

Why Is Low Blood Cholesterol Associated with Increased Late Life Mortality?

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Low cholesterol levels are associated with increased mortality risk in older adults, challenging the “lower is better” paradigm

Cholesterol plays crucial roles in cell membrane structure, hormone production, vitamin D synthesis and nerve function. Adequate levels are essential for optimal health, especially in older individuals

Low cholesterol is linked to higher diabetes risk in older adults. Both very low and very high levels increase risk, with the lowest risk occurring at moderate levels

Maintaining adequate cholesterol levels is important for brain health, particularly in post-menopausal women. Low levels may disrupt lipid rafts and myelin production, potentially affecting cognitive function

Recent research indicates a relationship between low cholesterol and increased risk of blood cancers. Cholesterol has protective effects on immune function and regulation of cancer cell proliferation

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You’ve likely heard that high cholesterol is bad for your health, however cholesterol is found in nearly every cell of your body and is vital for optimal functioning. If you have too little, your risk of health problems increases, including all-cause mortality.

Research published in *Frontiers in Endocrinology* found a revealing link between low total cholesterol (TC) levels and increased mortality risk in those aged 85 and above.¹ This research challenges the conventional dogma that lower cholesterol is always better, especially for older adults.

The study, which analyzed data from the Chinese Longitudinal Healthy Longevity Survey, found that individuals with TC levels below 3.40 mmol/L (131 mg/dL) had a significantly higher risk of all-cause mortality compared to those with higher levels.² In fact, the mortality risk increased by 12% for every 1 mmol/L reduction in TC.³ These findings suggest that maintaining higher cholesterol levels may benefit longevity in your later years.

Why Low Cholesterol Is Harmful in Late Life

Cholesterol, often misunderstood as merely harmful, plays several crucial roles in

maintaining bodily functions. This waxy substance serves as a fundamental building block for cell membranes, providing structural integrity and fluidity. It acts as a precursor for various essential hormones and is vital in the production of vitamin D when your skin is exposed to sunlight, contributing to bone health and immune function.

In your digestive system, cholesterol aids in the formation of bile acids, which are necessary for the absorption of fats and fat-soluble vitamins. Further, cholesterol is integral to myelin sheath formation, enhancing nerve signal transmission throughout your body. A balanced amount of cholesterol is indispensable for optimal health and plays a protective role as you age.

As for why low cholesterol increases risk of all-cause mortality in older adults, low TC levels may compromise cell function and increase your vulnerability to infections and other health problems. Additionally, cholesterol helps regulate inflammatory markers in your body. With lower TC levels, you might experience enhanced inflammation, which is associated with numerous age-related diseases.

The study found the protective effect of higher cholesterol is independent of nutritional status or chronic health conditions, suggesting a direct biological link between TC levels and longevity in advanced age. The researchers explained:⁴

“Although the biological pathways that link TC to mortality are poorly understood, several mechanisms may explain this inverse association. For example, blood lipids, which are an important component of cell membranes, may affect cell electrophysiology by modulating the distribution and function of some ion channels.

Low TC levels may contribute to the pathogenesis of some common diseases in older people, such as atrial fibrillation. Another potential mechanism is that TC may regulate inflammatory markers such as C-reactive protein and attenuate the biological response to inflammation. Therefore, individuals with low TC levels may be more vulnerable to physiological disorders because of enhanced inflammation.”

The study identified an optimal range for TC levels in those aged 85 years and over. Participants with TC levels between 3.40 and 4.39 mmol/L (131 to 170 mg/dL) and those with levels at or above 4.39 mmol/L (170 mg/dL) had significantly lower mortality risks compared to those with levels below 3.40 mmol/L.⁵

“Our findings contribute to the growing body of evidence challenging the ‘lower is better’ paradigm for cholesterol levels in older adults,” the researchers noted, proposing that the optimal TC range for older adults might lie between 3.40 and 5.18 mmol/L (131 to 200 mg/dL).⁶

Low Cholesterol Linked to Increased Diabetes Risk

Another important study of 3.26 million Chinese adults aged 65 and older also revealed the importance of properly optimizing your cholesterol. It found low cholesterol levels are associated with a higher risk of diabetes.⁷

The researchers observed a J-shaped relationship between total cholesterol and diabetes risk. This means that both very low and very high cholesterol levels were associated with

increased diabetes risk, with the lowest risk occurring at moderate levels. Specifically, TC levels below 4.04 mmol/L (156 mg/dL) were linked to higher diabetes odds. This “cholesterol paradox” could further explain why low cholesterol contributes to increased mortality in late life.

The findings even held true for [low-density lipoprotein](#) (LDL) cholesterol, often labeled as the “bad” cholesterol. The study found a similar J-shaped relationship between LDL cholesterol levels and diabetes risk. LDL cholesterol levels below 2.33 mmol/L (90 mg/dL) were associated with higher diabetes odds. For every 1 mmol/L increase in LDL cholesterol below this threshold, there was a 12% decrease in diabetes risk.⁸

This again challenges the “lower is better” approach to LDL management, especially for older adults. The protective effect of moderately higher LDL cholesterol levels could be another piece of the puzzle in understanding increased late-life mortality associated with low cholesterol — your body needs a certain level of LDL cholesterol for optimal health throughout life, including in your later years.

The Protective Role of Cholesterol in Brain Health

Maintaining adequate cholesterol levels is also crucial for your brain health, especially as you age. Cholesterol plays a vital role in the production and maintenance of cell membranes in your brain and is essential for the formation of lipid rafts, specialized regions in cell membranes that are crucial for synaptic function and plasticity.⁹

These processes are fundamental for learning and memory. When your cholesterol levels are too low, it can disrupt these lipid rafts, potentially affecting your memory consolidation and cognitive function. Additionally, cholesterol is necessary for myelin production, the protective sheath around nerve fibers that enables efficient signal transmission in your brain.

Low cholesterol levels might interfere with the repair and regeneration of myelin, leading to impaired information processing and potentially contributing to cognitive decline. Further, research indicates that women have a higher lifetime risk of developing Alzheimer’s disease compared to men, and cholesterol levels may play a role in this difference.

The study focused specifically on post-menopausal women, finding that those with total cholesterol levels below 153 mg/dL had a significantly higher risk of developing dementia.¹⁰ Even women with cholesterol levels above 201 mg/dL had a reduced risk of developing dementia compared to those with the lowest levels.¹¹

This suggests that maintaining adequate cholesterol levels may be particularly important for cognitive health in post-menopausal women. The researchers explained several reasons why low cholesterol may increase dementia risk in this population:¹²

“In neurons, lipid rafts are ... believed to be involved in synaptic function and plasticity, which are essential for learning and memory processes. Low cholesterol caused by drugs or toxins may disrupt lipid rafts, subsequently affecting memory consolidation and cognitive function and finally resulting in dementia.

In addition to lipid raft disruption, demyelination caused by low cholesterol levels might also be another important factor that interferes with the regeneration of myeline; therefore, signal (information) transformation and consolidation become disrupted.

Several factors including hyperglycemia, hypertension, toxins, infections, and many other factors that induce free radicals, oxidation, and the inflammation of myeline results in the aging process or the destruction of myelin. In this situation, a higher cholesterol level might be a rate-limited process for repairment and remyelination.

Without intact functional lipid rafts and myeline, information in the brain for conduction, consolidation, or plasticity is not possible.”

Link Between Low Cholesterol and Blood Cancer Risk Unveiled

Recent research from the UK Biobank study has also uncovered an unexpected relationship between low cholesterol levels and an increased risk of plasma cell neoplasms, including multiple myeloma.¹³

This large-scale study followed 502,507 participants for up to 14 years, revealing that individuals with lower levels of total cholesterol, LDL, high-density lipoprotein (HDL) and apolipoproteins had a higher likelihood of developing these blood cancers.¹⁴ While the exact mechanisms are not fully understood, this research points to the complex role of cholesterol in cellular health and immune function.

In the context of blood cancers, cholesterol appears to have protective effects. Higher levels of HDL and its associated apolipoprotein A have been linked to reduced inflammation and improved immune cell function. These lipids can regulate cancer cell proliferation and modify the function of macrophages and other immune cells.¹⁵

Additionally, cholesterol is crucial for the homeostasis of your hematopoietic system, which produces blood cells. The study suggests that very low cholesterol levels might disrupt this delicate balance, potentially increasing the risk of malignant transformations in plasma cells.¹⁶

The study found that the relationship between cholesterol and plasma cell neoplasms was particularly pronounced in males and individuals over 60 years old. The use of [cholesterol-lowering medications](#) didn't reduce the risk of these blood cancers, suggesting that artificially lowering cholesterol levels does not provide the same protective effects as naturally occurring higher levels.

Statin cholesterol-lowering medications are among the most-prescribed drugs in the U.S., but the number of people taking them may soon decline significantly. Based on previous guidelines, 45.4 million adults meet the [criteria to take statin drugs](#), but if updated guidelines from the American Heart Association are adopted, this will drop to 28.3 million.¹⁷

Optimizing Cholesterol Levels for Overall Health

Maintaining optimal cholesterol levels involves more than just focusing on the numbers. Your [gut health](#) plays a significant role in this complex equation. Oxygen-intolerant bacteria, which thrive in an oxygen-free gut environment, are vital for converting plant fibers into

beneficial fats. However, modern lifestyle factors can disrupt this delicate balance, potentially leading to a shift toward oxygen-tolerant bacteria that produce more potent endotoxins.

This shift can have far-reaching implications for your health. Endotoxemia, often resulting from this bacterial imbalance, is a significant underlying cause of septic shock — a condition that may be more prevalent than commonly recognized.

In fact, it could be a leading cause of death, surpassing even heart disease and cancer in some estimations. Many cases of heart disease or heart failure might actually be triggered by endotoxemia, underscoring the interconnectedness of your gut health and cardiovascular system.

To truly optimize your cholesterol levels and overall health, it's essential to look beyond conventional metrics and instead consider the following tests for a more comprehensive understanding of your heart disease risk:

- Omega-3 index
- HDL/total cholesterol ratio
- Fasting insulin level
- Fasting blood sugar level
- Triglyceride/HDL ratio
- Iron level

This personalized approach, combined with strategies to [improve mitochondrial function](#) and maintain a healthy gut ecosystem, offers a more holistic path to cardiovascular health. By addressing these underlying factors, you can naturally optimize your cholesterol levels while supporting your overall well-being.

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Notes

^{1, 2, 3, 5} [Front. Endocrinol, 12 June 2024](#)

^{4, 6} [Front. Endocrinol, 12 June 2024, Discussion](#)

^{7, 8} [Lipids Health Dis. 2024; 23: 167](#)

^{9, 10, 11} [Nutrients. 2023 Oct; 15\(20\): 4481](#)

¹² [Nutrients. 2023 Oct; 15\(20\): 4481, Discussion](#)

^{13, 14} [Cancer Med. 2023 Nov; 12\(22\): 20964-20975](#)

^{15, 16} [Cancer Med. 2023 Nov; 12\(22\): 20964-20975, Discussion](#)

¹⁷ [JAMA Internal Medicine June 10, 2024](#)

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