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Dietary Cholesterol and Cardiovascular Disease: The Triangular Relationship Between Evidence-Based Medicine, Public Health Policy, and the Food Industry as Seen Through the Evolution of Dietary Guidelines

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Abstract

The relationship between dietary cholesterol and cardiovascular disease is one of the most controversial topics in the history of nutritional science. This paper systematically reviews the historical evolution of dietary cholesterol recommendations in dietary guidelines since the mid-20th century, revealing the complex interplay among evidence-based medicine, public health policy, and the food industry that underlies this evolution. The study finds that the evolution of dietary cholesterol recommendations is not a simple narrative of scientific progress, but rather a tortuous process involving "hypothesis establishment—policy entrenchment—scientific revision—and interest-based bargaining." From the 1950s to the 1970s, Ancel Keys' "lipid hypothesis" was established as the dominant paradigm within a specific historical context, and strategic interventions by the sugar industry further reinforced the singular attribution of health risks to "fat and cholesterol." The first edition of the U.S. Dietary Guidelines in 1980 established a daily upper limit of 300 mg for dietary cholesterol, a standard adopted by many countries over the following four decades. However, the 2015 U.S. Dietary Guidelines' decision to remove the cholesterol limit marked a fundamental shift in scientific understanding—from a focus on individual nutrients to a holistic dietary pattern. The issue of industry influence exposed in the 2025 edition of the U.S. Dietary Guidelines reveals the tension between scientific consensus and policy-making. The "ultra-processed foods" classification system in the Brazilian Dietary Guidelines represents a new path away from the reductionist paradigm. This article argues that the essence of the dietary cholesterol controversy lies in the conflict between "reductionist" and "holistic" scientific paradigms. Public health decision-making requires the establishment of more robust mechanisms to prevent conflicts of interest, while future nutritional science should transcend debates over individual nutrients and return to the fundamentals of whole foods and dietary patterns.

Keywords: Dietary Cholesterol; Cardiovascular Disease; Dietary Guidelines; Evidence-Based Medicine; Food Industry; Commercial Determinants of Health

1. Introduction

Since the mid-20th century, cardiovascular disease has been a leading cause of death worldwide. In the quest to understand its causes, the relationship between dietary cholesterol and serum cholesterol, as well as the relationship between serum cholesterol and cardiovascular disease, has been a central focus of nutritional epidemiology (The Rockefeller University, 1994; Kepczyk & Moore, 2026). However, dietary cholesterol recommendations have undergone a dramatic shift over the past seven decades—from advocating for restriction in the 1960s, to the removal of the 300-milligram daily limit in the 2015 U.S. Dietary Guidelines, and finally to the implicitly contradictory stance in the 2025 guidelines.

This evolution is by no means a simple story of "scientific progress." It is interwoven with the accumulation and interpretation of scientific evidence, path dependence in public health policy, the interests of the food industry, and conflicts between different scientific paradigms. As historians have pointed out, the production of scientific knowledge never occurs in a vacuum but is deeply embedded within specific social, economic, and political contexts.

This paper aims to systematically trace the historical evolution of dietary guidelines regarding dietary cholesterol, analyze the multiple driving factors behind them, and explore the implications of this case for contemporary public health policy-making. The paper will proceed in four parts: first, a review of the evolution of scientific understanding regarding the relationship between dietary cholesterol and cardiovascular disease; second, an analysis of the historical evolution of cholesterol recommendations in dietary guidelines and their key turning points; third, an examination of the role of the food industry in scientific controversies and policy-making; and finally, a discussion of the profound implications of this case for evidence-based medicine and public health policy.

2. The Evolution of Scientific Understanding: From the "Lipid Hypothesis" to "Paradigm Shifts"

2.1. The Development and Establishment of the Lipid Hypothesis

Research into the link between dietary cholesterol and cardiovascular disease began in the early 20th century. In 1913, Russian pathologist Nikolai Anichkov, through feeding experiments on rabbits, first demonstrated that cholesterol can induce atherosclerotic lesions, providing early experimental evidence for cholesterol-related theories. However, this study had significant limitations: rabbits are herbivores, and their dietary cholesterol metabolism differs fundamentally from that of humans—a flaw that was not fully recognized at the time.

In the 1950s, the incidence of cardiovascular disease rose rapidly in Western countries, and myocardial infarction became the leading cause of death in the United States, prompting the

scientific community to accelerate its search for the underlying causes of the disease. Against this backdrop, Ancel Keys, a physiologist at the University of Minnesota, formally proposed the lipid-heart hypothesis, whose central tenet was that dietary saturated fat and cholesterol raise serum cholesterol levels, thereby triggering atherosclerosis and coronary heart disease.

Launched in 1958, the Seven Countries Study provided key support for the lipid hypothesis. The study compared dietary patterns and coronary heart disease mortality rates across seven countries, including Japan, Greece, and the United States, and concluded that there was a positive correlation between saturated fat intake and coronary heart disease mortality. Subsequent studies have pointed out significant methodological flaws in this research: Kees initially collected data from 22 countries but selected only the seven that supported his hypothesis for publication; countries such as France, which had high saturated fat intake but low rates of coronary heart disease, were deliberately excluded; and the study contained statistical biases such as selective reporting.

Despite scientific controversy, the Seven Countries Study had a significant impact on policy. In 1955, when U.S. President Eisenhower suffered a sudden heart attack, his attending physician publicly emphasized the health risks of saturated fat and cholesterol, bringing the lipid hypothesis into the spotlight of political attention. For decades thereafter, the fat-cholesterol paradigm became the dominant theoretical framework in the field of cardiovascular disease prevention.

2.2. The Accumulation and Revision of Scientific Evidence

In the second half of the 20th century, as research methodologies improved, the limitations of the lipid hypothesis gradually became apparent. First, numerous epidemiological studies confirmed that the association between dietary cholesterol and serum cholesterol was weaker than theoretically predicted. Research by Edward Arens at Rockefeller University demonstrated that there are significant individual differences in the metabolism of dietary cholesterol in humans; in some populations, high cholesterol intake did not lead to a significant increase in serum cholesterol, suggesting that a one-size-fits-all restriction on dietary cholesterol lacks a physiological basis (Liu & Zhao, 2017; Dean et al.,2024). Second, clinical trials of statins have prompted new academic reflection. While statins can significantly lower LDL cholesterol and reduce cardiovascular events, a large number of cardiovascular events remain unpreventable even when LDL cholesterol is reduced to extremely low levels. This suggests that interventions focused solely on cholesterol overlook other risk factors that have not been taken into account.

Since the beginning of the 21st century, several large-scale meta-analyses have re-evaluated the relationship between dietary cholesterol and cardiovascular disease. The results of meta-analyses incorporating dozens of prospective studies indicate that dietary cholesterol intake is not significantly and independently associated with the risk of coronary heart disease. At the same time, a growing body of evidence suggests that industrial trans fats, refined carbohydrates, and excessive added sugars pose a greater risk to the cardiovascular system than saturated fats and cholesterol found in natural foods.

During this period, significant breakthroughs were made in research on biomarkers of cardiovascular disease risk: Apolipoprotein B and non-HDL cholesterol are superior to LDL

cholesterol in predicting the total burden of atherogenic lipoprotein particles; the triglyceride-to-HDL cholesterol ratio effectively assesses insulin resistance and metabolic dysfunction; and lipoproteins, as independent genetic risk factors, can explain part of the mechanism underlying cardiovascular events. These findings confirm that the assessment of cardiovascular disease risk must move beyond the simplified paradigm centered on low-density lipoprotein cholesterol.

2.3. The Current Scientific Consensus: From the Cholesterol-Centric Model to the Multifactorial Model

Currently, the international nutrition community has reached a nuanced consensus regarding dietary cholesterol and cardiovascular disease: First, the effect of dietary cholesterol on serum cholesterol varies significantly among individuals; the population can be divided into high-responders and low-responders, with the majority exhibiting low sensitivity to dietary cholesterol; Second, dietary cholesterol intake is highly correlated with saturated fat intake, making it difficult to precisely distinguish their independent effects; third, the food matrix effect plays a critical role, as cholesterol from different sources—such as eggs and red meat—exhibits differences in metabolic effects.

More importantly, modern nutritional science has shifted from a reductionist paradigm focused on individual nutrients to an ecological perspective centered on holistic dietary patterns. The 2025–2030 Dietary Guidelines for Americans reflects this shift, with the core focus moving from restricting the intake of a single nutrient—such as cholesterol—to establishing healthy dietary patterns. It emphasizes the holistic combination of vegetables, fruits, whole grains, and high-quality protein, rather than evaluating individual nutrients in isolation. This paradigm shift reflects a deepening of scientific understanding: human diets are based on whole foods as the unit of intake, and the health effects of a diet are determined by the interactions between foods, processing methods, and sociocultural contexts.

3. The Evolution of Dietary Guidelines: From Restrictions to Liberalization and Beyond

3.1. 1980 First Edition Guidelines: Establishing Upper Limits for Cholesterol

In 1980, the U.S. Department of Agriculture and the Department of Health and Human Services jointly released the first edition of the *Dietary Guidelines for Americans*, which became a landmark document in modern nutrition policy. The guidelines explicitly recommended reducing the intake of total fat, saturated fat, and dietary cholesterol, based primarily on the finding that a high-fat, high-cholesterol diet increases the risk of heart disease.

The development of this edition of the guidelines was influenced by academic biases and conflicts of interest. Mark Hegerst, a core member of the drafting team and a nutritionist at Harvard University, had previously received funding from the Sugar Research Foundation to participate in the publication of a research review that attributed the causes of heart disease to fat rather than sugar; Frederick Starr, the founder of Harvard University's Department of Nutrition, had financial ties to the sugar industry. This background suggests that when the first edition of the guidelines established cholesterol restriction standards, sugar industry interest groups used

funding for targeted research to shift public and policy attention away from sugar and toward fat and cholesterol.

The guidelines established a core recommendation limiting daily cholesterol intake to no more than 300 milligrams, which became a long-standing standard for global nutrition education. Guided by this policy, the U.S. food industry launched a low-fat revolution, introducing a flood of low-fat, low-cholesterol processed foods onto the market. To compensate for the loss of flavor, the use of added sugars in processed foods generally increased.

3.2. A Turning Point in 2015: The Removal of Cholesterol Upper Limits

In 2015, the U.S. Dietary Guidelines Advisory Committee released a scientific report recommending the removal of the daily upper limit for dietary cholesterol intake. This recommendation was incorporated into the 2015–2020 Dietary Guidelines for Americans, marking the end of the era of cholesterol restrictions.

This policy adjustment is based on clear scientific evidence: current evidence does not support a dose-response relationship between dietary cholesterol and cardiovascular disease; the effect of dietary cholesterol on serum cholesterol varies among individuals; and the core of a healthy dietary pattern lies in the overall combination of foods, rather than the control of individual nutrients. This decision has also sparked controversy. Critics argue that removing the upper limit could be misinterpreted by the public as implying that cholesterol is harmless, while foods high in cholesterol are typically high in saturated fat and still require moderate consumption.

Another significant change in the 2015 Guidelines was the first-ever establishment of a limit on added sugar intake: added sugars should provide no more than 10% of total daily calories. This recommendation indirectly acknowledges the health risks associated with the previous dietary focus on low-fat, high-sugar diets (Nascimento et al., 2026; Physicians Committee for Responsible Medicine, 2026). From a historical perspective, the 2015 revision corrects the policy deviations of the past four decades, shifting the focus of research and policy from fat and cholesterol to other dietary risk factors, such as sugar.

3.3. 2025 Guidelines: Contradictions and Controversies

The Dietary Guidelines for Americans 2025–2030, released in January 2026, sparked widespread academic controversy. On the surface, the guidelines retained the restriction that saturated fat should account for no more than 10% of total energy intake, emphasized the consumption of vegetables, fruits, and whole grains, and, for the first time, called for the complete elimination of added sugars, reflecting a deepening understanding of the harms of sugar.

The guidelines contain fundamental flaws that have drawn criticism from both the academic community and the public health sector. A core contradiction lies in the fact that while the guidelines restrict saturated fat intake, they simultaneously prioritize animal protein and full-fat dairy products as recommended protein sources—both of which are major dietary sources of saturated fat. This coexistence of restrictions and recommendations has created confusion among the public.

Issues of scientific integrity are even more pronounced: of the nine experts providing the scientific basis for the guidelines, at least eight had conflicts of interest with the food industry. In

January 2026, the Physicians Committee for Responsible Medicine submitted a petition to the Office of the Inspector General of the U.S. Department of Health and Human Services and the Department of Agriculture, demanding the withdrawal and redrafting of the guidelines on the grounds of suspected unlawful industry influence, exposing the failure of conflict-of-interest prevention mechanisms in public health policymaking.

Furthermore, the guidelines represent a step backward in visual presentation; the new Food Guide Pyramid reverts to reductionist, abstract symbols that fail to reflect the complexity of modern food systems. In contrast, Brazil's dietary guidelines adopt the NOVA food classification system, which categorizes foods based on their degree of processing and explicitly recommends avoiding ultra-processed foods—representing a paradigm shift from a focus on nutrients to food itself, and from individual choice to the broader food environment.

3.4. International Comparison: Paradigm Innovation in the Brazilian Guidelines

Within the global dietary guidelines framework, Brazil has forged a distinctive research and policy path. The Brazilian Dietary Guidelines, published in 2014, moved away from the traditional nutrient-based perspective and instead built its framework around the degree of food processing. Using the NOVA classification system, it categorizes foods into four groups: fresh and minimally processed foods, cooking ingredients, processed foods, and ultra-processed foods.

The revolutionary value of this classification system lies in breaking free from the reductionist framework of "good" versus "bad" nutrients, demonstrating that industrial processing alters the food matrix and produces independent health effects. Ultra-processed foods are not only high in sugar, fat, and salt, but their physical structure and chemical composition have been profoundly altered, potentially disrupting satiety signals, gut microbiota, and metabolic responses. The Brazilian guidelines explicitly recommend basing diets on fresh and minimally processed foods while completely avoiding ultra-processed foods, a stance that aligns closely with mainstream epidemiological evidence.

The methodological innovation of the Brazilian guidelines is equally significant: the development process strictly excluded industry interference, was led by an independent academic team, and explicitly rejected industry funding; the content framework integrates public values such as social equity, environmental sustainability, and food sovereignty, embodying the core principle that nutrition policy serves the overall well-being of society rather than the interests of specific industries.

The Brazilian guidelines have had a profound impact on global nutrition policy. Many Latin American countries have adopted similar frameworks and implemented accompanying regulatory measures, such as warning labels and taxes on ultra-processed foods, thereby providing an alternative model for global public health governance and challenging the industry-friendly policy paradigm exemplified by U.S. guidelines.

4. The Role of the Food Industry: The Clash of Interests and the Shaping of Scientific Discourse

4.1. The Sugar Industry Lobby's Historical Strategies

Perhaps the most cautionary tale in the evolution of dietary cholesterol guidelines is the sugar industry's interference in scientific research and policymaking. In 2016, a historical analysis published in the *Journal of the American Medical Association: Internal Medicine* revealed a startling discovery: in 1967, the Sugar Research Foundation provided approximately $6,500 in funding to three Harvard scientists, commissioning them to publish a review attributing coronary heart disease to fat rather than sugar.

The three recipients included Frederick Stal, founder of the Department of Nutrition at the Harvard School of Public Health, and Mark Hegerst, who later drafted the first edition of the U.S. Dietary Guidelines. In 1967, they published a review in the *New England Journal of Medicine* concluding that "the only dietary change necessary to prevent coronary heart disease is a reduction in saturated fat and cholesterol intake," while making no mention of the link between sugar and heart disease. After its publication, this review became a highly cited paper in the field and had a profound impact on subsequent policy-making.

The success of the sugar industry's strategy lay in its exploitation of the complexity of scientific research. By funding specific studies, influencing academic publications, and suppressing dissenting voices, the sugar industry successfully shifted the scientific focus from sugar to fat. Ironically, when British nutritionist John Yudkin published Pure, White, and Deadly in 1972, systematically detailing the link between sugar and cardiovascular disease, he faced academic suppression orchestrated by Case and others and was stigmatized as a fringe figure "lacking scientific rigor." Yudkin's research career was thus derailed, while Keys, hailed as the "father of the Mediterranean diet," achieved fame and lived to be 100 years old.

4.2. The Food Industry's Ongoing Influence on Dietary Guidelines

The history of the sugar industry is just the tip of the iceberg. The controversy surrounding the 2025 edition of the U.S. Dietary Guidelines shows that the food industry's influence on nutrition policy has not ended but continues in more covert ways.

The core issue exposed during the development of the new guidelines is "conflicts of interest among experts." The vast majority of experts responsible for drafting the scientific reports had financial ties to the beef and dairy industries. This phenomenon highlights the "revolving door" problem: the boundaries between academic experts and industry are becoming increasingly blurred, and mechanisms to prevent conflicts of interest are virtually non-existent.

The consequences of this industry influence are evident in the specific content of the guidelines. While the new guidelines retain restrictions on saturated fat, they place animal protein and full-fat dairy products at the center of protein source recommendations. This contradictory strategy of "retaining restrictions while strengthening encouragement" essentially provides policy cover for the dairy and meat industries. When public health policies reframe systemic food environment issues as a moral narrative of "personal choice," industry responsibility is successfully sidestepped.

4.3. The Theoretical Framework of "Commercial Determinants of Health"

In recent years, the public health community has proposed the conceptual framework of "Commercial Determinants of Health" to analyze the role of corporate activities in shaping population health. This framework posits that commercial behavior influences health through multiple channels: direct effects, indirect effects, and structural effects.

The food industry's influence on dietary guidelines is a prime example of "commercial determinants of health." By funding research, participating in guideline development, and lobbying government agencies, the industry has successfully kept the policy focus on a track that benefits the sales of its products. U.S. dietary guidelines have long emphasized "individual choice" and "nutrient balance" while avoiding discussion of structural factors such as food processing, product formulation, and marketing strategies; this path dependence aligns closely with the industry's interests.

An analysis of international literature indicates that dietary guidelines in many countries do not faithfully reflect scientific evidence but rather reflect the combined influence of agricultural subsidy structures, trade agreements, and industry lobbying. Animal-based foods occupy a central position in most guidelines not because their health benefits surpass those of plant-based foods, but due to the weight and political influence of the livestock industry within the agricultural economy. This explanation helps clarify the fundamental divergence between the U.S. and Brazilian guidelines: the former is constrained by a powerful agribusiness complex, while the latter has chosen a path independent of industry interests.

5. Theoretical Reflection: The Paradigm Clash Between Reductionism and Holism

5.1. The Epistemological Dilemma in Nutritional Science

Behind the controversy over dietary cholesterol lies a deeper epistemological dilemma in nutritional science: how to strike a balance between "reductionism" and "holism"? The reductionist approach breaks down food into nutrients and uses randomized controlled trials and epidemiological studies to explore the relationship between individual nutrients and health outcomes. This approach has achieved significant historical milestones—the discovery of vitamins, the elucidation of the roles of essential fatty acids, and the establishment of nutrient targets in dietary guidelines.

However, the fundamental flaw of the reductionist approach lies in the fact that humans consume food, not individual nutrients; broader factors such as food matrix, processing methods, and dietary patterns are overlooked. The dietary cholesterol case clearly illustrates the limitations of reductionism—when scientific focus is overly concentrated on a single nutrient, it may neglect more important dietary determinants. The 2015 decision to remove the cholesterol intake limit was precisely a correction of this reductive oversimplification.

The holistic approach, in contrast, views the diet as a complex system, focusing on food combinations, processing methods, dietary patterns, and sociocultural contexts. The NOVA classification system in Brazil's dietary guidelines represents the application of this holistic

approach at the policy level: rather than telling the public how much cholesterol to limit, it recommends which foods should form the foundation of daily diets and which should be avoided. This framework acknowledges that the health effects of food cannot be reduced to the sum of its nutritional components.

5.2. Path Dependence in Public Health Decision-Making

The evolution of dietary guidelines also reveals the "path dependence" inherent in public health decision-making. Once a particular theoretical paradigm is established as the basis for policy, it becomes difficult to adjust the policy direction even when subsequent evidence calls it into question. The "cholesterol ceiling" established in 1980 became a fundamental tenet of global nutrition education over the following four decades; even as scientific evidence gradually accumulated to demonstrate its limitations, policy adjustments did not occur until as late as 2015.

The formation of path dependence involves multiple mechanisms: institutional lock-in, the solidification of professional consensus, and the stability of vested interests. These factors interact to create a massive inertia that must be overcome for policy shifts to occur.

The issue of industry influence exposed in the 2025 U.S. Dietary Guidelines demonstrates that path dependence is not merely a matter of scientific understanding, but also a matter of political economy. When specific industries gain institutionalized influence in policy-making, policy direction becomes systematically locked into a trajectory that favors industry interests. The inherent contradiction in the U.S. guidelines between "encouraging animal protein" and "restricting saturated fat" is a concrete manifestation of this locking effect.

5.3. Scientific Autonomy and the Prevention of Conflicts of Interest

The key lesson for contemporary public health policy drawn from the dietary cholesterol case is the need to establish more robust mechanisms to protect scientific autonomy and prevent conflicts of interest from eroding scientific integrity.

The controversy surrounding the 2025 U.S. guidelines has exposed the failure of existing mechanisms to prevent conflicts of interest. The fact that eight out of nine authors of the scientific report had industry ties demonstrates that the transparency and fairness of the expert selection process require fundamental improvement. Even more concerning is that these conflicts of interest were exposed by external oversight organizations after the guidelines were published, rather than being proactively disclosed by official bodies.

The experience with the Brazilian guidelines offers an alternative model worth emulating. Its development process explicitly rejected industry participation; all experts declared no conflicts of interest, and the final document genuinely reflected scientific evidence rather than industry demands. This model demonstrates that it is possible to develop dietary guidelines free from commercial influence; the key lies in political will and institutional design.

The international public health community has put forward several reform proposals: establishing an independent expert selection mechanism, mandating the disclosure of conflicts of interest, prohibiting experts with industry ties from participating in guideline development, and separating guideline review from industry lobbying. These proposals aim to place the control of "commercial determinants of health" at the core of public health governance.

6. Discussion

Looking ahead, nutritional science and public health policy must undergo a threefold shift: at the conceptual level, moving from "reductionism" to "holism," focusing on food systems and dietary patterns rather than individual nutrients; at the methodological level, establishing stricter mechanisms to prevent conflicts of interest to ensure the independence and integrity of scientific evidence; and at the governance level, incorporating "commercial determinants of health" into policy frameworks to address the food industry's impact on public health through structural interventions.

The story of dietary cholesterol is far from over. As nutritional science advances and food systems evolve, new scientific evidence will continue to emerge, and policies will continue to be adjusted. But the deeper lesson of this case goes beyond cholesterol itself—it reminds us that public health decision-making requires not only scientific evidence, but also critical awareness of the social context in which evidence is produced, as well as systematic safeguards against commercial interests. Only then can dietary guidelines truly serve public health, rather than the interests of specific industries.

7. Conclusions

The debate over the relationship between dietary cholesterol and cardiovascular disease appears to be a scientific issue, but in reality, it is a complex narrative intertwined with the triple logic of science, policy, and business. From Ancel Keys' "Seven Countries Study" to the industry controversy surrounding the 2025 U.S. Dietary Guidelines, seven decades of history reveal a clear trajectory: the establishment of scientific hypotheses is often constrained by specific historical conditions and social contexts; once policies are formed, they generate path dependence; and commercial interests continually seek to shape scientific discourse to maintain their own standing.

The core findings of this paper can be summarized in four points: First, the relationship between dietary cholesterol and cardiovascular disease is far more complex than early hypotheses suggested, with individual metabolic differences, food matrix effects, and overall dietary patterns all playing significant roles; Second, the evolution of dietary guidelines has undergone four stages: "hypothesis establishment—policy solidification—scientific revision—interest-based bargaining," and the removal of the cholesterol upper limit in 2015 marked a fundamental shift in scientific understanding; Third, strategic interventions by the sugar industry lobby in the 1960s and 1970s profoundly influenced the direction of early guidelines, and the issues of industry influence exposed in the 2025 guidelines indicate that this pattern persists; fourth, the Nova classification system and independent development model of Brazil's dietary guidelines offer a viable alternative pathway for breaking free from the reductionist paradigm and industry influence.

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