



**THE
WARRANTY**

THE POWER OF ZERO

Navigating the prognostic value of Coronary Artery Calcium (CAC) absence in asymptomatic and symptomatic populations.



**THE SOFT
SHIELD**

Based on 'The Power of Zero: Risk Stratification and Coronary Calcium Absence' by Peter Megdal, PhD.

Moving Beyond Binary Interpretation

The Warranty (Thesis)



Context: Asymptomatic Primary Prevention

Insight: CAC = 0 is a powerful negative risk marker allowing treatment de-escalation.

Metric: ~1% 10-year event rate (MESA).

The Soft Shield (Antithesis)



Context: Symptomatic / Chest Pain

Insight: Zero calcium does not exclude vulnerable soft plaque or necrotic core.

Metric: 15–20% of ACS patients present with CAC = 0.

The Integrated View (Synthesis)



Context: Clinical Decision Making

Insight: Risk stratification requires a Bayesian approach integrating pre-test probability, genetics, and plaque morphology.

The Paradigm Shift in Risk Stratification

1990s: Risk
Factor Counting

2000s: The
Research Tool

Today: Direct Disease
Visualization



Framingham
Models.



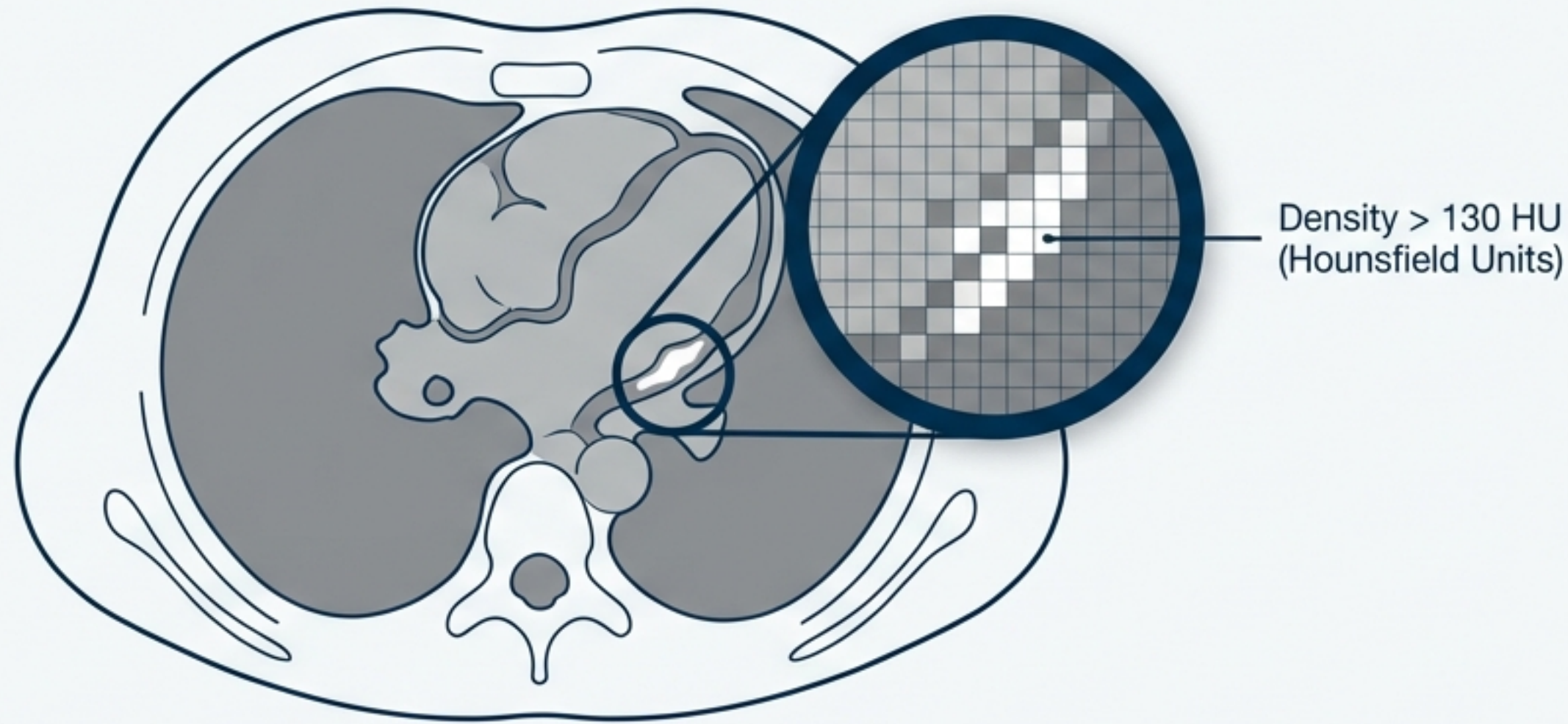
CAC Scoring as
"Truth Serum"

“The ‘power of zero’ has emerged as one of the most powerful negative risk markers in preventive cardiology.”

— *Circulation*, 2020

Over three decades, CAC scoring has evolved from a research tool to a central instrument in preventive cardiology. It serves as a biological "truth serum" that overrides traditional risk factor modeling.

What the Scan Sees: The Agatston Threshold

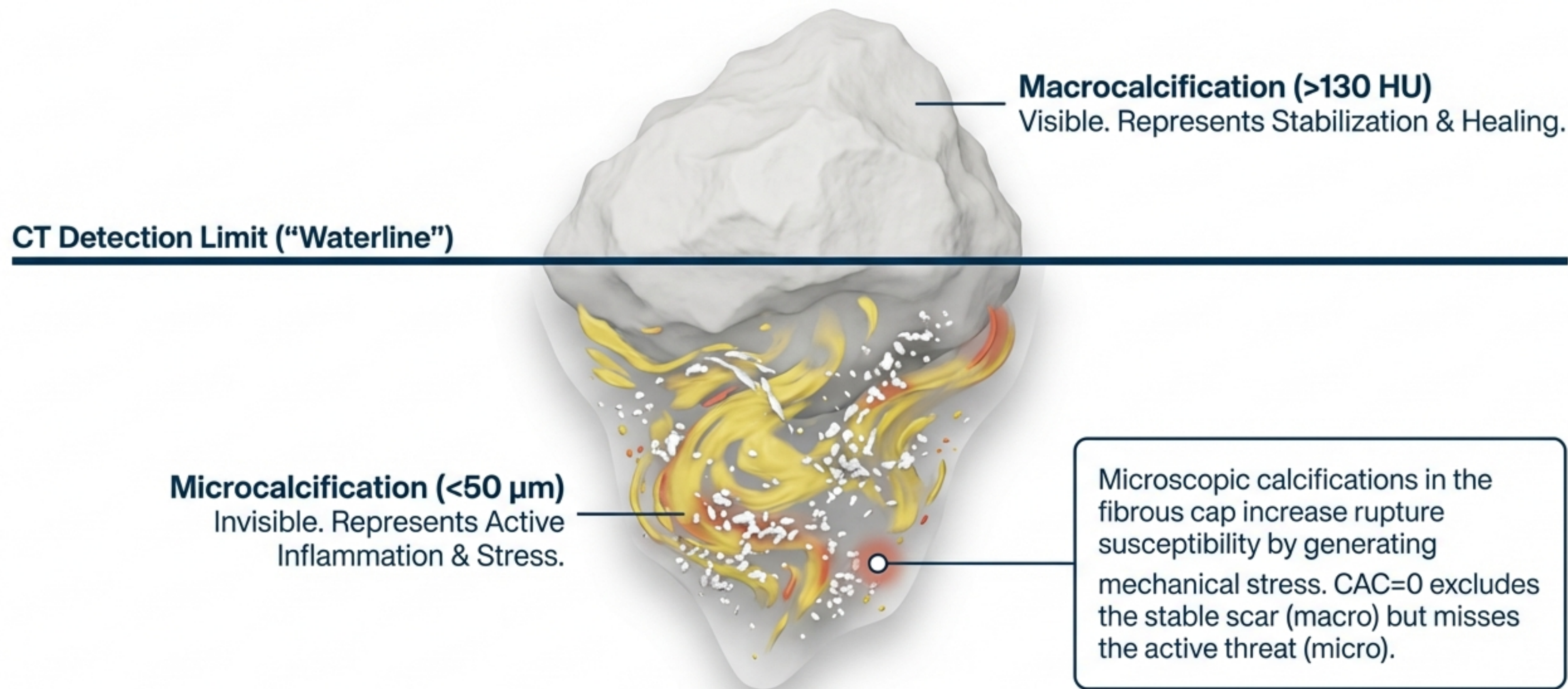


Calcification represents a biologic response to chronic lipid infiltration—specifically osteogenic differentiation and extracellular matrix changes.

Crucially, if the density is below 130 HU, the scan reads it as **“Zero”**.

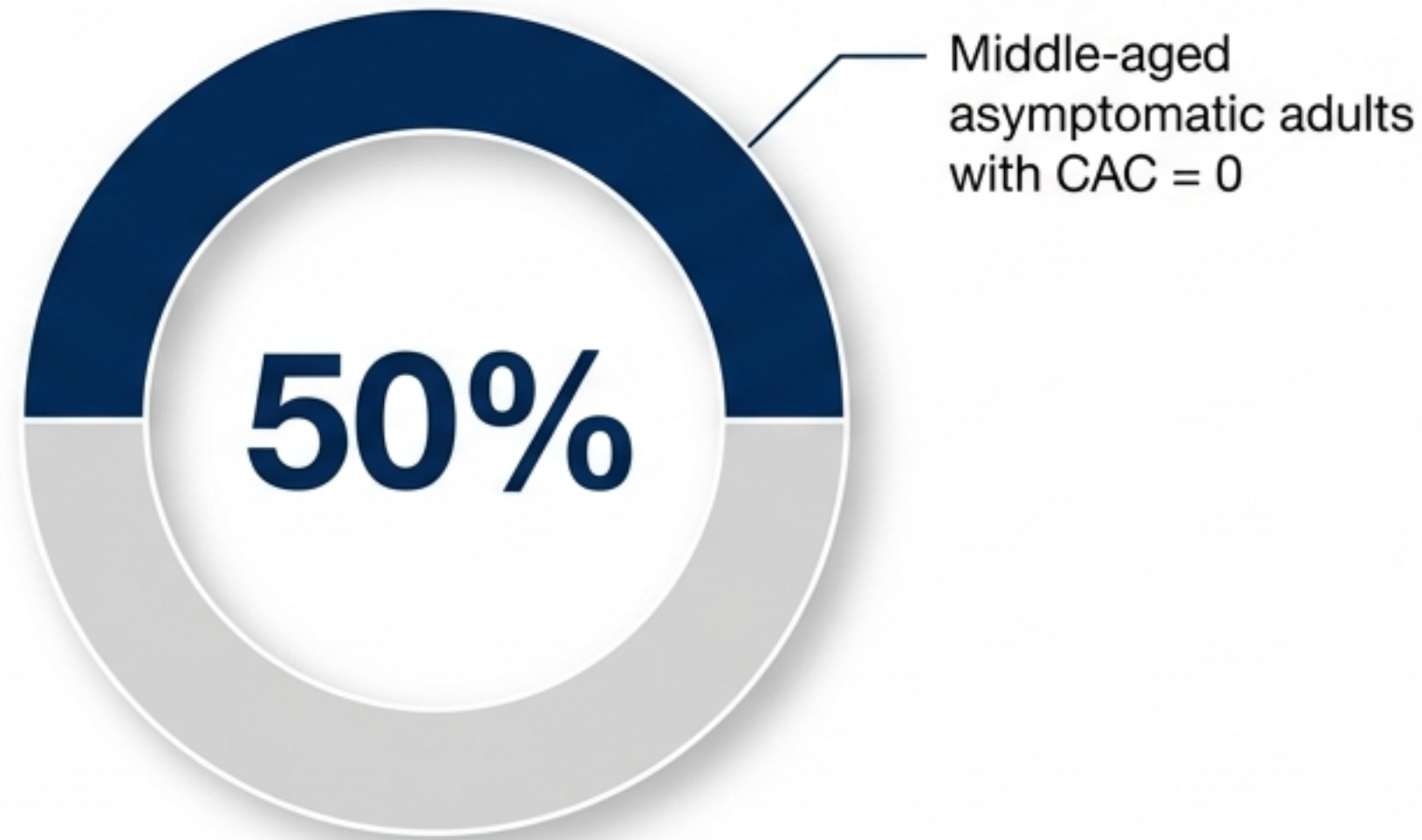
$$\text{Agatston Score} = \text{Plaque Area} \times \text{Density Factor}$$

The Iceberg Concept: Macro vs. Micro



The Power of Zero in Primary Prevention

Data from the Multi-Ethnic Study of Atherosclerosis (MESA)



1%

10-Year ASCVD Event Rate

Annualized risk ~0.1%

In the absence of symptoms, CAC = 0 represents a biologically distinct low-risk phenotype, not just the bottom of a linear scale.

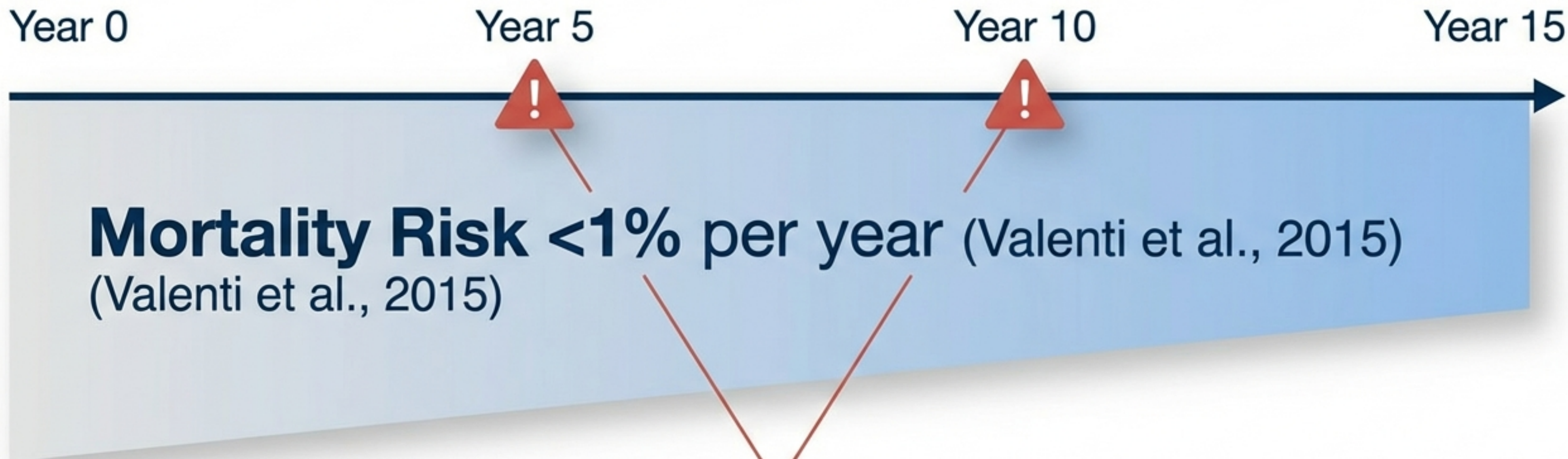
The 15-Year Warranty Period

Year 0

Year 5

Year 10

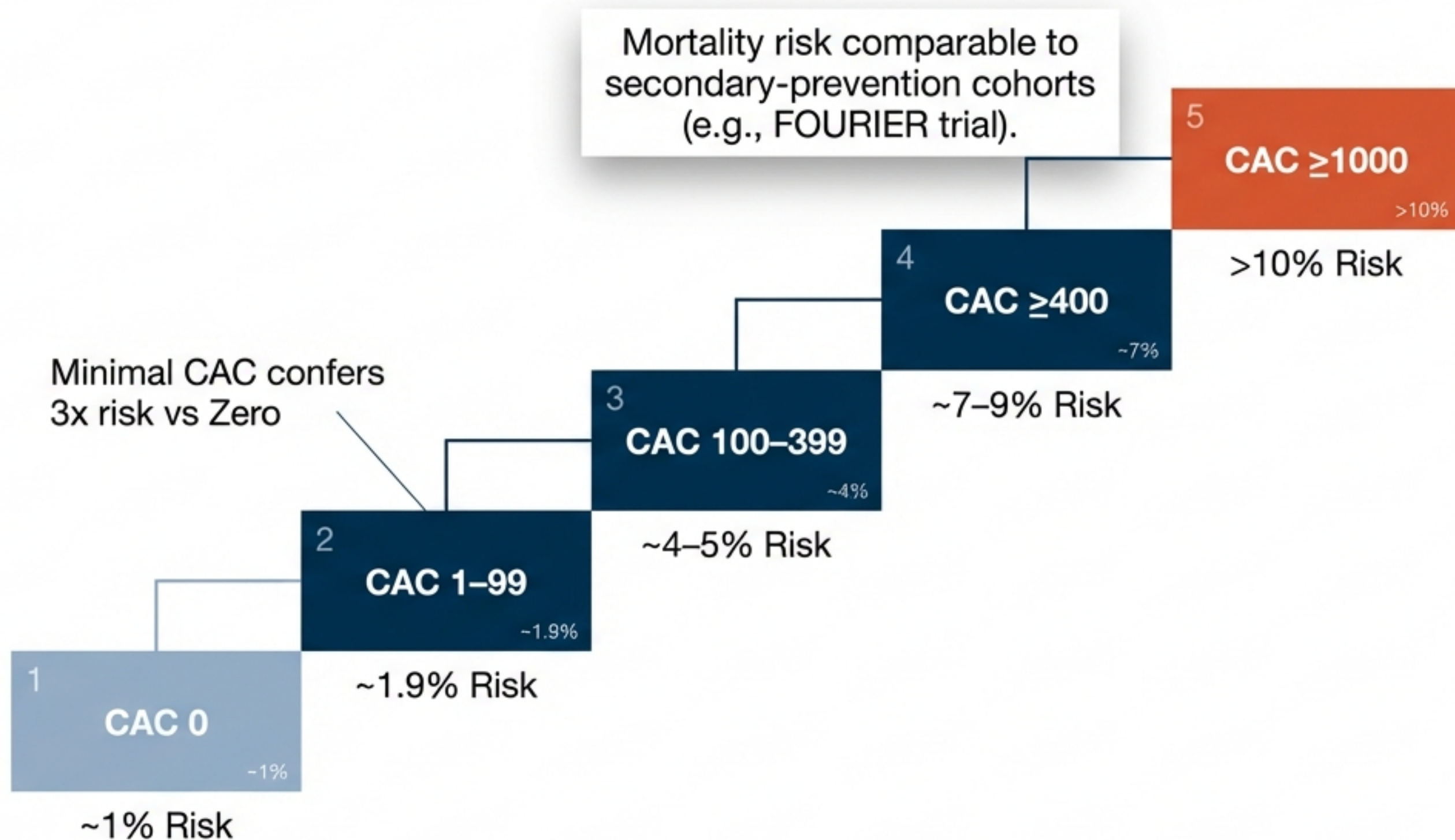
Year 15



Mortality Risk <1% per year (Valenti et al., 2015)
(Valenti et al., 2015)

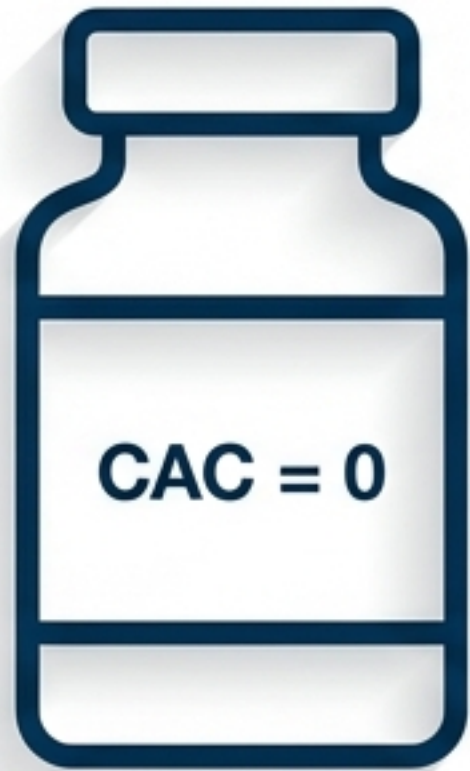
Caveat: The warranty shortens significantly for **Diabetics** and **Heavy Smokers** due to **accelerated plaque progression**.

Risk is Not Binary, It Is Graded



Refining Therapeutic Allocation

Number Needed to Treat (NNT) for Statin Benefit (5-Year)



NNT > 100

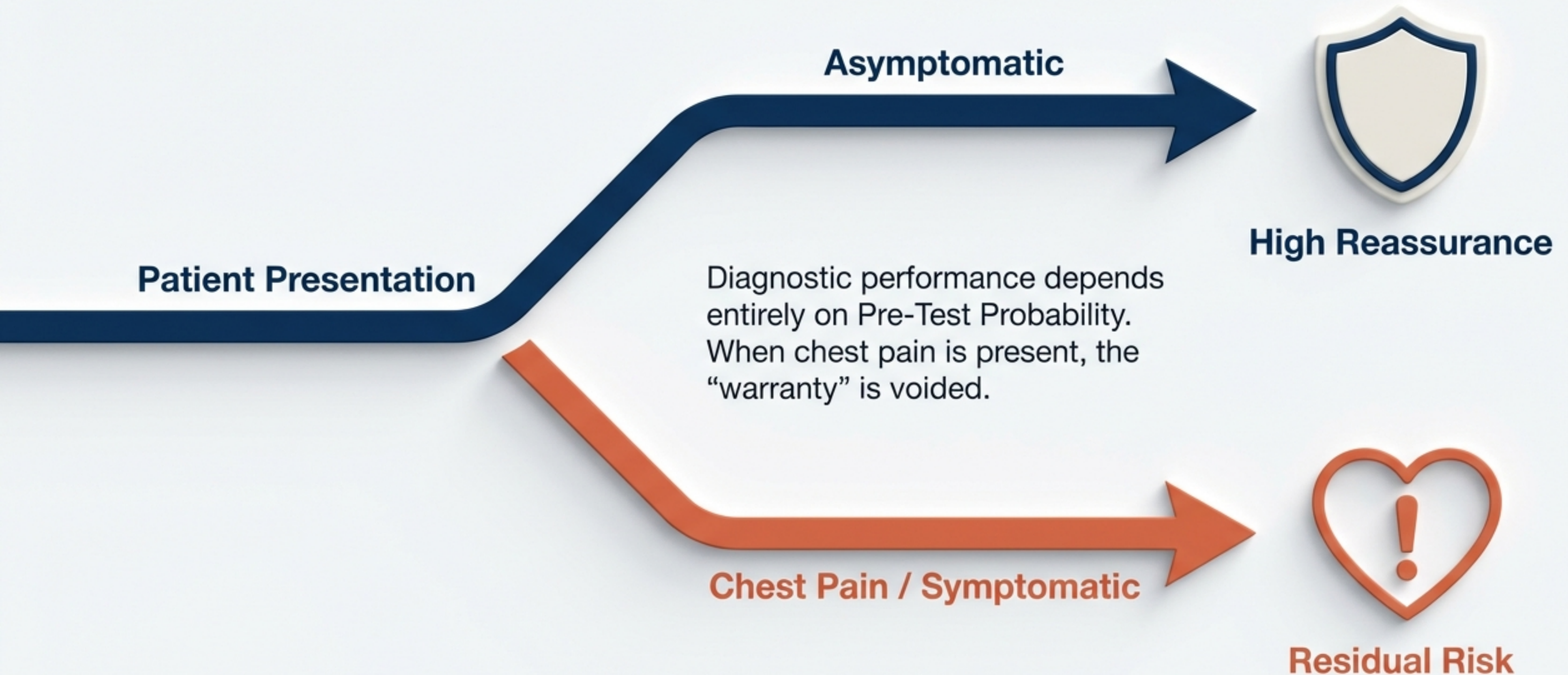
DEFER THERAPY



NNT 12–25

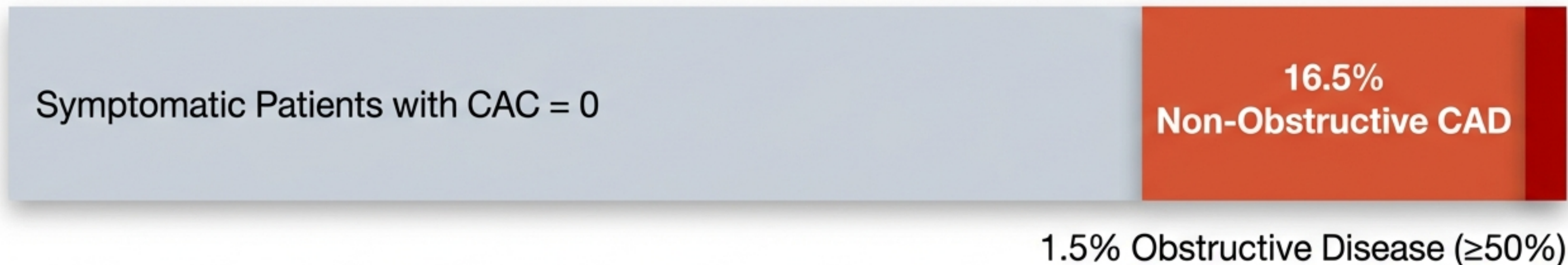
AGGRESSIVE LIPID LOWERING

The Symptomatic Pivot: When Zero \neq Safe



Residual Risk in Stable Chest Pain

Insights from the PROMISE Trial

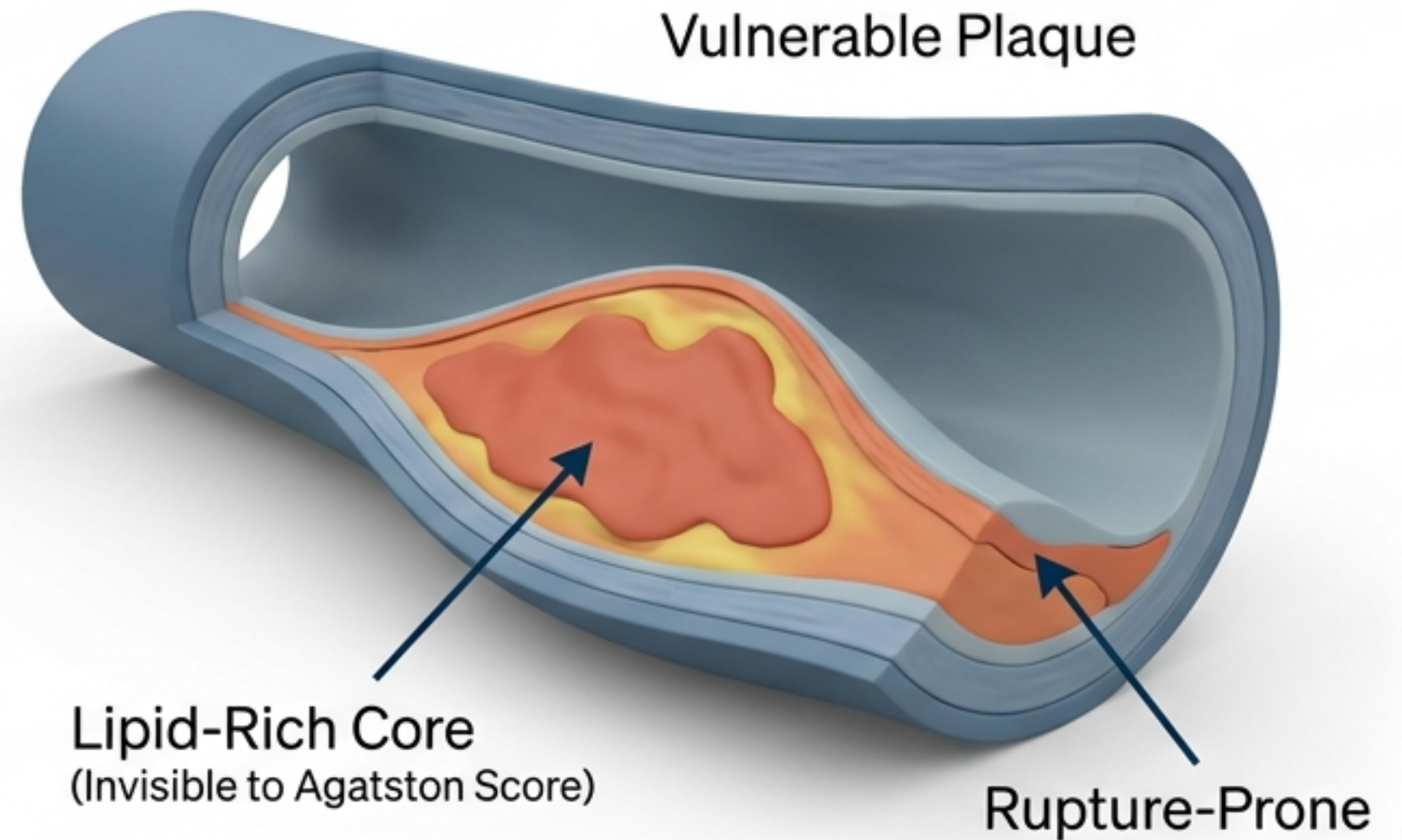


While obstructive disease is rare, the presence of non-obstructive soft plaque is common. Zero is a “soft shield” — better than a high score, but insufficient to rule out disease entirely.

The ACS Paradox

15–20%

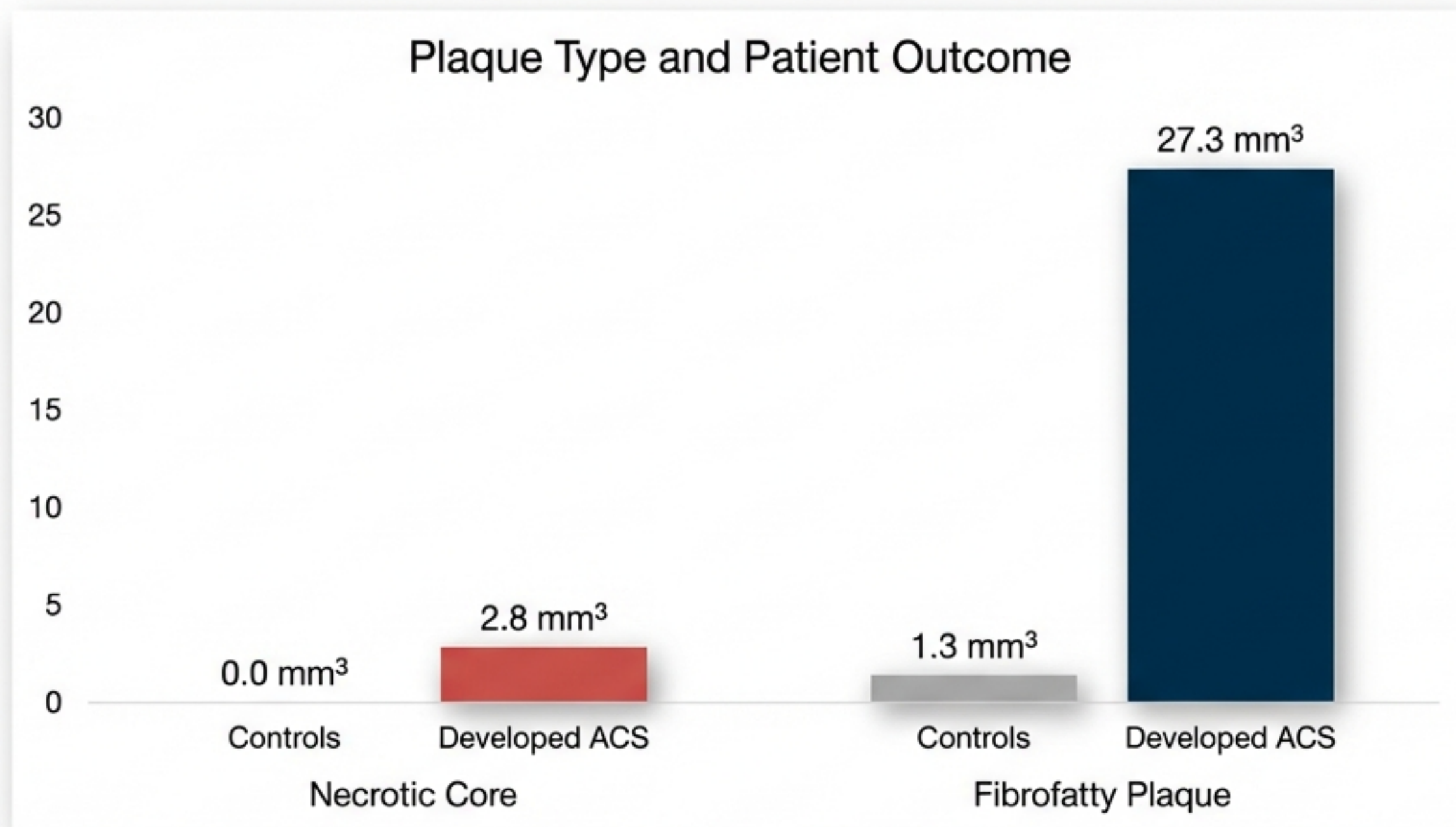
of patients presenting with Acute Coronary Syndrome (ACS) have CAC = 0.



Common in younger patients where soft plaque ruptures before calcification occurs.

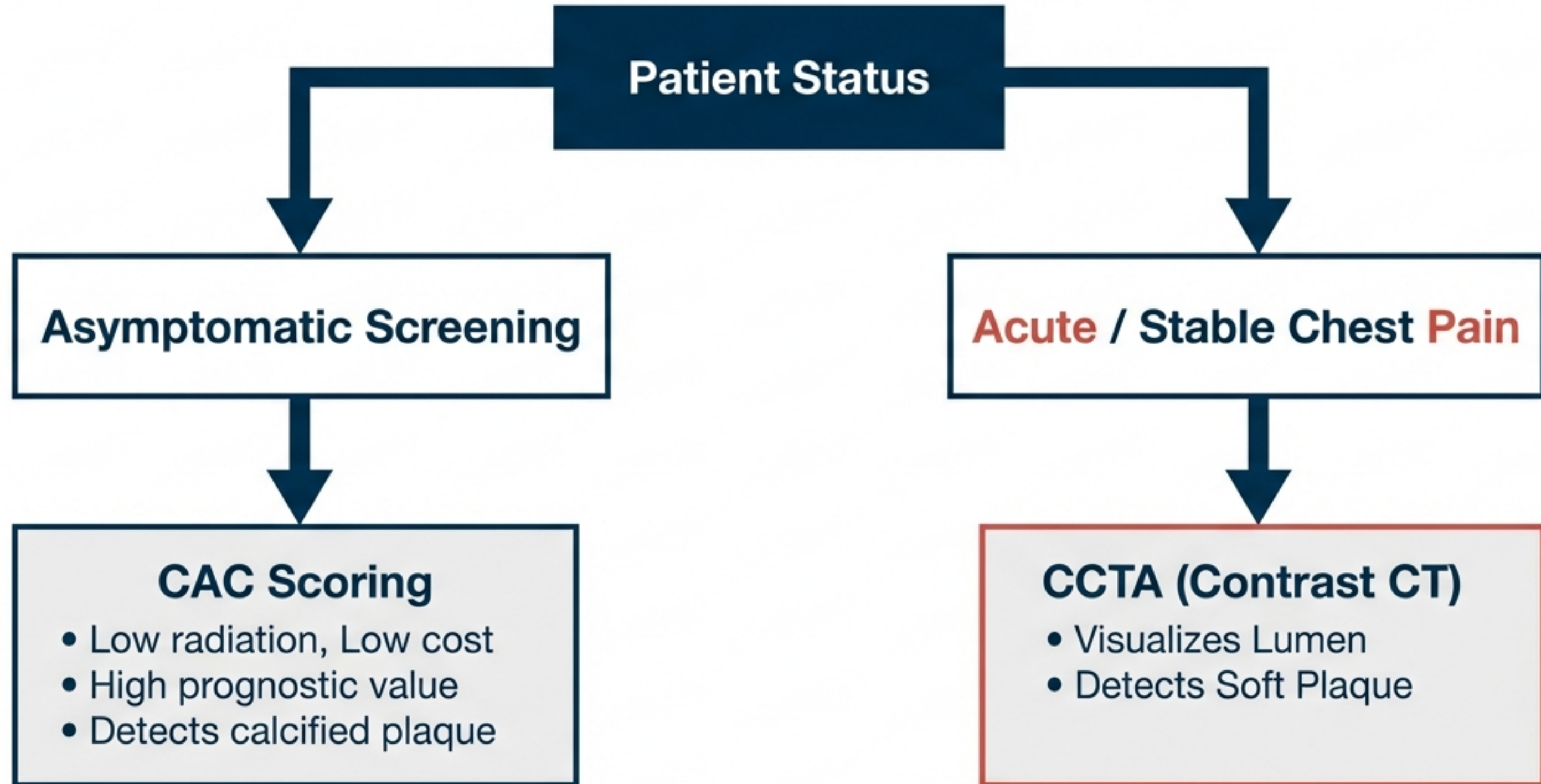
Quantifying the Invisible: ICONIC Insights

Plaque Volume (mm³) in Symptomatic CAC=0 Patients



Substantial vulnerable plaque burden (necrotic core) can exist and rupture in the complete absence of detectable calcification.

Guideline Divergence: The Right Scan for the Right Patient



The Sex-Specific Nuance



Lower absolute CAC prevalence.

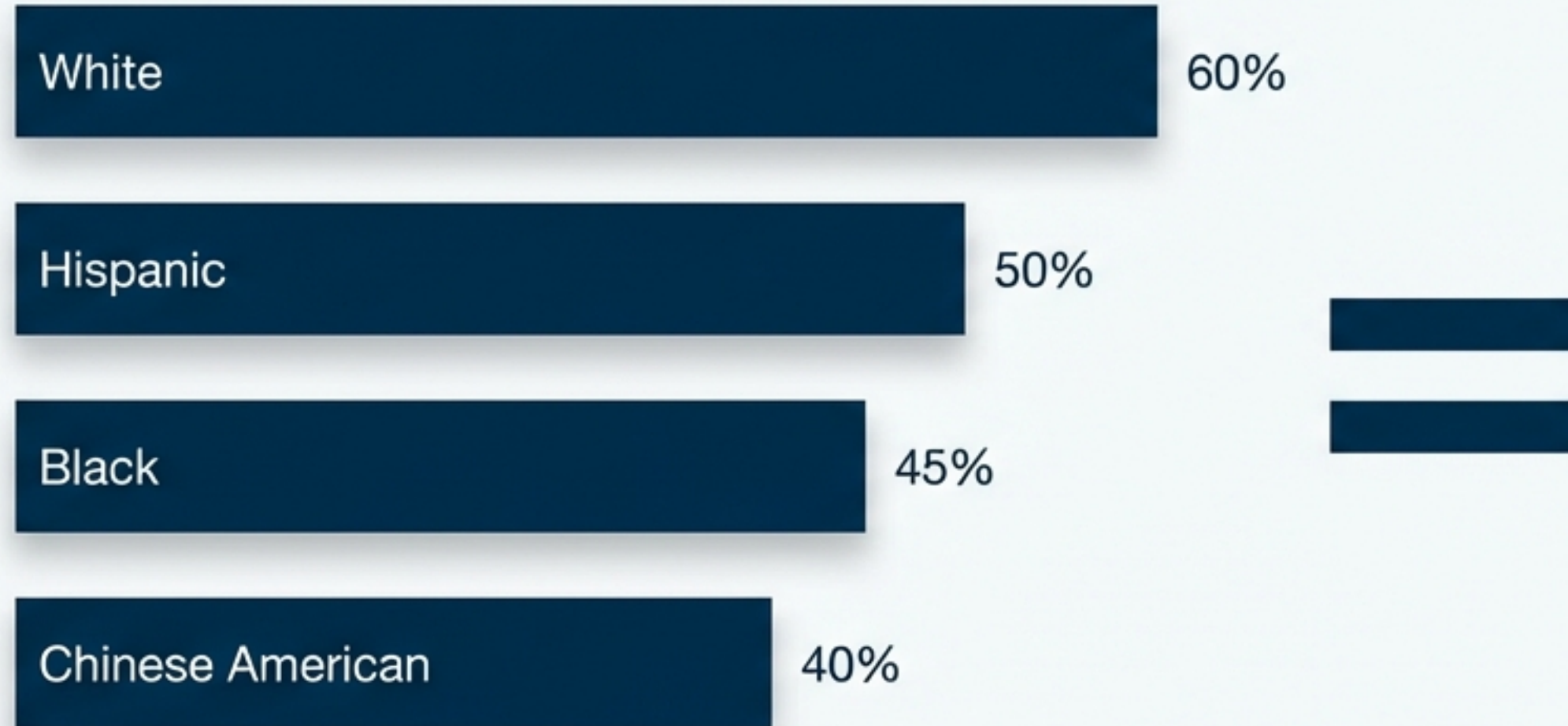
Higher proportion of Non-Calcified Plaque.

Higher prevalence of Microvascular Dysfunction.

Clinical Implication: Symptomatic women with CAC = 0 require cautious interpretation, as their pathology is often Agatston-negative.

Ethnic Variability and Risk Consistency

Prevalence of CAC



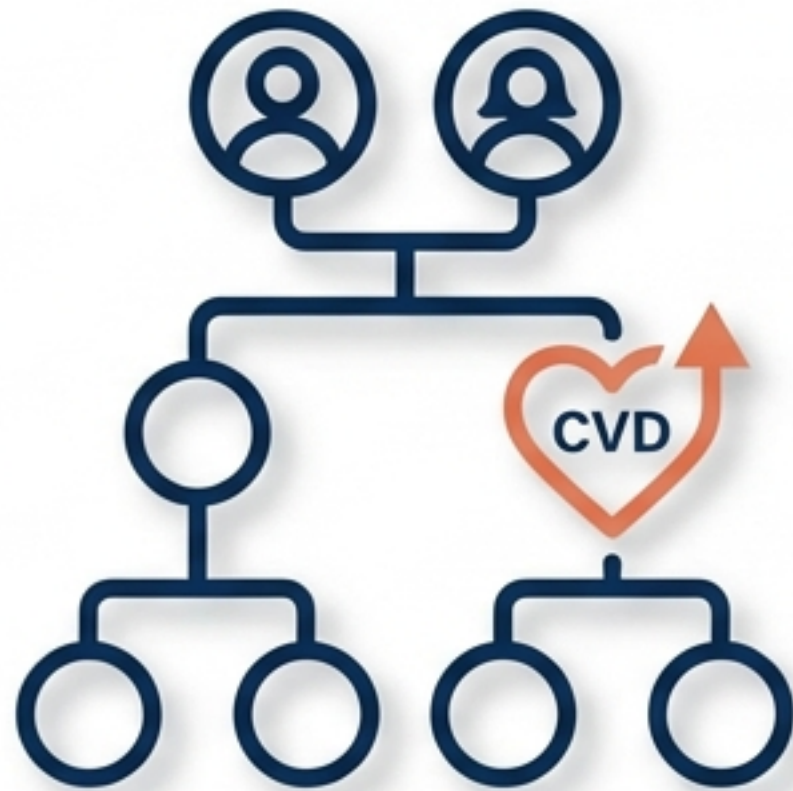
Prognostic Power is Identical

Despite prevalence differences, a Zero Score confers the same low-risk warranty across all ethnic groups (MESA).

Beyond the Score: Genetic Overrides

Certain biological factors elevate risk independent of calcification status.

Parental Premature CVD



History of premature heart disease in parents independently increases risk even if CAC = 0.

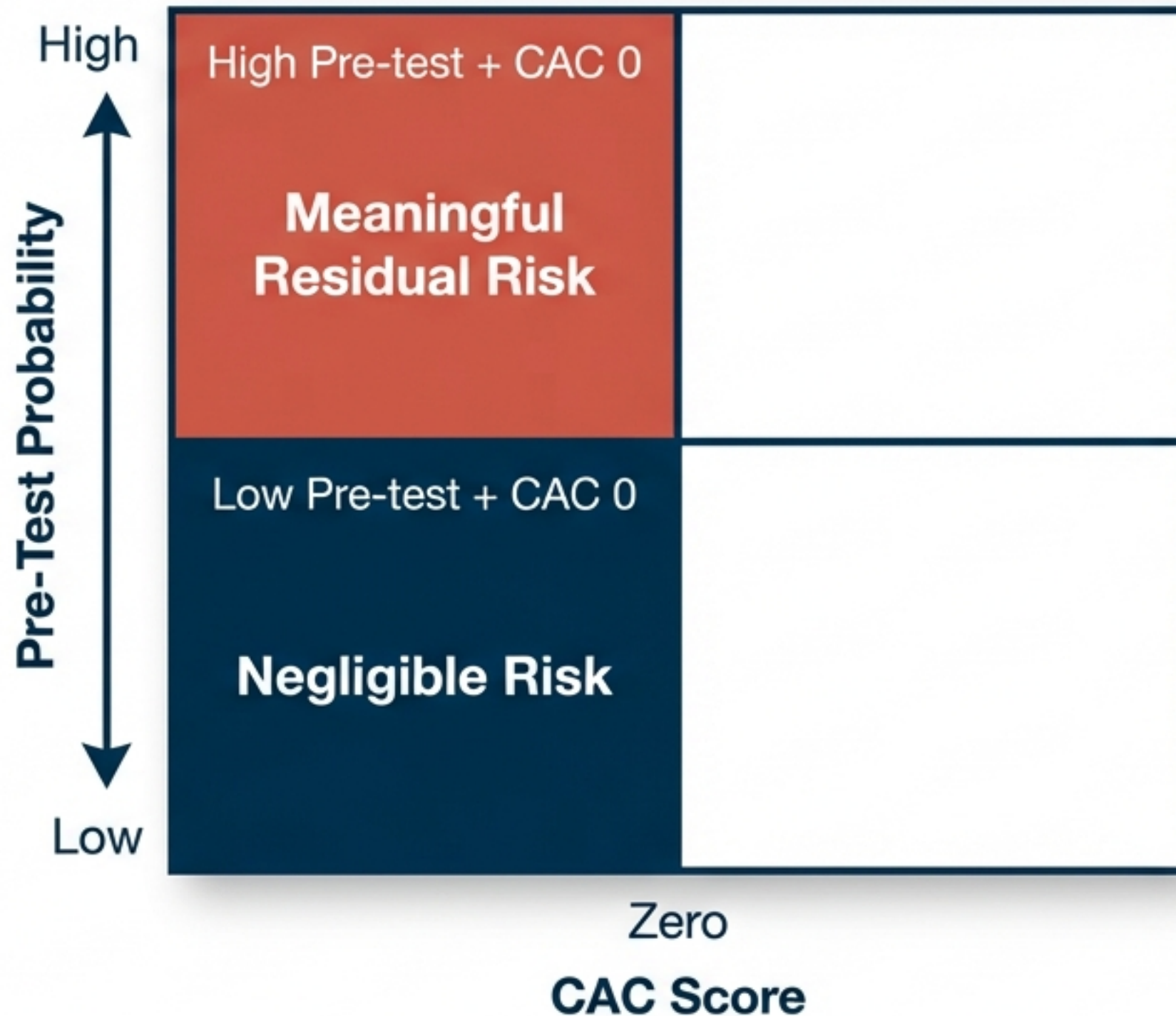
Atherogenic Index of Plasma (AIP)



Elevated AIP correlates with adverse events independent of traditional factors.

Do not rely on CAC alone in patients with strong **genetic loading**.

The Synthesis: A Bayesian Approach



We must move from a binary “Zero vs. Positive” mindset to an integrated assessment of clinical phenotype and plaque burden.

The Final Verdict

Asymptomatic



CAC = 0 is a durable “warranty” allowing safe de-escalation of therapy.

Symptomatic



CAC = 0 is a “**soft shield.**” It lowers probability but does not exclude obstructive or **vulnerable plaque.**

Future Direction



Risk stratification must evolve to integrate calcified and non-calcified plaque assessment (CCTA).

Key References

1. Blaha MJ et al. Zero Coronary Artery Calcium Score: Powerful, but What Does It Mean? *Circulation* 2020.
2. Budoff MJ et al. Long-term prognosis associated with coronary calcification. *JACC* 2007.
3. Douglas PS et al. Prognostic Value of Coronary Artery Calcium in the PROMISE Trial. *Circulation* 2015.
4. Al'Aref SJ et al. CTA-Derived Plaque Characteristics... in Patients With Coronary Artery Calcium Score of Zero. *AJR* 2024.
5. Grundy SM et al. 2018 AHA/ACC Multisociety Guideline on the Management of Blood Cholesterol.
6. Gulati M et al. 2021 AHA/ACC Guideline for the Evaluation of Chest Pain.