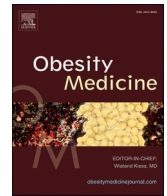


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## Ketosis or calories: The question of diabetes pseudoremission

## ARTICLE INFO

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## To the Editor,

We read with interest the recent article, “Type 2 diabetes remission with very low-energy ketogenic treatment: a retrospective real-world study” (Sofra et al., 2025). This single-centre retrospective study evaluated the effectiveness of a very low-energy ketogenic treatment (VLEKT) meal-replacement protocol in achieving diabetes remission among 38 overweight and obese adults with type 2 diabetes (T2DM). The authors reported that nearly half of participants achieved remission at 6 months, with approximately one quarter maintaining remission at 2 years. While the authors propose VLEKT as a safe and feasible adjunct to diabetes care with potential to support remission-focused strategies, caution is warranted in attributing the observed benefits to “ketosis” or considering euglycemia achieved through carbohydrate avoidance as evidence of true remission of the  $\beta$ -cell dysfunction underlying T2DM.

The prescribed intake of 600–800 kcal/day represents marked and intensive caloric restriction, long known to induce rapid euglycemia, often preceding substantial weight loss. Yet, the absence of systematic ketone monitoring leaves uncertain whether ketosis occurred. Even if present, the lack of a non-ketogenic very-low-calorie control group prevents distinguishing the effects of ketosis from those of caloric restriction. Notably, the most pronounced improvements arose during the active low-energy phase, paralleling outcomes from non-ketogenic VLCD programs such as DiRECT (Lean et al., 2018), which have achieved comparable remission rates. Furthermore, ketone concentrations in the DiRECT mechanistic study (Taylor et al., 2018) rose only modestly during the 800-kcal/day diet, far below levels seen in nutritional ketosis. These findings support the interpretation that energy restriction and weight loss, rather than ketosis, are the primary drivers of benefit.

Although the study applies the ADA/EASD definition of remission (HbA<sub>1c</sub> <6.5 % for  $\geq 3$  months without medication), euglycemia achieved through carbohydrate avoidance does not necessarily represent disease modification. Instead, it reflects a state of unchallenged  $\beta$ -cell function, analogous to artificial euglycemia induced by pharmacologic glucose lowering. Since the hallmark pathology of T2DM is impaired  $\beta$ -cell insulin secretion in response to carbohydrate stimuli (Suleiman et al., 2022), glycemic normalization without  $\beta$ -cell recovery may constitute only *pseudoremission*. We propose this term to describe cases in which remission criteria are met, but glycemic control depends on ongoing carbohydrate avoidance or pharmacotherapy rather than restoration of  $\beta$ -cell function.

Patients achieving euglycemia through carbohydrate avoidance may prematurely discontinue surveillance for diabetes complications. Although Sofra et al. employed remission criteria solely as an indicator of metabolic state, rather than advocating any broader clinical application, it remains essential to highlight the potential risks associated with pseudoremission. To mitigate the possibility of reduced clinical follow-up, clinicians should emphasize that remission does not obviate the need for ongoing surveillance. Routine HbA<sub>1c</sub> monitoring should continue, together with the standard schedule of screening for macrovascular and microvascular complications, including assessments for diabetic retinopathy, nephropathy, and peripheral neuropathy, as well as regular pedal and dental examinations. Until robust evidence demonstrates durable  $\beta$ -cell recovery, claims of diabetes remission achieved solely through carbohydrate avoidance, which leaves the  $\beta$ -cell activity unchallenged, must be interpreted with appropriate caution.”

With respect to potential conflicts of interest, the manuscript states that there are “no known competing interests,” while also

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indicating that some authors are affiliated with Pronokal®, the provider of the intervention. Given these authors' involvement in protocol design and training, more explicit disclosure of this affiliation, along with clarification of any measures implemented to mitigate potential bias, would further enhance transparency and strengthen the overall integrity of the study.


Finally, there is an urgent need for future research to clearly disentangle the metabolic effects of caloric restriction from those of nutritional ketosis. Rigorous, well-controlled trials incorporating standardized caloric intake, ketone biomarkers, objective measures of  $\beta$ -cell recovery, and longitudinal metabolic profiling are essential to determine whether the observed euglycemia arises from ketosis, caloric deficit, or their interaction—and whether this euglycemia represents true diabetes remission or merely a state of unchallenged pancreatic  $\beta$ -cells. Clarifying these mechanisms will be pivotal for developing precise, targeted nutritional strategies for the effective management of T2DM.

### Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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