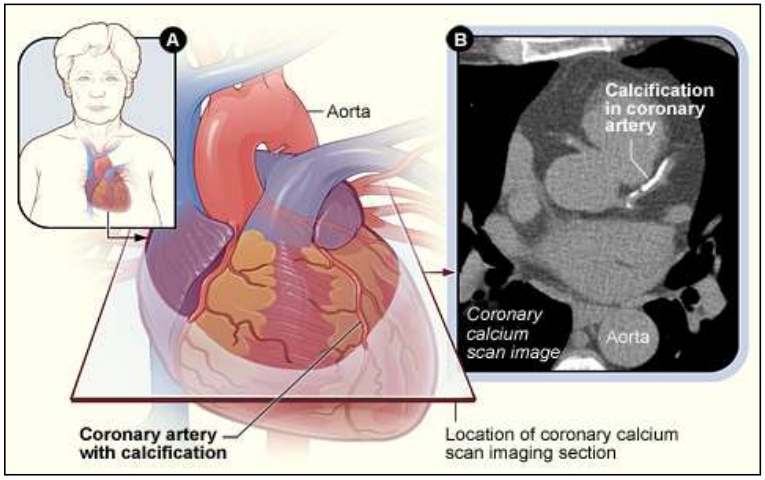
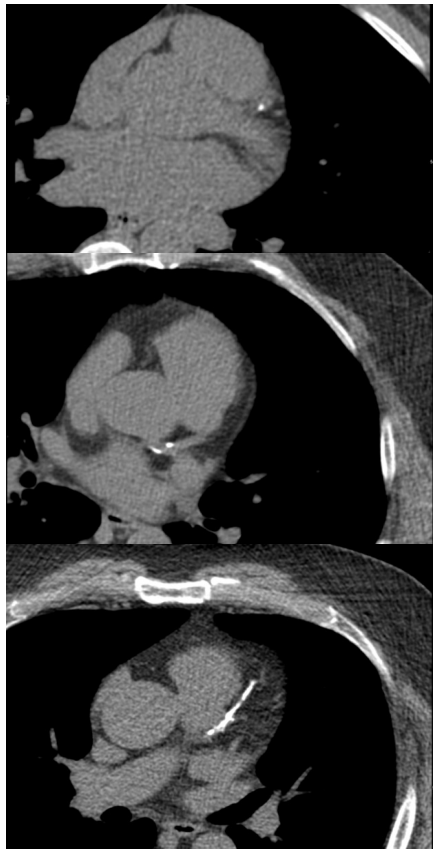
Coronary Artery Calcium Scoring





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Heart Check America
Founded 1992
First Scanners in Chicago and LA

MESA

NHLBI, 2000

ROTTERDAM STUDY

Many supporters, 1990

The Heinz Nixdorf RECALL (Risk Factors, Evaluation of Coronary Calcium and Lifestyle) Study

2000, many sponsors

Coronary Calcium as a Predictor of Coronary Events in Four Racial or Ethnic Groups

Robert Detrano, M.D., Ph.D., Alan D. Guerci, M.D., J. Jeffrey Carr, M.D., M.S.C.E., Diane E. Bild, M.D., M.P.H., Gregory Burke, M.D., Ph.D., Aaron R. Folsom, M.D., Kiang Liu, Ph.D., Steven Shea, M.D., Moyses Szklo, M.D., Dr.P.H., David A. Bluemke, M.D., Ph.D., Daniel H. O'Leary, M.D., Russell Tracy, Ph.D., Karol Watson, M.D., Ph.D., Nathan D. Wong, Ph.D., and Richard A. Kronmal, Ph.D.

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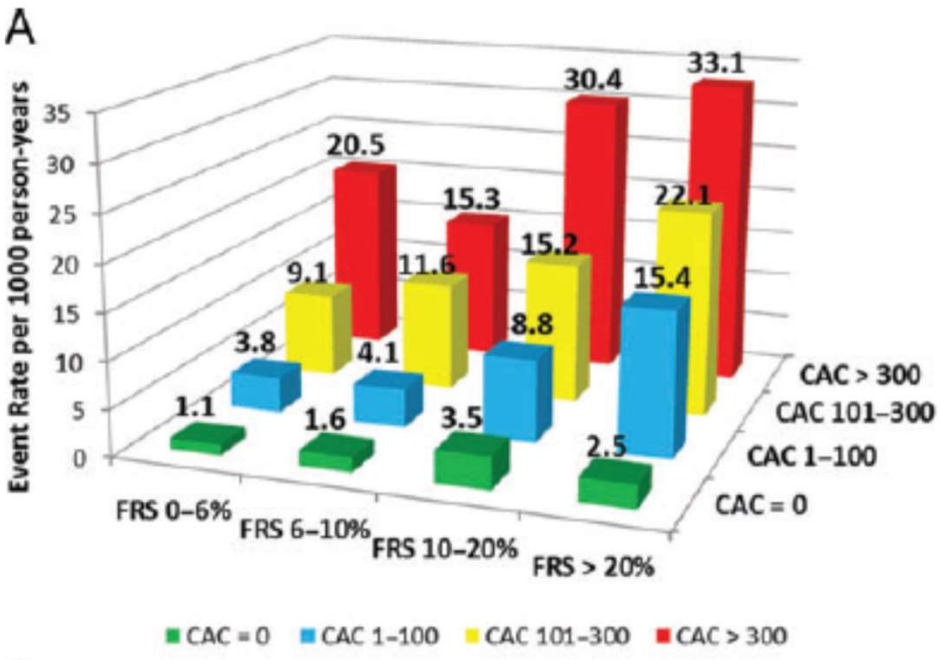
Table 3. Risk of Coronary Events Associated with Increasing Coronary-Artery Calcium Score after Adjustment for Standard Risk Factors.*

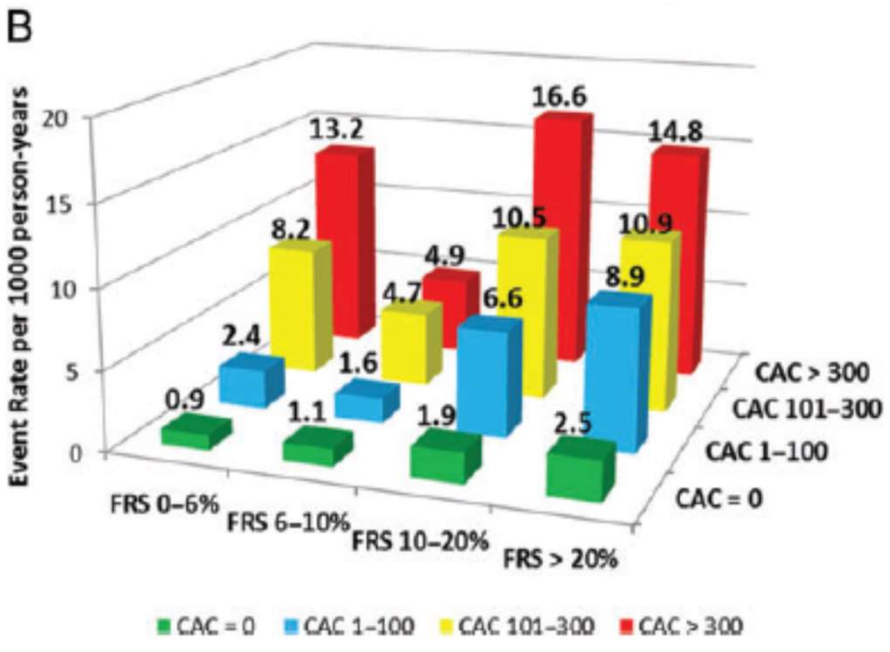
Coronary-Artery Calcium Score	Major Coronary Event†			Any Coronary Event		
	No./No. at Risk	Hazard Ratio (95% CI)	P Value	No./No. at Risk	Hazard Ratio (95% CI)	P Value
0	8/3409	1.00		15/3409	1.00	
1–100	25/1728	3.89 (1.72–8.79)	<0.001	39/1728	3.61 (1.96–6.65)	<0.001
101–300	24/752	7.08 (3.05–16.47)	<0.001	41/752	7.73 (4.13–14.47)	<0.001
>300	32/833	6.84 (2.93–15.99)	<0.001	67/833	9.67 (5.20–17.98)	<0.001
Log_2(CAC+1)‡		1.20 (1.12–1.29)	<0.001		1.26 (1.19–1.33)	<0.001

* CAC denotes coronary-artery calcium score, and CI confidence interval.
† Major coronary events were myocardial infarction and death from coronary heart disease.
‡ Each unit increase in $\log_2$(CAC+1) represents a doubling of the coronary-artery calcium score.

Adding CAC to Standard Risk Factors

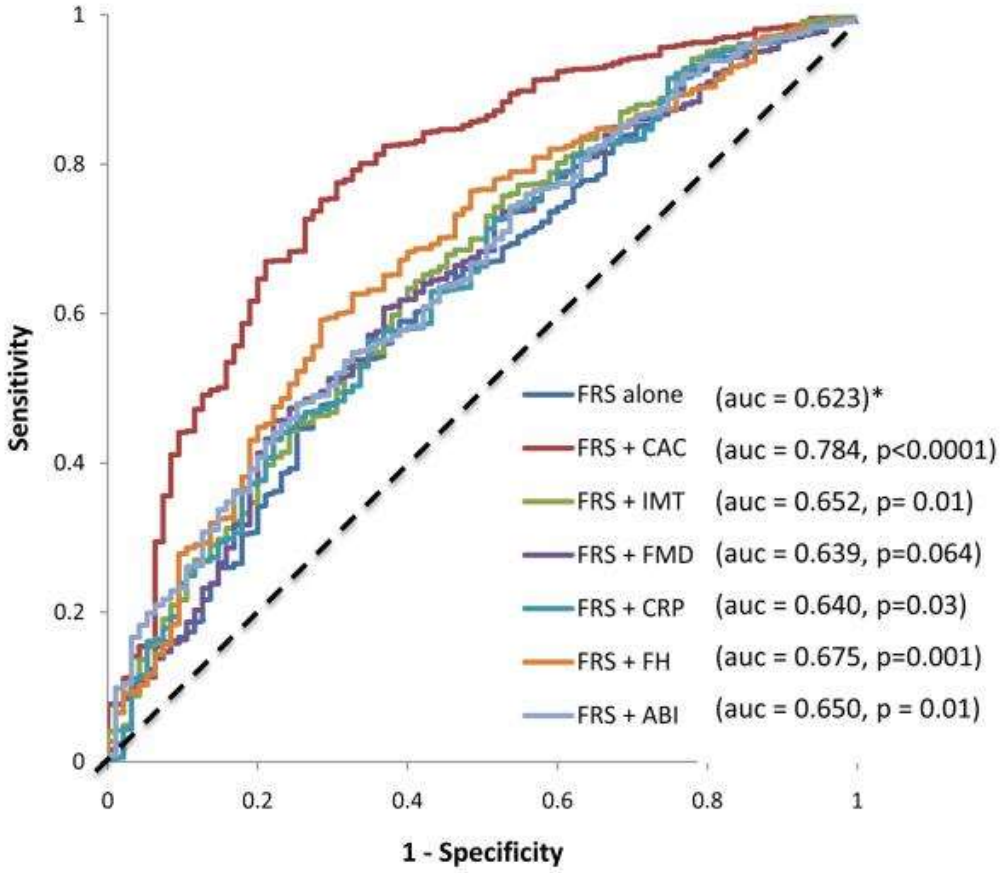


Total CHD



Hard CHD

CAC vs. Other Risk Markers



CAC improves ASCVD risk discrimination to a much greater degree than any other cardiovascular risk factor

Yeboah et al. *JAMA*. 2012;308:788-795

Using 10-year ASCVD risk estimate plus coronary artery calcium (CAC) score to guide statin therapy				
Patient's 10-year atherosclerotic cardiovascular disease (ASCVD) risk estimate:	<5%	5-7.5%	>7.5-20%	>20%
Consulting ASCVD risk estimate alone	Statin not recommended	Consider for statin	Recommend statin	Recommend statin
Consulting ASCVD risk estimate + CAC				
If CAC score =0	Statin not recommended	Statin not recommended	Statin not recommended	Recommend statin
If CAC score >0	Statin not recommended	Consider for statin	Recommend statin	Recommend statin
Does CAC score modify treatment plan?	✗ CAC not effective for this population	✓ CAC can reclassify risk up or down	✓ CAC can reclassify risk up or down	✗ CAC not effective for this population

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Greenland, P. et al. J Am Coll Cardiol. 2018;72(4):434-47.

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Risk Enhancing Factors

- **Family history of premature ASCVD** (males, age <55 y; females, age <65 y)
- **Primary hypercholesterolemia** (LDL-C, 160–189 mg/dL [4.1–4.8 mmol/L]; non–HDL-C 190–219 mg/dL [4.9–5.6 mmol/L])*
- **Metabolic syndrome** (increased waist circumference [by ethnically appropriate cutpoints], elevated triglycerides [>150 mg/dL, nonfasting], elevated blood pressure, elevated glucose, and low HDL-C [<40 mg/dL in men; <50 mg/dL in women] are factors; a tally of 3 makes the diagnosis)
- **Chronic kidney disease** (eGFR 15–59 mL/min/1.73 m2 with or without albuminuria; not treated with dialysis or kidney transplantation)
- **Chronic inflammatory conditions**, such as psoriasis, RA, lupus, or HIV/AIDS
- **History of premature menopause (before age 40 y) and history of pregnancy-associated conditions that increase later ASCVD risk, such as preeclampsia**
- **High-risk race/ethnicity** (e.g., South Asian ancestry)
- **Lipids/biomarkers**: associated with increased ASCVD risk
  - Persistently elevated,* primary hypertriglyceridemia (≥175 mg/dL, nonfasting)
  - If measured:
    - **Elevated high-sensitivity C-reactive protein** (≥2.0 mg/L)
    - **Elevated Lp(a)**: A relative indication for its measurement is family history of premature ASCVD. An Lp(a) ≥50 mg/dL or ≥125 nmol/L constitutes a risk-enhancing factor, especially at higher levels of Lp(a).
    - **Elevated apoB** (≥130 mg/dL): A relative indication for its measurement would be triglyceride ≥200 mg/dL. A level ≥130 mg/dL corresponds to an LDL-C >160 mg/dL and constitutes a risk-enhancing factor
    - **ABI** (<0.9)

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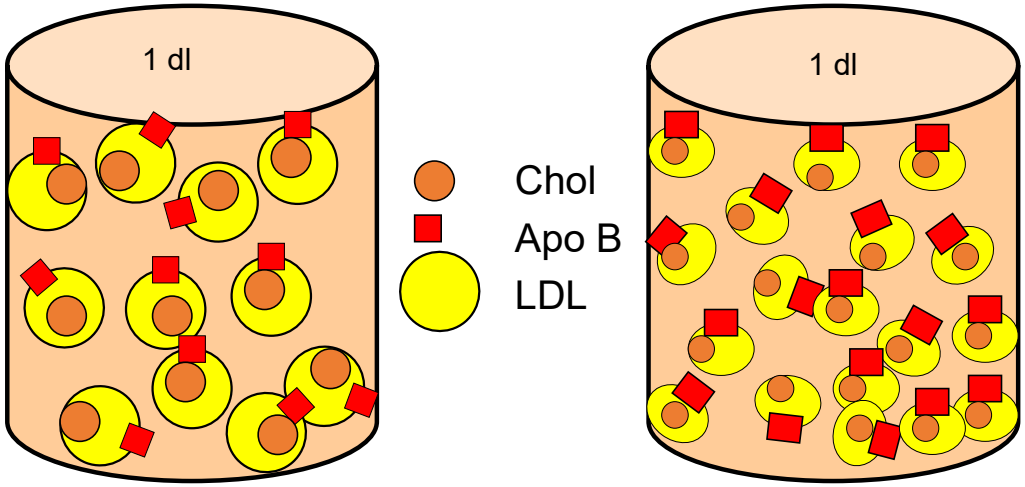
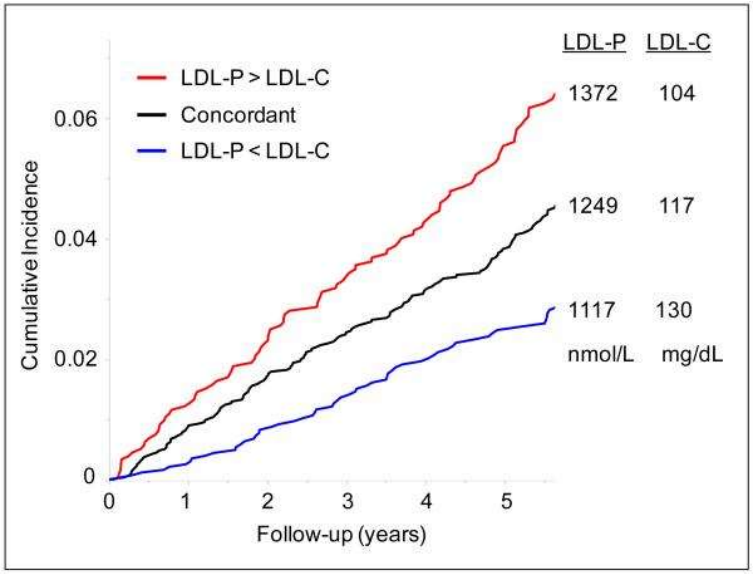
Advanced Lipoprotein Testing

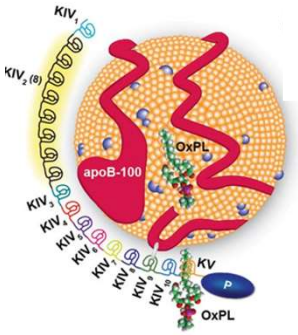


110 mg/dl	LDL-C	**110 mg/dl**
A	Pattern	**B**
1200 nmol/L	LDL Particle #	**1800 nmol/L**
90 mg/dl	Apo B	**120 mg/dl**
130 mg/dl	NHDL	**160 mg/dl**



Otvos et al. *J Clin Lipid*. 2011;5:105-113

Lipoprotein (a)



Prothrombotic

Inhibits fibrinolysis

plasminogen

↑ PAI 1

Platelet activation

Proatherosclerotic

Intimal retention

Proinflammatory

Carrier of ox-PL

- Plasma concentrations of lipoprotein(a) are primarily genetically determined (90% of plasma concentration)
- Both mass (mg/dL) and particle concentration (nmol/L) assays– cannot easily convert between these
  - Values ≥50 mg/dL or ≥125 nmol/L considered elevated
- ~20% of the population has elevated Lp(a)
  - Blacks have higher levels than whites

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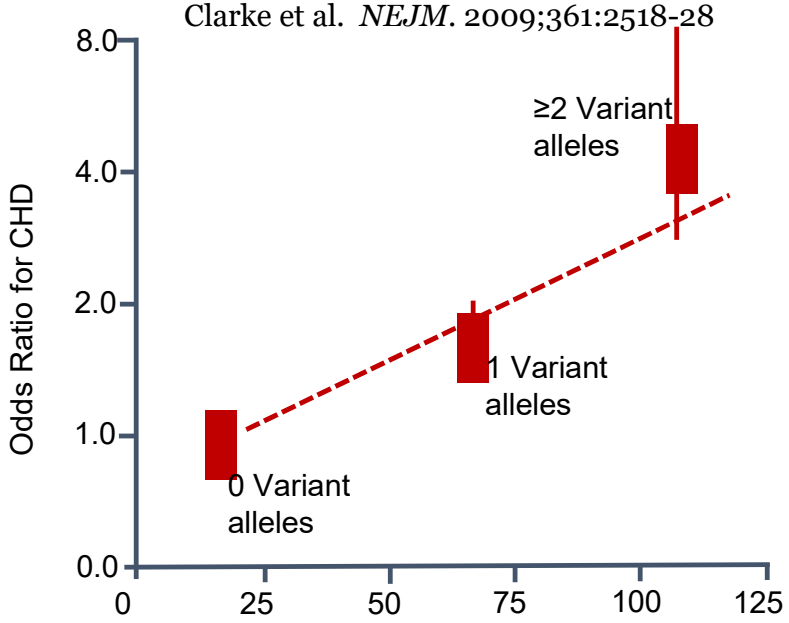
Clarke et al. *NEJM*. 2009;361:2518-28



3145 cases with CAD, 3352 control subjects

Gene score 0-4 variant alleles associated with Lp(a) and CHD

Circulation: Cardiovascular Quality and Outcomes
Volume 12, Issue 11, November 2019
https://doi.org/10.1161/CIRCOUTCOMES.119.006078

American Heart Association.

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CARDIOVASCULAR PERSPECTIVE

Do Risk-Enhancing Factors Enhance Risk Estimation?

Ralph H. Stern, PhD, MD and Robert D. Brook, MD

Key Words: cardiology ■ cholesterol ■ coronary artery disease ■ guideline ■ risk

"If REFs are to be considered, they must be incorporated into a validated model. Such models only exist for hsCRP (which does not improve population risk stratification) and CAC. Without such a model clinicians using a REF (or worse, many REFs) will erroneously stack the deck in favor of higher risks and over-value the information provided."

"Absent convincing evidence that REFs improve the risk stratification of the PCE and given the paucity of validated models that incorporate them, clinicians should continue to rely on the PCE for primary prevention decisions, understanding that the risk estimates represent frequentist probabilities."

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AHA SCIENTIFIC STATEMENT

Cardiovascular Health in African Americans

A Scientific Statement From the American Heart Association

RESULTS: The higher prevalence of traditional cardiovascular risk factors (eg, hypertension, diabetes mellitus, obesity, and atherosclerotic cardiovascular risk) underlies the relatively earlier age of onset of cardiovascular diseases among African Americans. Hypertension in

Carnethon et al. *Circulation*. 2017;136:e9393-e423

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Racial Differences in Cardiovascular Biomarkers in the General Population

Hackler et al. *JAHA*. 2019;8:e021729

Conclusions—Significant racial differences were seen in biomarkers reflecting lipids, adipokines, and biomarkers of endothelial function, inflammation, myocyte injury, and neurohormonal stress, which may contribute to racial differences in the development and complications of CVD. (***J Am Heart Assoc.*** **2019;8:e012729. DOI: 10.1161/JAHA.119.012729.)**

Differences in estimates for 10-year risk of cardiovascular disease in Black versus White individuals with identical risk factor profiles using pooled cohort equations: an in silico cohort study

Interpretation The PCE might generate substantially divergent cardiovascular disease risk estimates for Black versus White individuals with identical risk profiles, which could introduce race-related variations in clinical recommendations for cardiovascular disease prevention.

Vasan et al. *Lancet Dig Health*. 2022;4:e55-63

Thank you!

Questions/Discussion