Interesterified Triglycerides, Blood Viscosity, and Heart Disease Review

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Introduction

Gregory Sloop, John Weidman, and Joseph St Cyr's 2018 article, "Perspective: Interesterified Triglycerides, the Recent Increase in Deaths from Heart Disease, and Elevated Blood Viscosity," proposes that changes in manufactured dietary fats may contribute to cardiovascular mortality through effects on red blood cells and blood viscosity. The original review treats this proposal as if it were established by extensive causal evidence. That overstates what the article provides. It is a perspective piece that assembles historical trends, mechanistic reasoning, and indirect observations to generate a hypothesis. Interesterified fats are not the same as industrial trans fats, and the health effects of a fat depend on its fatty-acid composition, molecular structure, food matrix, dose, and the nutrient it replaces. Human trials have produced mixed findings, and current evidence does not establish interesterified fats as the primary cause of recent changes in heart-disease mortality or elevated blood viscosity. The article is valuable for identifying a research question, but it should be assessed with attention to study design, alternative explanations, and later experimental evidence (Sloop et al., 2018).

What Interesterification Means

Dietary triglycerides contain three fatty acids attached to a glycerol backbone. Interesterification rearranges the positions of fatty acids within or among triglyceride molecules. Food manufacturers use chemical or enzymatic processes to change melting behavior, texture, spreadability, and crystallization without necessarily changing the overall types of fatty acids present. This process became more prominent as manufacturers sought alternatives to partially hydrogenated oils, the main industrial source of artificial trans fat. Interesterification and partial hydrogenation are different. Partial hydrogenation creates trans double bonds and changes fatty-acid geometry; interesterification mainly changes where existing fatty acids sit on the triglyceride. Some interesterified products are rich in saturated fatty acids such as palmitic or stearic acid, while others may contain more unsaturated fat. A health evaluation must therefore compare complete fat formulations rather than attaching one risk level to every product described as interesterified.

Industrial Trans Fat and Regulatory Change

The strongest evidence discussed around manufactured fats concerns industrial trans fatty acids from partially hydrogenated oils. Controlled feeding studies and epidemiological research linked higher intake with an unfavorable LDL-to-HDL cholesterol profile and increased cardiovascular risk. The United States required trans fat declaration on Nutrition Facts labels beginning in 2006. In 2015, the Food and Drug Administration determined that partially hydrogenated oils were no longer generally recognized as safe for use in human food, and later regulatory actions removed remaining authorized uses. These changes are important to the 2018 perspective because interesterified fats were among the technologies used to replace partially hydrogenated oils. However, the harms of trans fat cannot simply be transferred to the replacement process. A substitute may be better, worse, or similar depending on its composition and how it compares with the fat or carbohydrate it replaces (U.S. Food and Drug Administration, 2015).

The Blood-Viscosity Hypothesis

Sloop and colleagues focus on blood viscosity, the resistance of blood to flow. Viscosity is influenced by hematocrit, plasma proteins, temperature, red-cell aggregation, and the ability of erythrocytes to deform while passing through small vessels. The authors propose that straight-chain saturated and trans fatty acids incorporated into cell membranes may increase intermolecular interactions, reduce membrane fluidity, impair red-cell deformability, and thereby raise viscosity. Higher viscosity could theoretically contribute to vascular resistance and thrombosis. This chain is biologically plausible enough to investigate, but plausibility is not proof. To establish it, researchers would need controlled exposure measurements, validated changes in membrane composition and deformability, clinically meaningful viscosity effects, and evidence that those changes increase cardiovascular events independent of established risk factors. The perspective does not supply that full causal sequence (Sloop et al., 2018).

Historical Trends Are Not Causal Tests

The article compares periods of fat production, consumption, regulation, and cardiovascular mortality. Such ecological patterns can generate hypotheses, but they cannot determine what caused an individual event or population trend. Heart-disease mortality changes with smoking prevalence, blood-pressure treatment, cholesterol-lowering medication, diabetes, obesity, diagnostic definitions, emergency care, aging, socioeconomic inequality, air pollution, and many dietary factors. Production data also do not show individual intake or the exact triglyceride structures consumed. If two trends rise at similar times, the relationship may be causal, coincidental, confounded, or partly mediated by other variables. The original review calls the historical comparisons validation, but that term is too strong. They are contextual observations that require testing through trials, prospective cohorts,

biomarker studies, and mechanistic experiments (Sloop et al., 2018).

Evidence from Human Feeding Trials

Human trials do not support a simple conclusion that the interesterification process is uniformly harmful. An earlier trial comparing a vegetable-fat blend before and after chemical interesterification found no adverse difference in fasting blood lipids, enzymes, or hemostasis markers when fatty-acid composition was held similar. Other studies have reported different metabolic responses depending on the test fats. A 2021 randomized trial found that palmitic-acid-rich fats, whether interesterified or not, produced more atherogenic postprandial lipoprotein features than a monounsaturated-fat-rich oil; importantly, interesterification itself did not materially change fat digestion or measured lipid metabolism. A 2024 randomized crossover trial comparing commercially relevant spreads assessed acute triglyceride and vascular responses, illustrating that current research focuses on specific formulations rather than a universal category. These studies are generally short and use surrogate outcomes, so they cannot prove long-term safety. They do show why composition and comparator must be separated from processing method (Meijer et al., 2001; Berry et al., 2021).

Fatty-Acid Composition and Replacement Matter

A diet does not replace a fat with nothing. Removing industrial trans fat may lead to replacement with unsaturated oil, saturated fat, interesterified blends, or refined carbohydrate. Cardiovascular implications differ among those choices. Replacing trans fat with polyunsaturated or monounsaturated fat is generally more favorable than replacing it with a highly saturated formulation. If an interesterified product contains substantial palmitic acid, observed effects may reflect saturated-fat composition more than interesterification. The position of fatty acids on triglycerides can affect digestion and postprandial metabolism, but current evidence does not justify ignoring the total dietary pattern. Evaluation should include LDL cholesterol, triglyceride-rich remnants, glucose and insulin responses, inflammation, endothelial function, blood pressure, body weight, and actual cardiovascular outcomes. Focusing only on viscosity risks overstating one mechanism within a multifactorial disease (Berry et al., 2021).

Thrombosis and Cardiovascular Disease

Arterial thrombosis commonly develops when an atherosclerotic plaque ruptures or erodes and triggers platelet activation and coagulation. Blood viscosity may influence flow and vascular stress, but thrombosis cannot be explained as the inevitable result of thickened blood. Atherosclerosis develops through lipoprotein retention, inflammation, endothelial dysfunction, immune activity, and other processes over time. Cardiovascular mortality also includes conditions that do not share one mechanism. The perspective is useful in reminding researchers that red-cell rheology receives less

public attention than cholesterol. It becomes misleading only when a proposed viscosity pathway is presented as the dominant explanation for population mortality. Strong causal inference would require evidence that the exposure predicts clinical outcomes, that the effect is reproducible, and that competing mechanisms do not account for the association.

Interpreting Denmark and New York Evidence

The original review cites declines in cardiovascular mortality after restrictions on industrial trans fat in Denmark and selected New York jurisdictions. Such policy evidence supports the decision to reduce trans fat, especially when considered with biological and clinical evidence. It does not validate a claim about interesterified triglycerides. Policies may coincide with other health changes, and their effects are estimated through statistical comparison rather than by observing a single before-and-after number. More importantly, a reduction in harm from partially hydrogenated oils does not mean every replacement is harmless or harmful. It means reformulation should be monitored. Researchers should measure what fats replaced trans fat, how product composition changed, and whether risk markers or outcomes shifted. The 2018 perspective correctly asks regulators and scientists not to assume replacement ingredients require no evaluation, but it blurs distinct exposures when it treats trans-fat experience as direct proof against interesterification.

Labeling and Consumer Information

Consumers can identify trans fat on the Nutrition Facts label and partially hydrogenated oils in ingredient lists, although current U.S. regulatory changes have greatly reduced their use. “Interesterified fat” is not ordinarily presented as a separate nutrient line with a health-based daily value. Whether additional process labeling would improve health decisions is an empirical and regulatory question. A label can inform only when terminology is meaningful, consistently defined, and linked to evidence consumers can use. Listing a technical process without explaining fatty-acid composition could create alarm while revealing little about comparative risk. Public-health policy may be better served by transparent ingredient identification, monitoring of food-supply reformulation, limits on harmful components, and dietary guidance emphasizing unsaturated fats and minimally processed foods. The perspective raises a legitimate transparency issue but does not demonstrate that a special warning label is scientifically warranted.

Strengths of the Perspective

The article’s main strength is intellectual: it connects food technology, membrane biology, hemorheology, epidemiological trends, and regulation in a testable hypothesis. It also challenges complacency about reformulation. When an unsafe ingredient is removed, manufacturers and regulators should evaluate what replaces it rather than assuming that technical functionality equals

nutritional equivalence. The authors identify specific measurements—fat production, consumption, red-cell properties, blood viscosity, and cardiovascular outcomes—that could be studied. Perspective articles can advance science by drawing attention to neglected mechanisms, particularly when they clearly distinguish speculation from evidence (Sloop et al., 2018).

Limitations and Research Needs

The central limitation is causal overreach. Ecological timing, mechanistic plausibility, and selected policy observations cannot show that interesterified fats produced a national increase in heart-disease deaths. The category of interesterified fat is chemically diverse, exposure data are limited, and long-term randomized outcome trials are unavailable. Future research should characterize specific products, compare interesterified and non-interesterified fats with matched fatty-acid composition, measure membrane incorporation and rheology, and follow cardiometabolic outcomes over sufficient periods. Studies should disclose funding and formulation details. Population surveillance could track replacement fats and dietary patterns after trans-fat removal. Researchers should also determine whether any observed effect comes from interesterification, saturated-fat content, caloric excess, food matrix, or another component.

Conclusion

Sloop, Weidman, and St Cyr offer a provocative hypothesis that interesterified triglycerides may affect cardiovascular risk through red-cell membrane properties and blood viscosity. The proposal deserves investigation, but the original review incorrectly treats it as validated fact and repeatedly merges interesterified fats with industrial trans fats. Current human evidence is mixed and often indicates that fatty-acid composition and replacement nutrient are more important than the interesterification process by itself. Regulatory action against partially hydrogenated oils was based on strong evidence about trans fat; it does not establish equivalent harm from all interesterified products. The article’s best contribution is its call for transparent data and targeted research. A scientifically responsible conclusion is neither that interesterified fats are proven dangerous nor that they are automatically safe, but that specific formulations should be assessed with controlled human studies, realistic exposure information, multiple risk markers, and long-term outcomes (Sloop et al., 2018; Meijer et al., 2001; Berry et al., 2021).

References

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