

# Revisiting Saturated Fat's Role in Cardiovascular Disease – The Case for C15:0

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May 31, 2026

## STORY AT-A-GLANCE

- › Cardiovascular disease remains the world's leading cause of death, and decades of blaming all saturated fat alike have overlooked important distinctions, including the protective role of the odd-chain saturated fat pentadecanoic acid (C15:0)
- › C15:0 is found mainly in full-fat grass fed dairy. My narrative review on C15:0 highlights its potential role in supporting cardiovascular and metabolic health markers
- › Long-term population studies and meta-analyses show that higher blood levels of C15:0 predict healthier cholesterol, less inflammation, and reduced cardiovascular events
- › Early supplementation trials using purified C15:0 at 100 milligrams daily improved triglycerides, cholesterol balance, and inflammatory markers
- › Nutrition guidelines may eventually shift the view on saturated fats, with C15:0 standing out as a fat that warrants further investigation in the context of cardiovascular health

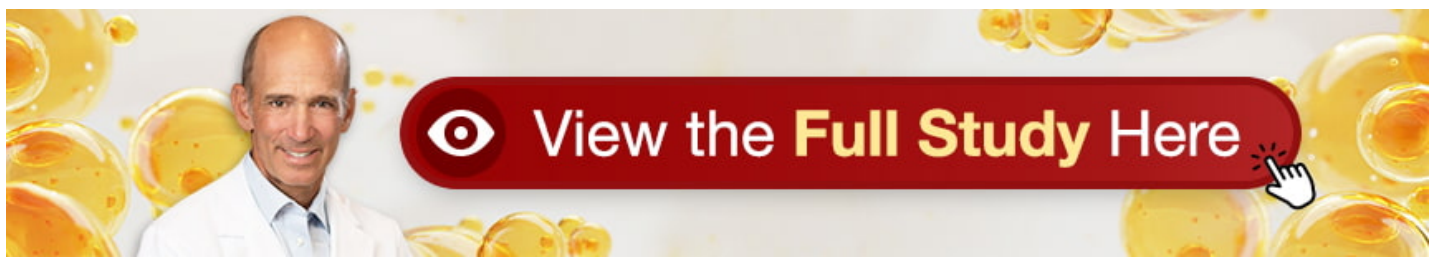
Cardiovascular disease remains the leading cause of death worldwide,<sup>1</sup> even with decades of medical progress. For much of the past century, saturated fat was labeled a primary driver of clogged arteries and heart attacks, shaping dietary advice, food production, and the way entire populations eat.<sup>2</sup> Yet research has revealed that this blanket condemnation overlooked important distinctions in fats.

In 2025, I published a narrative review in the *World Journal of Cardiology*, an internationally recognized, peer-reviewed journal known for advancing understanding of cardiovascular disease and its prevention. In this work, I highlight an emerging paradigm: not all saturated fats are the same, and the odd-chain saturated fat pentadecanoic acid (C15:0) – primarily found in dairy fat – appears to have meaningful effects on several cardiovascular and metabolic markers, according to studies.

The framework I present challenges long-standing dietary guidance that restricts all saturated fats as a single category. Instead, my review synthesizes evidence showing that C15:0 supports healthier lipoprotein profiles, inflammation, insulin sensitivity, and mitochondrial function – mechanisms that, taken together, are being investigated for their relevance to cardiovascular risk.

By reframing C15:0 as a "good" saturated fat, this paper provides the scientific foundation for re-evaluating dietary recommendations and exploring whether C15:0 intake – through food or supplementation – fits into broader cardiovascular research.

Below, I summarize its central findings; however, I also encourage you to read the paper (linked below), or download a copy of the simplified version of it (see link at the end of the article), so you can better understand why this unique fat is so important for heart health.



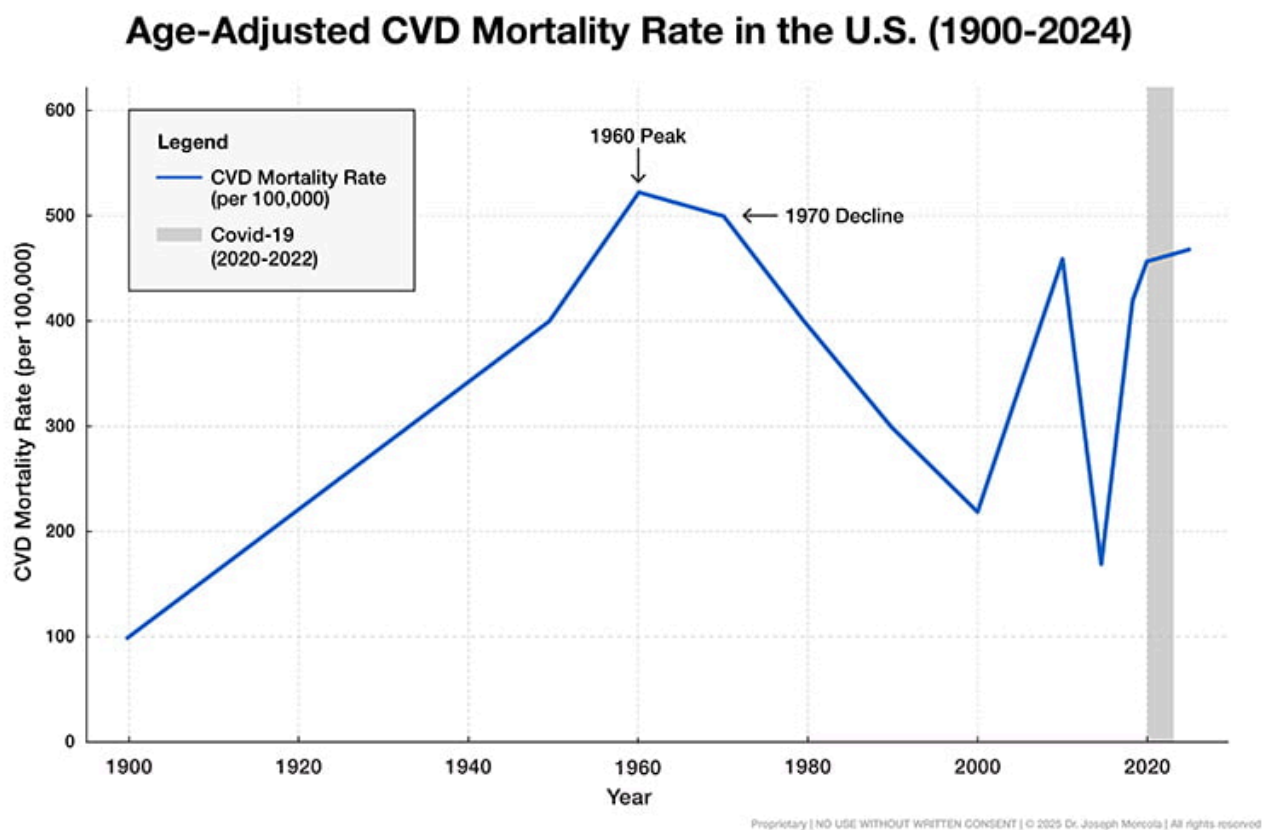
## **Shifts in Heart Disease and Dietary Guidance**

Heart disease rose sharply in the United States during the first half of the 20th century. In 1900, infectious diseases were still the leading cause of death, and cardiovascular disease was a relatively minor concern. By 1950, however, coronary heart disease and

stroke had surged to the forefront, claiming more lives each year and quickly becoming the nation's most pressing health threat.

- **By the 1960s, cardiovascular mortality reached its peak** – Age-adjusted cardiovascular mortality in the U.S. peaked in 1968, when it reached 520 deaths per 100,000 people. At that time, nearly 40% of all deaths in the U.S. were from heart disease and stroke combined. This marked the highest burden ever recorded.<sup>3</sup>

From the 1970s up to the early 2010s, age-adjusted cardiovascular mortality fell by roughly 50% to 70% in many high-income countries. In the U.S., the heart disease death rate dropped to about 168 per 100,000 by 2015.<sup>4</sup>



**Figure 1.** Age-adjusted cardiovascular mortality in the United States fell steeply after 1960 but rebounded during the COVID-19 era, underscoring the persistent public-health burden of heart disease.

- **Several major public health measures contributed to this improvement** – Cigarette smoking, once pervasive, declined sharply after large-scale anti-smoking campaigns. Blood pressure screening and treatment became widespread, lowering the prevalence of uncontrolled hypertension.

Improved management of risk factors like cholesterol and blood pressure, along with advances in emergency cardiac care, surgical techniques, and secondary prevention, steadily increased survival. Together, these factors drove down mortality across multiple decades.

- **From 2010 to 2019, the pace of decline slowed** – During this period, the age-adjusted cardiovascular death rate fell only modestly, from 456.6 to 416 deaths per 100,000 adults. Much of this slowdown was attributed to rising levels of obesity, Type 2 diabetes, and metabolic syndrome, which increased risk despite continued progress in treatment and acute care.<sup>5</sup>
- **The COVID-19 pandemic reversed much of this progress** – Between 2020 and 2022, cardiovascular mortality rose by 9%, the largest increase in decades. In that short span, there were approximately 228,000 more cardiovascular deaths than expected based on prior trends.<sup>6</sup>

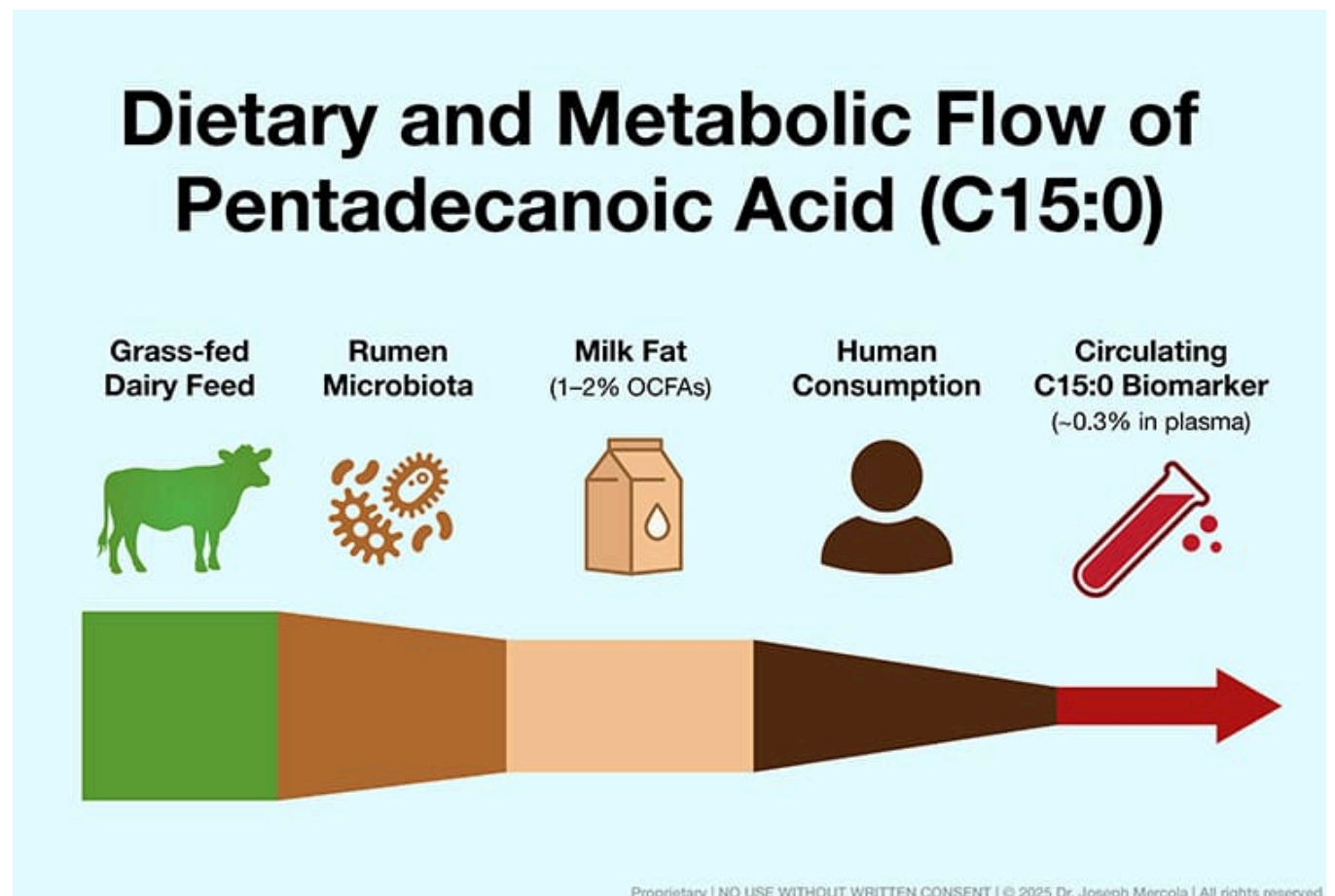
Contributing factors included the cardiovascular complications of COVID-19 infection, interruptions in medical care, and worsening control of chronic conditions during the pandemic. By 2022, mortality rates had climbed back to the levels seen in 2010.<sup>7</sup>

- **Dietary fat has been central to cardiovascular prevention efforts since the 1950s** – The diet-heart hypothesis, which proposed that saturated fat intake increased cholesterol and directly caused cardiovascular disease, shaped both research and public policy. This flawed theory guided decades of dietary recommendations, which encouraged the replacement of animal fats with vegetable oils and the widespread adoption of low-fat products.<sup>8</sup>
- **These policies reshaped the food environment in the U.S. and many other countries** – Butter, lard, and full-fat dairy products were displaced by margarine, refined vegetable oils, and skim or low-fat dairy. Refined carbohydrates often filled

the gap left by reduced fat intake. This shift reduced population exposure to some fatty acids that were not well studied at the time, including odd-chain saturated fats such as C15:0.

## From Rumen Microbes to Your Plate – How C15:0 Enters the Diet

C15:0 originates primarily from ruminant animals, with full-fat dairy being the richest dietary source. Whole milk, butter, cheese, and yogurt contain the highest levels, and in cow's milk fat, odd-chain fatty acids make up about 1% to 2% of total fats, with C15:0 and C17:0 being the most abundant.



**Figure 2.** Major exogenous pathway for pentadecanoic acid: microbial synthesis in ruminants yields C15:0-rich milk fat that, once ingested, produces characteristic circulating C15:0 signatures usable as objective dairy-intake biomarkers.

- **Microbes, not cows, make odd-chain fats** – When the microbes in the rumen (the first stomach of a ruminant animal) ferment dietary fiber, they generate propionate, a short-chain fatty acid (SCFA), which is converted into propionyl-CoA. This is then

added to the front end of growing fatty acids, resulting in odd-chain fats like C15:0 and C17:0, which are incorporated into the cow's tissues and released into its milk.

- **Dairy fat is the dominant dietary source** — Because of this microbial process, dairy fat contains much higher amounts of C15:0 than other foods. Since C15:0 is located in the milk-fat portion, foods like whole milk, butter, and cheese provide meaningful amounts, whereas reduced-fat and skim milk contain far less. Ruminant meats supply smaller amounts, while certain fish and plants provide only trace levels.
- **C15:0 is a reliable biomarker of dairy fat intake** — Because food diaries and questionnaires are often inaccurate, researchers use C15:0 levels in the blood as an objective measure of dairy consumption. It can be detected in plasma phospholipids, cholesterol esters, and red blood cell membranes, reflecting intake over weeks to months.

In one trial, a 10-fold increase in full-fat dairy consumption led to a proportional increase in plasma C15:0. Conversely, replacing dairy fat with other fats caused circulating C15:0 to drop. These results indicate that blood levels of C15:0 serve as a direct nutritional indicator of dairy fat intake.

- **Endogenous production is minimal in humans** — While animal studies show that gut-derived propionate can be converted to odd-chain fats, in humans, this pathway contributes little. A 2021 controlled feeding trial found that boosting fiber intake (and colonic propionate) did not significantly raise blood C15:0 or C17:0. Thus, C15:0 needs to be regarded primarily as a dietary nutrient.
- **Ratios confirm diet is the main source** — Human plasma shows a C15:0 to C17:0 ratio of roughly 1:2, while dairy fat has a ratio closer to 2:1. This mismatch suggests selective metabolism after intake but supports the conclusion that diet is the major source of circulating C15:0.

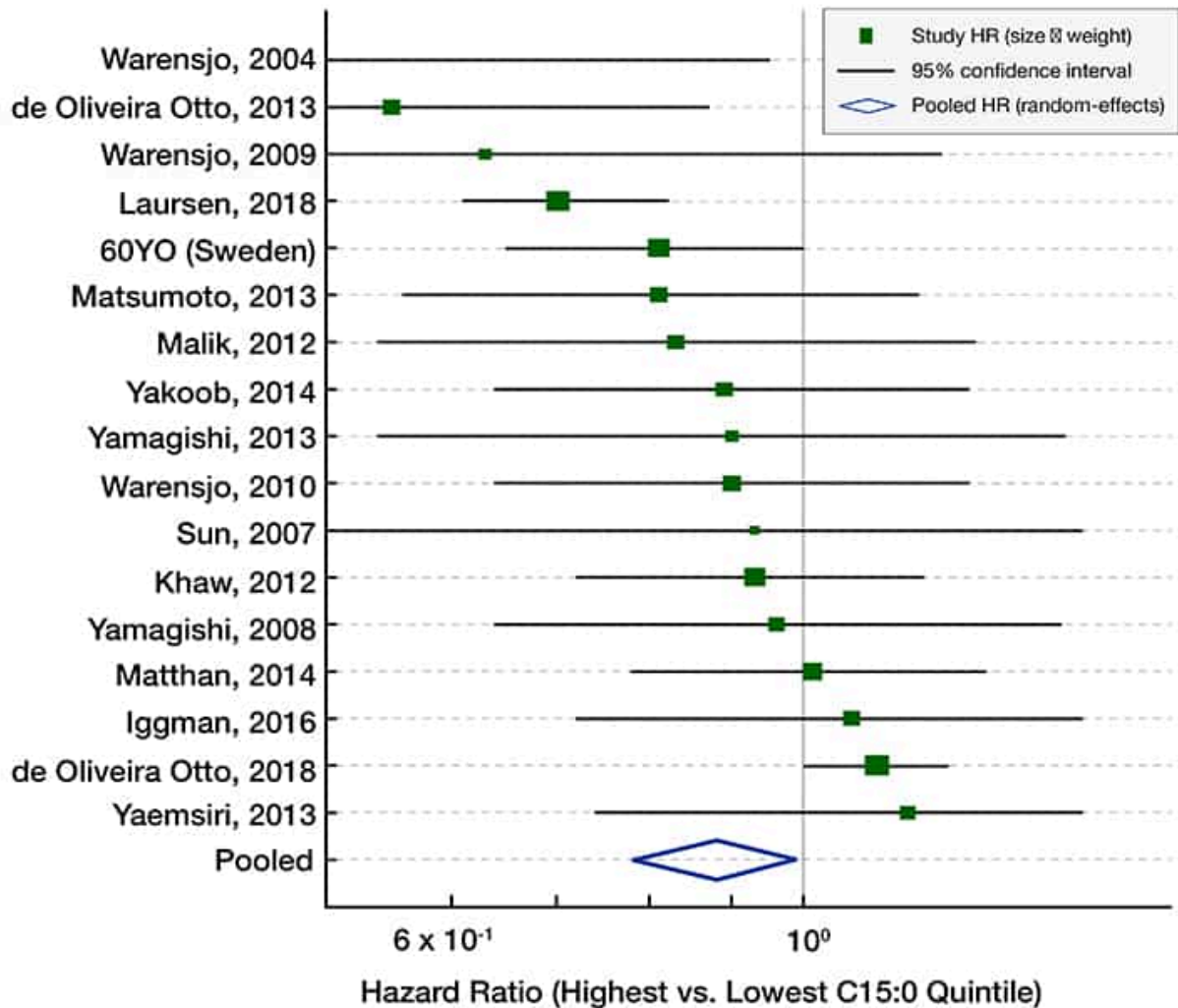
With the shift toward low-fat dairy and more plant-based foods, average blood levels of C15:0 have declined in recent decades. This trend raises concerns that lowering odd-chain saturated fats in the diet may carry unintended health consequences.

## What Long-Term Studies Reveal About C15:0

A growing number of studies have tracked C15:0 levels in thousands of people worldwide, following participants for years to see how this nutrient relates to long-term health. These studies provide a window into how C15:0 behaves in real-world settings, beyond short-term experiments or laboratory models, particularly in heart health.

- **Swedish cohort links C15:0 to lower CVD risk** — A 2021 study measured baseline serum C15:0 and followed participants for cardiovascular outcomes. Those in the highest quintile had a 25% lower risk of their first cardiovascular event compared with the lowest quintile. The relationship was linear for CVD, but all-cause mortality was U-shaped, with the lowest death rates near the median C15:0 level, suggesting there may be an optimal range.<sup>9</sup>
- **Pooled evidence strengthens the association** — A 2021 systematic review and meta-analysis combined results from 18 prospective studies across Europe, the U.S., Asia, and Australia. Participants with the highest C15:0 levels had a reported 12% lower risk of cardiovascular disease compared to the lowest, while C17:0 carried a 14% lower risk. These associations held even after adjusting for traditional risk factors such as age, smoking, and cholesterol.<sup>10</sup>

## Prospective Evidence Linking Circulating C15:0 to Cardiovascular Events



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**Figure 3.** Pooled analysis of 18 prospective cohorts shows a 12% lower risk of incident cardiovascular disease among participants in the highest quintile of circulating C15:0 compared with the lowest, with minimal between-study heterogeneity ( $I^2 = 14\%$ ).

- Coronary artery disease outcomes are particularly notable** – In the Cardiovascular Health Study, each standard-deviation increase in plasma C15:0 was linked to a 19% lower risk of coronary heart disease.<sup>11</sup> Similar findings came from the MESA study, where higher odd-chain fatty acids correlated with less coronary calcium and fewer cardiac events, though some associations weakened with full statistical adjustment.<sup>12</sup>

- **Stroke risk appears lower with higher C15:0** – Evidence is more limited, but a Dutch cohort reported that elevated odd-chain dairy fat biomarkers were associated with reduced stroke risk, especially for hemorrhagic stroke.
- **C15:0 may protect against heart failure** – In the long-term Cardiovascular Health Study, pentadecanoic acid, along with nervonic acid, was the only saturated fat inversely linked to incident heart failure after accounting for competing risks. Over 22 years of follow-up, participants with lower C15:0 had more new cases of heart failure.
- **Type 2 diabetes risk is consistently lower** – Multiple prospective cohorts also show strong inverse associations between C15:0 and diabetes. A meta-analysis of eight studies found that each standard deviation increase in C15:0 corresponded to a 14% reduction in diabetes risk. Across studies, those in the top quartile of C15:0 often had about half the risk of Type 2 diabetes compared with those in the lowest quartile.<sup>13</sup>

Together, these population studies demonstrate that higher C15:0 consistently tracks with better cardiovascular and metabolic outcomes. You can learn more about the health benefits of C15:0 in "[C15:0 – Found in Dairy – May Be an Essential Fat](#)."

## **Mechanisms of Action – How C15:0 May Support Heart Health**

C15:0's observed effects on cardiometabolic markers are not explained by a single pathway. Instead, researchers have found that this fat works through multiple mechanisms at once, influencing several of the body's core systems that determine cardiovascular resilience, including:

- **Blood lipids – C15:0 improves cholesterol and triglyceride balance in both animal and human studies** – In animal-model supplementation studies, researchers observed reductions in total cholesterol, triglycerides, and hepatic fat accumulation,

with proposed activation of PPAR- $\alpha$  and PPAR- $\delta$  – nuclear receptors that regulate fat metabolism.

PPAR- $\alpha$  promotes fatty acid oxidation and raises HDL cholesterol, while PPAR- $\delta$  enhances energy use in muscle. Its activation of PPAR- $\delta$  in vascular smooth muscle may also contribute to arterial flexibility and reduced vascular resistance.

In human cohorts, higher C15:0 is consistently linked to higher HDL and lower triglycerides, with neutral or inconsistent effects on LDL. A 12-week trial using 100 milligrams of purified C15:0 increased circulating levels and improved triglycerides, non-HDL cholesterol, and the total cholesterol-to-HDL ratio.<sup>14</sup>

- **Inflammation and endothelial health** – C15:0 helps calm inflammation by lowering signaling proteins such as IL-6, TNF- $\alpha$ , and MCP-1. These proteins, called cytokines, act like chemical messengers that can fuel chronic inflammation when present at high levels.

In studies with obese mice, C15:0 lowered these cytokines by turning on certain pathways in cells, including PPAR- $\alpha$  and PPAR- $\delta$  (switches that control fat burning and inflammation) and AMPK (an enzyme that senses energy levels and helps regulate metabolism). Together, these changes quiet NF- $\kappa$ B, a master switch that drives inflammation throughout the body.

C15:0 also appears to support endothelial function in experimental studies. It helps your endothelial cells – the thin lining inside your blood vessels – work properly by keeping nitric oxide available. Nitric oxide is a gas your body makes to relax and widen blood vessels. When harmful fats like palmitic acid disrupt this function, adding C15:0 can preserve nitric oxide levels and reduce the damage caused to the cells.

- **Insulin sensitivity and metabolic health** – Higher levels of C15:0 in the blood are strongly linked to a lower risk of Type 2 diabetes and metabolic syndrome. In fact, one analysis of eight large studies found that people with higher C15:0 had a 14% lower risk of developing diabetes for every step up in their levels.<sup>15</sup>

On a cellular level, C15:0 helps your body use insulin more effectively. It does this by activating AMPK, an energy-sensing enzyme that improves metabolism. AMPK then switches on AS160, which removes the brakes on GLUT4 – a protein that acts like a door, moving glucose (sugar) from the bloodstream into muscle cells. This chain reaction increases how much sugar your muscles can absorb, keeping blood sugar levels steadier.

In lab studies with muscle cells, adding C15:0 improved both regular glucose uptake and insulin-stimulated uptake. In animal studies, it lowered fasting blood sugar and insulin, improved how the body responded to insulin, and boosted fat burning.

- **Mitochondrial function** – C15:0 restores the function of the mitochondrial membrane, reduces reactive oxygen species (ROS), and enhances ATP output. In cell studies, micromolar doses cut ROS by about 30% and boosted complex II activity, a component of the mitochondrial electron transport chain that drives ATP production.

In animal hearts, supplementation increased ATP production and improved recovery after ischemia, leading to less scarring and better pumping function. In animal studies, supplemented groups also showed stronger red blood cells and less anemia – markers that researchers interpret as consistent with improved oxygen delivery.

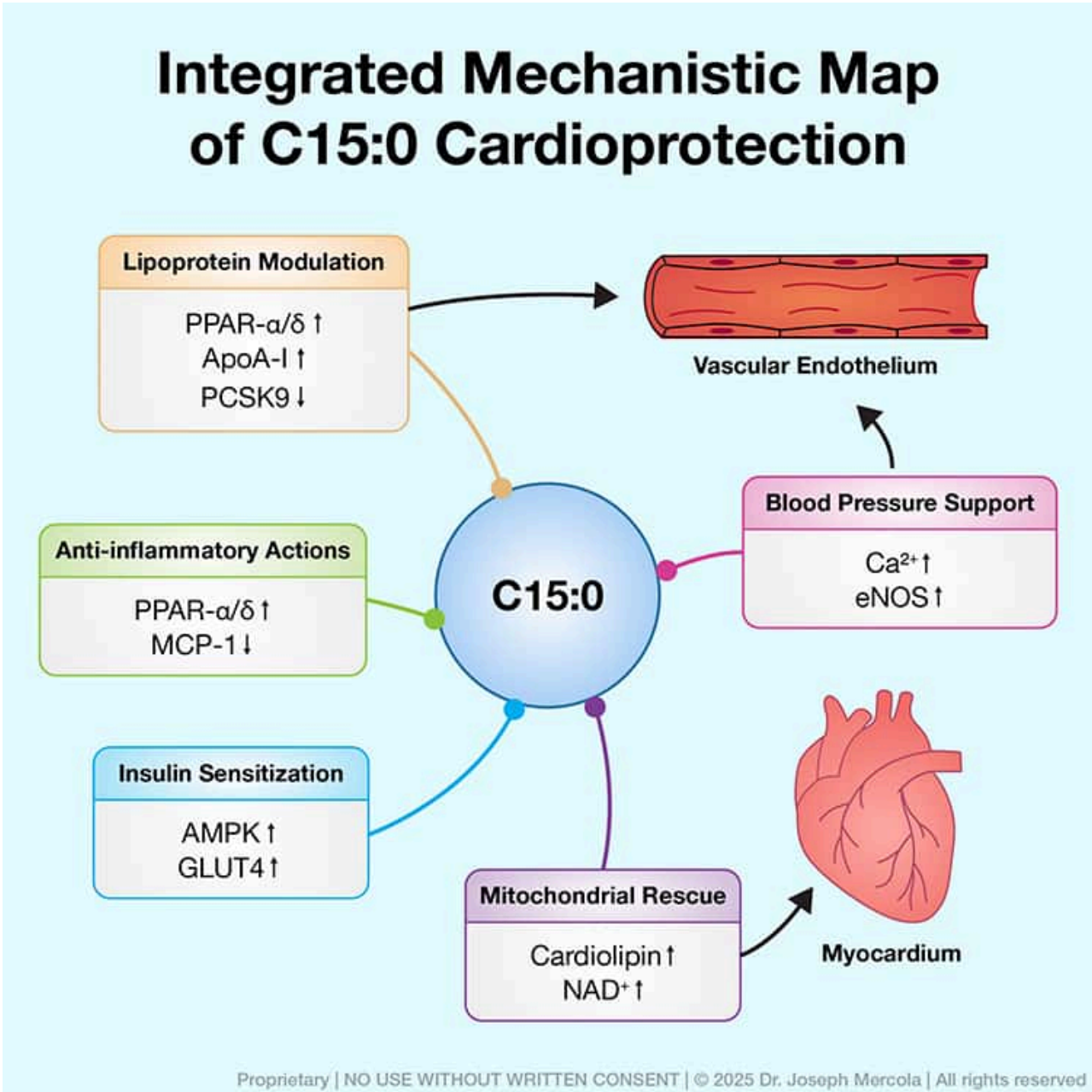
- **Blood pressure regulation** – Observational studies link higher levels of odd-chain fats to slightly lower blood pressure and fewer cases of high blood pressure. Experimental models show that C15:0 stimulates nitric oxide (NO) release from endothelial cells, promoting vasodilation and vascular relaxation.

Its metabolite, pentadecanoylcarnitine, further supports vascular health by engaging multiple receptor pathways that help maintain vessel tone and resilience.

- **Microbiome connections** – As you read earlier, the gut microbiome plays a role in producing propionate, the precursor for odd-chain fats. While this pathway contributes little to your circulating C15:0, the connection highlights how dietary

patterns that support both dairy intake and microbial health may work together to influence cardiovascular outcomes.

The figure below maps these interconnected mechanisms, showing how C15:0 has been linked in research to lipid, inflammatory, metabolic, and mitochondrial pathways relevant to atherosclerosis and cardiometabolic health.



**Figure 4.** Pentadecanoic acid engages lipid, inflammatory, metabolic, and mitochondrial pathways that collectively attenuate atherosclerosis and improve cardiometabolic health. Abbreviations: AMPK, AMP-activated protein kinase; MCP-1, monocyte chemoattractant protein-1.

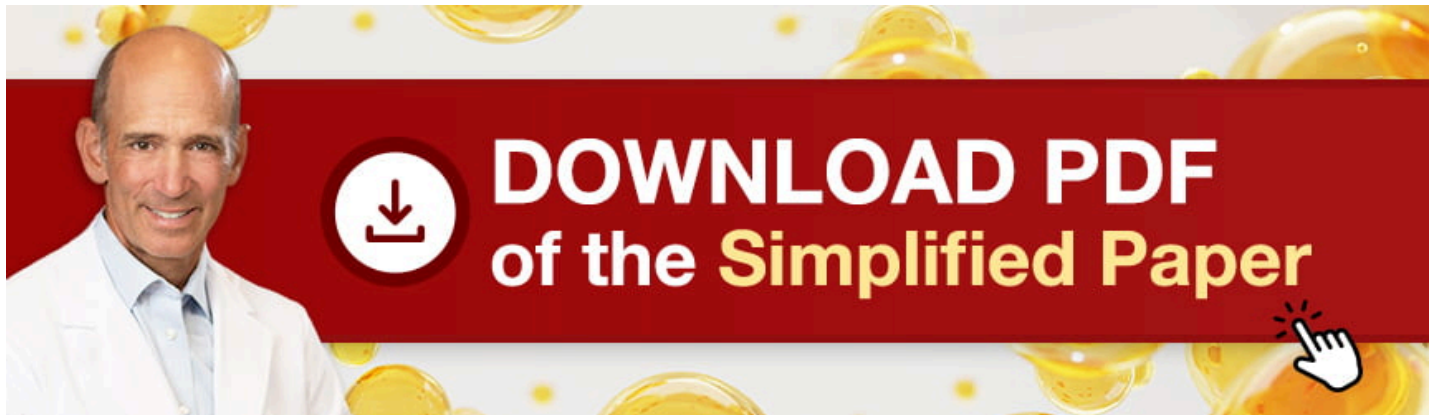
# Practical Strategies to Increase Your C15:0 Intake

Given the emerging research on C15:0, here are some dietary approaches you may wish to consider:

- **Incorporate it through your diet** — You can raise your C15:0 levels by choosing foods naturally rich in this fat, including:
  - Raw, grass fed full-fat dairy where legally available, or the highest-quality grass fed full-fat dairy you can access. Note that a single cup of whole milk provides about 100 milligrams of C15:0<sup>16</sup>
  - Grass fed beef, which contains more C15:0 than grain-fed beef
  - Lamb, especially Australian lamb, which is particularly high in C15:0
  - Fish such as mullet and catfish, which have C15:0 levels comparable to milkfat
  - Butter, ideally from grass fed cows
  - Full-fat cheese made with animal rennet
  - Organic pasture-raised eggs
  - Traditional fermented dairy foods, such as kefir or cultured butter
- **Supplementation** — In addition to dietary sources, supplementation has been studied as a way to raise circulating levels. Research has evaluated doses in the 100- to 250-milligram daily range. If you're considering supplementation, discuss it with your health care provider first.

C15:0 may eventually be recognized as a meaningful nutrient within broader cardiovascular health discussions. To explore the evidence and mechanisms in detail, I encourage you to download and read the simplified version of my paper.

*These findings include results from clinical, observational, animal, and laboratory studies. Findings from animal or in vitro research may not directly apply to human health, and results from any single study may not apply to all individuals.*



## **Frequently Asked Questions (FAQs) About C15:0 and Cardiovascular Disease**

**Q: Why should I care about C15:0 if I've always heard that saturated fat is bad for me?**

**A:** Most dietary guidelines lump all saturated fats together, but your body doesn't treat them the same way. Evidence now shows that odd-chain saturated fats like C15:0 behave differently from harmful fats that dominate processed foods. Higher C15:0 levels in your blood are linked to lower risks of heart disease, diabetes, and metabolic problems.

**Q: What are the proposed mechanisms by which C15:0 may influence heart health?**

**A:** Research suggests C15:0 may influence cholesterol and triglyceride balance, inflammation markers, insulin sensitivity, mitochondrial function, and vascular tone in laboratory and observational studies. Whether these effects translate into lower rates of heart attacks or other clinical events in supplement form has not been

established and is the subject of ongoing investigation.

**Q: What foods do I need to eat to get more C15:0?**

**A:** You'll find the richest amounts in full-fat dairy from grass fed cows, including milk, butter, and cheese. Organic pasture-raised eggs and fermented dairy foods such as kefir or cultured butter also contribute.

**Q: Why does grass fed dairy matter more than low-fat dairy?**

**A:** C15:0 lives in the fat portion of milk, so when fat is removed, you lose most of it. Grass fed dairy also contains more C15:0 than grain-fed dairy. Choosing whole, grass fed dairy provides meaningful amounts of this nutrient.

**Q: Is supplementing with C15:0 safe?**

**A:** Early human trials using 100 milligrams per day of purified C15:0 found it was safe and well-tolerated, while improving cholesterol and inflammatory markers. Higher doses are being studied. Researchers have evaluated values in the 100- to 250-milligram daily range. If you're considering supplementation, consult your health care provider first.

*This article is for informational purposes only and does not constitute medical advice. Consult a qualified health care provider before making changes to your health regimen.*

## Sources and References

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