The Modern Heart Check: Risk Stratification and Lipid Lowering Insights

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Agenda

CVD is #1 killer in US with just under 1,000,000 deaths annually

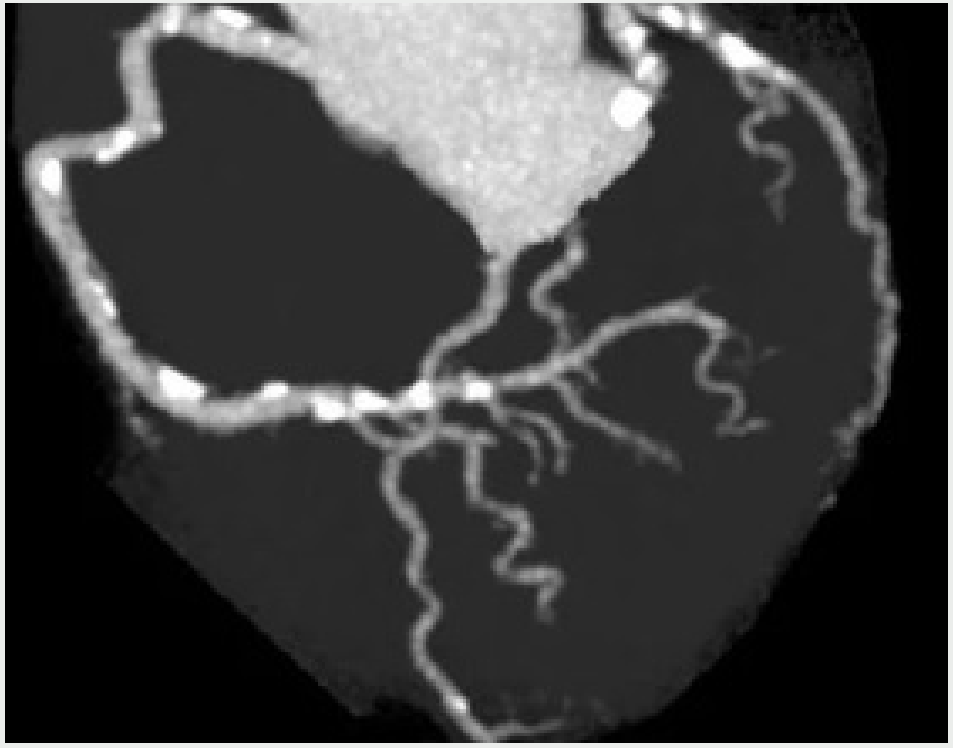
Calcium scores and CTA Coronary

Lp(a), Apo B

Risk Calculators

Statin management

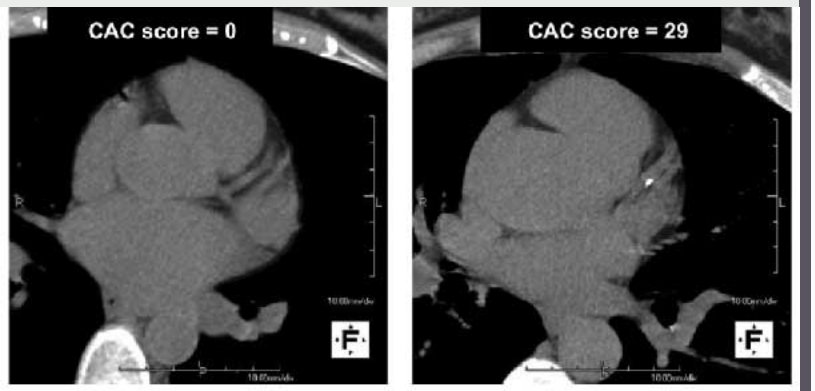
CALCIUM SCORES AND CORONARY CTA

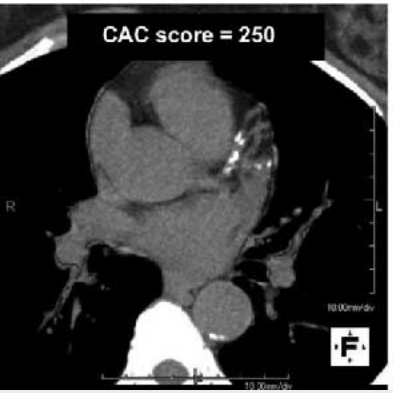


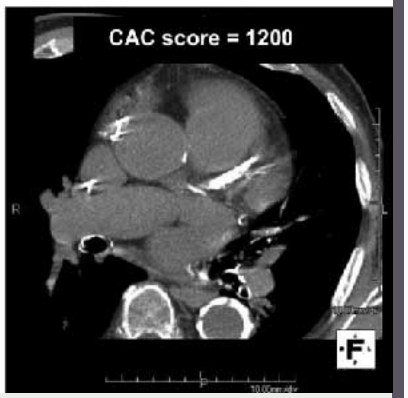
Calcium Score

- Coronary artery calcium (CAC) test
- Coronary calcium CT scan
- Heart CT calcium scan

- CT scan done with Low dose (1-1.5 mSv), typically 3 mm slices
- Equivalent to 4 months of normal exposure in US



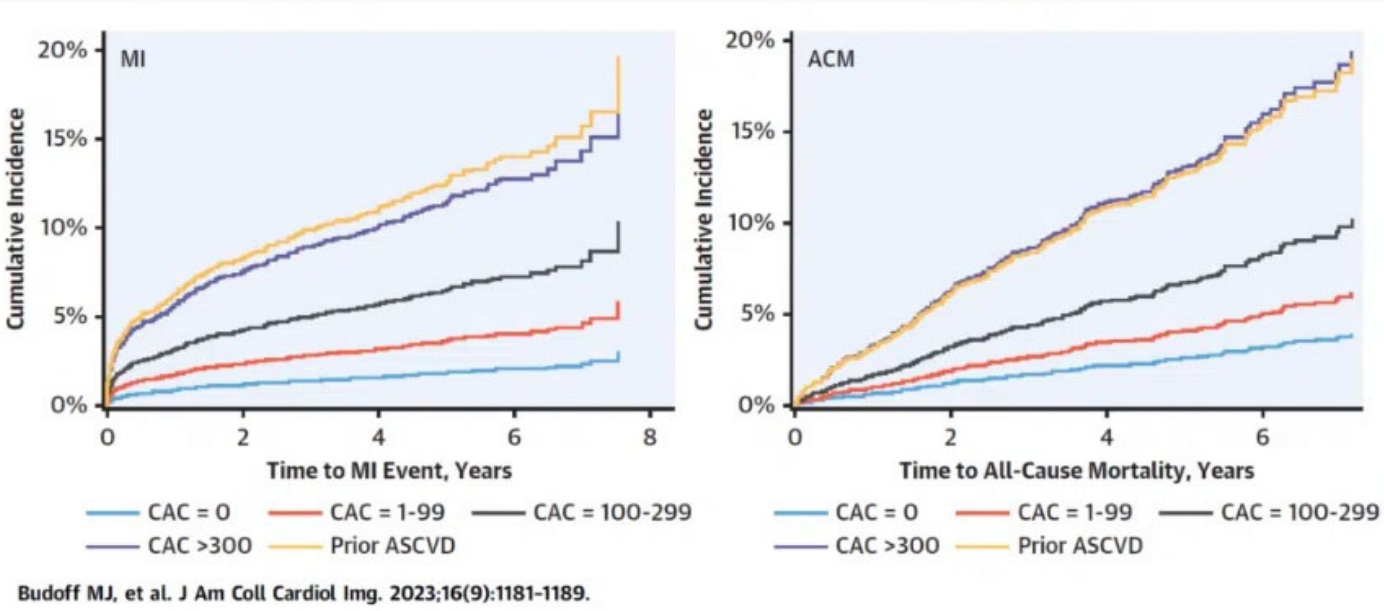




Calcium Score

Calcium Score	Interpretation
0	No identifiable atherosclerotic plaque. Very low cardiovascular disease risk. Less than 5% chance of presence of coronary artery disease. A negative examination.
1-10	Minimal plaque burden. Significant coronary artery disease very unlikely.
11-100	Mild plaque burden. Likely mild or minimal coronary stenosis.
101-400	Moderate plaque burden. Moderate non-obstructive coronary artery disease highly likely.
Over 400	Extensive plaque burden. High likelihood of at least one significant coronary stenosis (>50% diameter).

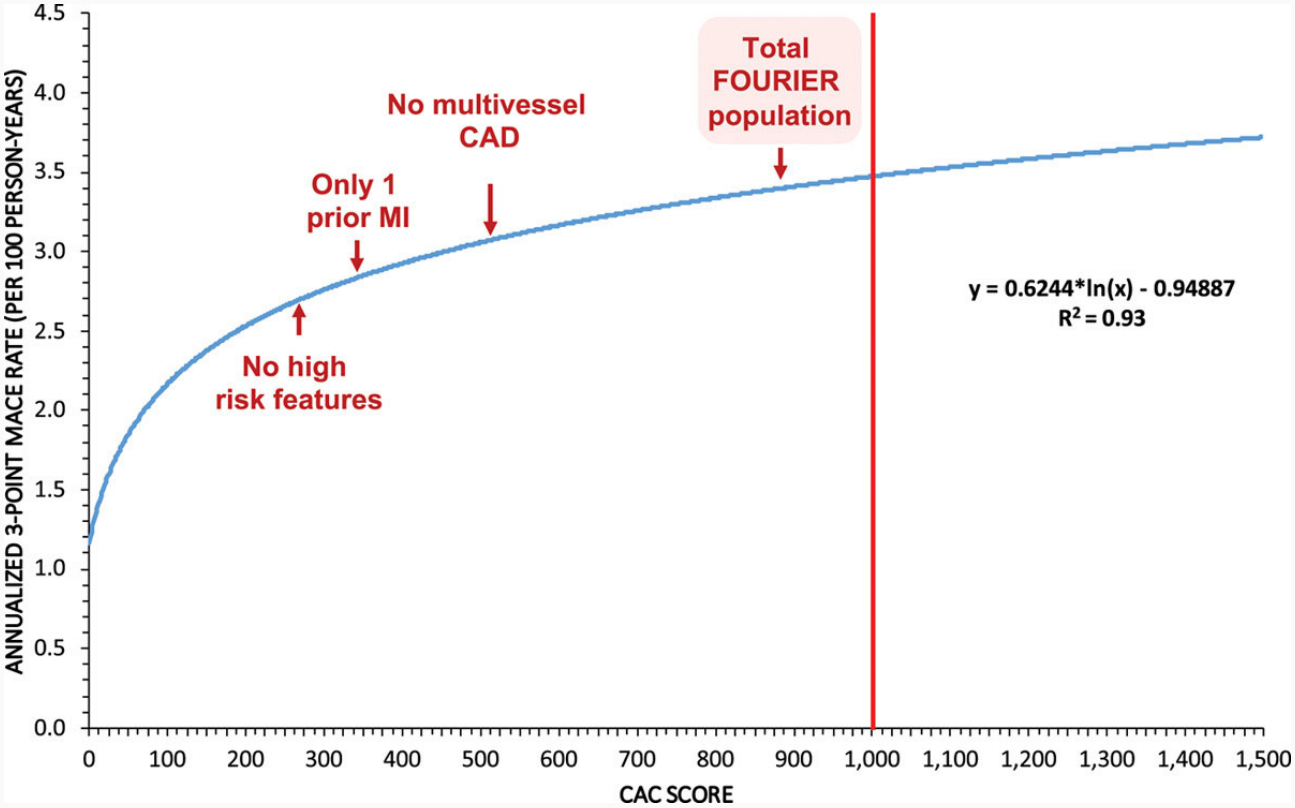
Calcium Score

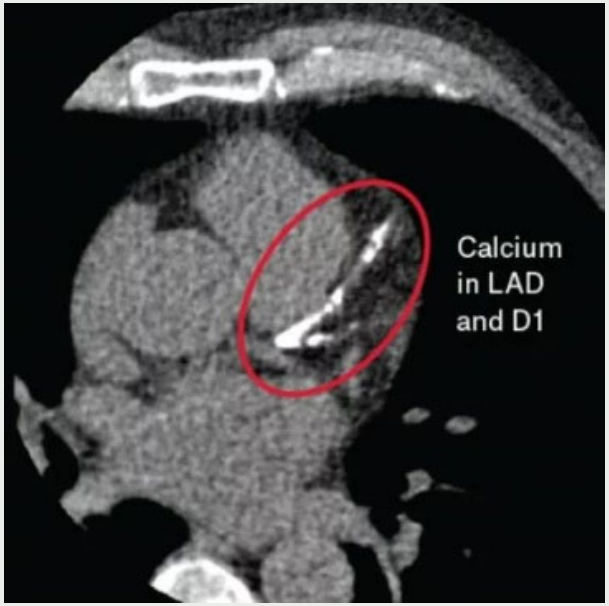


Budoff MJ, et al. J Am Coll Cardiol Img. 2023;16(9):1181-1189.

Event rates by coronary artery calcium (CAC) score distribution for major adverse cardiovascular events (MACE) **(upper left)**, MACE + late revascularization (LR) **(upper right)**, myocardial infarction (MI) **(lower left)**, and all-cause mortality (ACM) **(lower right)**. Follow-up was consistent for all endpoints, and each endpoint demonstrates that the event rates for CAC >300 are similar to those of patients who have established cardiovascular disease. ASCVD = atherosclerotic cardiovascular disease.

Calcium Score





CALCIUM SCORE

Consider For Patients:

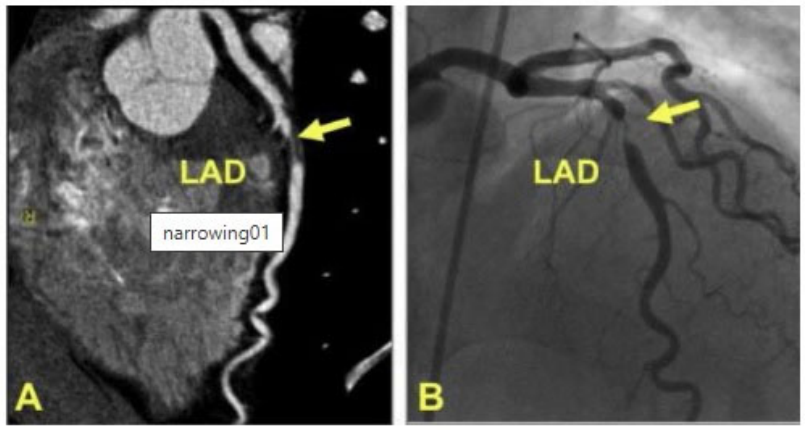
Asymptomatic adults, 40 or older

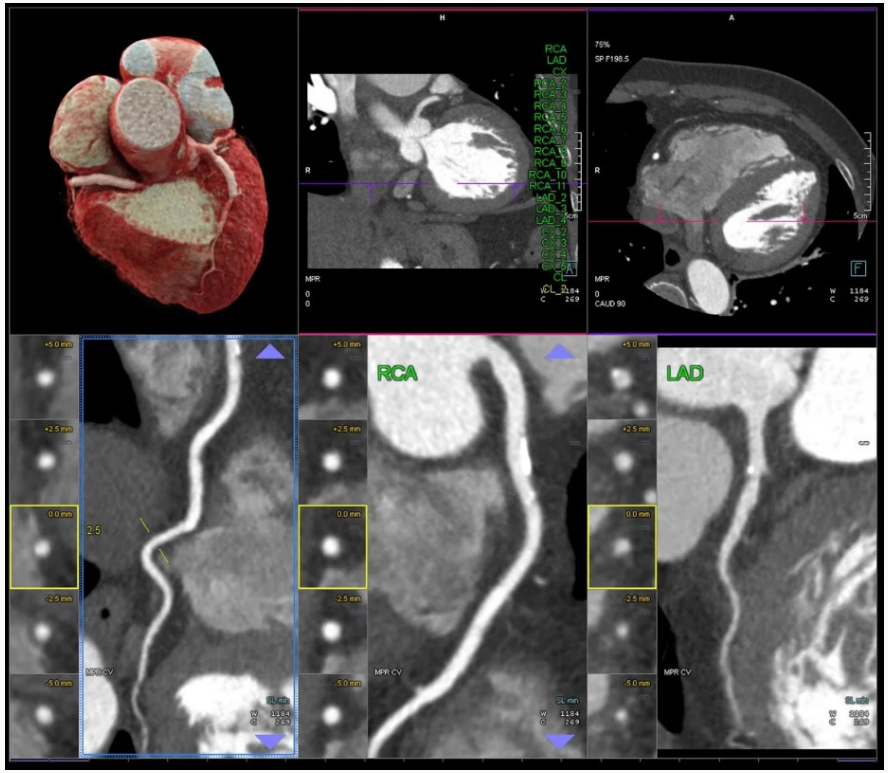
- **Family history CAD**
- **Smoking history**
- **High cholesterol**
- **High blood pressure**
- **Diabetes**
- **Obesity**

CORONARY CTA

Coronary CTA

- 3D, gated reconstruction of coronary anatomy
  - Calcified plaque
  - Soft Plaque
  - Anomalous coronary anatomy
  - Aorta/Pulmonary artery anatomy
- CT scan
  - Modern Avg: 4-7 mSv (historically ~20)
  - Ultra-low dose: 1-2 mSv

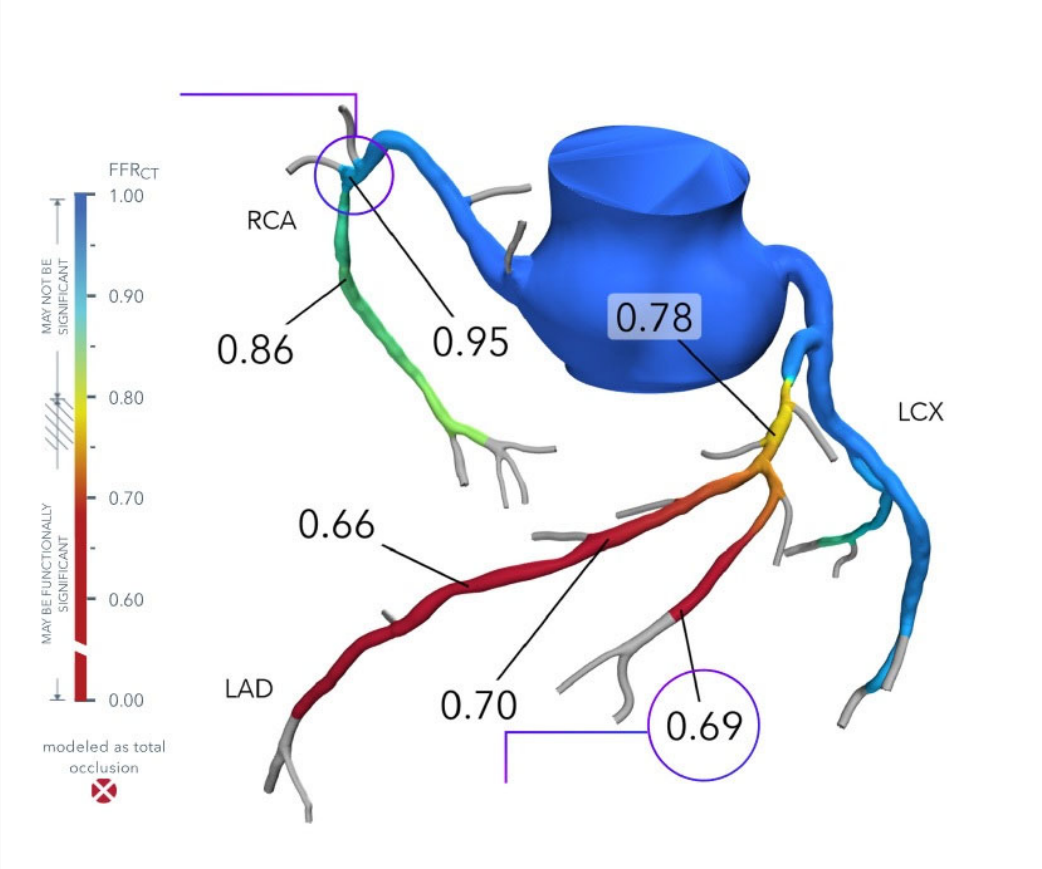




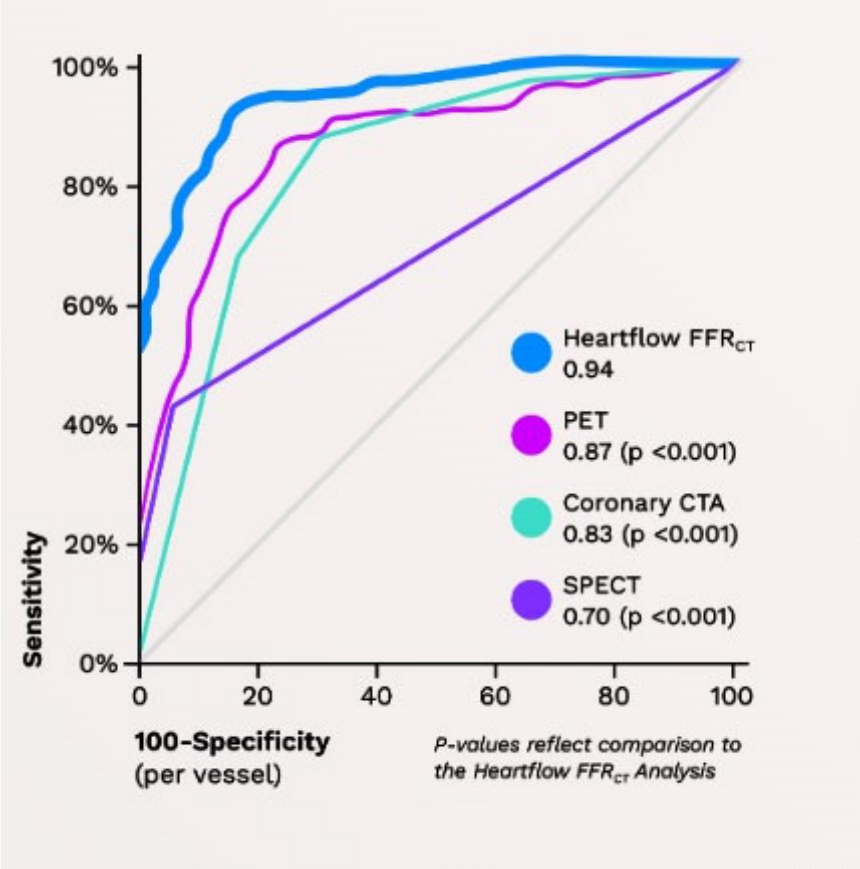
- ≥64-slice scanner with ECG gating
- Nitroglycerin
- Metoprolol, typically 50-100 mg
  - Ideally <70 bpm
- IV contrast, typically 90-130 cc
- Breathhold
- Ideally regular rhythm
  - Retrospective ECG-gated acquisition for irregular rhythms

Coronary CTA

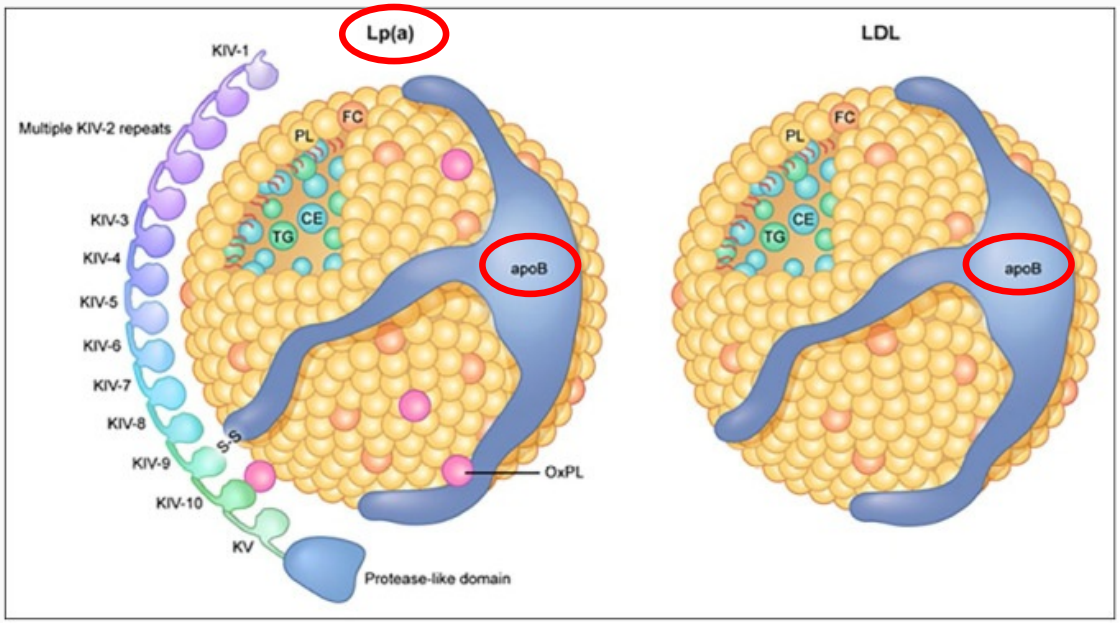
HEARTFLOW


FFRCT
1.00
0.90
0.80
0.70
0.60
0.00
MAY NOT BE SIGNIFICANT
MAY BE FUNCTIONALLY SIGNIFICANT
modeled as total occlusion
RCA
0.86
0.95
0.78
LCX
0.66
LAD
0.70
0.69

HEARTFLOW


100%
80%
60%
40%
20%
0%
Sensitivity
0
20
40
60
80
100
100-Specificity
(per vessel)
Heartflow FFR$_{CT}$
0.94
PET
0.87 (p <0.001)
Coronary CTA
0.83 (p <0.001)
SPECT
0.70 (p <0.001)
P-values reflect comparison to the Heartflow FFR$_{CT}$ Analysis

Lipoprotein A and Apolipoprotein B



Lp(a)

- Lipoprotein particle with an Apolipoprotein a and apolipoprotein B bound to it
- "LDL-like" moiety
- Carries oxidized phospholipids, which are proinflammatory
- 6x more atherogenic than LDL
- **90% of level is genetically driven**

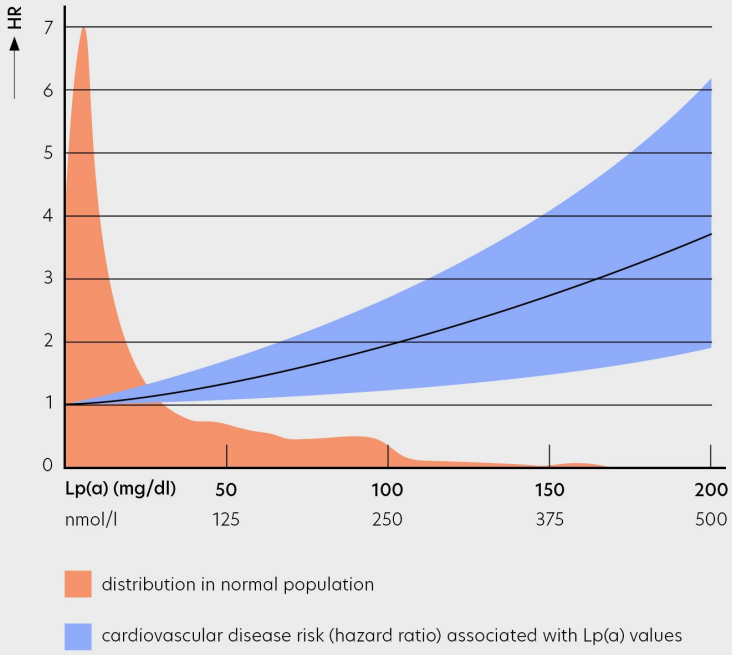
    -Other factors: age, ethnicity, liver/kidney disease

    -Level established in childhood

- 10-15% higher in women

Lp(a)

- Independent ASCVD risk factor
- Elevated in 20-30% of world population
- Hazard Ratio approaching 4x baseline with Lp(a) of 200
- Most current guidelines suggest ONE TIME screening in everyone



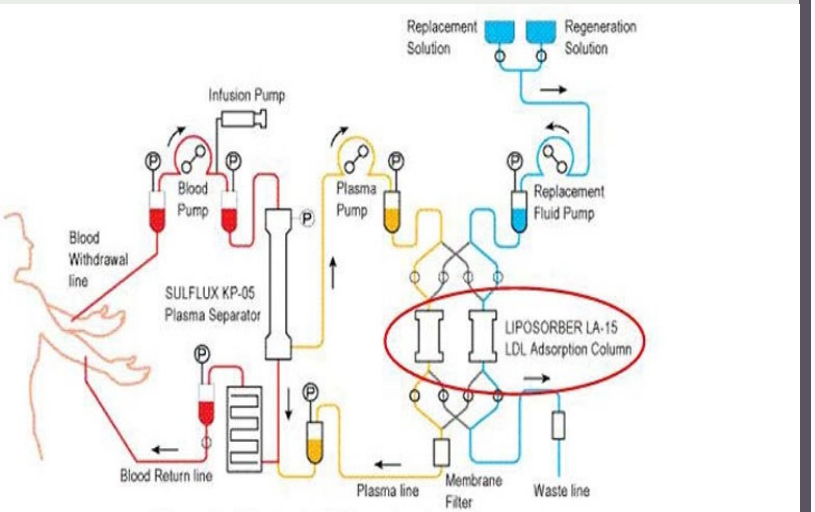
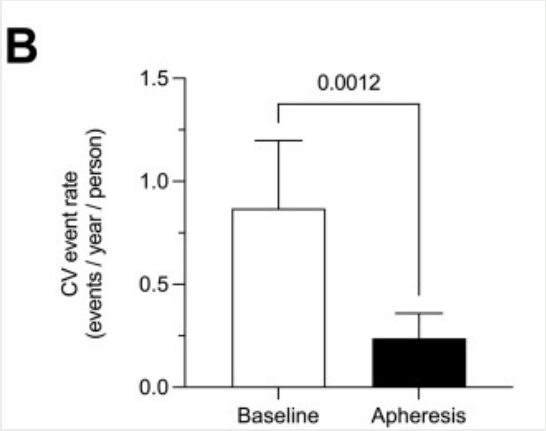


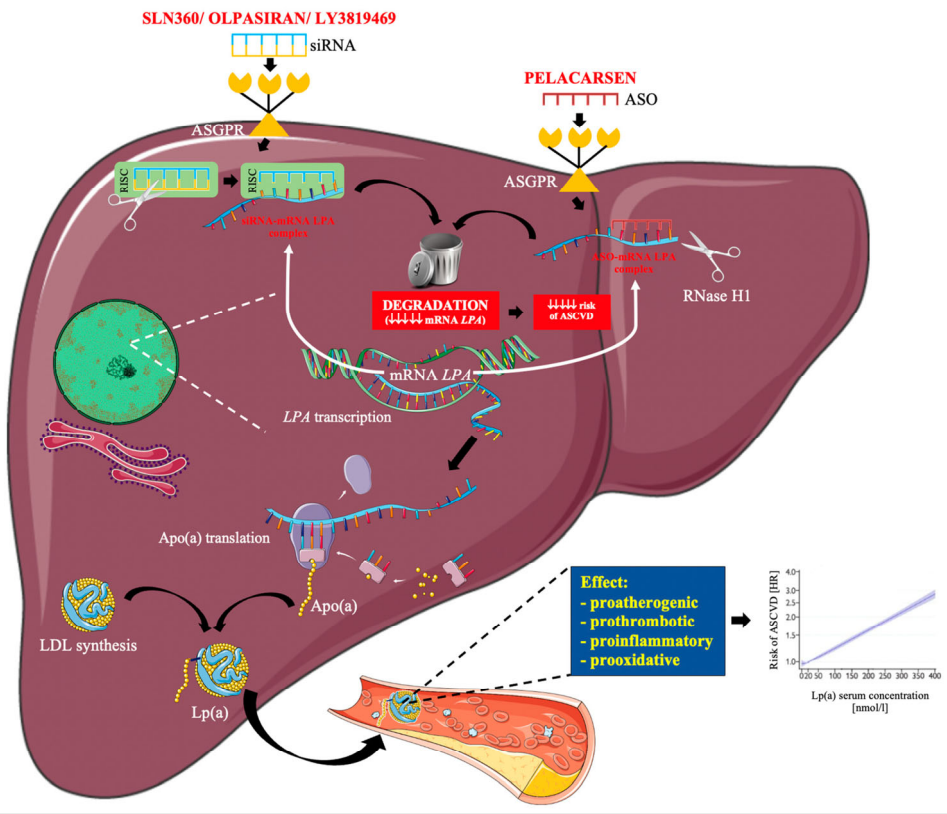
Figure 2. Schematic of Liposorber Operation



Lp(a) Therapeutics

- **Apheresis**
  - Only currently FDA approved therapy
  - HeFH, LDL>100, established CVD, Lp(a)>60
  - Weekly or biweekly schedule, 2-4 hrs
  - Yearly major adverse cardiac event (MACE) rate was reduced from 0.34 to 0.006 (Schumann)

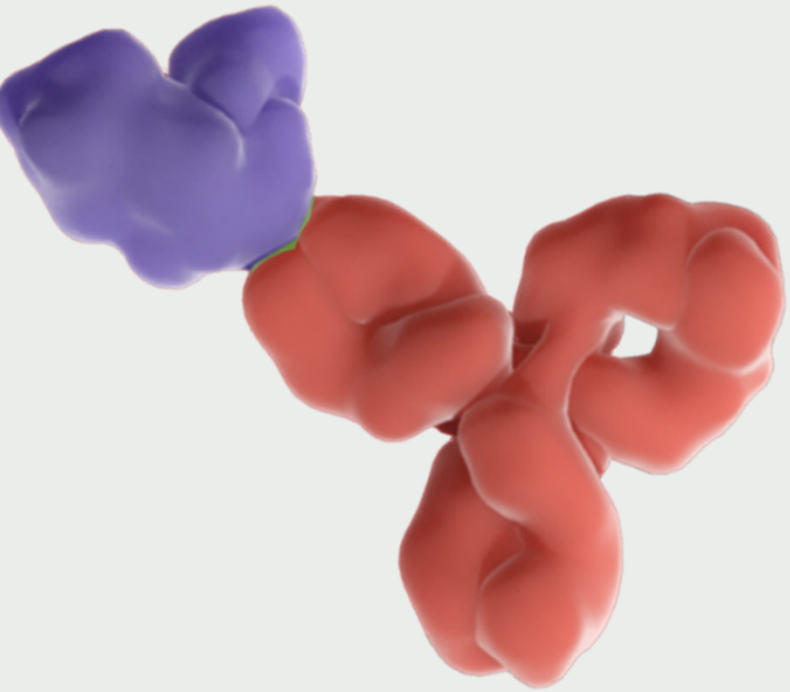
Lp(a) Therapeutics



Apo(a) messenger RNA targets

- **Pelacarsen (antisense oligonucleotide)**
- **Olpasiran (RNA silencer)**

- **80-90% reduction in Lp(a) levels**
- **Elevated Lp(a) and ASCVD**
- **Both phase III trials by end of 2026**

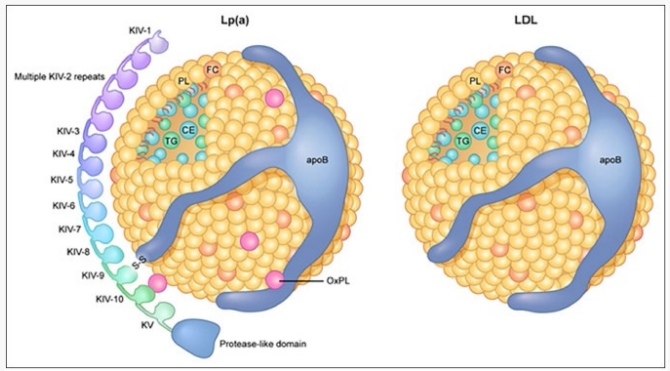


Lp(a) Therapeutics

- PCSK9 inhibitors
  - 20-30% Lp(a) reduction
  - Likely enhanced benefit in patients with high Lp(a)
- Niacin
  - Reduces Lp(a), but no evidence clinical benefit
- Statins
  - May increase Lp(a) up to 24%.
  - No data for harm, unclear if mitigates benefit

- Moral of the story (for now): Maximize ASCVD risk factors and LDL reduction

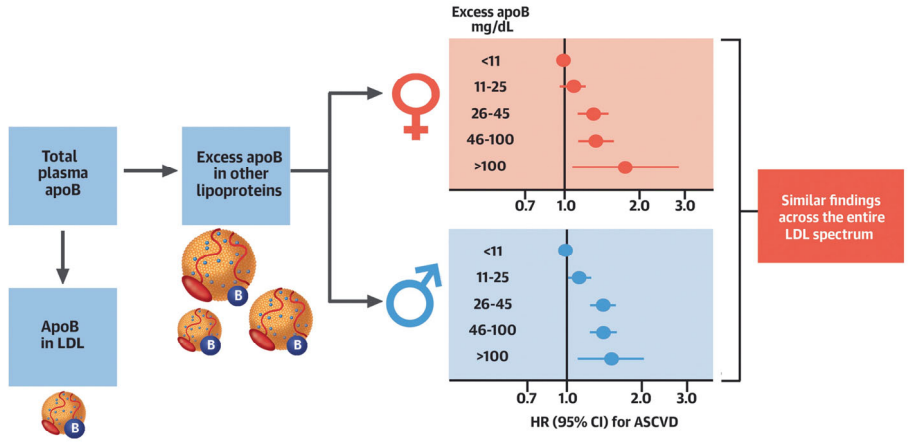
Apolipoprotein B



- Primary structural protein on all “atherogenic” lipoproteins (None on HDL)
- 2 main isoforms of ApoB
  - ApoB100 (VLDL, ILDL, LDL, Lp(a)
  - ApoB48 (chylomicrons and remnants)
- 1 molecule on each

Apolipoprotein B

CENTRAL ILLUSTRATION: Excess Apolipoprotein B in Risk of Atherosclerotic Cardiovascular Disease



Johannesen CDL, et al. J Am Coll Cardiol. 2024;83(23):2262-2273.

- Given variable size of atherogenic particles, more reliable risk marker of ASCVD than LDL-c
- Reliability even higher in hypertriglyceridemia
- Unaffected by fasting

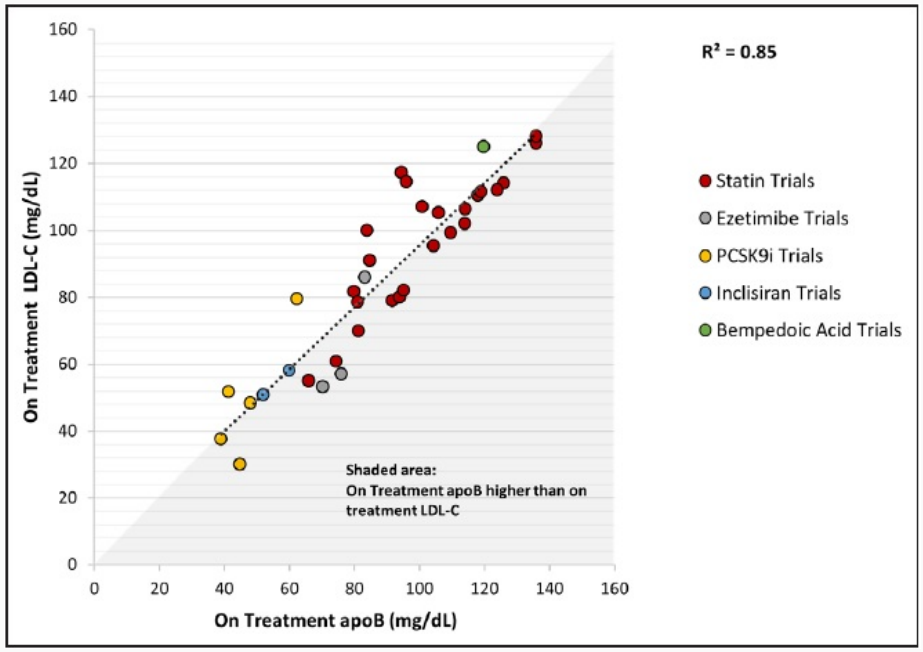
Apolipoprotein B

ASCVD Risk Profile	LDL-C Target	Non-HDL-C Target	Apob Target
Very High (Secondary Prevention)	<1.4 mmol/L (<55mg/dL)	<2.2 mmol/L (<85 mg/dL)	<50
High Risk - CAC>300, FH	<1.8 mmol/L (<70mg/dL)	<2.5 mmol/L (<100mg/dL)	<60
Moderate	<2.5 mmol/L (<100mg/dL)	<3.4 mmol/L (<130 mg/dL)	<80

THERAPEUTICS

- Unlike Lp(a), ApoB declines with atherogenic particles on standard therapies
- Slowly working into guidelines
- For the most part, LDL-c and ApoB reductions correlate

Apolipoprotein B



THERAPEUTICS

- Unlike Lp(a), ApoB declines with atherogenic particles on standard therapies
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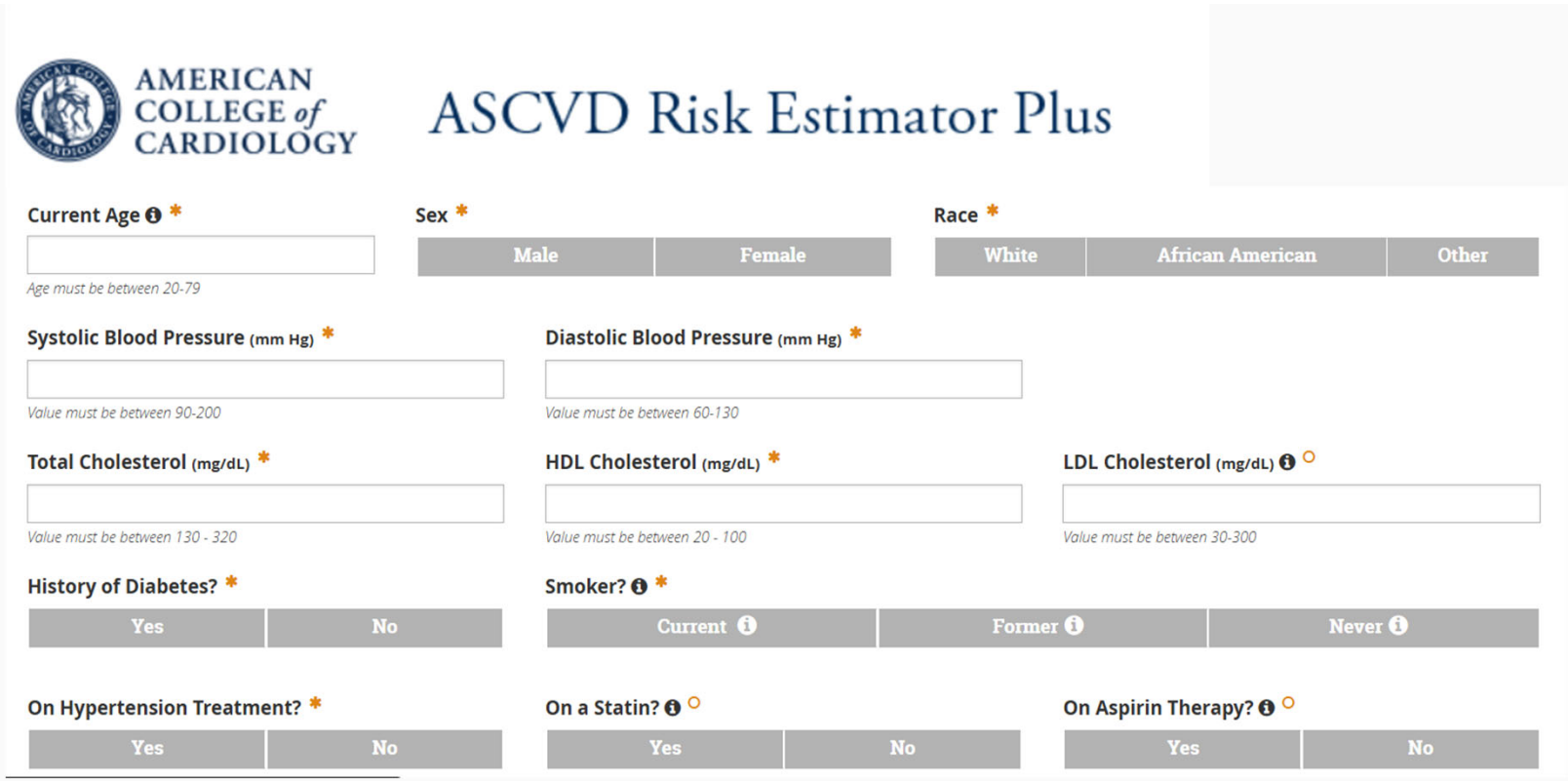
So how do we incorporate this into the risk calculators we've been using for years?

Risk Calculators

- No calculators incorporate Lp(a)
- Only MESA CHD and Mayo incorporates CAC
- Adjunctive to Lp(a), ApoB, calcium scores

Newer	Older
PCE* (ACC)	Framingham
PREVENT (AHA)	Reynolds
SCORE2 (ESC)	QRISK
MESA CHD	
Mayo (pooled from ACC, MESA, Framingham)	

*Pooled Cohort Equations



Risk Calculators

Risk Calculators

MESA 10-Year CHD Risk with Coronary Artery Calcification

1. Gender	Male ○	Female ○			
2. Age (45-85 years)		Years			
3. Coronary Artery Calcification		Agatston			
4. Race/Ethnicity	Choose One				
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		mg/dL	or		mmol/L
9. HDL Cholesterol		mg/dL	or		mmol/L
10. Systolic Blood Pressure		mmHg	or		kPa
11. Lipid Lowering Medication	Yes ○	No ○			
12. Hypertension Medication	Yes ○	No ○			

Calculate 10-year CHD risk

Using the Coronary Artery Calcium Score

10 Year risk of a CHD Event	Coronary Age	Difference from Chronologic Age

Without Considering the Coronary Artery Calcium Score

10 Year risk of a CHD Event	Coronary Age	Difference from Chronologic Age

So shifting gears...

We've decided to treat our patient, but they aren't taking their statin...

Statin Management Tips

- True intolerance to statins is not trivial
- 5-10% based on pooled analyses
- Up to 75% can be managed with changing dose or statin

Statin Management Tips

- Rule out secondary causes
  - Hypothyroidism
  - Vitamin D deficiency
  - *New exercise routine*
  - Drug interactions
- More frequent lipid checks, education

Statin Management Tips

- Creatine Kinase (CK)
  - If >5x normal, STOP statin
  - If 3-5x normal, discontinue
    - Once CK normalizes lower dose or change statin
  - If CK <3x normal, OK to monitor

Statin Management Tips

- Low dose high-potency statin
  - Atorvastatin 10 mg, rosuvastatin 5 mg daily
  - May achieve 33-45% LDL reduction
- Intermittent Dosing high potency statin
  - 20-40% LDL reduction

Statin Management Tips

- Switch to hydrophilic statin
  - Rosuvastatin, pitavastatin, lovastatin
- RACING study
  - Rosuvastatin 10 mg + ezetimibe 10 mg
  - Greater LDL reduction, lower discontinuation than rosuvastatin 20 mg monotherapy

Statin Alternatives

- **Ezetimibe**
  - 1st line for primary prevention, given cost
  - 18-20% reduction in CVD events as monotherapy

Statin Alternatives

- **PCSK9 inhibitors**
  - Evolucumab, Alirocumab, Inclisiran
  - Reduce LDL by ~50%
  - 15-25% incremental decrease in CVD events when added to statins
- Enlicitide
  - Oral PCSK9 inhibitor in phase III trial

Statin Alternatives

- **Bempedoic acid**
  - ACL inhibitor (ATP-citrate lyase)
  - Lowers LDL by ~22%
  - 13-23% CVD event decrease

Final tips & takeaways

- **CVD is #1 killer in US with just under 1,000,000 deaths annually**
- Several tools exist to evaluate risk
  - Calcium scoring/CTA
    - Lipid testing
  - Risk calculators
- **Statins are foundational in ASCVD management**
  - 20-45% reduction in events/mortality
  - Intolerance is 5-10%
  - 1st step is to adjust dosing
- **For true intolerance there are several good options**
  - Ezetimibe, PCKS9 inhibitors, bempedoic acid

THANK YOU

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