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Study on the efficacy and safety of lower-carbohydrate dietary patterns in MAFLD: A systematic review and meta-analysis of randomized controlled trials

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Citation 1 change
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REVIEW TITLE AND BASIC DETAILS

Review title 1 change
Study on the efficacy and safety of lower-carbohydrate dietary patterns in MAFLD: A systematic review and meta-analysis of randomized controlled trials

Original language title 1 change
Study on the efficacy and safety of lower-carbohydrate dietary patterns in MAFLD: A systematic review and meta-analysis of randomized controlled trials

Review objectives
Metabolic associated fatty liver disease (MAFLD) was renamed from nonalcoholic fatty liver disease (NAFLD) in 2020, and the incidence rate showed a rising and younger trend. In recent years, an increasing number of studies have focused on the potential therapeutic effects of low carbohydrate dietary patterns on MAFLD. This study collected randomized controlled trials of low carbohydrate dietary intervention for MAFLD to evaluate its therapeutic effect and provide evidence-based medicine for clinical work.

Keywords
Lower-carbohydrate dietary patterns; Low-carbohydrate diet; very-low carbohydrate, high-fat ketogenic diet; Metabolic associated fatty liver disease; Randomized controlled trials; Systematic review

SEARCHING AND SCREENING

Searches 1 change
Retrieve from databases such as PubMed, Embase, \Web of Science, Cochrane Library, China National Knowledge Infrastructure (CNKI), China Biomedical Literature Database (CBM), China Science and Technology Journal Database (VIP), Wanfang Database, etc., with a time range from database establishment to June 1, 2025.

Study design 1 change
Only randomized study types will be included.

Included
Inclusion criteria:Randomized controlled trial.Exclusion criteria:Non-randomized controlled trial.

ELIGIBILITY CRITERIA

Condition or domain being studied
Non alcoholic fatty liver disease is a chronic progressive liver disease caused by overnutrition and insulin resistance in genetically susceptible individuals. The disease spectrum includes non-alcoholic fatty liver disease, non-alcoholic fatty hepatitis and its related fibrosis and cirrhosis. In 2020, the International Fatty Liver Expert Group recommended renaming NAFLD to MAFLD, emphasizing the core role of metabolic abnormalities in the pathogenesis of fatty liver. The risk factors for MAFLD include high-fat and high calorie dietary structure, sedentary lifestyle, metabolic syndrome and its components. Currently, lifestyle changes to promote weight loss are considered the first-line treatment for MAFLD, with diet being the cornerstone of lifestyle interventions. However, there is currently no consensus on whether specific dietary patterns should be recommended to MAFLD patients.

Population 1 change
Inclusion criteria:Subjects who meet the diagnostic criteria for MAFLD.Exclusion criteria: Animal experiments.

Intervention(s) or exposure(s) 1 change
Inclusion criteria:Lower-carbohydrate dietary patterns (Energy<26% or Carbohydrate<130g/d), and understanding the proportion of constant nutrient intake (carbohydrates, fats, proteins).Exclusion criteria:Lower-carbohydrate dietary patterns, but not understanding the proportion of constant nutrient intake.

Comparator(s) or control(s) 1 change
Inclusion criteria:Non lower-carbohydrate dietary patterns, or only providing lifestyle guidance without intervention measures.Exclusion criteria:During the trial, other

interventions such as drug therapy and exercise therapy were carried out.

Context 1 change
Currently, lifestyle changes to promote weight loss are considered the first-line treatment for MAFLD, with diet being the cornerstone of lifestyle interventions. It is generally believed that appropriate calorie restriction and a reasonable low-fat diet are beneficial for improving the condition of MAFLD patients, and in recent years, LCDP has gradually become a hot topic of concern. However, the lack of a universally accepted standard definition for LCDP in the past has posed obstacles to determining dietary guidance related to LCDP. In 2024, the "Expert Consensus on Nutrition and Lower Carbohydrate Diets" clearly defined LCDP (Energy<26% or Carbohydrate<130 g/d) and distinguished between two subtypes of LCDP: LCD (Energy 10-25% or Carbohydrate 50-129 g/d) and VLCKD (Energy<10% or Carbohydrate 20-50 g/d). The clarification of this dietary pattern will have a positive impact on controlling the occurrence and development of MAFLD, therefore it is necessary to conduct a systematic analysis. This study collected randomized controlled trials of LCDP intervention in MAFLD to evaluate its therapeutic effect and provide evidence-based medicine for clinical work.

OUTCOMES TO BE ANALYSED

Main outcomes
Including: weight, waist circumference, waist to hip ratio, visceral fat, BMI, triglycerides, total cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, aspartate transaminase, alanine transaminase, gamma glutamyl transferase, fasting blood glucose, glycated hemoglobin, insulin resistance index, systolic blood pressure, diastolic blood pressure, controlled attenuation parameters, etc.

Additional outcomes
None

DATA COLLECTION PROCESS

Data extraction (selection and coding)
In terms of literature screening, the search results were first imported into EndNote X7 software for initial screening. Two researchers independently excluded duplicate literature through the bibliography, and then read the abstracts one by one to exclude literature unrelated to this study. After the initial screening, the literature was re screened by reading the full text, and the screening results were cross checked against the inclusion and exclusion criteria to retain studies that met the inclusion criteria. If there is a disagreement, it can be decided whether to include it through joint discussion, and if necessary, a third researcher can assist in resolving it. If the information in the article is incomplete or unclear, the original research author will be contacted and information will be obtained through email consultation. Finally, summarize the outcome measures and exclude literature with less than 3 outcome measures. The extraction of literature information includes: basic research information (first author name, publication year, research country), trial type and patient data (number of participants, gender, average age, diagnostic method),

intervention measures (intervention period, intervention method), possible biases, outcome measures, and other necessary information.

Risk of bias (quality) assessment

To evaluate the quality of the included studies, we used the Cochrane ROB method in Review Manager 5.3 software for methodological quality assessment: ① selection bias, ② implementation bias, ③ measurement bias, ④ follow-up bias, ⑤ reporting bias, ⑥ other biases; Determine the risk levels of "low risk", "high risk", and "uncertain" based on the bias risk assessment table for each item.

PLANNED DATA SYNTHESIS

Strategy for data synthesis

Perform meta-analysis using RevMan 5.3 software. The effect size was combined by evaluating the standardized mean difference (SMD) and corresponding 95% confidence interval (CI) of the included studies. Cochran Q test and I^2 test were used to evaluate the existence and severity of heterogeneity. When $I^2 \leqslant 50\%$ and $P \geqslant 0.10$, it was considered that the heterogeneity of the study was small, and a fixed effects model was used to study the obtained data. When heterogeneity $I^2>50\%$ or $P<0.10$, it was considered that the heterogeneity of the study was large, and a random effects model was used for analysis; And explore the sources of heterogeneity through sensitivity analysis and subgroup analysis. Sensitivity analysis involves sequentially removing individual studies and then re merging the effect sizes, and evaluating the difference in the combined effect sizes before and after removing the study, in order to examine the impact of a particular study on the combined effect sizes. Subgroup analysis mainly involves grouping based on research type and intervention duration as variables to explore the sources of heterogeneity. Use funnel plot and Egger method to test for publication bias.

Analysis of subgroups or subsets

According to the lower-carbohydrate dietary patterns, it is divided into two subgroups: low carbohydrate diet and extremely low carbohydrate high-fat ketogenic diet. According to the intervention period, it is divided into three subgroups: 2 weeks, 8 weeks, and 12 weeks.

REVIEW AFFILIATION, FUNDING AND PEER REVIEW

Review team members 1 change

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No conflict of interest declared.

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No conflict of interest declared.

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No conflict of interest declared.

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No conflict of interest declared.

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Funding source

None

TIMELINE OF THE REVIEW

Review timeline

Start date: 1 January 2025. End date: 1 June 2025.

Date of first submission to PROSPERO

21 November 2024

Date of registration in PROSPERO

02 December 2024

CURRENT REVIEW STAGE

Publication of review results

The intention is not to publish the review once completed.

Stage of the review at this submission

Review stage	Started	Completed
Pilot work	✓	✓
Formal searching/study identification	✓	✓
Screening search results against inclusion criteria	✓	✓
Data extraction or receipt of IPD	✓	✓
Risk of bias/quality assessment	✓	✓
Data synthesis	✓	✓

Review status

The review is completed.

ADDITIONAL INFORMATION

PROSPERO version history 1 change

- Version 2.0, published 22 Jun 2025
- Version 1.3, published 22 Jun 2025
- Version 1.2, published 22 Jun 2025
- Version 1.1, published 02 Dec 2024
- Version 1.0, published 02 Dec 2024

Review conflict of interest
None known

Country
China

Medical Subject Headings
Dietary Carbohydrates; Dietary Patterns; Evidence-Based Medicine; Humans; Incidence; Non-alcoholic Fatty Liver Disease; Randomized Controlled Trials as Topic

Revision note 1 change
Update the progress of system reviews and meta-analyses.

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