

# Cholesterol: From Heart Health Villain to Longevity Superhero

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Rethinking a Misunderstood Molecule



METABOLIC HEALTH  
Arizona



LIFE'S BEST  
MEDICINE

PODCAST

WITH BRIAN LENZKES, MD



LOW CARB MD  
PODCAST

WITH  
With Dr. Tro and Dr. Lenzkes

# The Current Landscape of Metabolic Health Assessment

## Limitations of Traditional Markers

- **Common Metabolic Markers**

Reliance on indicators such as Body Mass Index (BMI), Hemoglobin A1c (HbA1c), and standard lipid panels.

- **Inherent Limitations**

These markers often fail to provide a complete metabolic picture.

- **BMI Limitations**

Does not differentiate between fat and muscle mass, potentially misclassifying metabolic health.

- **HbA1c Limitations**

Offers a long-term average of blood glucose but misses crucial daily glycemic variability.

- **Lipid Panel Limitations**

Can be insufficient without considering particle size, number, and the triglyceride-to-HDL ratio.

There is a clear need for more comprehensive and predictive tools to accurately assess metabolic health and identify individual risk.

# Understanding Cholesterol Carriers

Lipoproteins: The Body's Transport System



## High-Density Lipoprotein (HDL)

Known as "good" cholesterol, HDL removes excess cholesterol from cells and arteries, returning it to the liver for processing.



## Low-Density Lipoprotein (LDL)

Referred to as "bad" cholesterol, LDL transports cholesterol from the liver to cells; high levels can cause arterial plaque buildup.

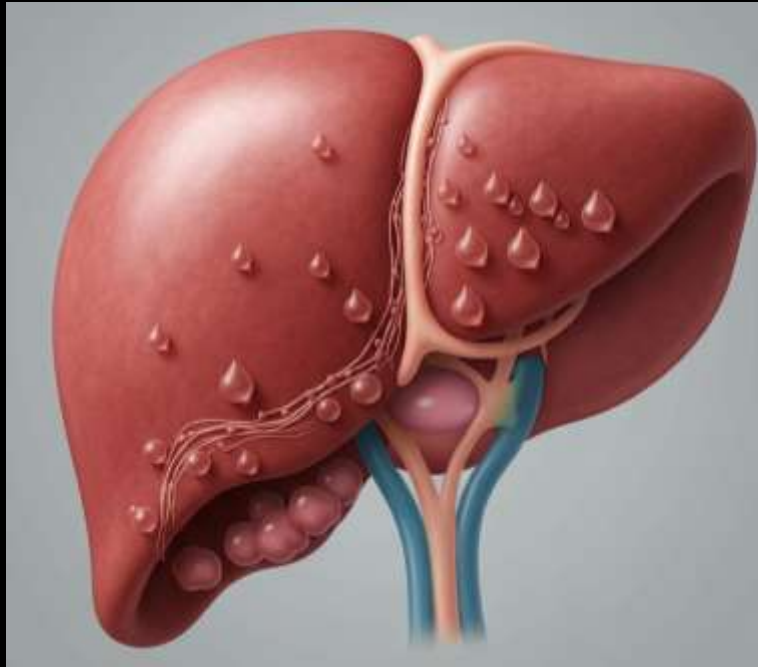


## Very-Low-Density Lipoprotein (VLDL)

Primarily carries triglycerides and cholesterol from the liver to tissues; it is a precursor to LDL.

# Understanding VLDL: The Triglyceride Carrier

Visualizing Lipoprotein Transport



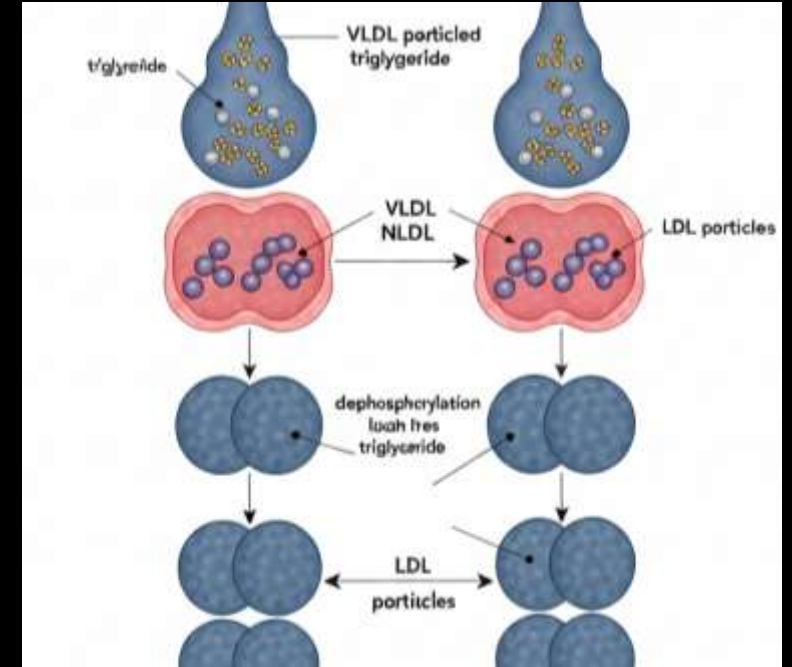
## VLDL: The Liver's Transport Particle

Very Low-Density Lipoprotein (VLDL) is produced by the liver and its primary role is to transport triglycerides (fats) to cells throughout the body.



## The VLDL Transport Boat

Imagine VLDL as a cargo ship, with triglycerides as its main payload.

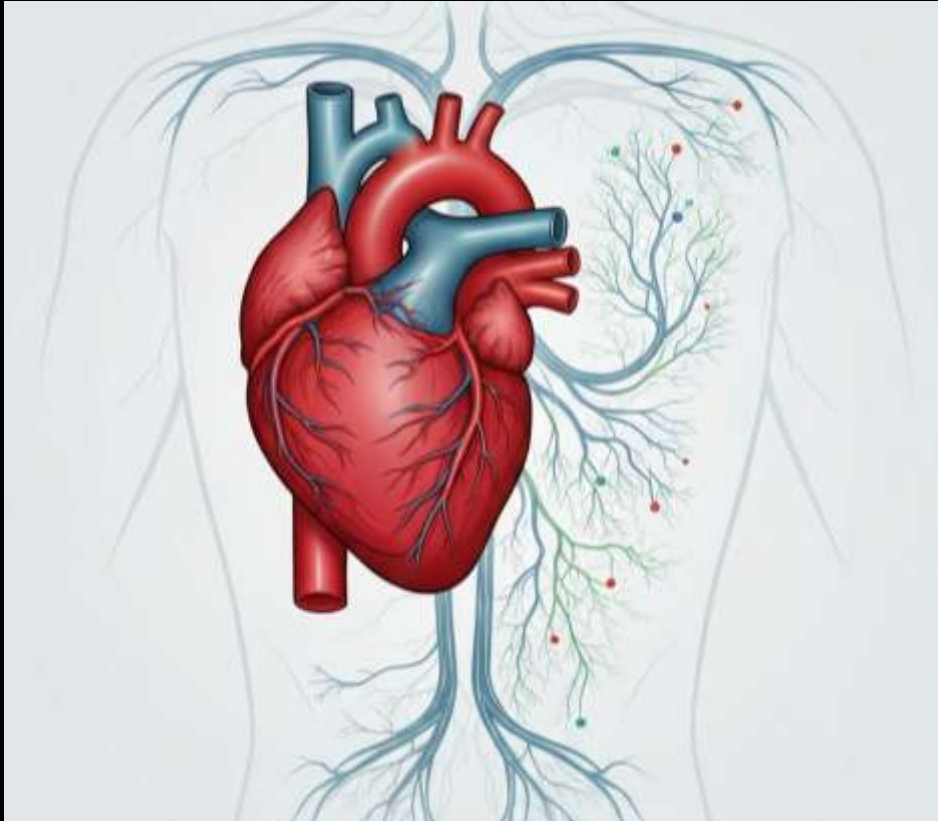


## Transformation After Cargo Delivery

As VLDL unloads its triglyceride cargo, it becomes smaller and denser, eventually transforming into other lipoproteins, such as LDL.

# Triglycerides: Key Indicators of Metabolic Health

Balancing Lipids for a Healthier Heart



- **Understanding Triglycerides**

A type of fat in your blood. High levels are linked to obesity, metabolic syndrome, type 2 diabetes, and increased heart disease risk.

- **Importance of Lowering Triglycerides**

Reducing high levels improves metabolic health, decreases risk of heart attack and stroke, and helps prevent pancreatitis.

- **Triglyceride to HDL Ratio**

A powerful predictor of cardiovascular risk. A high ratio indicates increased risk, while a low ratio suggests better metabolic health.

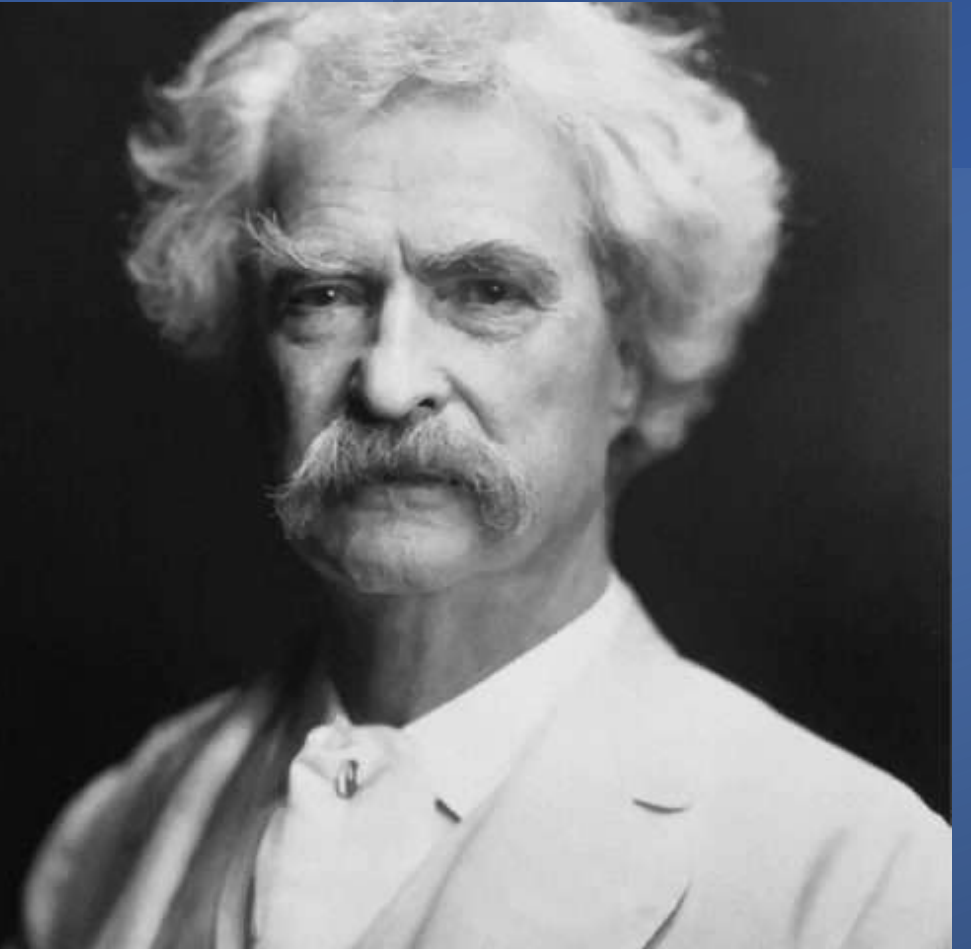
- **Factors Influencing Levels**

Diet (refined carbs, unhealthy fats), lack of exercise, weight gain, and genetics impact triglyceride levels.

Managing triglyceride levels is crucial for overall metabolic well-being and reducing cardiovascular disease risk.

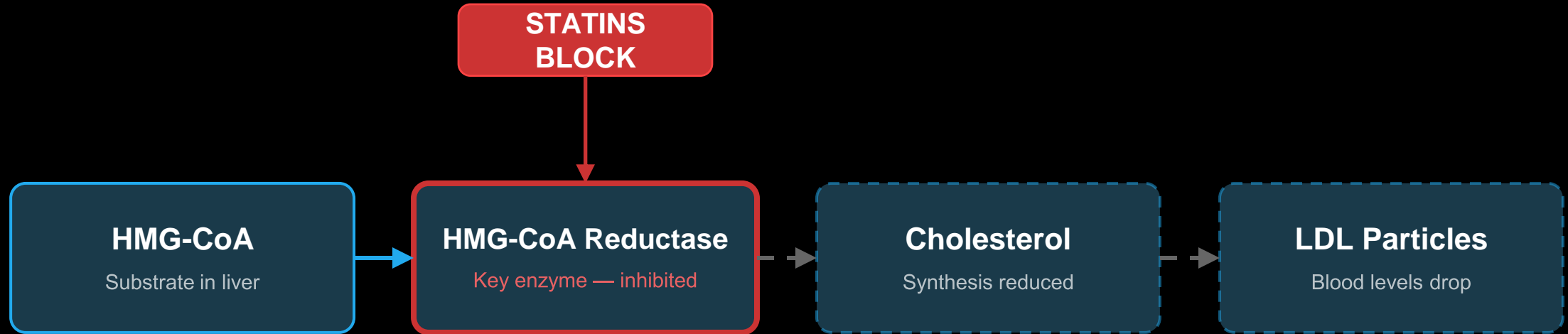
It ain't what you don't know  
that gets you into trouble. It's  
what you know for sure that  
just ain't so.

*Mark Twain*



# How Statins Block LDL Cholesterol Formation

The cholesterol synthesis pathway in the liver and where statins intervene



- **Mechanism:** Statins competitively inhibit HMG-CoA reductase, the rate-limiting enzyme in hepatic cholesterol synthesis.
- **Downstream effect:** Reduced cholesterol production prompts the liver to upregulate LDL receptors, clearing more LDL from the bloodstream.
- **Result:** Lower circulating LDL cholesterol levels, reducing cardiovascular risk.

# Impact of Statin Medications

Understanding the Risks and Benefits



## Mechanism of Action

Statins inhibit HMG-CoA reductase, an enzyme essential for cholesterol production in the liver.



## Muscle Pain & Weakness

A common side effect, ranging from mild discomfort to more severe myopathy.



## Liver Enzyme Elevations

Requires regular monitoring to detect potential liver stress.



## Increased Risk of Type 2 Diabetes

A potential risk, particularly for individuals with pre-existing diabetes risk factors.



## Cognitive Issues

Some patients may experience temporary memory loss or confusion, often reversible upon discontinuation.



## Digestive Problems

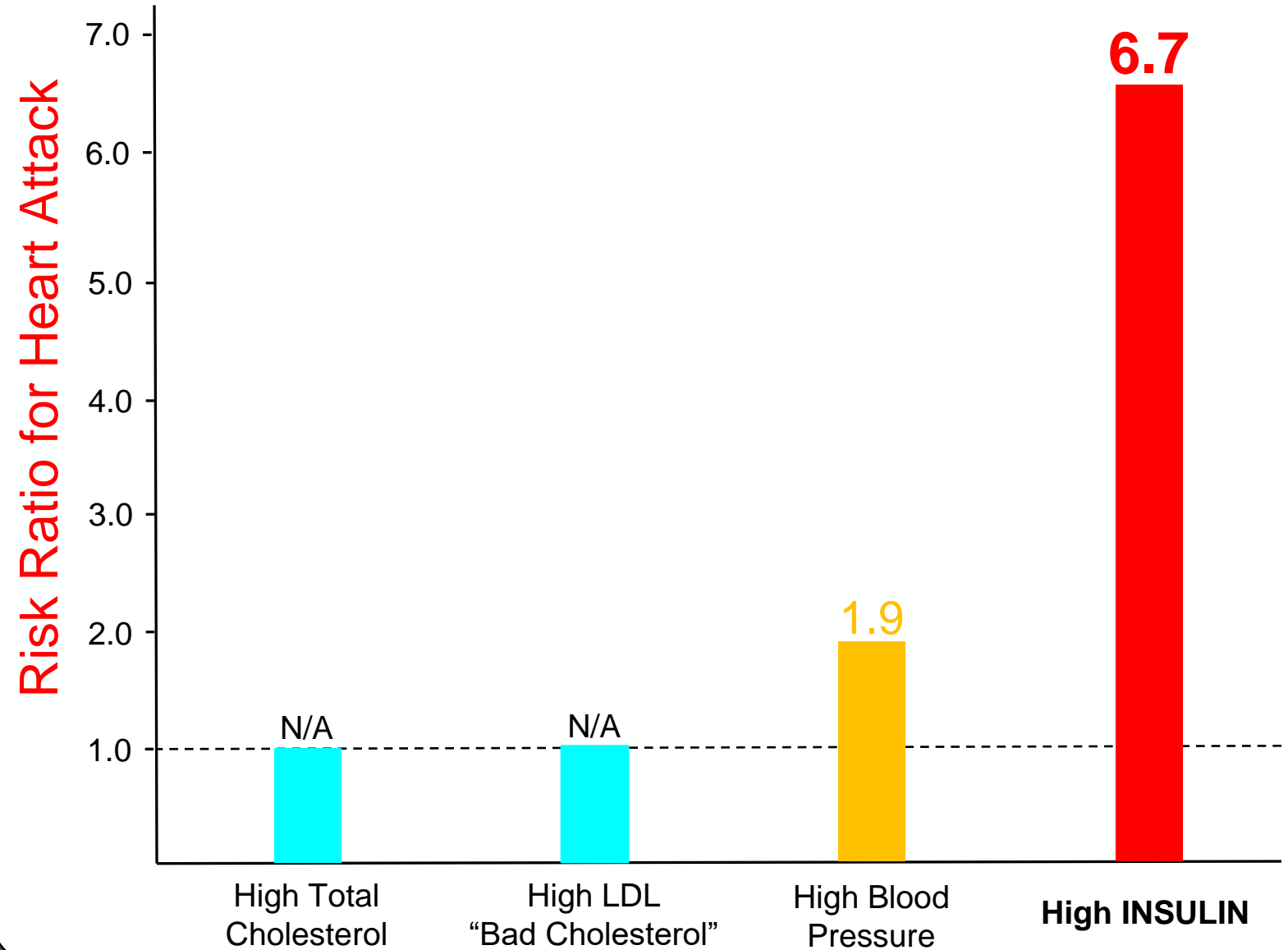
May include symptoms like nausea, diarrhea, or constipation.



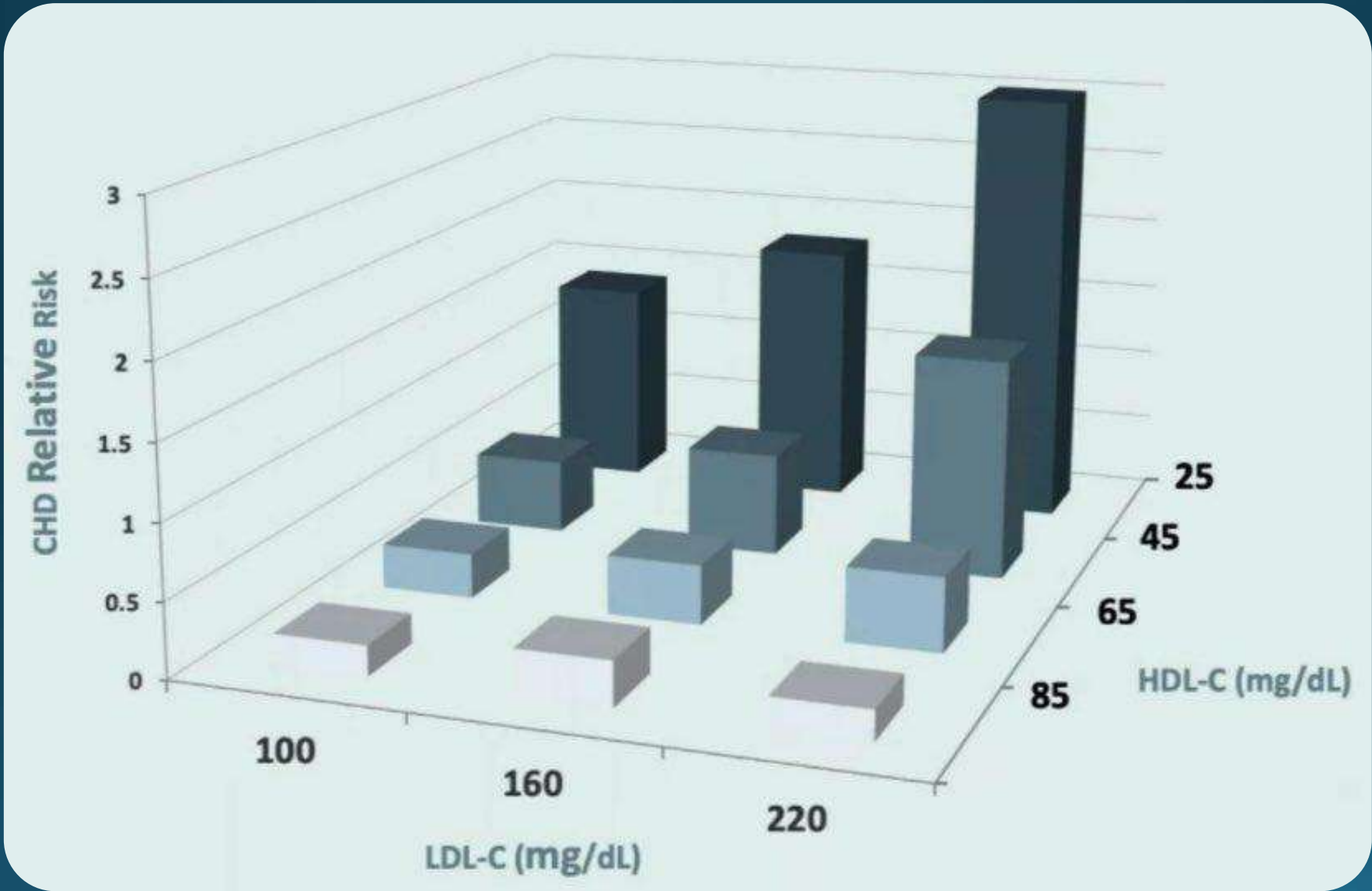
## Rhabdomyolysis

A rare but severe condition involving significant muscle breakdown, requiring immediate medical attention.

What else, unlike LDL – strongly predicts outcomes?



# Don't Underestimate the importance of HDL!!



# HDL: The Unsung Hero of Metabolic Health and Heart Protection

More Than Just 'Good Cholesterol'



- **Reverse Cholesterol Transport**

HDL actively removes excess cholesterol from tissues and artery walls, transporting it to the liver for processing and excretion, thus preventing plaque buildup.

- **Anti-inflammatory Properties**

HDL inhibits inflammatory processes in the arteries, protecting the vascular endothelium and reducing heart disease risk.

- **Antioxidant Effects**

HDL contains enzymes that neutralize harmful free radicals, protecting LDL from oxidation and its role in plaque formation.

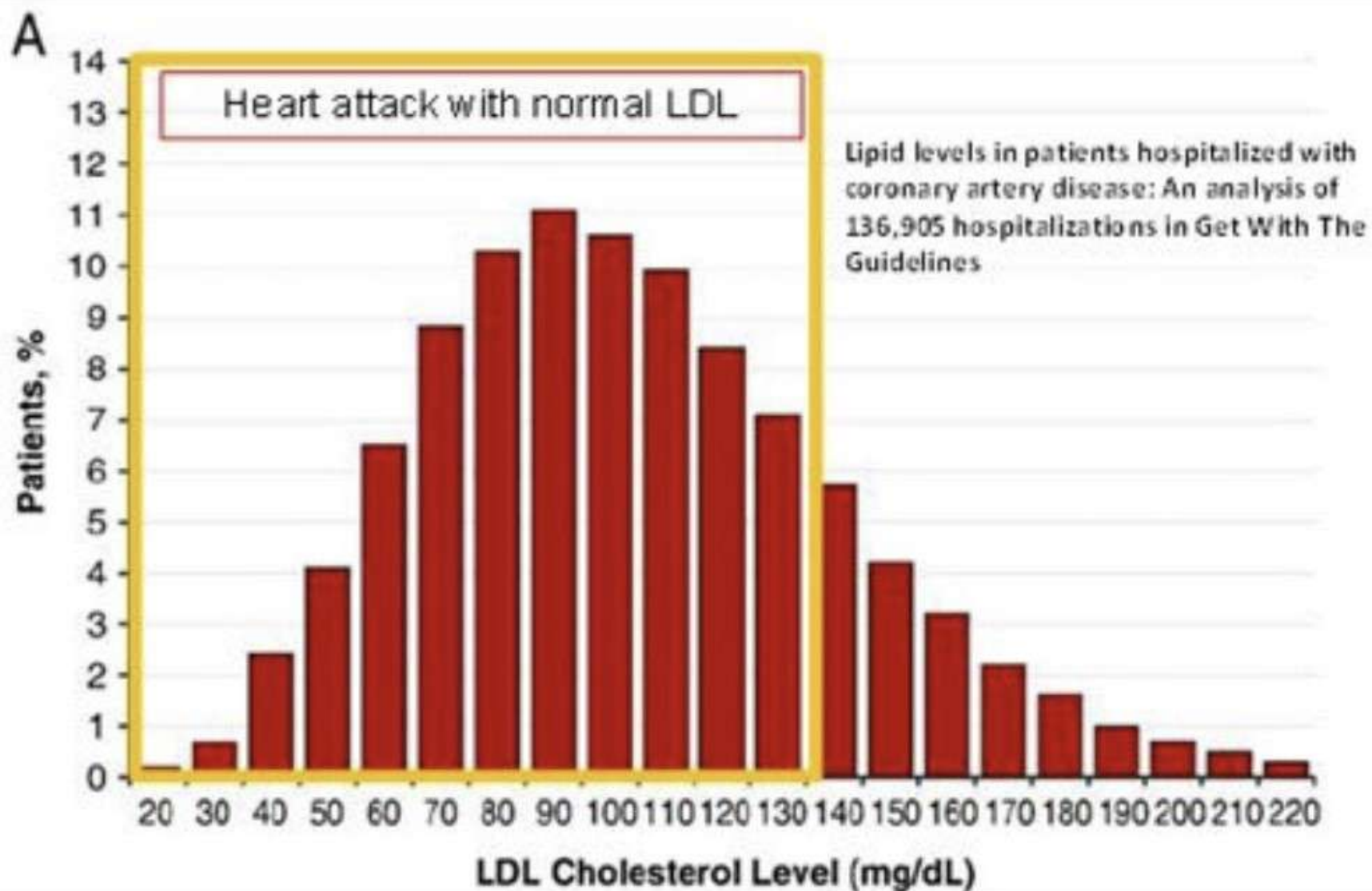
- **Metabolic Regulation**

Emerging research suggests HDL plays a role in glucose metabolism and insulin sensitivity, contributing to overall metabolic health.

- **Protective Factor**

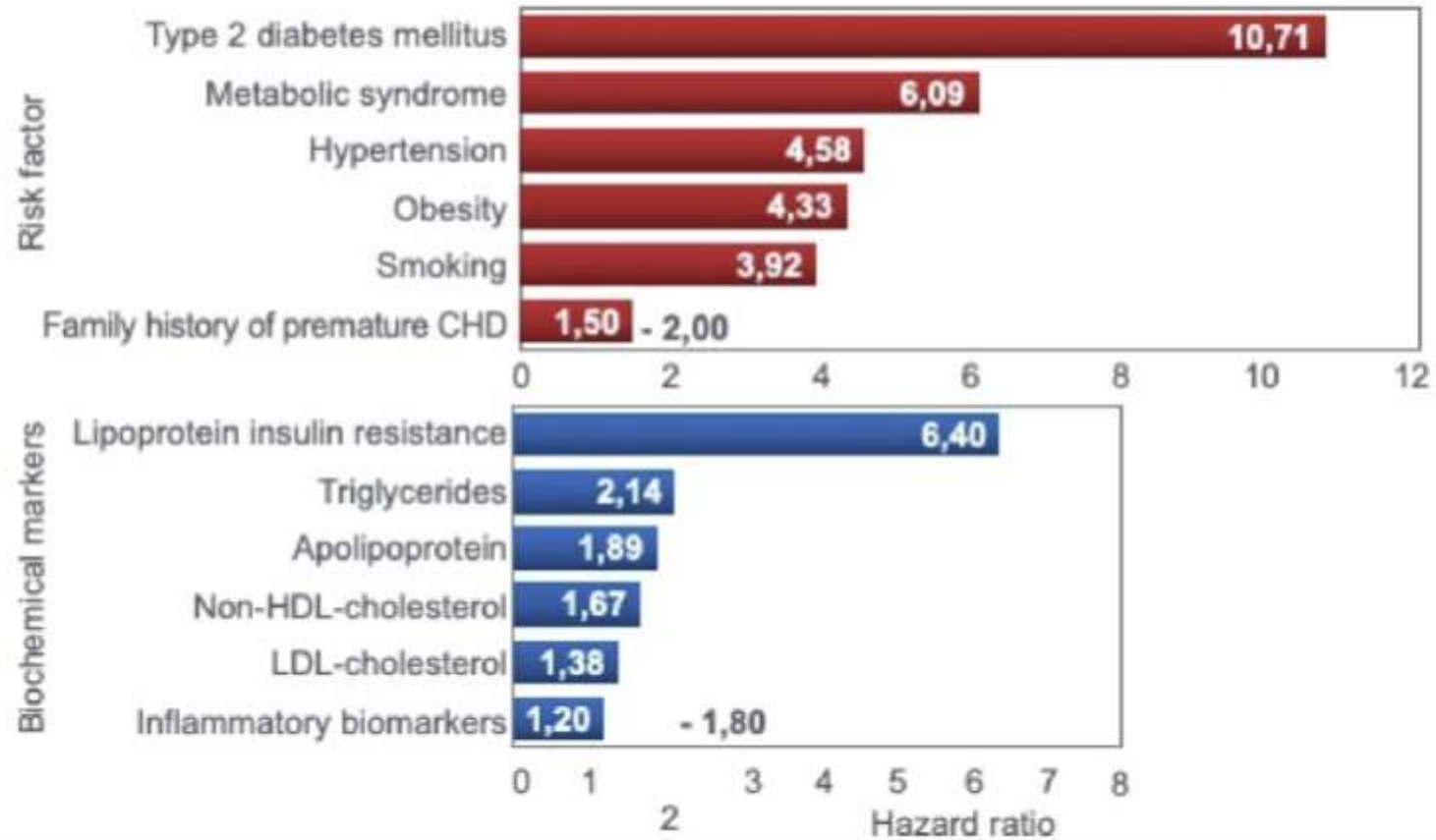
Higher HDL levels are consistently associated with a lower risk of cardiovascular events like heart attacks and strokes.

Of 136,905 patients hospitalized with heart disease, more than 75% had "normal" cholesterol levels below 130 mg/dl



# HAZARD RATIOS FOR DEVELOPMENT OF CORONARY HEART DISEASE

21.4 year follow-up. Women's Health Study





# Beyond the Bad Rap: Cholesterol's Essential Functions

The Unsung Hero of Human Physiology

- **Cellular Integrity**

Cholesterol is a fundamental component of cell membranes, maintaining their structure and fluidity.

- **Hormone Production**

It's the precursor for vital steroid hormones, including estrogen, testosterone, and cortisol.

- **Vitamin D Synthesis**

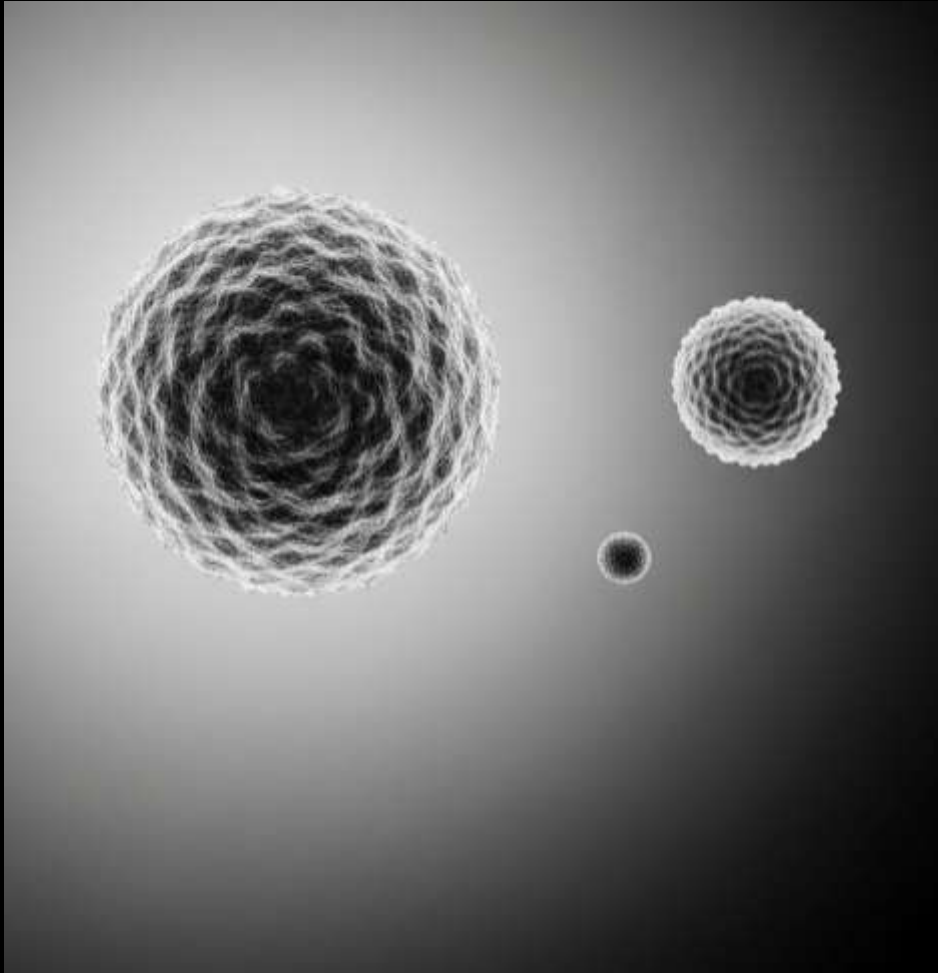
Essential for converting sunlight into Vitamin D, crucial for bone health and immune function.

- **Bile Acid Production**

Aids in fat digestion and nutrient absorption.

# Small Dense LDL vs. Large Fluffy LDL

## A Tale of Two Particles



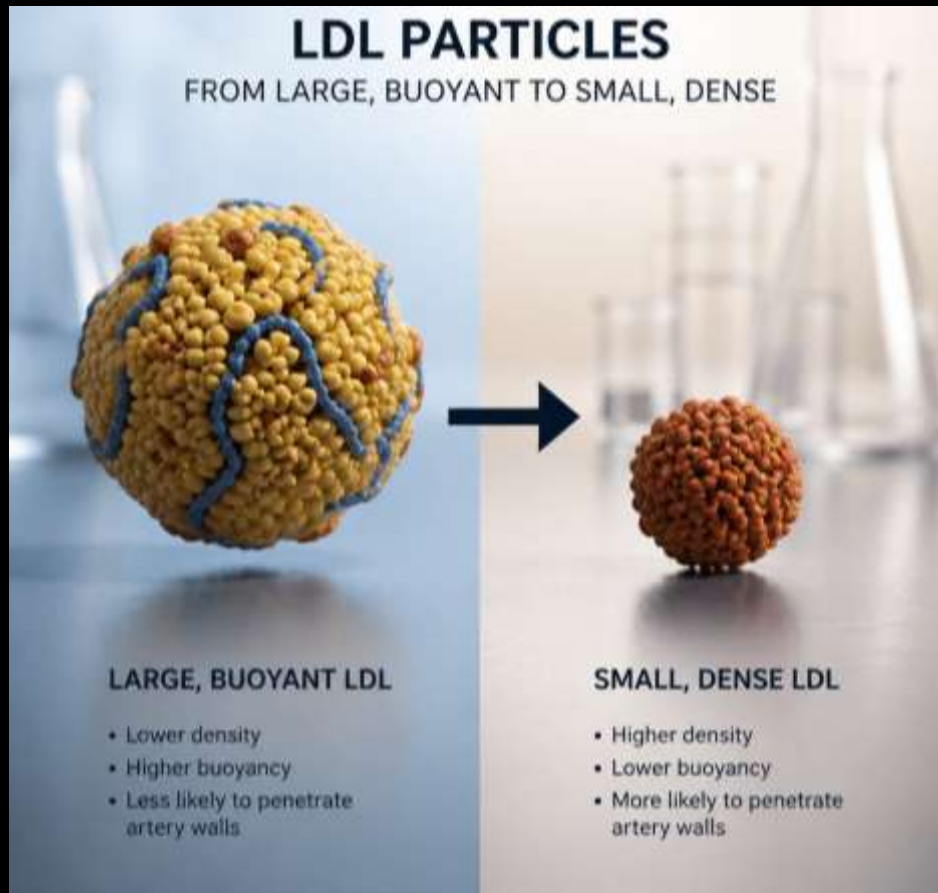
- **Small Dense LDL (sdLDL): The More Dangerous Particle**

More atherogenic, prone to penetrating artery walls and becoming oxidized. Associated with increased risk of heart disease and stroke, particularly in individuals with insulin resistance, metabolic syndrome, high triglycerides, and low HDL cholesterol.
- **Large Fluffy LDL (lLDL): The Less Harmful Particle**

Less likely to penetrate arterial walls or become oxidized, generally considered less atherogenic.
- **The Conversion Process: Lifestyle's Role**

An atherogenic lifestyle, insulin resistance, high triglycerides, and low HDL promote sdLDL. Regular exercise, a heart-healthy diet, weight loss, and management of insulin resistance can help convert sdLDL to lLDL.

# Factors Driving the Conversion of Large Buoyant LDL to Small Dense LDL



- **Elevated Triglycerides**

High triglyceride levels lead to triglyceride-rich lipoproteins (TRLs) and increased substrate for lipases.

- **Hepatic Lipase (HL) Activity**

Increased HL activity hydrolyzes triglycerides in LDL particles, transforming them into smaller, denser forms.

- **Insulin Resistance & Metabolic Syndrome**

These conditions are associated with dyslipidemia, including an increase in small dense LDL particles.

- **Dietary Factors**

Diets high in refined carbohydrates and sugars promote hepatic VLDL production and triglyceride synthesis.

- **Oxidative Stress & Inflammation**

These factors can modify LDL particles and influence lipase activity, promoting aggregation and uptake.

# The Protective LDL Profile in Metabolic Health

Why metabolically healthy individuals have LDL that is predominantly large, buoyant, and less atherogenic

## METABOLIC HEALTH MARKERS

### ✓ High insulin sensitivity

Reduces hepatic VLDL overproduction, leading to fewer small dense LDL particles

### ✓ Low triglycerides

Less CETP-mediated lipid exchange, preserving large buoyant LDL structure

### ✓ High HDL cholesterol

Efficient reverse cholesterol transport and anti-inflammatory signaling

### ✓ Low inflammation

Minimal oxidative stress and endothelial dysfunction, reducing LDL oxidation risk

### ✓ TG/HDL ratio < 2

Strong surrogate marker for insulin sensitivity and favorable LDL subclass distribution

## THE PROTECTIVE LDL PROFILE

### Predominantly Large Buoyant LDL

- Less susceptible to oxidation than small dense LDL
- Less likely to penetrate arterial walls
- Cleared more efficiently by LDL receptors

### Lower ApoB / Particle Number

- For any given LDL-C level, fewer total particles
- Each large LDL particle carries more cholesterol per particle

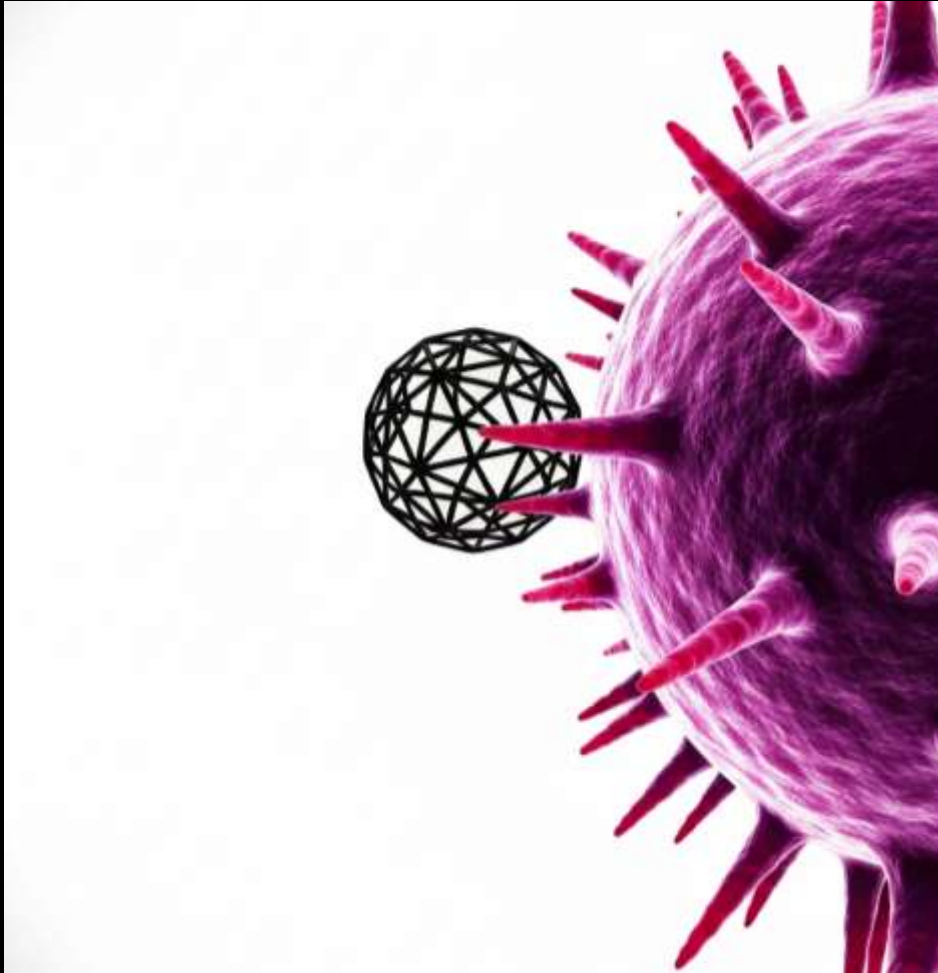
### Dietary Influence

- High-fat / low-carb diets shift LDL toward larger particles
- Reliably reduces small dense LDL concentration

**Key insight:** LDL-C alone does not capture risk — metabolic context determines whether LDL particles are protective or atherogenic

# LDL Cholesterol: An Unexpected Immune Ally

Beyond Arterial Plaque: Supporting Immune Defenses



- **Lipid Delivery**

LDL particles deliver essential lipids to immune cells, fueling their activity and function.

- **Antimicrobial Properties**

LDL can directly bind to and neutralize certain bacterial toxins and pathogens, acting as a first line of defense.

- **Modulating Inflammation**

While modified LDL can be pro-inflammatory, native LDL plays a role in regulating immune responses and can help dampen excessive inflammation.

- **Immune Cell Support**

Adequate LDL levels are crucial for the proper functioning of various immune cells, including macrophages, contributing to pathogen clearance and tissue repair. Heals myelin sheaths around nerves.



THE DATA

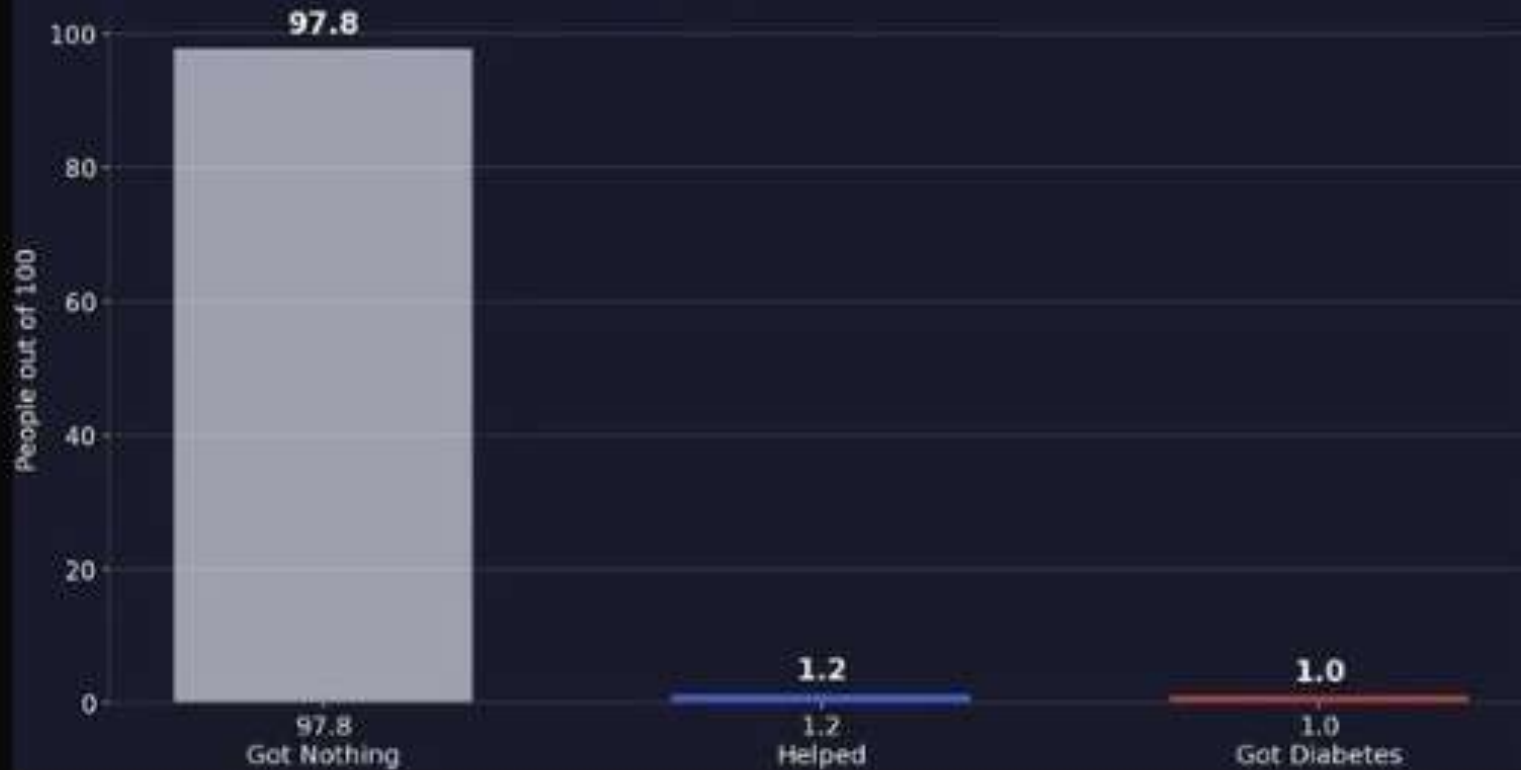
# 100 People Take Statins. What Actually Happens?

USPSTF Systematic Review - NNT Primary Prevention

HealthTrust

healthtrust.us/news

## 100 People Take Statins for 5 Years What Actually Happens?



# Higher LDL-C Associated with Lower Dementia Risk in Older Adults

Key Observational Studies in Community-Dwelling Elderly (70+)



- West et al. (2008)
- Katsumata et al. (2013)
- Schroevers et al. (2024)
- Lv et al. (2016) & Zhou et al. (2018)
- Lee et al. (2022)

# Padala et al. (2012): Statin Withdrawal Improves Cognition in Alzheimer's Dementia

## Prospective Withdrawal and Rechallenge Pilot Study

### Study Design

- 18 older adults (mean age ~79) with mild-to-moderate Alzheimer's dementia
- Already on statins
- 6 weeks statin withdrawal → 6 weeks rechallenge with same statin/same dose

### Conclusion

This pilot study found an improvement in cognition with discontinuation of statins and worsening with rechallenge. Statins may adversely affect cognition in patients with dementia.

Discontinuation of Statin:



MMSE + +1.9 points  
(p = 0.014)

Rechallenge with Statin:



MMSE + -1.9 points  
(p = 0.007)

Overall significance: p = 0.018 (repeated-measures AVOVA)



# The Cholesterol Paradox in the Elderly

## Higher LDL-C & Total Cholesterol Linked to Better Longevity & Lower All-Cause Mortality in Older Adults (65–85+)

### Key Pattern

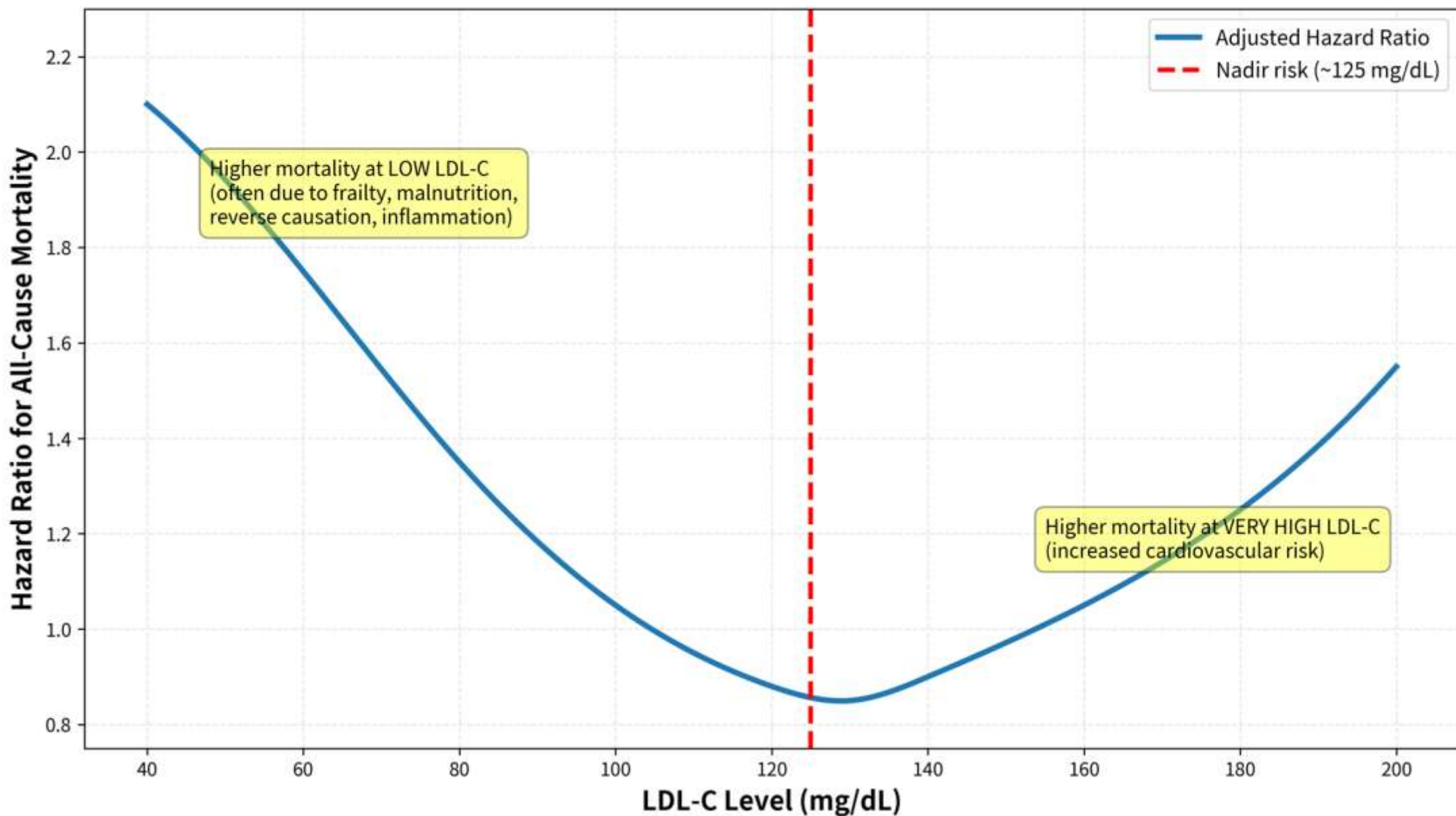
- Inverse or U-shaped relationship observed in multiple large observational studies
- Moderate-to-higher cholesterol levels associated with **lowest mortality risk**
- Often called the “**Cholesterol Paradox**” in seniors
- **Weverling-Rijnsburger (1997) – Leiden 85+ Study:** Higher TC ~ 15% lower mortality per 1 mmol/L
- **Ravnskov (2016) – Systematic review (19 cohorts):** High LDL-C inversely associated in 92% of elderly
- **Turusheva (2020), Kip (2024), Zhou (2024):** Clear U-shaped curves (nadir ~125-130 mg/dL LDL-C)
- **Hu (2024), Errigo (2025):** Strongest benefit in oldest-old (85+ / nonagenarians)

**Conclusion:** Very low cholesterol in the elderly often signals frailty, malnutrition, or preclinical illness (reverse causation). **Findings are observational — not proven causation.**



## U-Shaped Curve: LDL-C and All-Cause Mortality

(Based on restricted cubic spline models from Liu et al. 2021 NHANES, Kip et al. 2024, Zhou et al. 2024, and similar cohorts)



# Cholesterol in Seniors: A Key to Longevity?

Emerging Evidence from Research



## The Cholesterol Paradox

Unusually low cholesterol levels in older adults are paradoxically linked to increased mortality.



## Brain Health

Essential for neuronal function and repair. Adequate levels may protect against age-related cognitive decline.



## Immune Function

Crucial for a robust immune response, helping seniors fight infections.



## Increased Longevity

Studies indicate moderate to slightly elevated cholesterol may correlate with longer, healthier lives in seniors.

# Benefits of NMR Lipid Panel vs. Standard Lipid Panel

Advanced Lipoprotein Analysis for Superior Cardiovascular Risk Assessment

Standard Lipid Panel (Basic Test)	NMR Lipoprotein Panel (Advanced Test)
<ul style="list-style-type: none"><li>• Measures cholesterol mass only (Total-C, LDL-C, HDL-C, Triglycerides)</li><li>• LDL-C often calculated (inaccurate when triglycerides are high)</li><li>• Does NOT show LDL particle number or size</li><li>• Misses “discordance” — normal LDL-C but high risk</li><li>• Less accurate in metabolic syndrome, diabetes, or low-carb diets</li></ul>	<ul style="list-style-type: none"><li>• Directly measures LDL particle Number (LDL-P) — strongest predictor of plaque</li><li>• Determines LDL particle size (large buoyant vs. small dense)</li><li>• Measures ApoB (one protein per atherogenic particle)</li><li>• Assesses HDL particle subclasses and remnant particles</li><li>• Identifies hidden high-risk patterns even when standard LDL-C looks “normal”</li></ul>

**Key Advantage: It's the NUMBER and TYPE of LDL particles that drive atherosclerosis — not just the amount of cholesterol they carry.**

Especially valuable for metabolically healthy individuals & low-carb/keto diets • Evidence-based personalized heart health.

# Coronary Calcium Scan: A Window Into Your Heart

How a simple, non-invasive scan empowers patients to take control of cardiac risk.

- **See Your Risk, Not Just a Number**

A CAC score gives you a visual picture of calcium buildup in your arteries — making heart disease real and personal, not just abstract lab values.

- **Motivation to Change**

Patients who see their own calcium deposits are significantly more likely to adopt diet, exercise, and medication changes than those who only receive lab numbers.

- **Avoid Unnecessary Medication**

A zero calcium score can help patients with elevated LDL avoid statins when their actual arterial health is excellent, preventing side effects from unneeded treatment.

- **Quick, Low-Cost, No Downtime**

The scan takes under 10 minutes, requires no injection or dye, typically costs \$75–\$150, and delivers results the same day with minimal radiation exposure.

# MVX Plus and Global Mortality Risk Factors

Mapping MVX biomarkers to the GBD 2023 top modifiable risk factors for death and disability

## GBD 2023 TOP 10 RISK FACTORS

1. High systolic blood pressure
2. Particulate matter air pollution
3. Smoking
4. **High fasting plasma glucose** ◀ MVX
5. Low birthweight / short gestation
6. **High body mass index** ◀ MVX
7. **High LDL cholesterol** ◀ MVX
8. **Kidney dysfunction** ◀ MVX
9. Child growth failure
10. Lead exposure

*Highlighted = metabolic risks captured by MVX biomarkers*

## WHAT MVX PLUS MEASURES

### Inflammation Vulnerability Index (IVX)

- **GlycA** — systemic inflammation marker
- **Small HDL particles** — lipid metabolism dysfunction

### Metabolic Malnutrition Index (MMX)

- **Valine, Leucine, Isoleucine** — branched-chain amino acids reflecting protein/nutritional status
- **Citrate** — energy metabolism and mitochondrial function

### Why This Matters

- MVX captures 4 of the top 10 GBD risk factors through a single NMR-based blood test
- Also detects underlying inflammation and malnutrition that drive mortality independently of individual risk factors
- Nearly half of all global death and disability is preventable by modifying these metabolic risk factors (GBD 2023)
- MVX = Composite of IVX and MMX (Score 1-100)

MVX for Toxicity Screening

# MVX and Toxicity Assessment

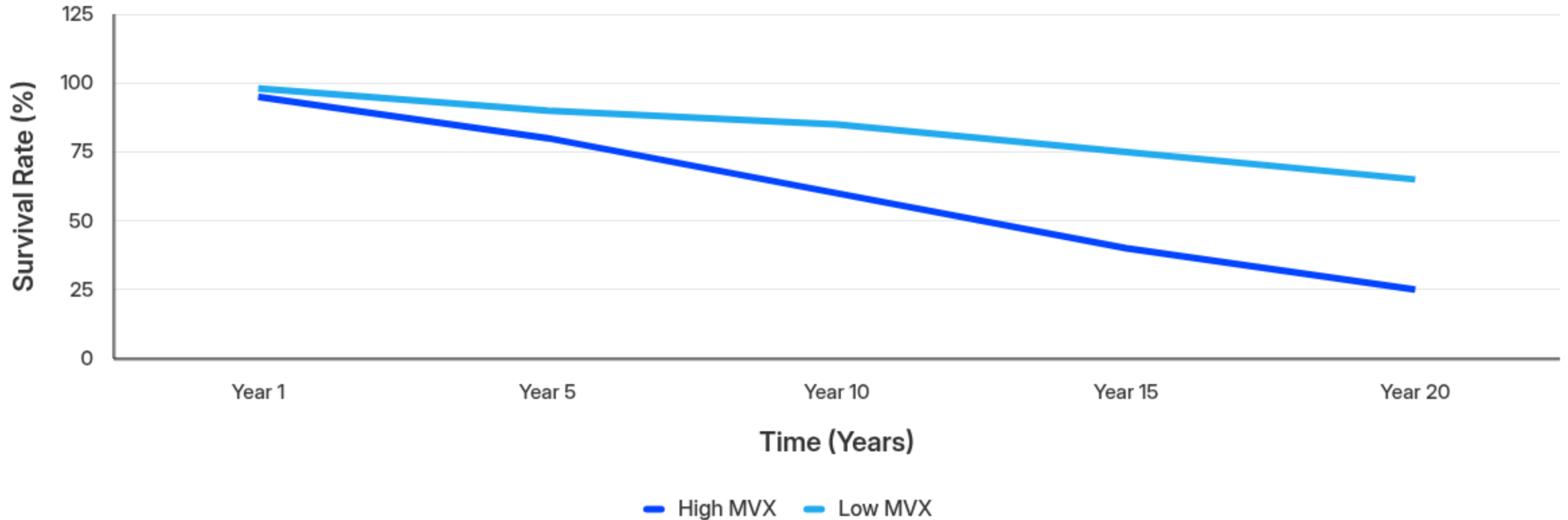
- Relationship with Toxins: Explores the connection between MVX and exposure to environmental, dietary, and other toxins.
- Cellular Burden & Response: Demonstrates how MVX can identify the cellular impact of toxins and the body's adaptive mechanisms.



MVX offers the capability to detect subclinical toxic effects, identifying issues before overt symptoms manifest.

# The Predictive Power of MVX for All-Cause Mortality

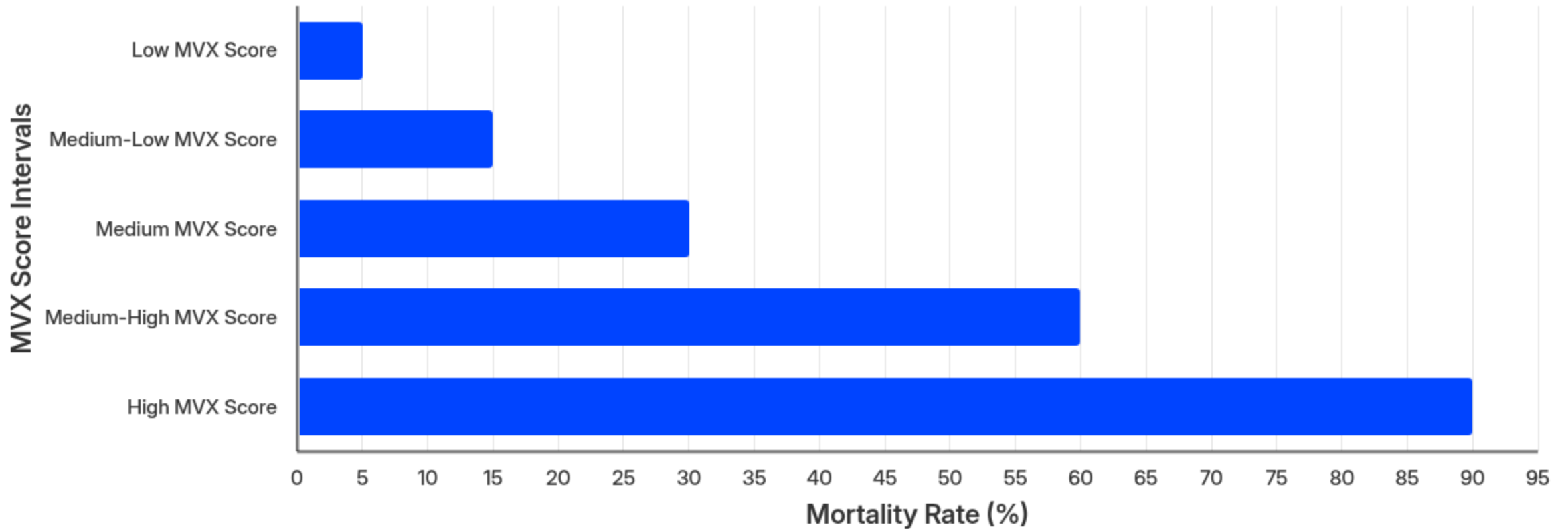
Evidence and Studies on MVX and Longevity



MVX levels are a significant predictor of all-cause mortality.

# MVX Scores vs. 5-Year Mortality Rates

Visualizing the Correlation



A clear positive correlation exists between MVX scores and 5-year mortality rates.

# Benefits of MVX Plus for Predicting All-Cause Mortality

Evidence-based advantages from peer-reviewed studies across multiple cohorts.

- **Strong Predictive Accuracy**

HR of 1.73 (95% CI: 1.49–2.01) for highest-quartile MVX in MESA (5,887 adults, 17.9-year follow-up).

- **Captures Hidden Metabolic Risk**

Integrates inflammation (IVX) and malnutrition (MMX) sub-indices from six NMR-derived metabolites missed by conventional panels.

- **Validated Across Populations**

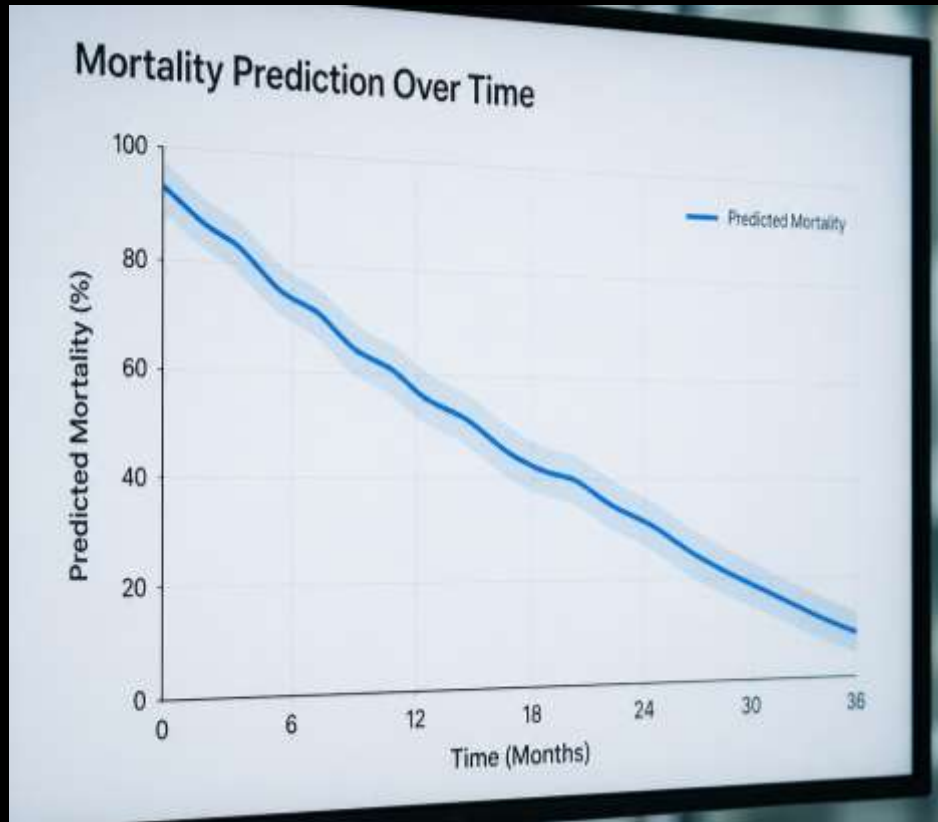
Replicated in CATHGEN (n=5,876), Intermountain Heart (n=2,888), PREVEND (n=5,446), and UK Biobank (n=218,635) cohorts.

- **Enables Early Intervention**

Identifies at-risk patients before symptoms appear, guiding targeted anti-inflammatory, nutritional, or personalized therapies for better outcomes.

# Summary and Key Takeaways

Consolidating Insights



- **MVX Testing for Metabolic Health**

Offers a comprehensive assessment of metabolic health and toxicity.

- **Predictive Power**

MVX is a powerful predictor of all-cause mortality.

- **Clinical Potential**

Significant potential for clinical application in risk stratification and personalized medicine.

Call to Action: Consider MVX testing for a deeper understanding of patient metabolic profiles.

## Key Takeaways – Why MVX Plus Matters

- Powerful, independent predictor of all-cause mortality across cohorts (HF, cardiac cath, general population)
- Graded risk even in low-risk patients
- Identifies treatable metabolic/inflammatory drivers
- Enables personalized lifestyle & intervention strategies

**MVX Plus provides superior/additive risk stratification beyond standard markers**

# Holistic Longevity

Beyond Medication: Lifestyle Interventions for a Healthier Life



## Dietary Wisdom

Focus on whole, unprocessed foods, healthy fats, and high-fiber fruits and vegetables.



## Mindful Movement

Engage in regular, moderate physical activity combining aerobic, strength, and flexibility training.

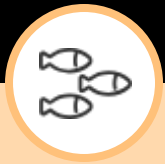


## Stress Management

Practice mindfulness, meditation, yoga, and prioritize adequate sleep hygiene.

# Nutrient Synergy for Longevity

Focusing on Key Nutrients



## Omega-3 Fatty Acids

Support heart and brain health. Found in fatty fish and flaxseeds.



## Antioxidants

Combat oxidative stress. Found in colorful fruits and vegetables (Vitamins C & E, beta-carotene).



## Magnesium

Involved in hundreds of bodily processes, including muscle and nerve function.

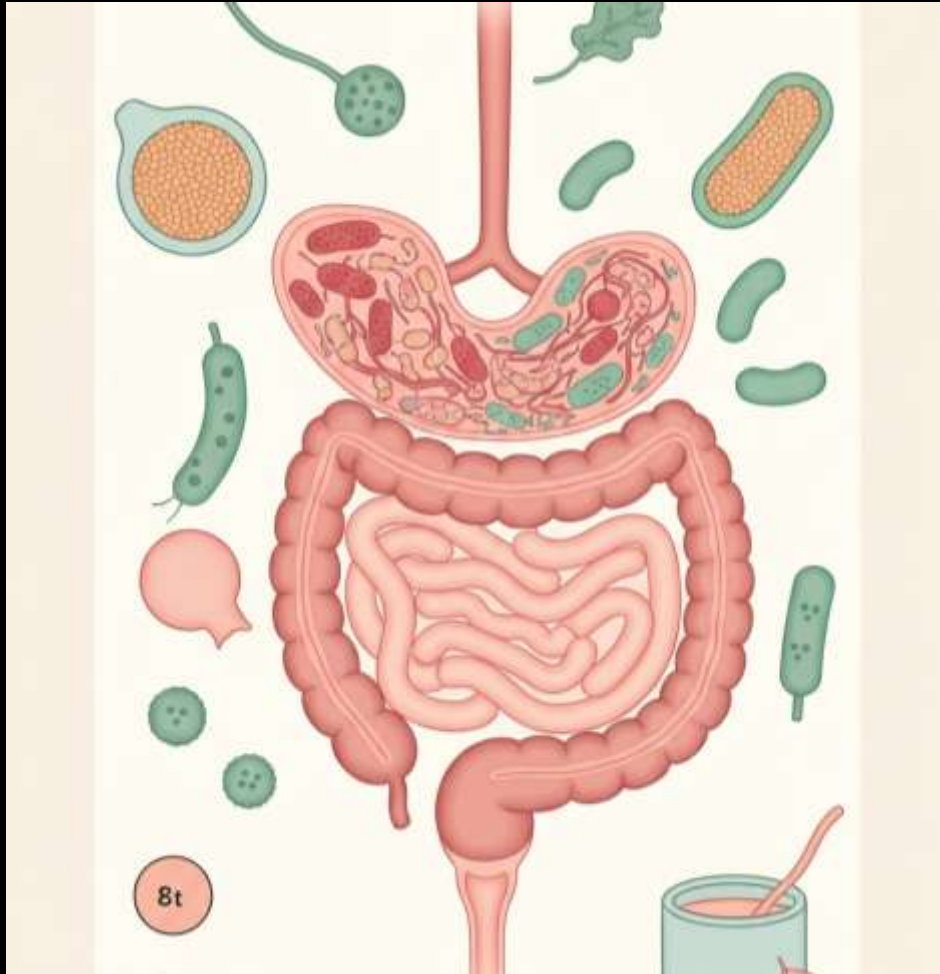


## Fiber

Aids digestion, helps manage cholesterol levels, and promotes gut health.

# The Gut-Brain Connection & Longevity

## Nurturing Your Microbiome



- **The Microbiome's Role**

A diverse gut microbiome is linked to better immune function, mood regulation, and reduced inflammation.

- **Prebiotics**

Fuel beneficial bacteria (e.g., onions, garlic, bananas).

- **Probiotics**

Introduce beneficial bacteria (e.g., yogurt, kimchi, sauerkraut).

- **Limit Processed Foods**

These can negatively impact microbial diversity.

# Key Takeaways for Longevity

Integrating Knowledge for a Healthier Future



- **Reframe Cholesterol**

Understand its vital functions beyond just heart disease risk.

- **Prioritize Lifestyle**

Diet, exercise, sleep, and stress management are powerful tools for longevity.

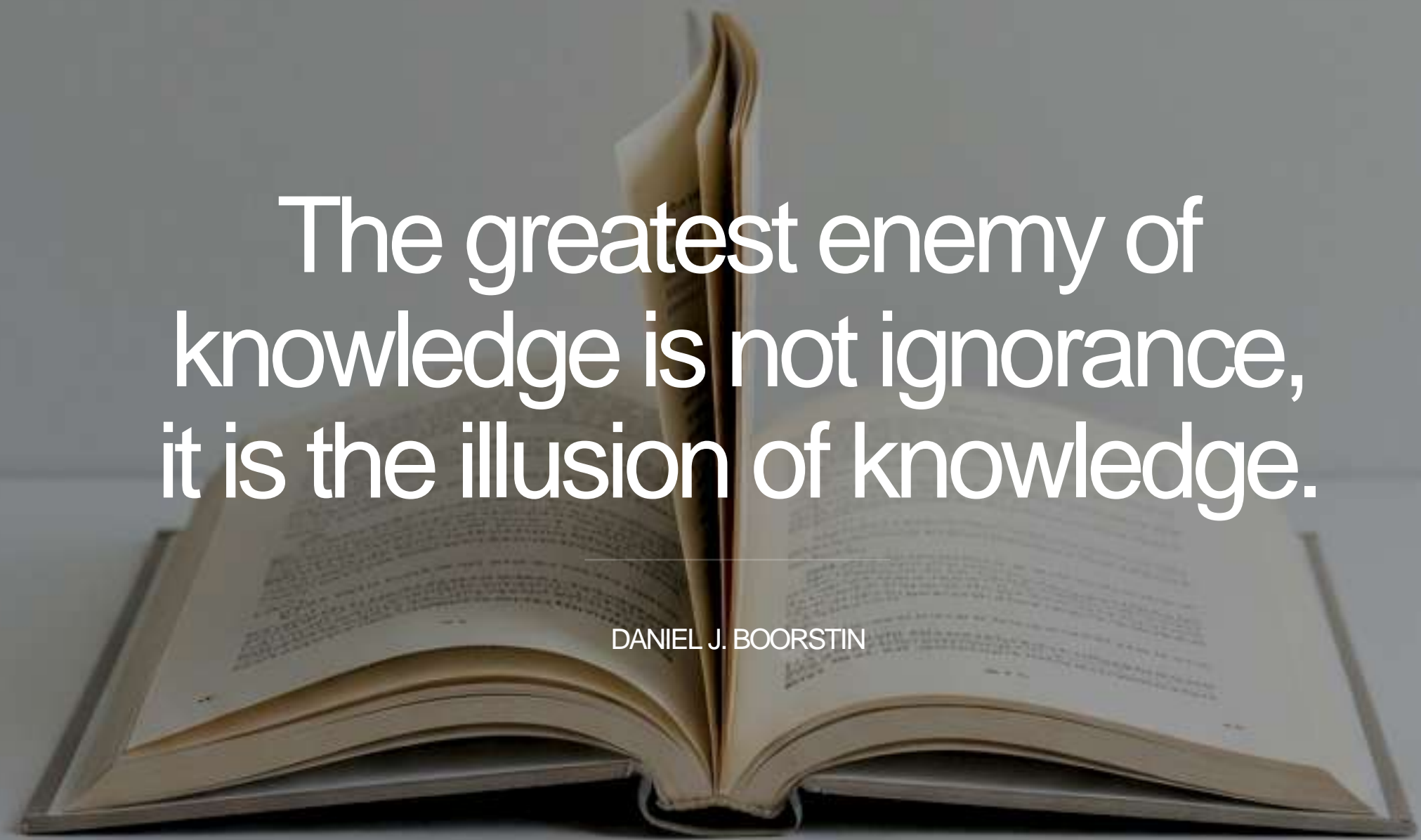
- **Informed Decisions**

Discuss medication risks, benefits, and alternatives with healthcare providers.

- **Holistic Approach**

Nurture your body and mind for sustained well-being.

Embrace a proactive and informed approach to health for a longer, more vibrant life.

An open book is shown from a top-down perspective, lying flat. The pages are filled with dense, small text, which is mostly obscured by a large white quote. The book is centered in the frame against a light gray background.

The greatest enemy of  
knowledge is not ignorance,  
it is the illusion of knowledge.

DANIEL J. BOORSTIN

**The Science Is Not Settled**



THE  
**CHOLESTEROL  
CODE**



Discussion Points

# Questions & Discussion

- Open floor for questions.
- Encouraging a personalized approach to health and longevity.

