What’s the next best test - in the asymptomatic patient?

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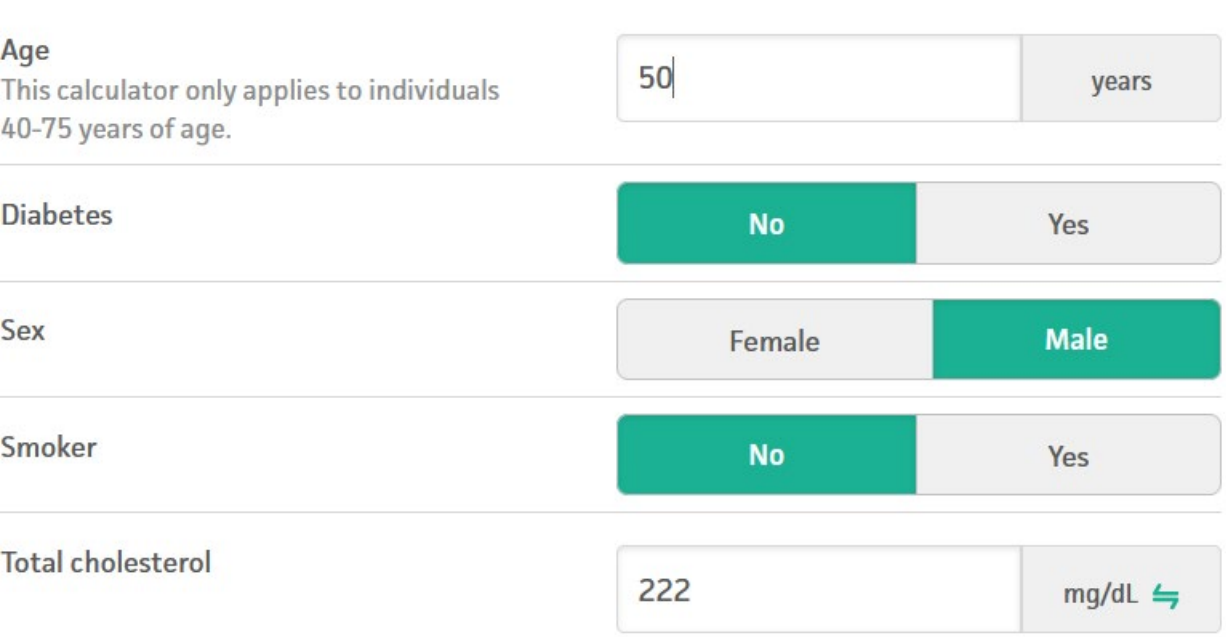
The asymptomatic patient – quantifying risk

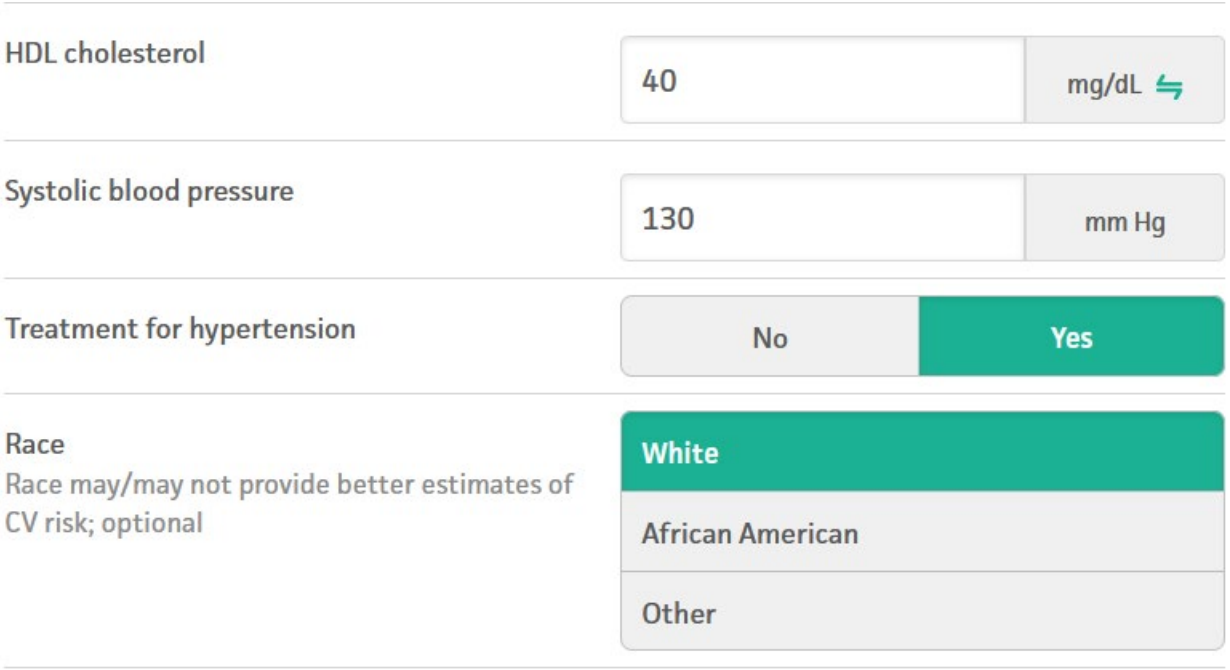
- Why it matters
- + early identification enables preventative strategies or helps guide intensity of interventions.
- + informs shared decision making on statins, aspirin, BP control and lifestyle intervention

Clinical decision framework based on risk in the asymptomatic patient

Risk Category	Suggested Approach
<5% (Low)	Lifestyle counseling
5–7.4% (Borderline)	Consider CAC if uncertain about statins
7.5–19.9% (Intermediate)	Favor statin; discuss intensifying lifestyle changes
≥20% (High)	Strong statin indication; aggressive risk reduction

The asymptomatic patient – quantifying risk





The asymptomatic patient – quantifying risk

Age
This calculator only applies to individuals 40-75 years of age.
50 years

Diabetes
No | Yes

Sex
Female | Male

Smoker
No | Yes

Total cholesterol
222 mg/dL ⇋

HDL cholesterol
40 mg/dL ⇋

Systolic blood pressure
130 mm Hg

Treatment for hypertension
No | Yes

Race
Race may/may not provide better estimates of CV risk; optional
White | African American | Other

Moderate-intensity statin recommended because of 10-year risk between 5-7.5%.

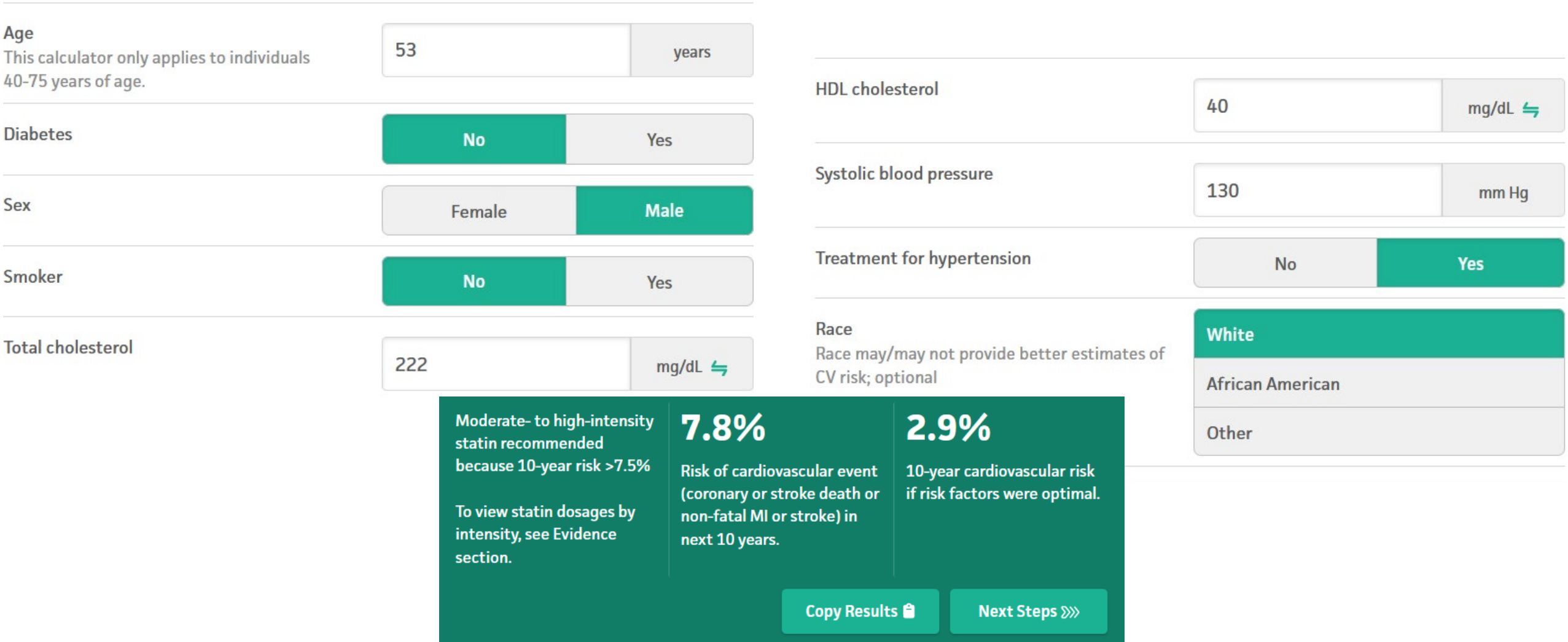
To view statin dosages by intensity, see Evidence section.

6.1%
Risk of cardiovascular event (coronary or stroke death or non-fatal MI or stroke) in next 10 years.

2.1%
10-year cardiovascular risk if risk factors were optimal.

Copy Results | Next Steps »

The asymptomatic patient – quantifying risk



The asymptomatic patient – understanding risk

- Based on the pooled cohort equation (PCE).

$$Risk = 1 - S_0(t)^{\exp(\Sigma\beta X - MeanRisk)}$$

The asymptomatic patient – understanding risk

$$Risk = 1 - S_o(t)^{\exp(\Sigma \beta X - MeanRisk)}$$

The BETA coefficients are the weight or influence each variable has in he model

For a white male the beta coefficients are:

Variable	β Coefficient
ln(Age)	12.344
ln(Total Cholesterol)	11.853
ln(HDL Cholesterol)	−7.990
ln(Age) × ln(Total Cholesterol)	−2.664
ln(Age) × ln(HDL)	1.769
ln(Systolic BP, untreated)	1.764
ln(Systolic BP, treated)	1.797
Smoking Status (yes)	7.837
ln(Age) × Smoker	−1.795
Diabetes Status (yes)	0.658

$$Risk = 1 - S_0(t)^{\exp(\Sigma \beta X - MeanRisk)}$$

Obvious limitations

Characteristic	Patient A	Patient B
Age	42 years	65 years
Sex	Male	Male
Race	White	White
Total Cholesterol	200 mg/dL	200 mg/dL
HDL Cholesterol	50 mg/dL	50 mg/dL
Systolic BP	120 mmHg (untreated)	120 mmHg (untreated)
Smoker	No	No
Diabetes	No	No
10-Year ASCVD Risk	**~2–3%**	**~15–20%**

Obvious limitations

Characteristic	Patient A	Patient B
Age	42 years	65 years
Sex	Male	Male
Race	White	White
Physical Activity	Sedentary	Regular exercise
Diet	High in saturated fats	Mediterranean-style
BMI	31 *(obese)*	24 *(healthy weight)*
Smoker	No	No
Diabetes	No	No
10-Year ASCVD Risk	**~2–3%**	**~15–20%**

What tests can we order to help stratify the risk?

- Coronary artery calcium (CAC) – direct measurement of calcific plaque burden on computed tomography (CT).
- High sensitivity CRP (hs-CRP) – systemic inflammation
- Anke Brachial index (ABI) – Peripheral artery disease
- Lipoprotein (a) – genetic atherogenic lipoprotein
- Apolipoprotein B (ApoB) – total number of atherogenic particles

Coronary artery calcium score

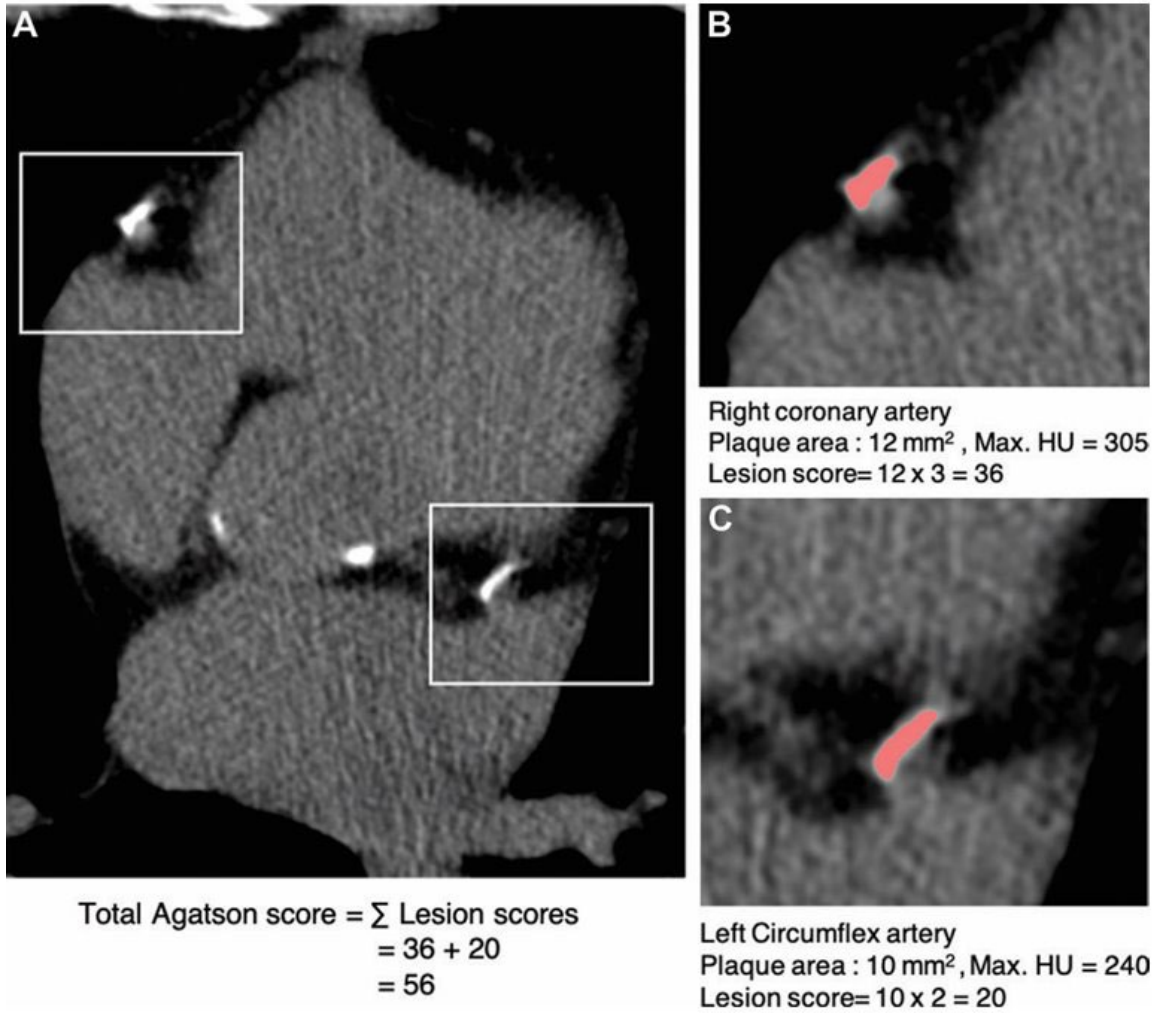


Figure 3. Agatson CAC score calculation in a 53-year-old man. After CT scan acquisition, the coronary artery calcifications (square outlines in **A**, red areas in **B** and **C**) are segmented by using a semiautomatic method in the vendor-provided software. The software also provides plaque area and maximal plaque attenuation values, which when multiplied by the attenuation weighting factor yield the calcium score for the plaque. The individual scores of all the coronary plaques are then added and reported as a single number (56 in this example).

Back to MESA CAC

Input your age, select your gender and race/ethnicity, input (optionally) your observed calcium score and click "Calculate".

Age (45-84):

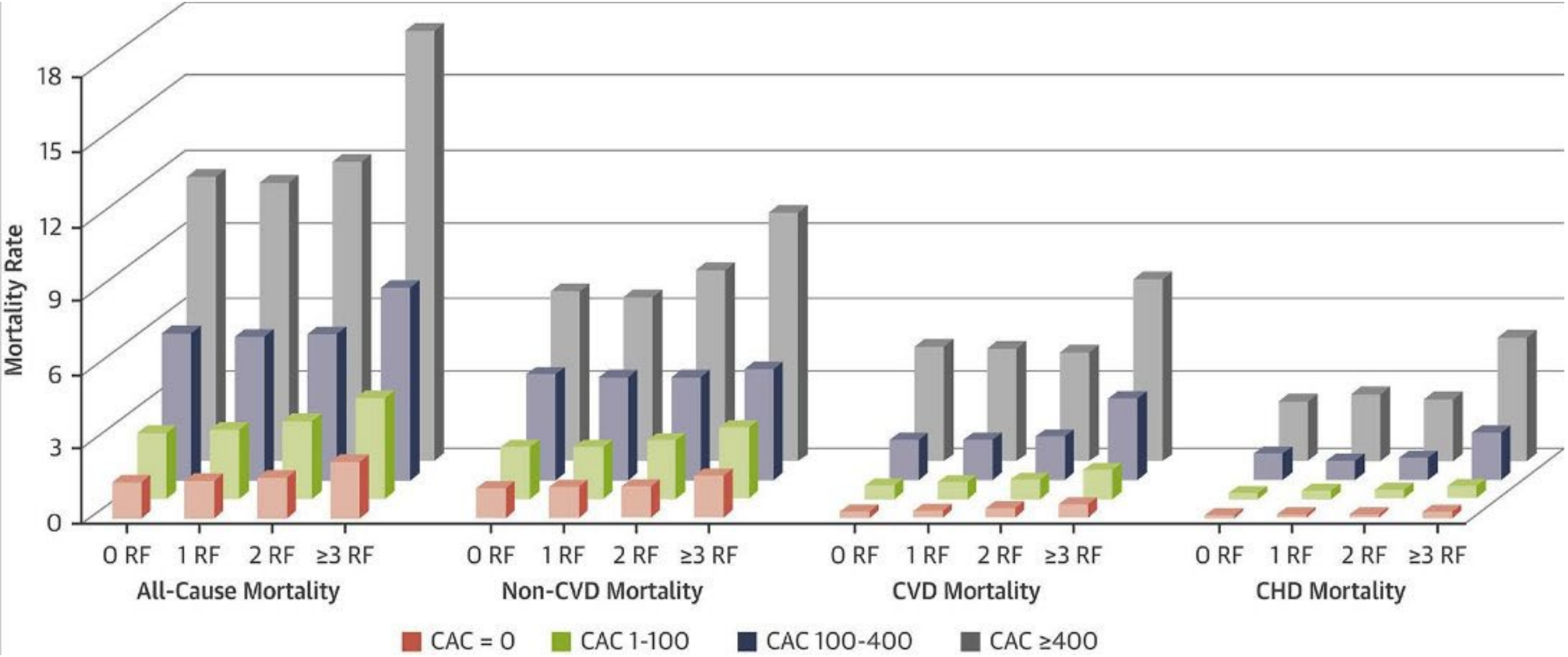
Gender: female

Race/Ethnicity: chinese

Observed Agatston Calcium Score (optional):

Calculate

The simple truth is risk scores miss patients with CAC



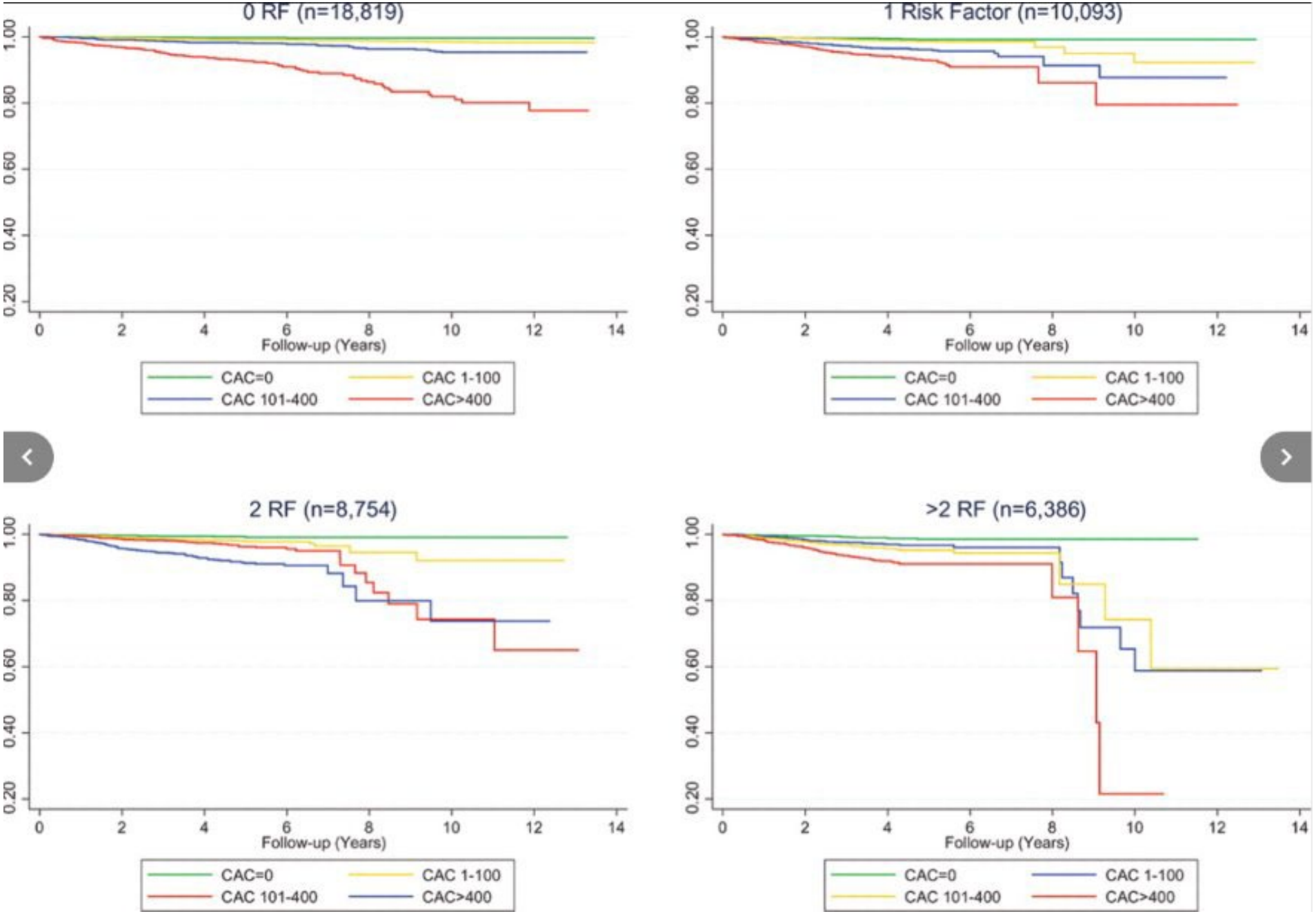
How about a combo risk score? – The power of addition

MESA 10-Year CHD Risk with Coronary Artery Calcification

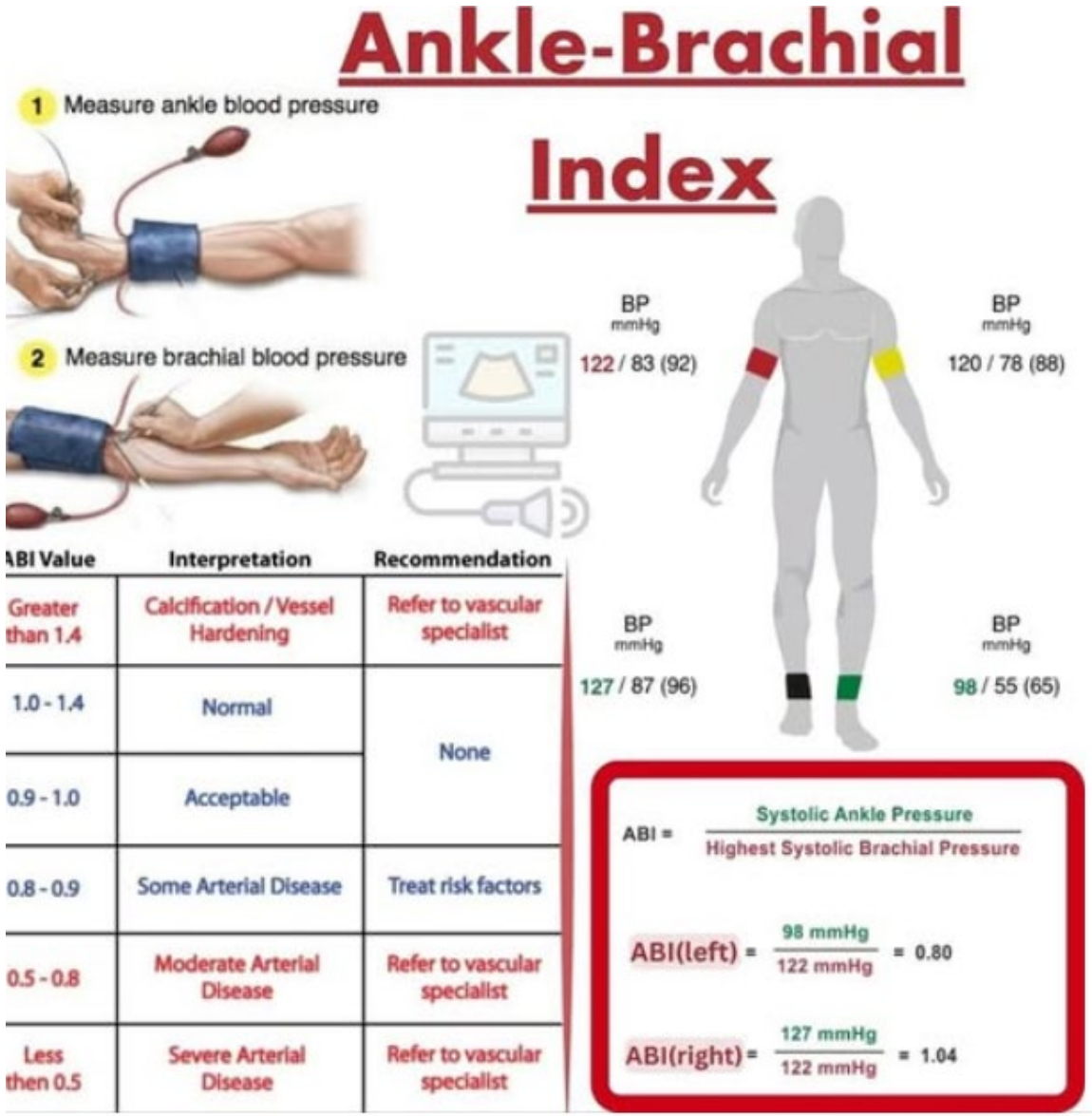
1. Gender	Male ◉	Female ○			
2. Age (45-85 years)	65	Years			
3. Coronary Artery Calcification	0	Agatston			
4. Race/Ethnicity	Caucasian				
5. Diabetes	Yes ○	No ◉			
6. Currently Smoke	Yes ○	No ◉			
7. Family History of Heart Attack (History in parents, siblings, or children)	Yes ○	No ◉			
8. Total Cholesterol	200	mg/dL	or	5.2	mmol/L
9. HDL Cholesterol	50	mg/dL	or	1.3	mmol/L
10. Systolic Blood Pressure	120	mmHg	or	16.0	kPa
11. Lipid Lowering Medication	Yes ○	No ◉			
12. Hypertension Medication	Yes ○	No ◉			

Using the Coronary Artery Calcium Score

10 Year risk of a CHD Event	Coronary Age	Difference from Chronologic Age
2.2%	36	-29


0 RF (n=18,819)
1 Risk Factor (n=10,093)
2 RF (n=8,754)
>2 RF (n=6,386)
1.00
0.80
0.60
0.40
0.20
0
2
4
6
8
10
12
14
Follow-up (Years)
Follow up (Years)
CAC=0
CAC 1-100
CAC 101-400
CAC>400

Other tests - ABI



ABI = (Ankle Systolic BP) / (Brachial Systolic BP)

Normal range: **1.0–1.4**

<0.9 suggests **peripheral artery disease (PAD)**

>1.4 may indicate **non-compressible arteries**, often due to medial calcification (e.g., in diabetes or CKD)

Benefits of ABI

- Improves risk stratification/prognostic: ABI < 0.9 associated with 2-4x increased risk of MI, CVA and CV mortality. Can reclassify borderline ASCVD patients
- Non-invasive not expensive. With proper tools and training can be performed in office in <15 minutes
- Especially useful in special populations: diabetic patients, smokers, older adults, in patients in whom peripheral arterial disease (PAD) is suspected

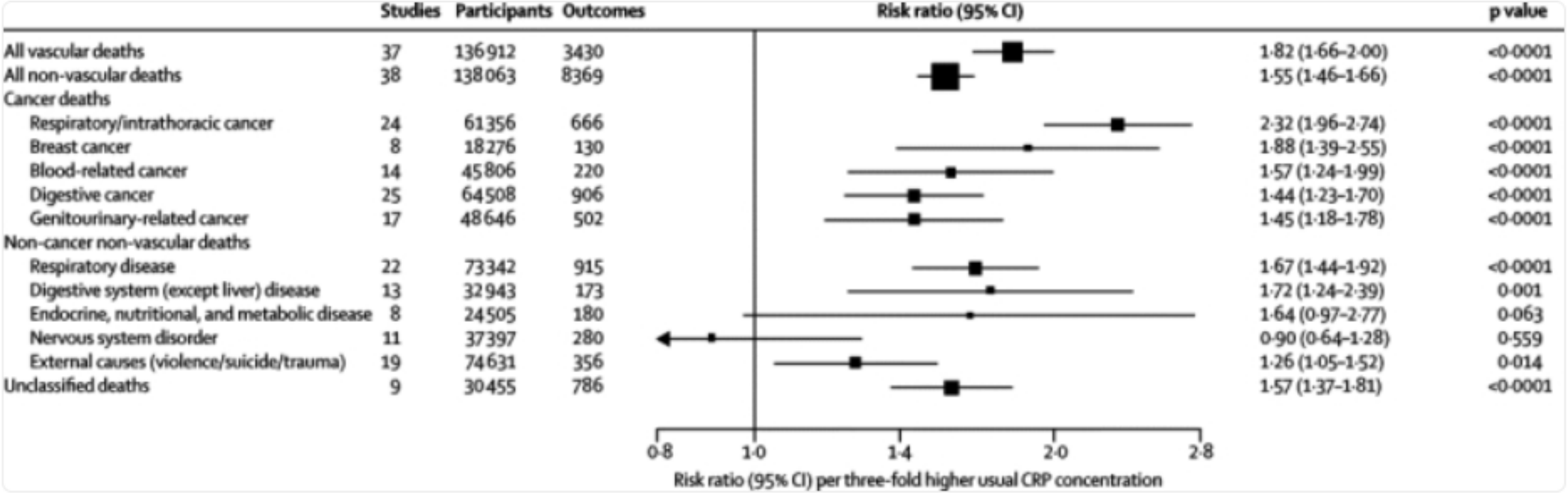
Framingham Offspring Study	~2,800 asymptomatic adults	ABI <0.9 was independently associated with a 2–3× increased risk of MI, stroke, and CV death, even after adjusting for traditional risk factors.
Meta-analysis (Ankle Brachial Index Collaboration, JAMA 2008)	48,294 participants	ABI <0.9 associated with a **hazard ratio of 1.63** for total mortality and **1.96 for CV mortality**. ABI improved risk classification beyond Framingham Risk Score.

hsCRP – an independent predictor of MI, stroke, CV death

- Refines risk in intermediate patients: adds granularity in intermediate risk patients.
- hsCRP can help identify patients who will benefit from statin despite LDL-C <130mg/dL, leading to lower CV events an mortality, based on Jupiter trial.
- Widely available, low cost, does not require fasting. Minimal patient risk

hsCRP

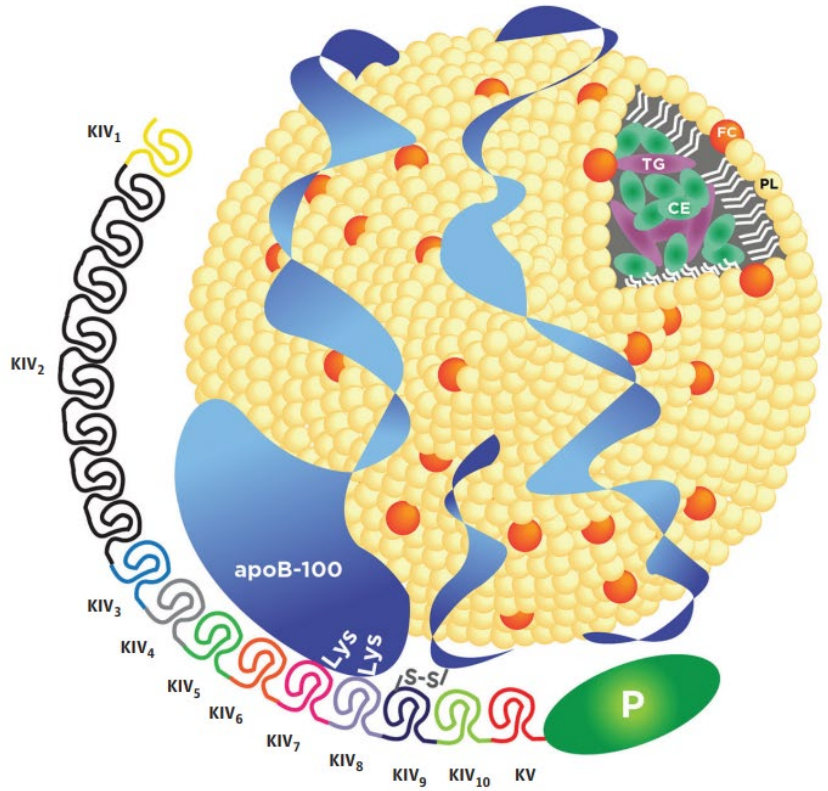
- <1.0mg/L: low risk
- 1.0 – 3.0mg/L: intermediate risk
- >3.0mg/L: high risk



Lipoprotein(a)

- AHA scientific statement (2022): Lp(a) is genetically determined, causal, and prevalent risk factor for ASCVD.

Figure 1. Lipoprotein(a) Structure



Lipoprotein(a) is a low-density lipoprotein–like particle covalently bound to apolipoprotein(a) via a disulfide linkage. Apolipoprotein(a) consists of 10 subtypes of kringle domain IV (KIV_{1-10}), kringle domain V (KV), and an inactive protease domain (P). KIV_2 can expand into more than 40 identically repeated copies. apoB-100 indicates apolipoprotein B-100; CE, cholesterol ester; FC, free cholesterol; Lys, lysine residue; PL, phospholipid; TG, triglyceride.

Lipoprotein(a)

- Associated with 2-3x increased risk of ASCVD and aortic valve stenosis, independent of LDL-C
- Low cost: $50-150 if not covered by insurance
- Low risk of harm
- Threshold of 50mg/dL (125nmol/L) is often used as cutoff for increased risk
- Lp(a) >99^{th} percentile linked to 3.4x higher MI risk compared to <20^{th} percentile

In summary

- We discussed risk
- The benefits of understanding how that risk is calculated
- Tests that can help us refine our understanding of each asymptomatic patient’s risk.

Thank you