Qeios

Peer Review

Review of: "From Carbohydrates to Ketones: Mitochondrial Reprogramming via β-Hydroxybutyrate Signaling for Non-Pharmacological Treatment of Metabolic Syndrome"

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The narrative frequently blends calorie restriction, low-carbohydrate diets, and true ketogenic diets, making it difficult to isolate effects attributable specifically to nutritional ketosis.

Numerous claims rely on mechanistic studies without consistently assessing the quality, heterogeneity, or limitations of the corresponding human evidence.

Study heterogeneity (macronutrient ratios, fat quality, ketosis verification, trial duration) is repeatedly acknowledged but insufficiently addressed when drawing conclusions.

Evidence selection appears biased toward positive outcomes, with limited discussion of null or contradictory findings, particularly for LDL-C, apoB, and long-term cardiovascular safety.

Several mechanistic pathways are described as established despite largely being derived from animal models or short-term human studies that lack causal confirmation.

Safety considerations are discussed briefly but do not sufficiently address long-term risks, vulnerable populations, or potential adverse effects beyond transient symptoms.

The translational framework is proposed but lacks clear methodological criteria for how mechanistic biomarkers should be integrated into future trial design.

The review occasionally presents speculative biochemical links (e.g., bile-acid shifts, FGF21/GDF15 signaling) as clinically actionable without evidence that they predict outcomes in MetS populations.

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Declarations

Potential competing interests: No potential competing interests to declare.