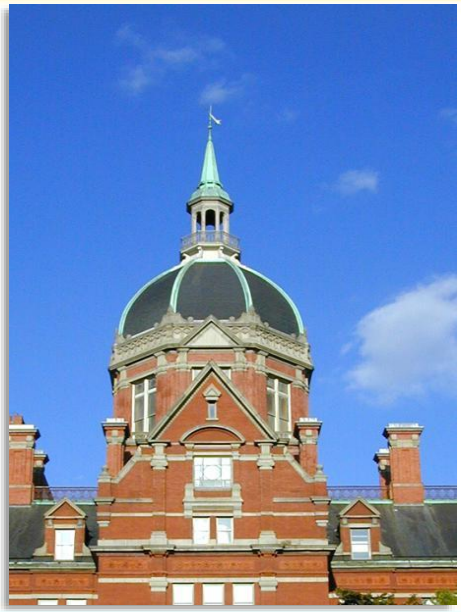

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CAC Score to Guide CV Risk Assessment When Decision to "Statin" Uncertain"

Erin D. Michos, MD, MHS, FACC, FAHA
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Johns Hopkins University School of Medicine

American College of Osteopathic Internists, May 9, 2019

@ErinMichos

Learning Objectives

- To review 2019 ACC/AHA Primary Prevention Guidelines for the Assessment of ASCVD Risk
- To discuss which type of patients may benefit from assessment of subclinical atherosclerosis by **CAC** score to refine ASCVD Risk Assessment and guide the **Clinician-Patient Risk Discussion** and treatment decisions

CASE Patient: Mr. J

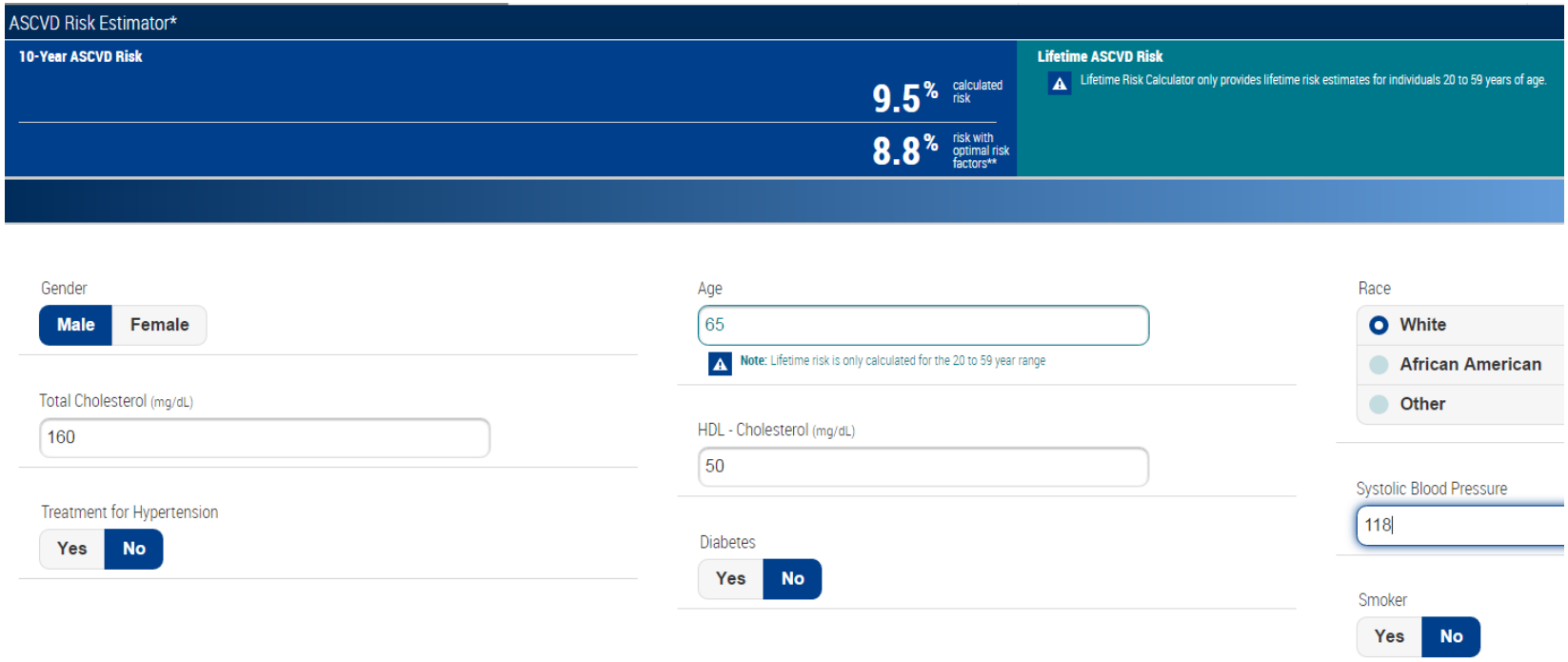
- Mr. J comes in for routine visit
  - 65 yo white male, asymptomatic
  - Never smoker
  - Runs 4x/ week, healthy diet
  - BMI 23
  - Untreated SBP 118 mm Hg
  - No diabetes
  - No family Hx of premature CAD
  - Total chol 160, HDL 50 mg/dl, TG 66, LDL 98

STATIN or
No STATIN?

CASE Patient: Mr. J

10-year ASCVD Risk is **9.5%**

STATIN or No STATIN?



CASE Patient: Mr. J
MOC QUESTION

Which of the following is appropriate at this time?

- a) Aspirin therapy for primary ASCVD prevention
- b) Consider statin therapy because 10-year ASCVD risk is ≥7.5%
- c) Engage in shared decision making discussion with patient about his concerns, values, and preferences
- d) Additional testing may be considered to inform treatment decisions
- e) b, c, d

Why Assess Risk?

Rationale for Absolute Risk Estimation

JOHNS HOPKINS MEDICINE

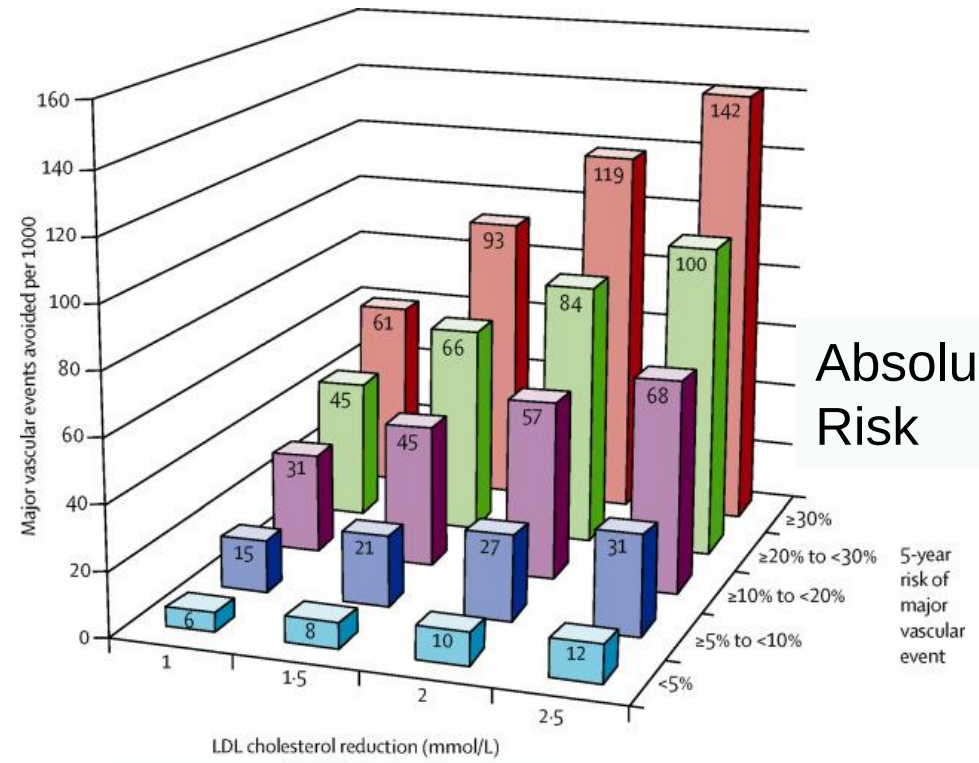
- Most important way to prevent CVD is to follow a healthy lifestyle throughout one's lifetime.

- When considering drug therapy, estimation of risk facilitates matching intensity of therapy to one's **absolute risk** to:
  - Maximize anticipated benefits of therapy
  - Minimize harms of over-treatment

Why Assess Risk?

Rationale for Absolute Risk Estimation

Cholesterol Treatment Trialists



Absolute Risk

LDL-C Reduction

CTT, Lancet 2012; Lloyd-Jones et al., Circ and JACC 2018

- Allows identification of patients at sufficient risk to merit treatment with higher likelihood of net individual and societal benefit
- Allows direct comparison of potential benefits and harms from drug therapy

2019 ACC/AHA Guideline on the Primary Prevention of CVD

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Assessment of 10-year ASCVD Risk

Recommendations for Assessment of Cardiovascular Risk		
COR	LOE	Recommendations
I	B-NR	For adults 40 to 75 years of age, clinicians should routinely assess traditional cardiovascular risk factors and calculate 10-year risk of ASCVD by using the pooled cohort equations (PCE).

Arnett D, Blumenthal RS,….Michos ED.. et al. Circulation 2019

2019 ACC/AHA Primary Prevention Guidelines

Assessment of 10-year ASCVD Risk

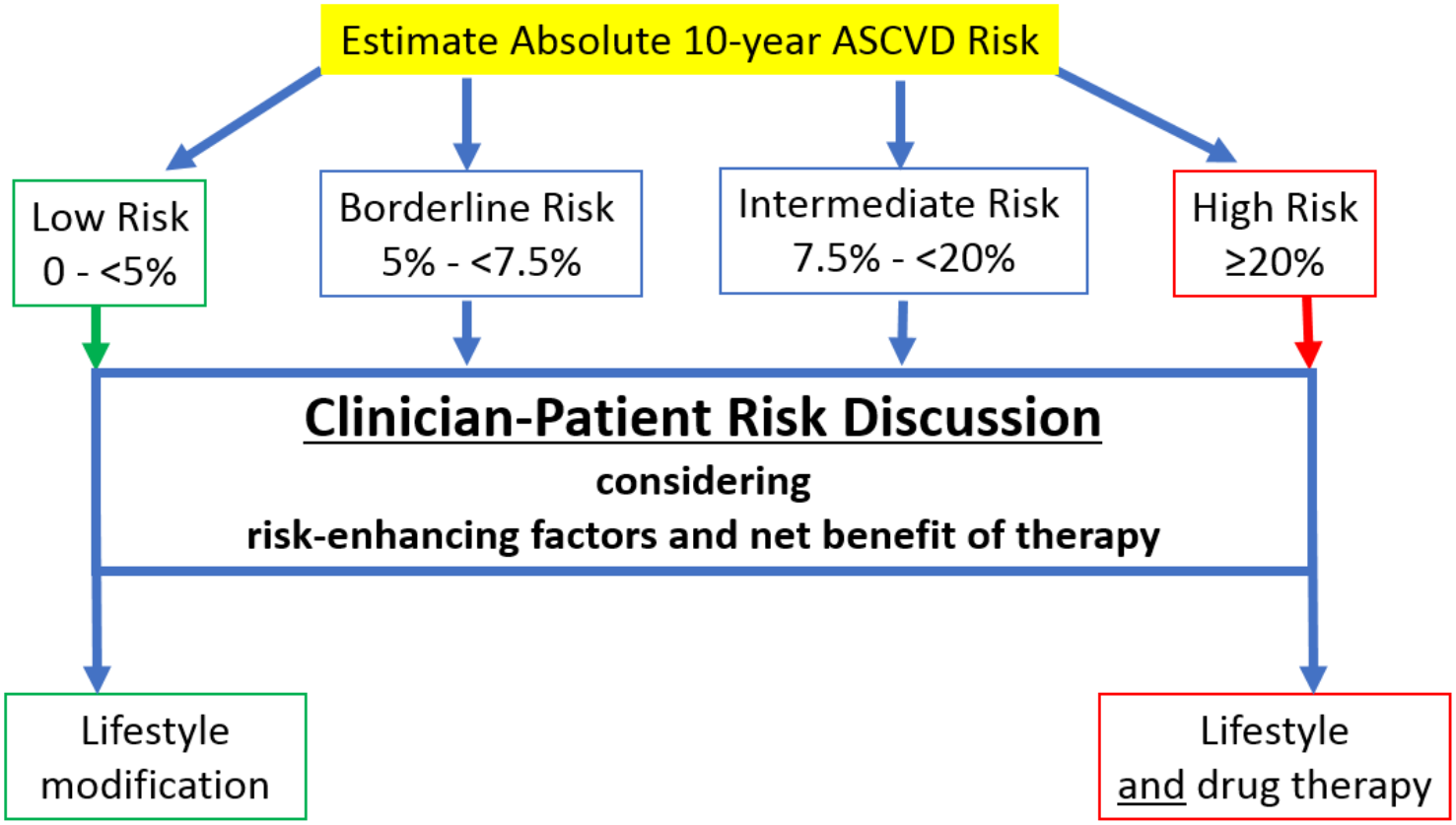
AHA ASCVD Risk Calculator (online/app)
http://static.heart.org/riskcalc/app/index.html#!/baseline-risk

Risk Factor	Units
Sex	M or F
Age	Years
Race	AA or WH
Total Cholesterol	mg/dL
HDL-Cholesterol	mg/dL
Systolic Blood Pressure	mm Hg
Treatment for Hypertension	Y or N
Diabetes	Y or N
Smoker	Y or N

- Based on multiple cohorts; sex and race-specific
- Stroke included in addition to MI and CHD mortality

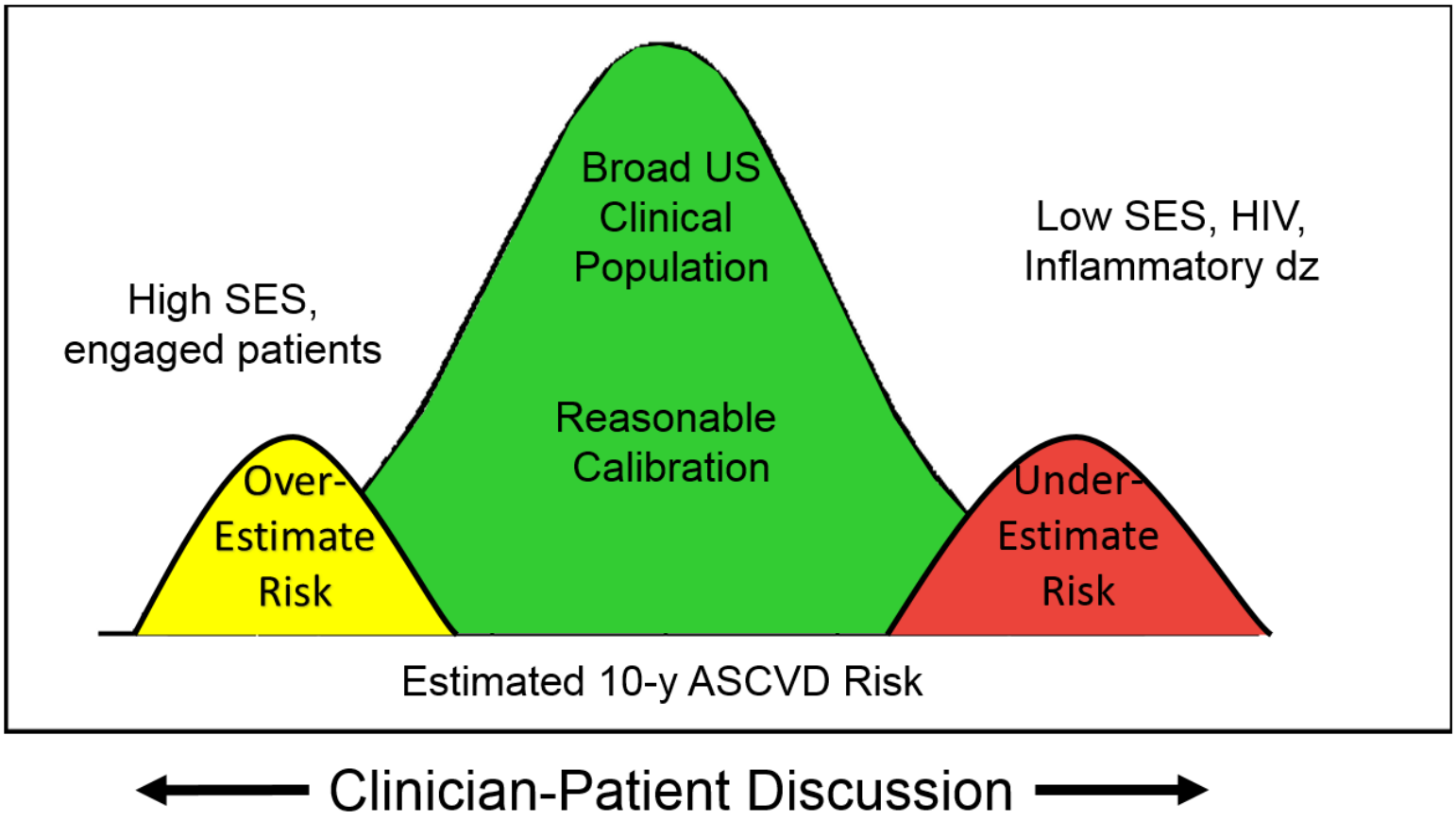
2019 ACC/AHA Primary Prevention Guideline

Refining Risk Estimates for Individual Patients



2019 ACC/AHA Primary Prevention Guidelines

Performance of PCE in Diverse Populations



PCE: Pooled Cohort Equations; SES, socioeconomic status

2019 ACC/AHA Primary Prevention Guidelines

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Assessment of ASCVD Risk: Risk Enhancing Factors

Recommendations for Assessment of Cardiovascular Risk		
COR	**LOE**	**Recommendations**
IIa	B-NR	In adults at **borderline risk** (5% to <7.5% 10-year ASCVD risk) or **intermediate risk** (≥7.5% to <20% 10-year ASCVD risk), it is reasonable to use additional **risk-enhancing factors** to guide decisions about preventive interventions (e.g., statin therapy).

Arnett DK, Blumenthal RS,….Michos ED…et al. Circulation 2019

2019 ACC/AHA Primary Prevention Guidelines

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Assessment of ASCVD Risk: Risk Enhancing Factors

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 m^2 with or without albuminuria; not treated with dialysis or kidney transplantation) • **Chronic inflammatory conditions,** such as psoriasis, RA, lupus, or HIV/AIDS

ABI, ankle-brachial index; AIDS, acquired immunodeficiency syndrome; apoB, apolipoprotein B; ASCVD, atherosclerotic cardiovascular disease; eGFR, estimated glomerular filtration rate; HDL-C, high-density lipoprotein cholesterol; HIV, human immunodeficiency virus; LDL-C, low-density lipoprotein cholesterol; Lp(a), lipoprotein (a); and RA, rheumatoid arthritis.

Risk Enhancing Factors, Cont'd

Risk-Enhancing Factors
• **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)

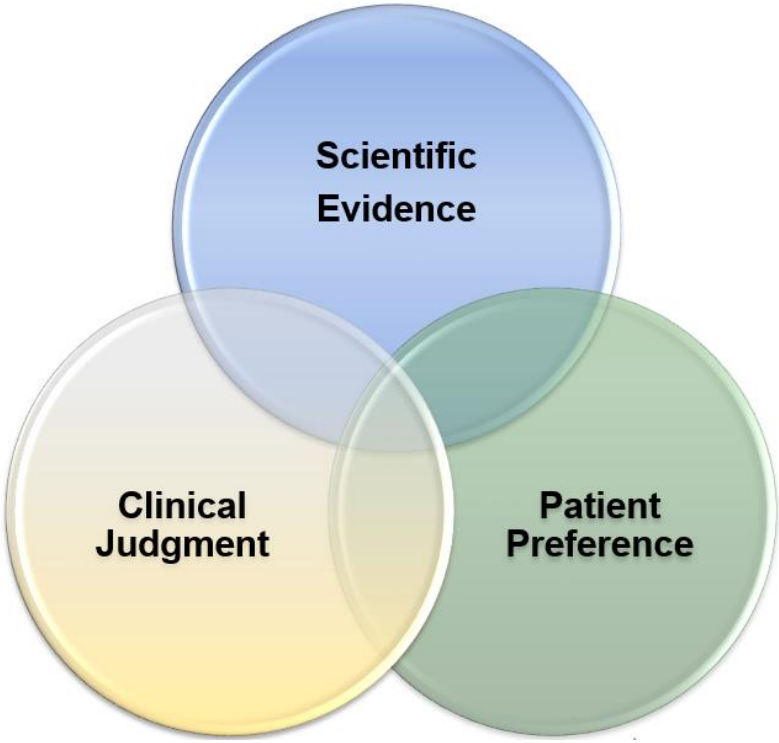
2019 ACC/AHA Primary Prevention Guidelines

Clinician-Patient Risk Discussion

Initiating Treatment in Primary Prevention

Clinicians and patients should discuss:

1. Estimated 10-yr risk, major risk factors, & risk-enhancing factors
2. Potential ASCVD risk reduction benefits of lifestyle + drug therapy
3. Potential adverse effects, drug interactions, & costs
4. Patient Preferences & values in shared decision-making



2019 ACC/AHA Primary Prevention Guideline

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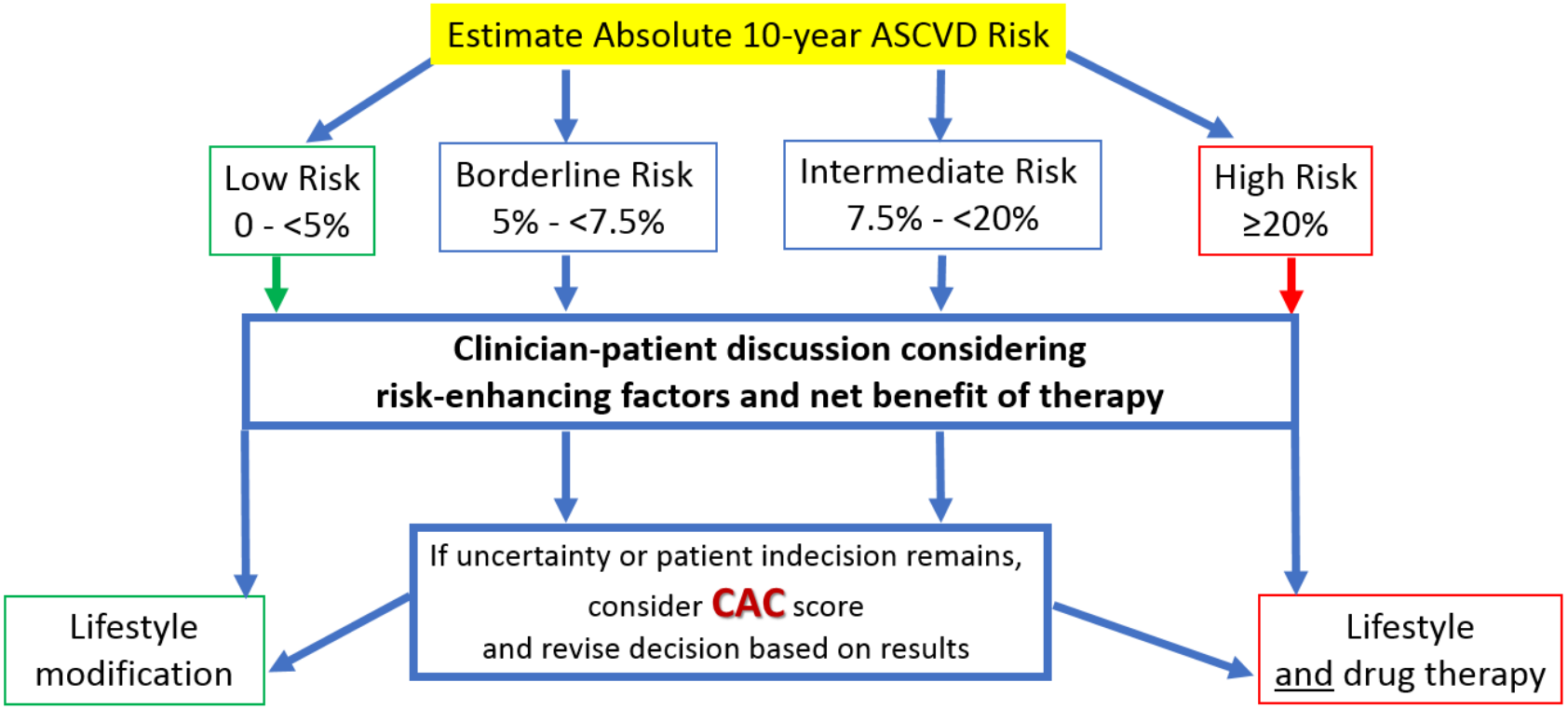
Assessment of ASCVD Risk: Use of CAC

Recommendations for Assessment of Cardiovascular Risk		
COR	**LOE**	**Recommendations**
IIa	B-NR	In adults at intermediate risk (≥7.5% to <20% 10-year ASCVD risk) or selected adults at borderline risk (5% to <7.5% 10-year ASCVD risk), if risk-based decisions for preventive interventions (e.g., statin therapy) remain uncertain, it is reasonable to measure a coronary artery calcium (CAC) score to guide clinician–patient risk discussion.

Arnett DK, Blumenthal RS,….Michos ED…et al. Circulation 2019

2019 ACC/AHA Primary Prevention Guideline

Assessment of ASCVD: Use of CAC

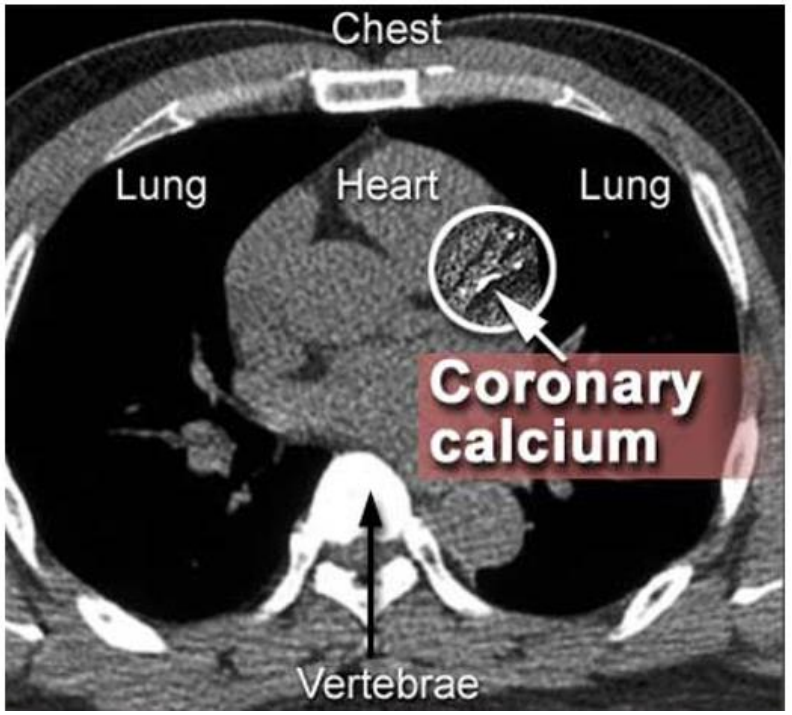


2019 ACC/AHA Primary Prevention Guideline

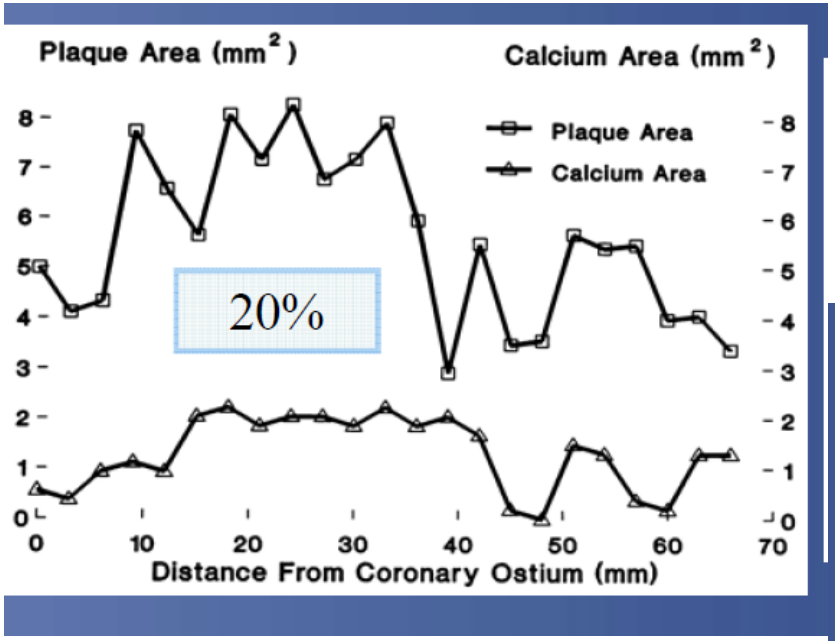
Assessment of ASCVD: Use of CAC

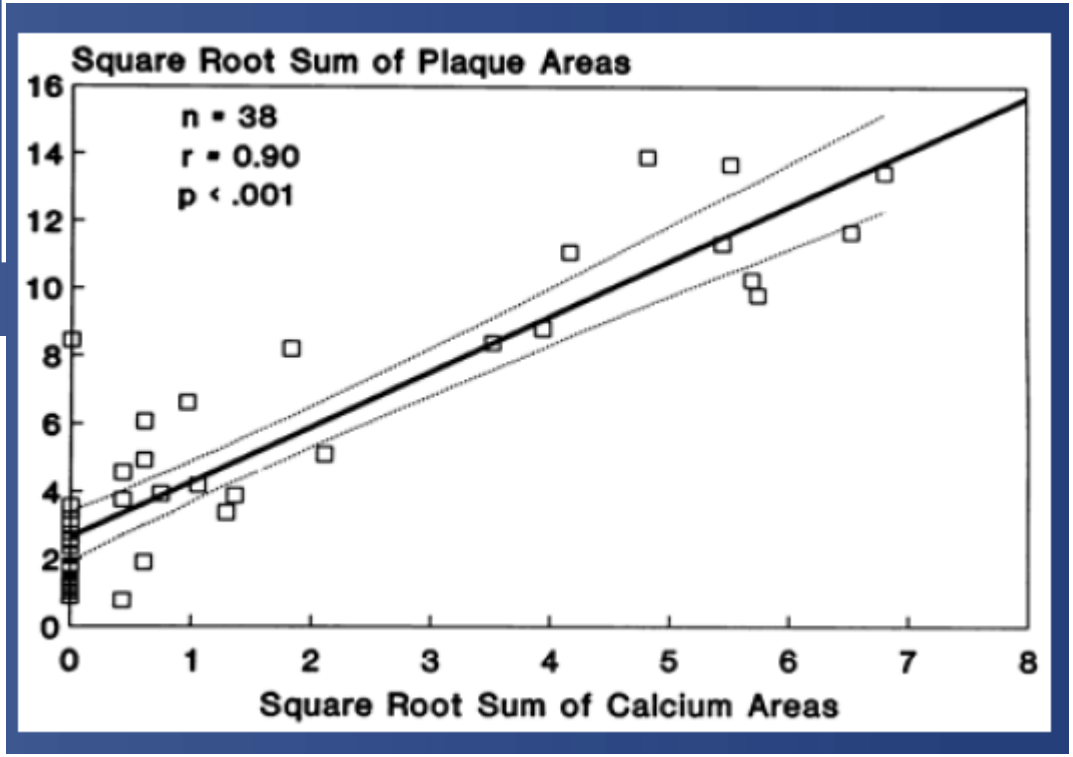
Coronary Artery Calcium (CAC) obtained by non-contrast cardiac CT

~1 mSv



Relationship of Calcification to Atherosclerotic Plaque Area



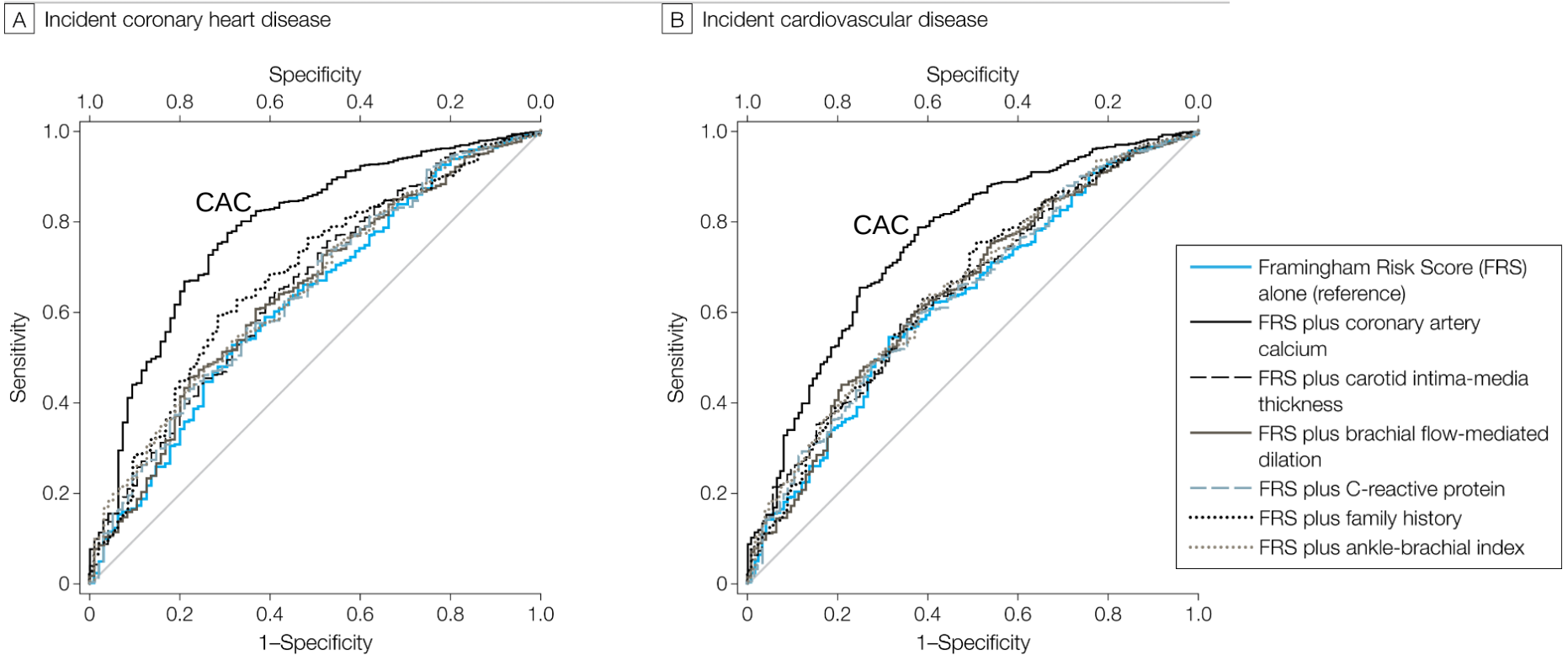


Rumberger, Circulation 1995

Comparison of Novel Risk Markers for Improvement in ASCVD Risk Assessment in Intermediate-Risk Individuals: MESA

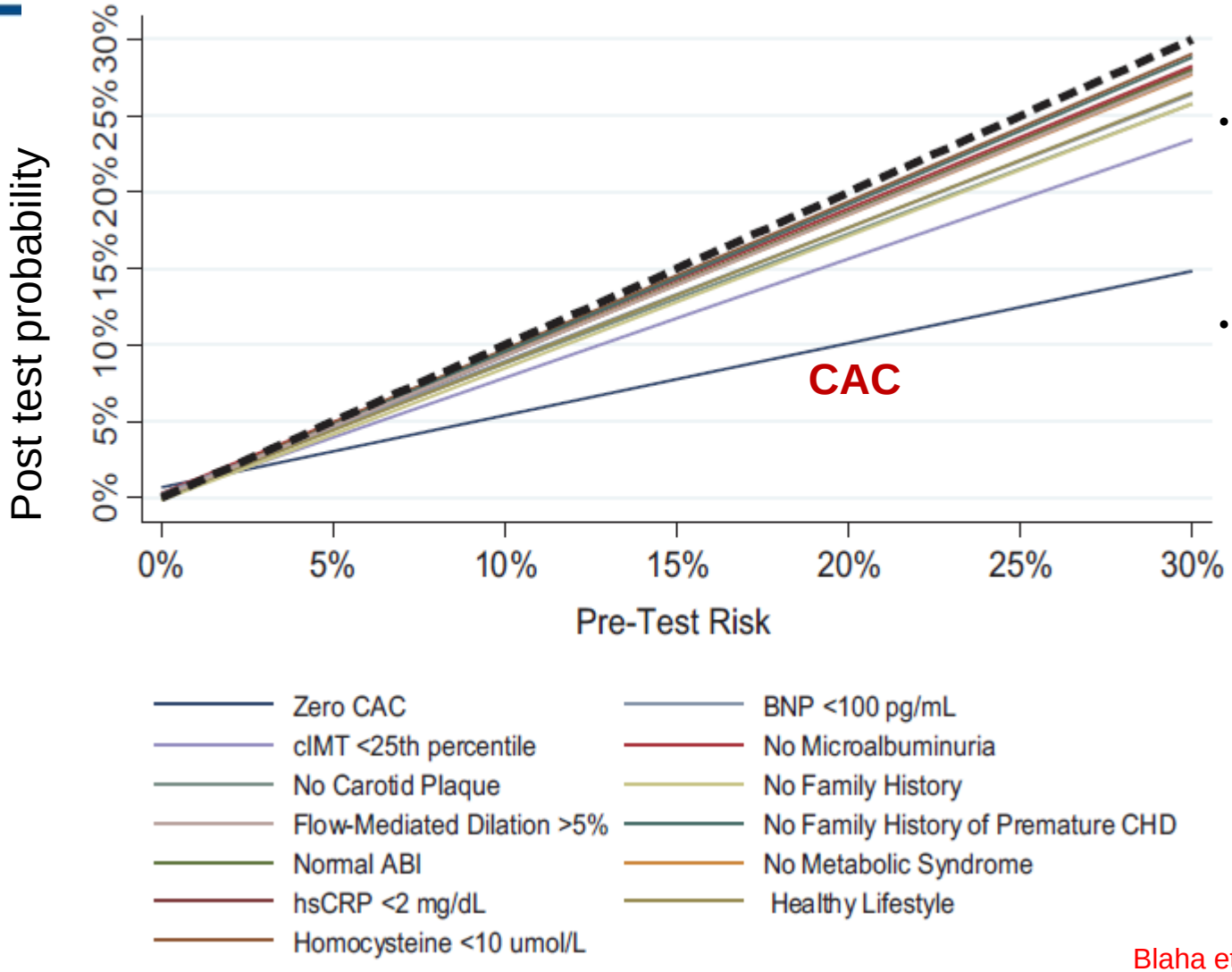
CHD

CVD



Yeboah J et al. JAMA. 2012;308(8):788-795.
doi:10.1001/jama.2012.9624

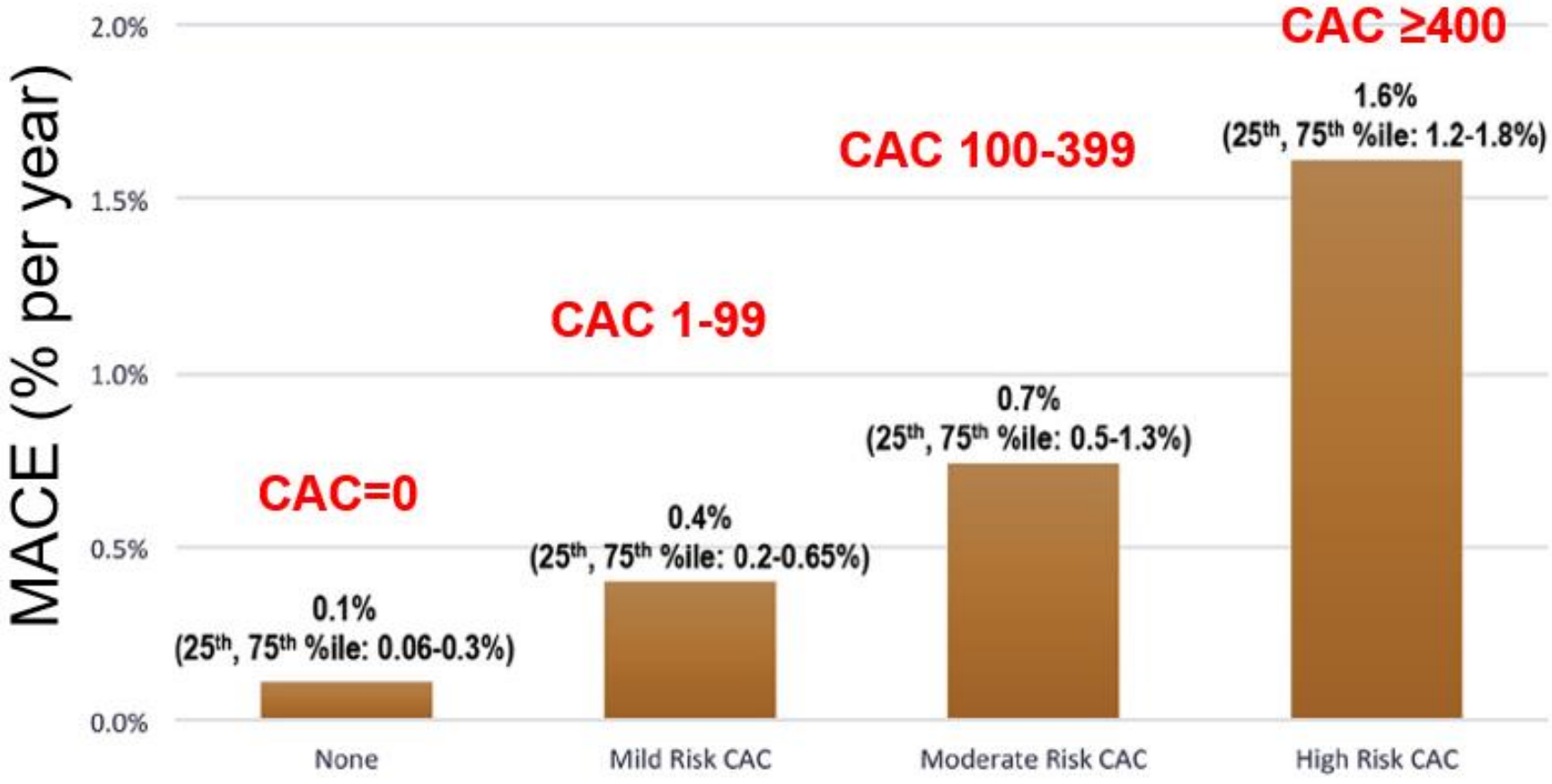
Negative Risk Markers for CVD: MESA



- CAC score of zero is the strongest "negative risk factor" for the development of ASCVD.
- **Imaging Hypothesis** – due to superior sensitivity, imaging tests for subclinical atherosclerosis are excellent at "ruling out" or "downgrading" risk estimates.

Blaha et al. Circulation 2016; 33:849-858

Major Adverse Cardiac Events by CAC scores: data from 7 registries

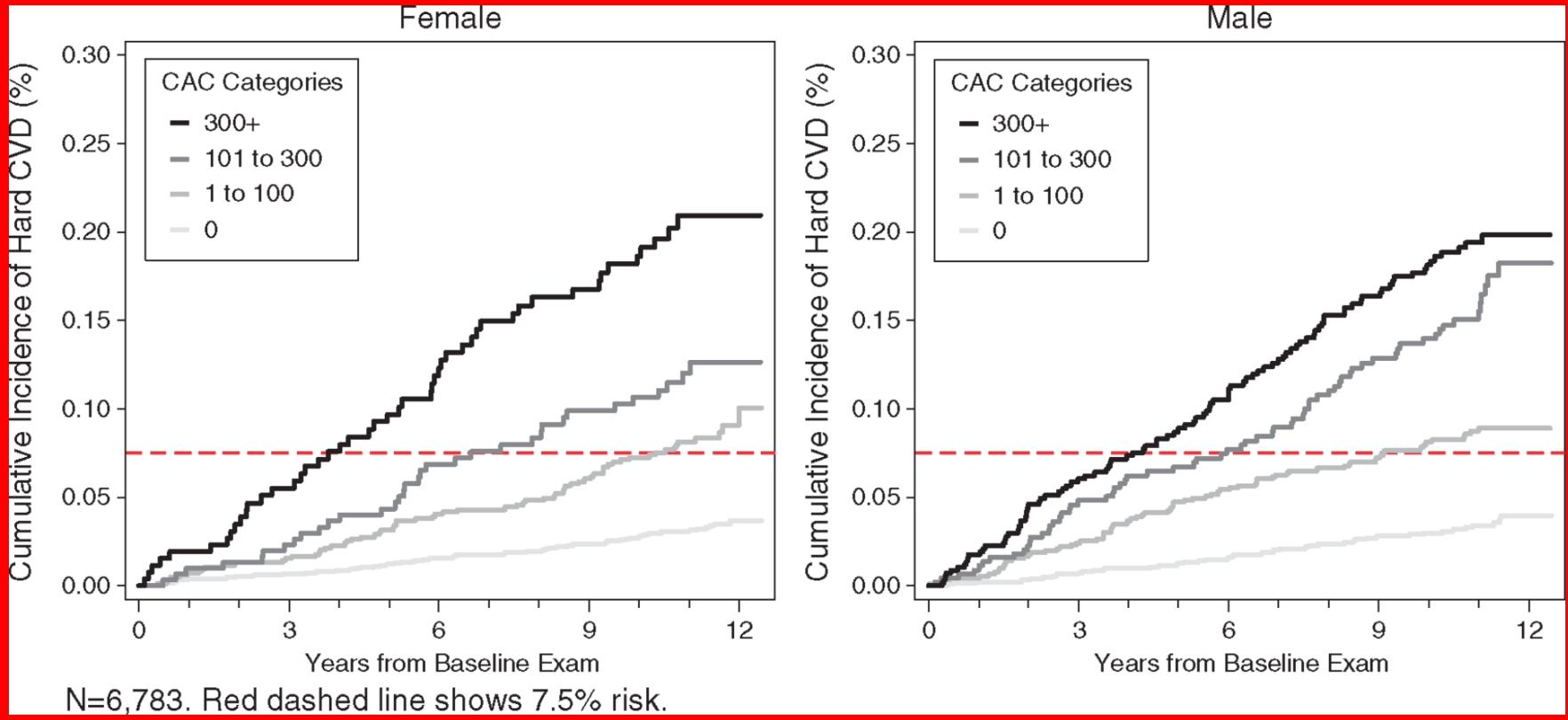


H. Hecht et al. / Journal of Cardiovascular Computed Tomography 11 (2017) 157–168

10-yr ASCVD risk by CAC Score:
Multi-Ethnic Study of Atherosclerosis by gender

Women

Men

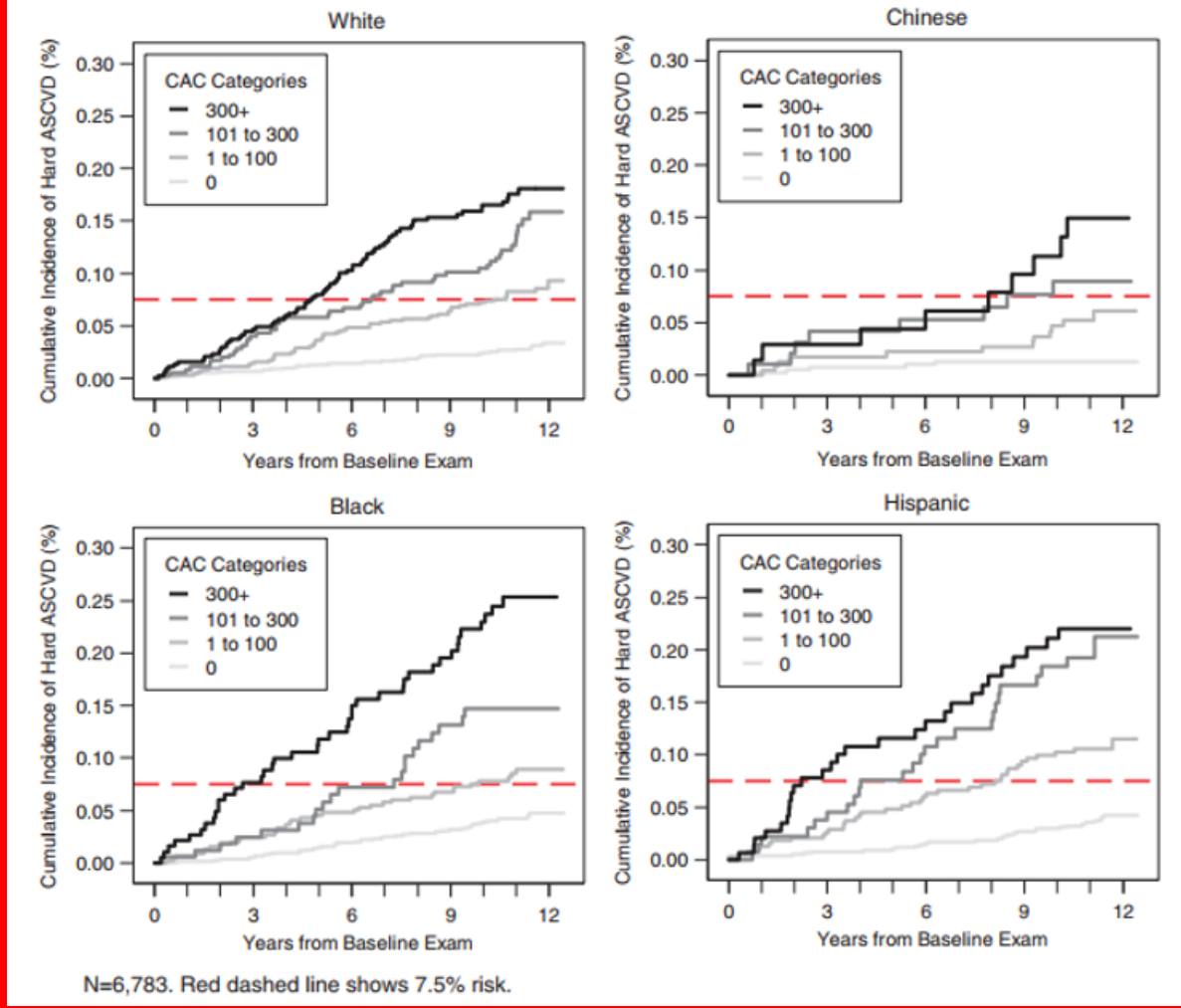


Budoff MJ…..**Michos ED**….et al. European Heart Journal (2018) 0, 1–10

10-yr ASCVD risk by CAC Score by race/ethnic groups

The Multi-Ethnic Study of Atherosclerosis (MESA)

- Whites
- Blacks
- Chinese
- Hispanics



Budoff MJ…..**Michos ED**….et al. European Heart Journal (2018)

10-yr ASCVD risk by CAC Score:

The Multi-Ethnic Study of Atherosclerosis (MESA)

By Age Groups

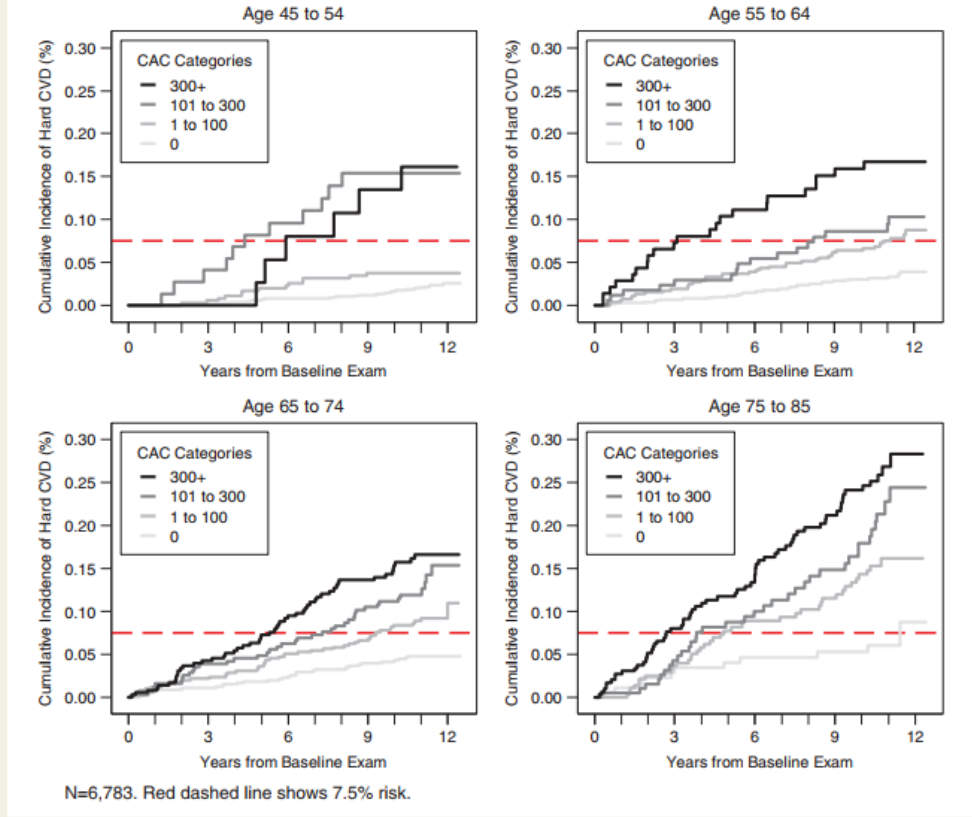


Figure 2 Unadjusted Kaplan–Meier cumulative incidence curves for hard atherosclerotic cardiovascular disease events by categories of coronary artery calcium and age. *n* = 6783. Red dashed line shows 7.5% risk.

Budoff MJ…..**Michos ED**….et al. European Heart Journal (2018)

"A man is as old as his coronaries…."

Syndenham 1689.

Are you really as old as your *Arteries*?

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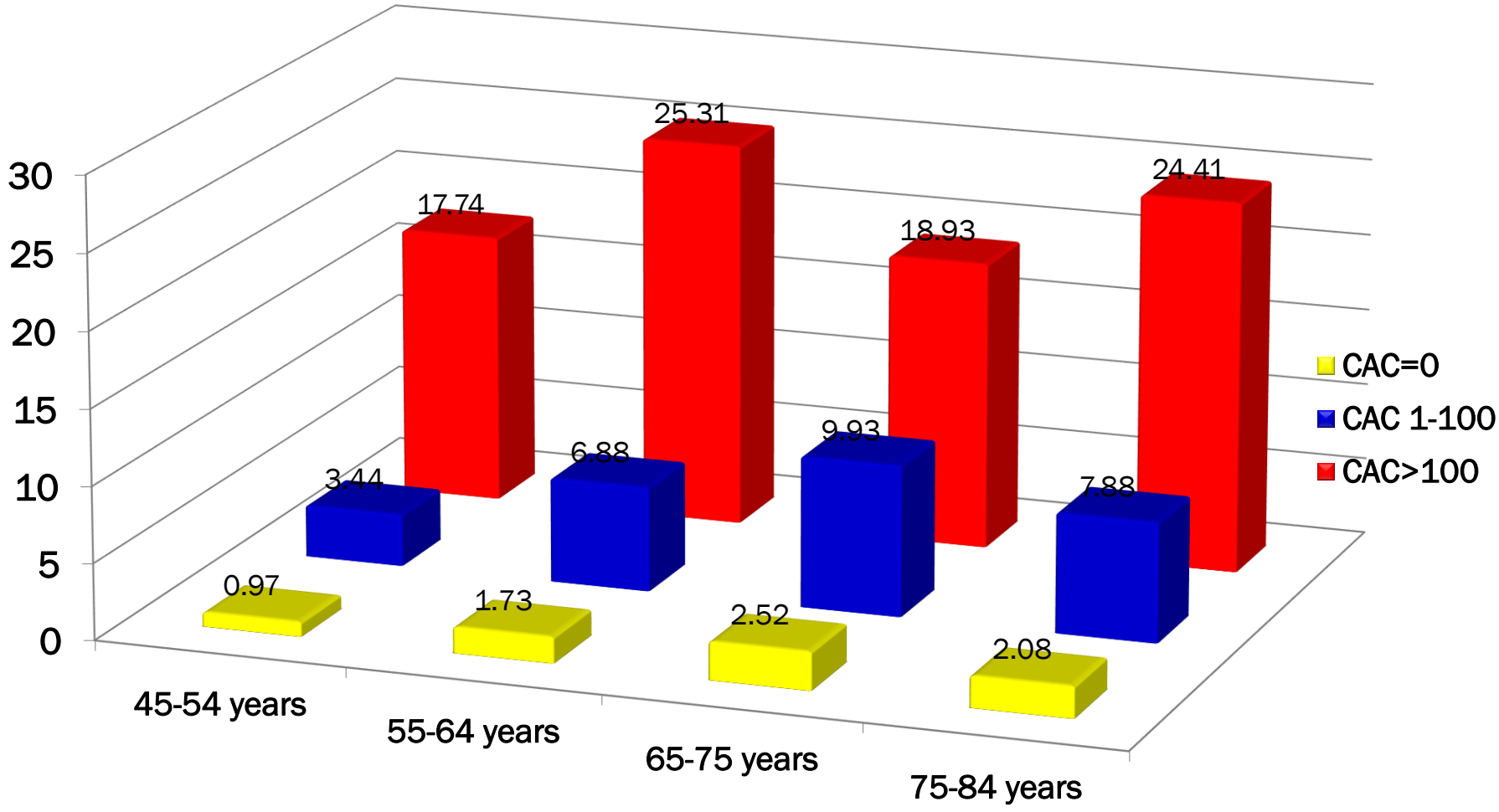
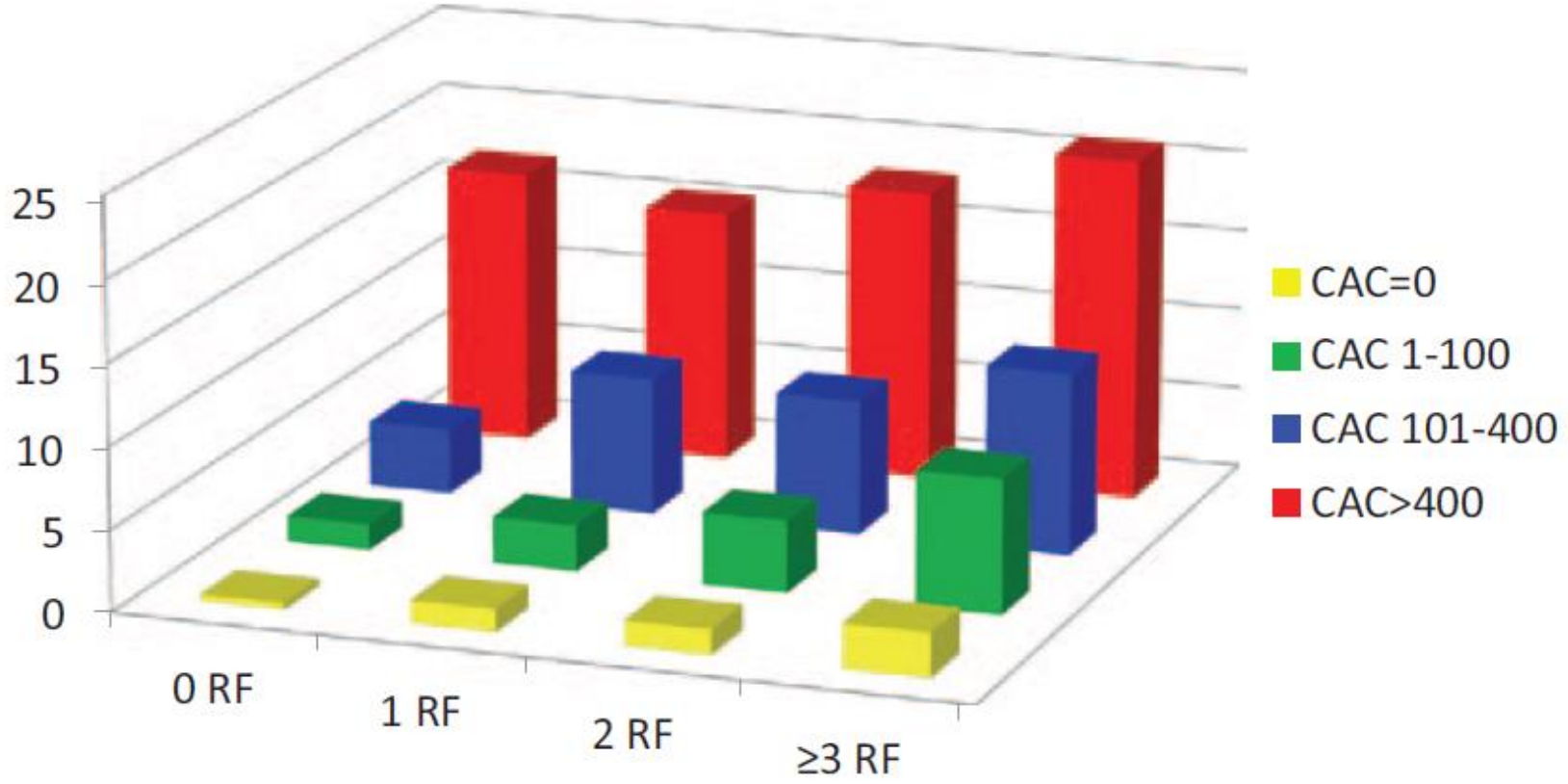
CHD events per 1000 person years (data from MESA)



Tota Maharaj R, Blaha MJ, Nasir K, et al. European Heart Journal. 2012.

All Cause Mortality (per 1000 person years)

Over 44,000 asymptomatic adults referred for CAC testing



Risk factors: smoking, dyslipidemia, diabetes, hypertension, family history of premature CHD

Nasir K, et al. ***Circ Cardiovasc Imaging***. 2012; 5:467-473.

CAC to guide discussion of statin initiation in primary prevention

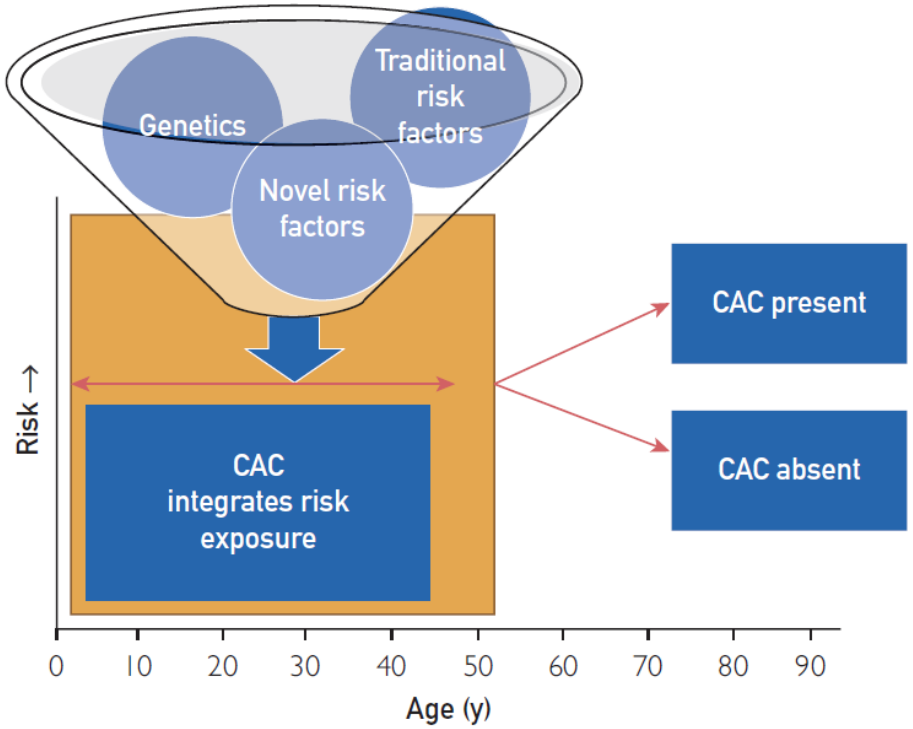


FIGURE 2. The coronary artery calcium (CAC) score integrates lifetime exposure of traditional and nontraditional risk factors for atherosclerotic cardiovascular disease.

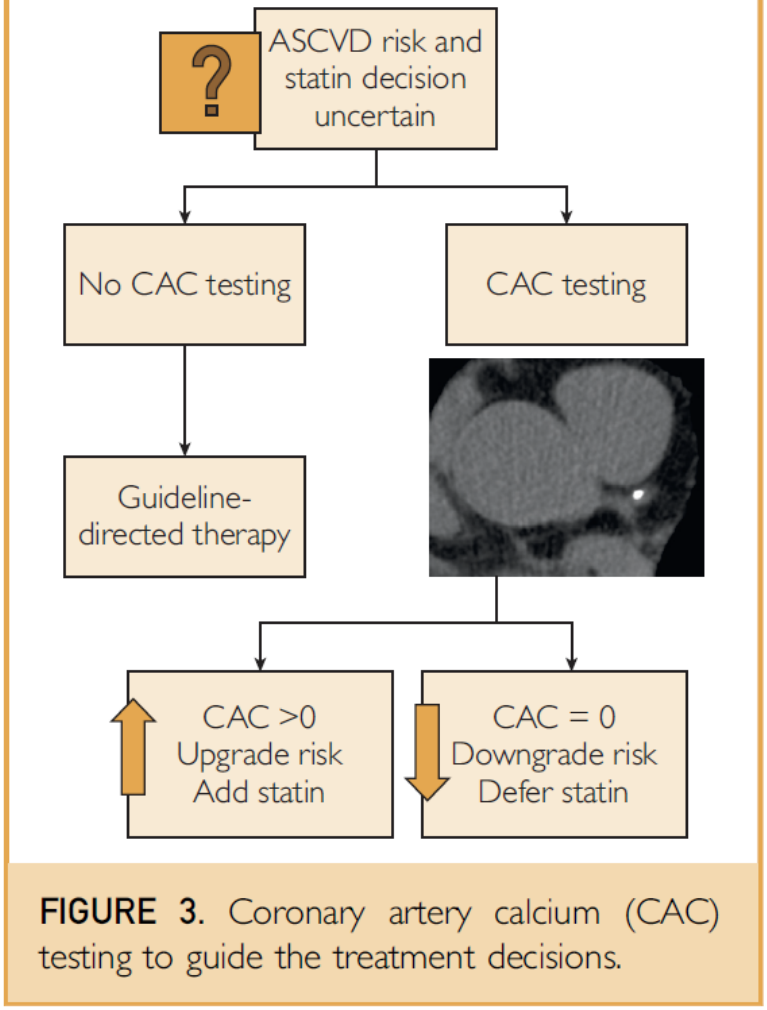


FIGURE 3. Coronary artery calcium (CAC) testing to guide the treatment decisions.

Michos ED et al. Mayo Clin Proc. 2017;92(12):1831-1841

Use of CAC=0 to "de-risk"

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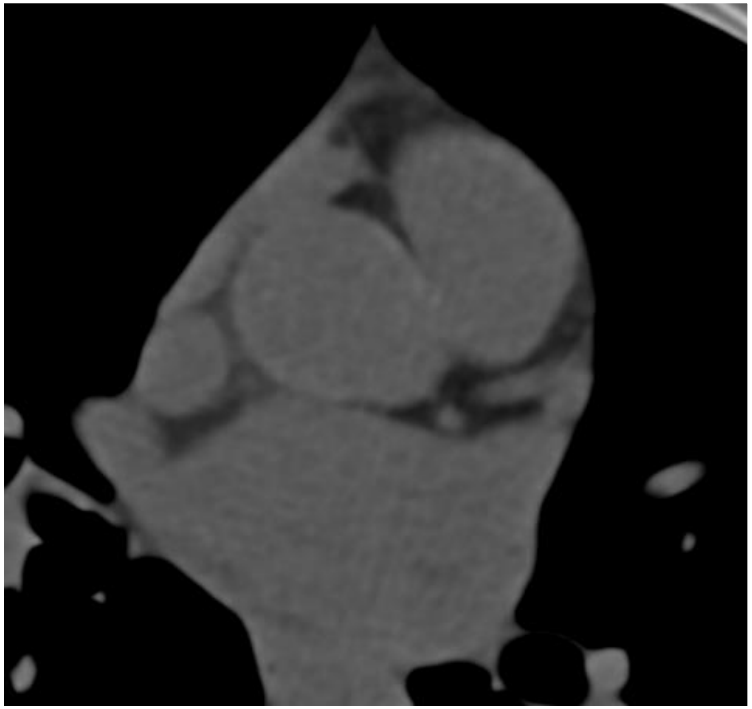
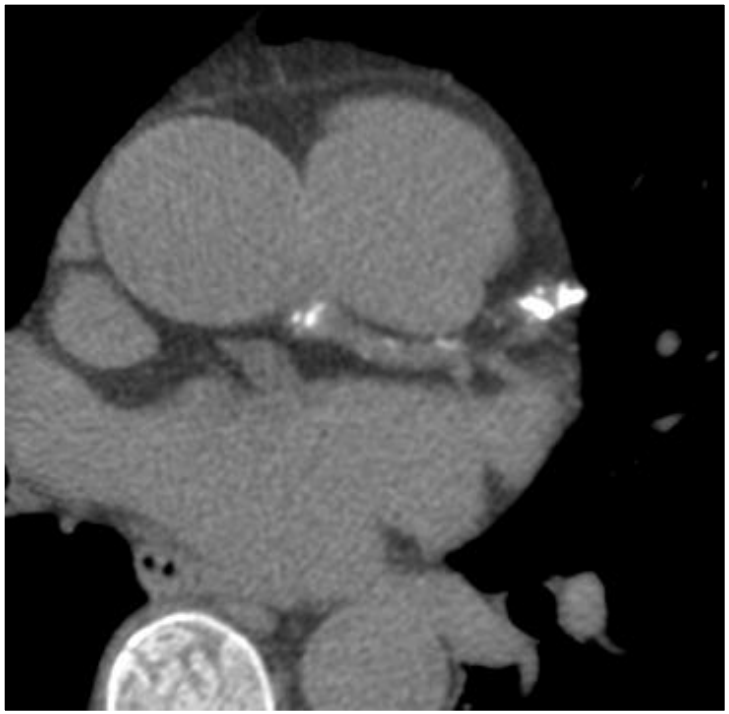
CAC = 0



NNT > 500

CAC = 242



NNT ~ 25

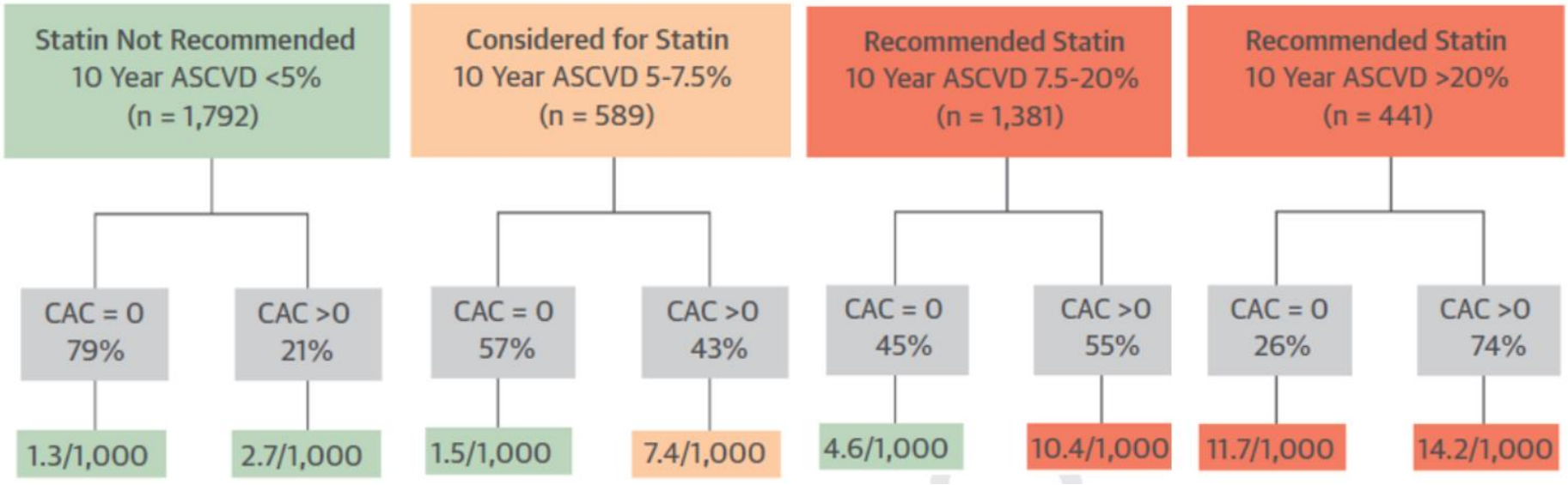
Bittencourt JACC 2014 (MESA)
Blaha LANCET 2011 (MESA)
Blankstein JACC 2011 (MESA)

Primary Prevention Adults 40 to 75 Yrs With LDL-C 70-189

Impact of CAC Results		
COR	**LOE**	**Recommendations**
IIa	**B-NR**	**In intermediate-risk adults or selected borderline-risk adults & CAC measured for making Rx decision:** • **If CAC=0 → reasonable to withhold statin & reassess in 5 -10 yrs, as long as higher risk conditions are absent (i.e. Familial Hypercholesterolemia, Diabetes, Family h/o premature CHD, smoking)** • **If CAC = 1 – 99 or > 75% → reasonable to initiate statin** • **If CAC ≥100 → initiate statin**

Impact of CAC on Baseline Risk and Statin Eligibility

Why? CAC in Borderline and Intermediate Risk Groups

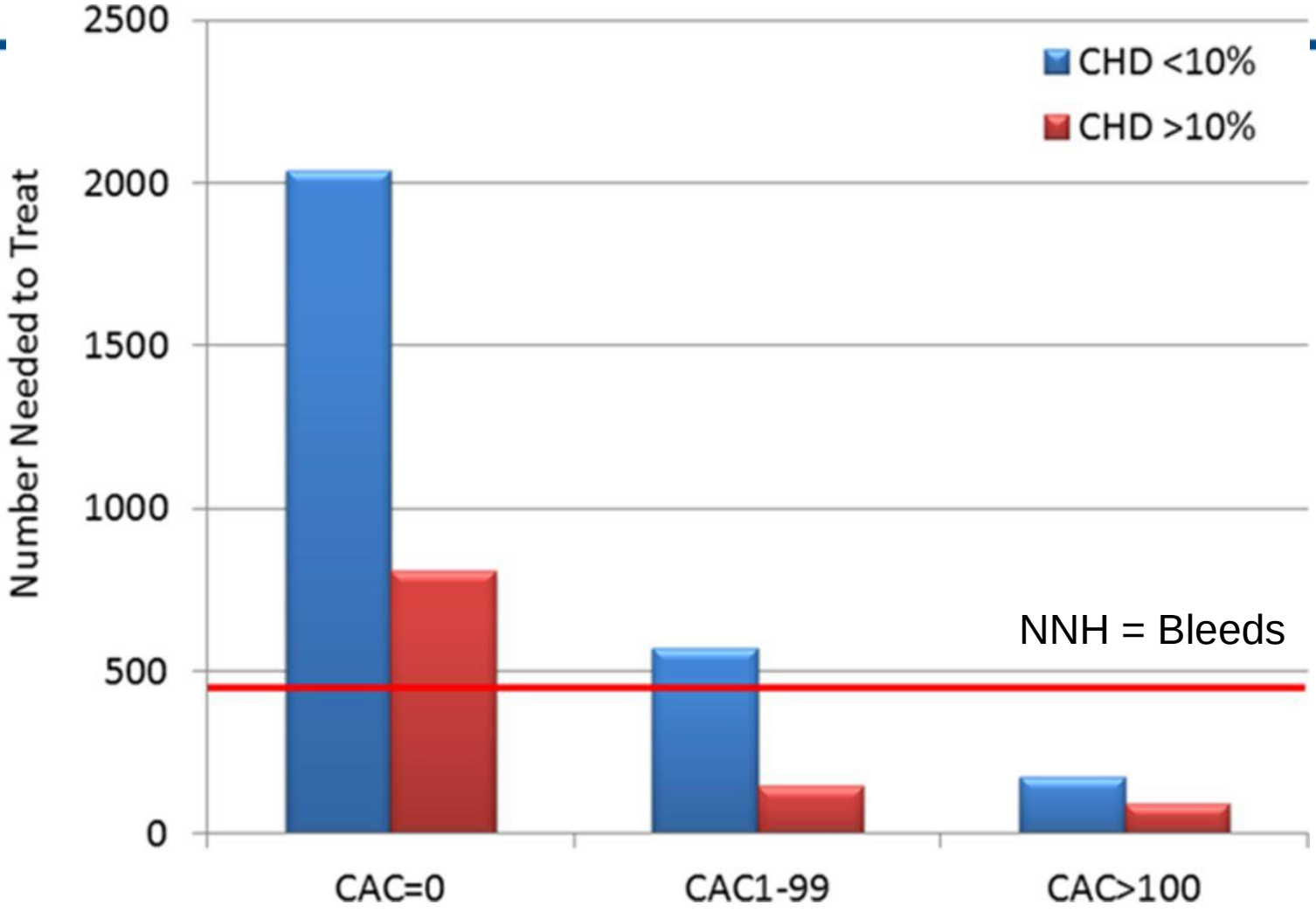


CENTRAL ILLUSTRATION **Impact of the Absence of CAC in Reclassifying Risk Below the Threshold for Statin Consideration Suggested by ACC/AHA Cholesterol Management Guidelines Across the Spectrum of Estimated 10-Year ASCVD Risk Score (Nondiabetic Patients with LDL-C of 70 to 189 mg/dl)**

Datasource: MESA

Nasir K et al. JACC 2015

Can CAC inform Aspirin Decision? (modelling from MESA)



Michael D. Miedema et al. Circ Cardiovasc Qual Outcomes. 2014;7:453-460

2019 ACC/AHA Primary Prevention Guideline

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Updated 2019 recs for aspirin in the primary prevention of ASCVD

Recommendations for Aspirin Use		
COR	**LOE**	**Recommendations**
IIb	A	1. Low-dose aspirin (75-100 mg orally daily) might be considered for the primary prevention of ASCVD among select adults 40 to 70 years of age who are at higher ASCVD risk but not at increased bleeding risk.
III: Harm	B-R	2. Low-dose aspirin (75-100 mg orally daily) should not be administered on a routine basis for the primary prevention of ASCVD among adults >70 years of age.
III: Harm	C-LD	3. Low-dose aspirin (75-100 mg orally daily) should not be administered for the primary prevention of ASCVD among adults of any age who are at increased risk of bleeding.

Arnett D, Blumenthal RS,….Michos ED.. et al. Circulation 2019

How to Use CAC to Guide Pharmacotherapy for ASCVD 5-20% risk

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Score	Treatment Recommendations
0	Statin not recommended (excludes FH)
1-99	Moderate intensity statin if <75th %tile Moderate to high intensity if >75th %tile
100-299	Moderate to high intensity statin + ASA 81 mg
>300	High intensity statin + ASA 81 mg

Clinical indications for coronary artery calcium scoring in asymptomatic patients: Expert consensus statement from the Society of Cardiovascular Computed Tomography

H. Hecht et al. / Journal of Cardiovascular Computed Tomography 11 (2017) 157–168

@ErinMichos

CASE Patient: Mr. J
MOC QUESTION - ANSWER

Which of the following is appropriate at this time?

a) Aspirin therapy for primary ASCVD prevention

b) Consider statin therapy because 10-year ASCVD risk is ≥7.5%

c) Engage in shared decision making discussion with patient about his concerns, values, preferences

d) Additional testing may be considered to inform treatment decisions

e) b, c, d

RESPONSE

- His ASCVD risk was 9.5%. Age 65. No other risk factors. 2019 ACC/AHA Guidelines give Aspirin a IIB indication for ages 40-70. Likely not indicated for most adults.
- 2018 ACC/AHA Lipid Guidelines indicate that an ASCVD risk ≥7.5% is a “statin benefit” group, and a moderate intensity statin should be considered (Class I recommendation, for ages 40-75).
- This decision should be made as part of a Clinician-Patient Risk Discussion (IIa recommendation) and if risk is uncertain, additional testing such as CAC can be considered (IIa recommendation)

CASE Patient: Mr. J

Case patient: Mr. J is somewhat reluctant to take a statin

- **Worried about muscle pains affecting his running**
- **Doesn't understand why he has to take a statin if his cholesterol is "good"**
- **Desires more information to refine his risk** → CAC

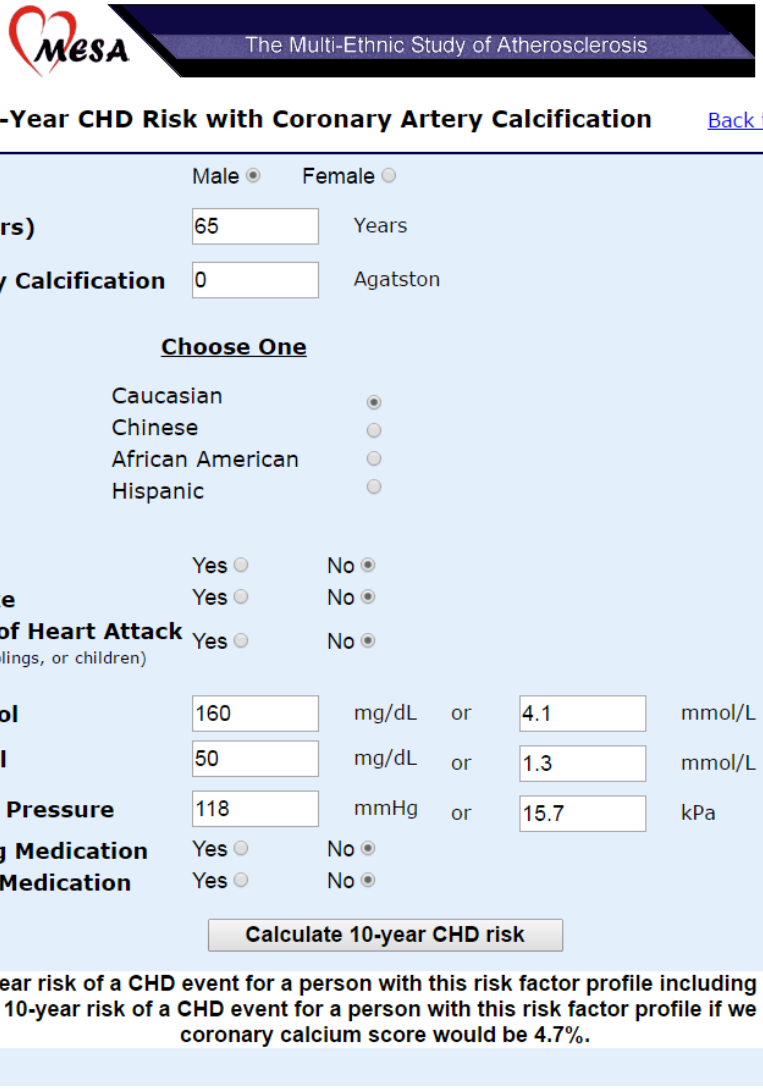
Quantifying the Utility of Taking Pills for Cardiovascular Prevention

Robert Hutchins, MD, MPH; Anthony J. Viera, MD, MPH; Stacey L. Sheridan, MD, MPH; Michael P. Pignone, MD, MPH

A survey found that more than 8% of people were willing to trade as much as two years of life to avoid taking daily medication for ASCVD, while roughly 21% would trade between one week and a year of their lives

Hutchins R et al. Circ Cardiovasc Qual Outcomes. 2015;8:155-163.

CASE Patient: Mr J
MESA CHD Risk Score if CAC=0



1.9% 10-yr CHD Risk

CASE Patient: Mr. J

- Mr. J's CAC score came back 0, which placed him at <25th age/sex/race percentile.
- Using the MESA CHD risk score incorporating his risk factors and CAC score, his estimated 10-year risk for CHD events would only be 1.9%.
- Mr. J decided that he wishes to defer statin therapy for now and continue to follow his heart-healthy lifestyle.
- A repeat CAC scan might be considered in ~5 years if still statin-reluctant.

Limitations CAC Testing

- **Radiation**
  - ~1 mSv – about same as bilateral mammogram
  - Lower than annual background radiation in US
- **Incidental findings**
  - pulmonary nodules in 4-8%, may need repeat testing to document stability
- **Downstream testing**
  - CAC should not trigger stress test/angiography referral
- **CAC progression**
  - rescan not usually indicated for those with CAC>0
- **Lack of RCT for CAC-guided therapy**
  - ROBINSCA (Netherlands: CAC vs RF screening)
  - No RCT for ASCVD risk scores either!

Top 7 Indications for CAC Testing (primary prevention)

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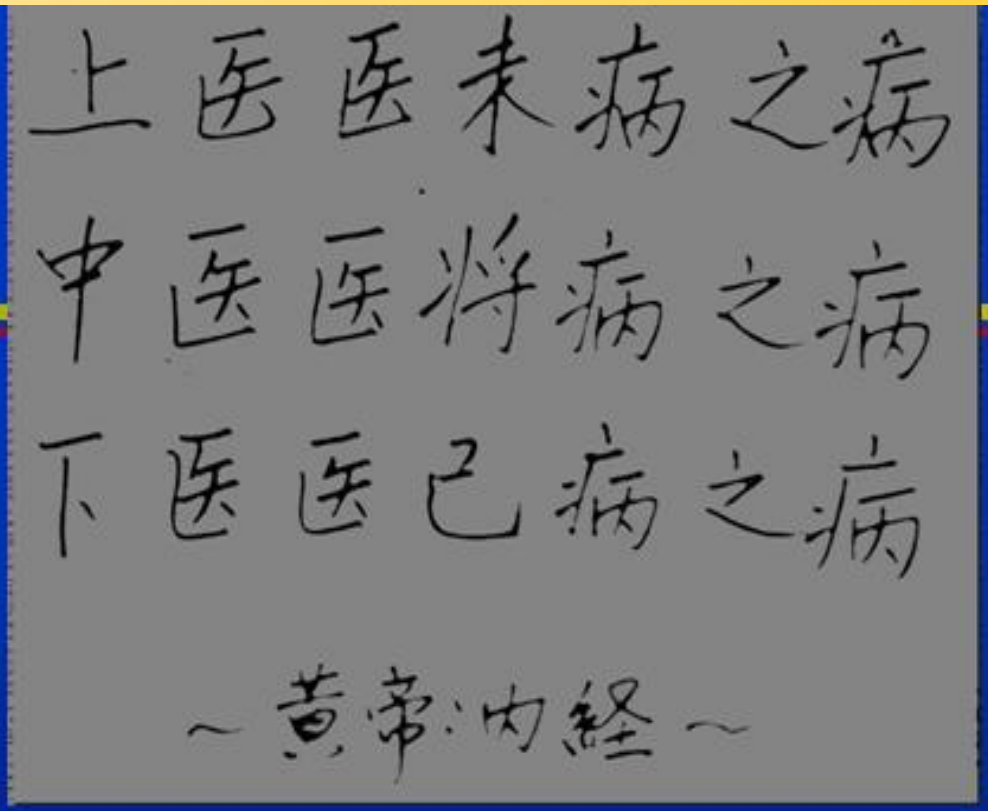
1. "Intermediate" Risk Patient
   - ASCVD 5-20%, Risk Uncertain
   - Family History, low risk diabetes
2. Statin Reluctant Pt
3. Statin Intolerant Pt
4. Decisions for Non-Statin Rx
5. Decisions For Aspirin Rx
6. Low Risk Chest Pain Syndrome
7. MOTIVATION!



Superior doctors prevent the disease.
Mediocre doctors treat the disease
before evident. **Subclinical Atherosclerosis**
Inferior doctors treat the full-blown disease.
--Huang Dee: Nai-Ching
(2600 BC First Chinese Medical Text)

2019 ACC/AHA Primary Prevention Guideline

JOHNS HOPKINS MEDICINE

Assessment of ASCVD Risk: Conclusions

1. Adults age 40 to 75 years of age should undergo **10-year ASCVD risk estimation by PCE**
2. Engage in **Clinician–Patient Risk Discussion** before starting on pharmacological therapy, such as antihypertensive therapy, a statin, or aspirin.
3. Presence or absence of additional **risk-enhancing factors** can help guide decisions about preventive interventions
4. If clinical uncertainty or patient indecision remain, consider **CAC** measurement in intermediate (7.5% - 19.9%) and **selected borderline (5 - 7.4%) risk patients**

2019 ACC/AHA Primary Prevention Guideline

Assessment of ASCVD Risk: Conclusions

1. Adults age 40 to 75 years of age should undergo **10-year ASCVD r** **y PCE**
2. Engage i **nt Risk Discussion** before starting o therapy, such as antihyper statin, or aspirin.
3. Presence or absence of additional **risk-enhancing factors** can help bout preventive interventions
4. If clinical ent indecision remain, consider **CAC** mea mediate (7.5% - 19.9%) and **selected** **4%) risk patients**

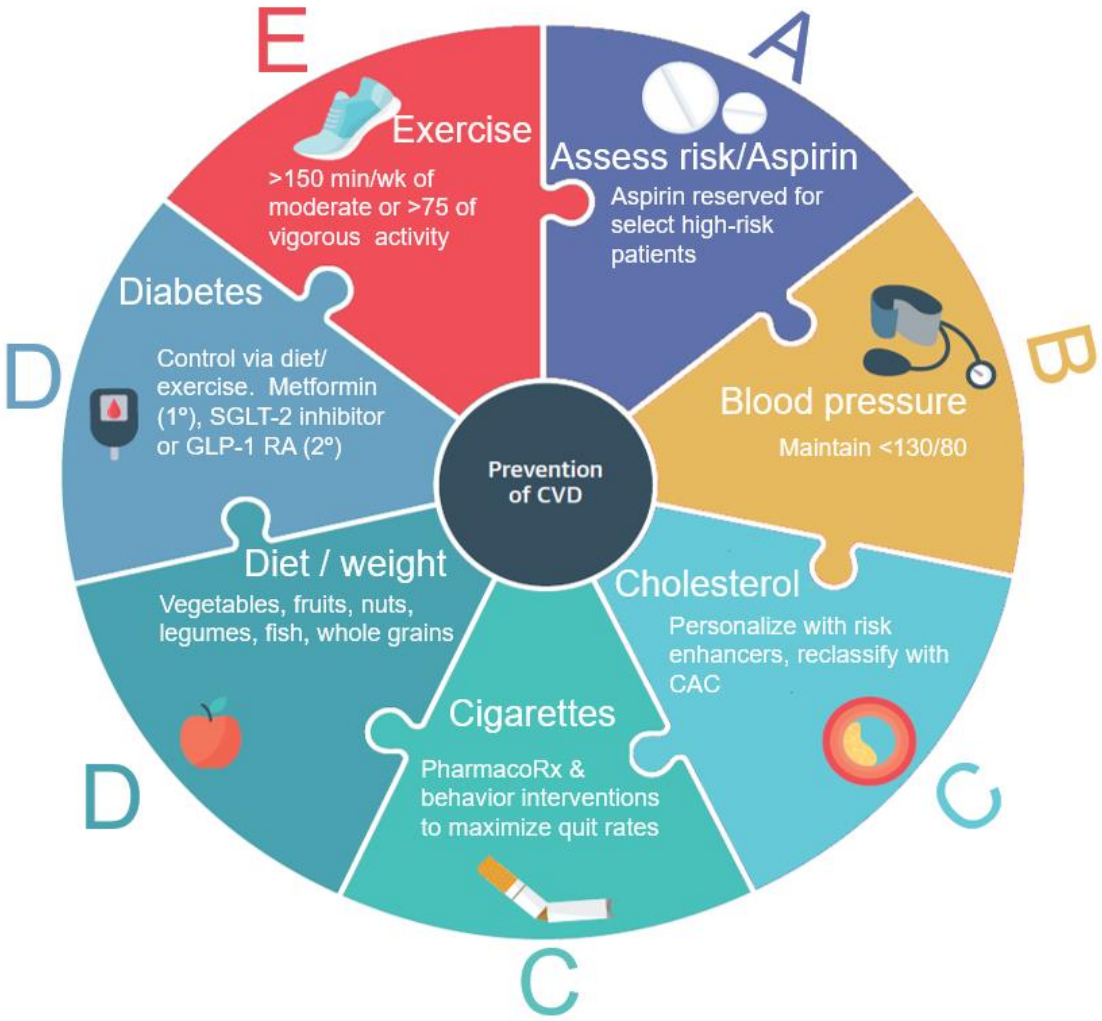
Estimate

Personalize

Reclassify

Shared Decision Making

ABCDE's of Prevention



Arnett DK, Blumenthal RS,….Michos ED…et al. Circulation 2019

Thanks! Questions??