FAST FACTS

Low and very low carbohydrate diets for diabetes remission

Dietary interventions that restrict carbohydrate intake for the management of diabetes are of particular interest to researchers, healthcare providers, and patients. Based on evidence of moderate to low certainty from 23 randomized trials (n=1357), evidence synthesis suggests that patients who adhere to low or very low carbohydrate diets for six months might achieve diabetes remission without adverse consequences. But the definition of low and very low carbohydrate diets, the long term health effects of carbohydrate restricted diets, and the working definitions of diabetes remission are debated, requiring further investigation, particularly for longer term health outcomes based on evidence from randomized trials.

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Definition of low or very low carbohydrate diets

Carbohydrate restriction has a long history of use in the management of diabetes, and authoritative organizations have recently highlighted the potential benefits and harms of low carbohydrate diets.¹ The definition of such diets can, however, vary widely and can be confusing to both patients and providers.²

Over the past few decades, the average carbohydrate intake for adults in the United States has been estimated to range between 39% and 51% of daily kilocalories (subsequently referred to as calories).² Historically, authoritative organizations have recommended carbohydrate intake varying from 45% to 65% of daily calories. Diets with a carbohydrate intake of less than 45% of daily calories therefore have been commonly considered as carbohydrate restricted.³

What is meant by a low carbohydrate diet can vary depending on the reference source. For example, a formal definition was proposed in 2015, defining a low carbohydrate diet as one where less than 26% of daily calories are derived from carbohydrates (<130 g/day),³ yet in its review of the literature the 2019 American Diabetes Association consensus statement on nutrition therapy for diabetes and prediabetes describes “a low-carbohydrate eating pattern as reducing carbohydrates to 26-45% of total calories” (<225 g/day of a 2000 calorie diet).¹

The definitions of very low carbohydrate diets also vary (eg, thresholds ranging from <10% to <26% of daily caloric intake).^{1,3} This difference is substantive because diets with substantially lower intakes of carbohydrate (eg, <10% of daily calories) have been shown to induce nutritional ketosis.⁴ In this physiological state, ketone bodies are produced and used as an alternative energy source, especially by the brain,⁴ with these diets commonly referred to as ketogenic. Conversely, very low carbohydrate diets, defined as an intake of <26% of daily calories, do not consistently induce ketogenesis.

Until the consensus on definitions is clear, researchers should explicitly define their use of the

terms low and very low carbohydrate diets, and readers of the literature should take note of these definitions when interpreting and applying the results from research. Further, when interpreting results, readers should look for evidence of adherence to carbohydrate restrictions and how adherence impacts study results.⁶

Why this matters

Very low carbohydrate diets, particularly those that induce ketogenesis, are controversial. The controversy is primarily related to the conventional, although debated,⁵ nutritional advice that is related to the suggested adverse health consequences of a diet high in saturated fat, which often occurs among those who follow carbohydrate restricted diets. We recently conducted the most comprehensive review of randomized trials among patients with diabetes who followed a low carbohydrate diet for six and 12 months and found no statistically significant or clinically important increase in total or serious adverse events.⁶ Such were, however, poorly reported, and major adverse cardiovascular outcomes could take longer to develop. So far, randomized trials of low carbohydrate diets for people with diabetes are limited to only a few trials with a duration of more than 12 months, and even these studies do not go beyond 24 months.⁶ Long term observational studies with a mean follow-up of 25 years suggest a U-shaped relation with both higher and lower extremes of carbohydrate intake, showing an increased mortality risk, although confounding cannot be excluded.⁷

In addition to the potential adverse health risks, advocates for plant based diets have raised environmental and ethical concerns about carbohydrate restricted diets, typically high in animal products.⁸ However, extensive carbohydrate restrictions can indeed be achieved, and individualized, using a vegetarian or vegan diet, although vegan ketogenic diets are more challenging without caloric restriction.

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Additional considerations—defining diabetes remission

Diabetes remission is an outcome of importance to patients, clinicians, and policy makers. How remission is defined also varies. In general, among contemporary definitions of diabetes remission, three factors are considered: a glycated hemoglobin (HbA1c) threshold, use of antidiabetes drugs, and duration of remission. Although an international body of diabetes experts published a consensus paper in 2009 attempting to formalize the definitions of remission,⁹ these were never formally adopted. Further, a scoping review of definitions in 2020 showed continued heterogeneity in how diabetes remission is defined.¹⁰ For example, the most commonly used HbA1c thresholds were <42 mmol/mol (6.0%) and <48 mmol/mol (6.5%).¹⁰ In terms of drug treatment use, the cessation of certain beneficial treatments, such as metformin, might be seen as unethical; thus, there is some resistance to definitions that require drug treatment cessation. As to proposed durations of remission, these can range from 30 days to five years depending on the reference source.¹⁰

Until the diabetes research community agrees on a formal definition of remission, researchers should explicitly state the conditions of their own definitions. Given the debate, researchers might use several definitions. Our group, for example, has attempted to manage this lack of consensus by reporting meta-analytic results on diabetes remission using four a priori definitions among trials reporting outcomes at six and 12 months.⁶

Conclusion

The terminology, evaluation, and application of carbohydrate restricted diets for diabetes remission are at the center of evidence informed decision making among patients, clinicians, and policy makers. Until consensus is reached, when the efficacy and safety of carbohydrate restricted diets are evaluated for diabetes management, researchers should be clear in their a priori definitions of low and very low carbohydrate diets as well as diabetes remission, and consumers of the research literature should be aware of which definitions are being used, while being cognizant of any sensitivity or subgroup analysis used to compare results across definitions.

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