Efficacy and safety of low-carbohydrate diets: a systematic review

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CRD summary
This review evaluated low-carbohydrate diets for the treatment of obesity. The authors concluded that there was insufficient evidence to make recommendations for or against the use of low-carbohydrate diets. The methods of the review were not well reported, and the search was limited and restricted to English language publications. It is possible that some studies were missed.

Authors' objectives
To evaluate changes in weight, serum lipids, fasting glucose, fasting serum insulin levels and blood-pressure among adults using low-carbohydrate diets in the out-patient setting.

Searching
MEDLINE was searched for studies published in the English language between 1966 and February 2003. The search terms were given in paper. The bibliographies of retrieved articles and conference proceedings were also checked.

Study selection
Study designs of evaluations included in the review
The inclusion criteria did not include details of study design. The included studies were randomised controlled trials (RCTs), randomised crossover trials, other studies with a control or comparison group, sequential studies and pre-test post-test studies. For crossover and sequential studies, only data from the first diet interval were included.

Specific interventions included in the review
The inclusion criteria specified either low-carbohydrate, ketogenic, higher protein or higher fat diets. The included studies had to report sufficient data to calculate both the carbohydrate content (g/day) and total calories consumed (kilocalories per day, kcal/day). Diets of less than 500 kcal/day, of duration less than 4 days, or with a requirement that the participants be hospitalised or confined to a diet or research centre, were excluded. Although the authors were interested in an exercise component of the treatment, a lack of information in the included studies meant that this was excluded from any analyses. In the included studies, the carbohydrate content varied from 0 to 901 g/day, the energy content from 525 to 4,629 kcal/day, and the study duration from 4 days to one year.

Participants included in the review
The inclusion criteria specified adults who were not hospitalised. Pregnant women were excluded. The participants in the included studies were male and female healthy volunteers, obese or diabetic persons. The mean ages ranged from 21 to 64 years. The diets were grouped according to their carbohydrate content. The body mass index (BMI) and weight before diet were given as the mean of the mean values in each of the two groups: BMI 36.3 and 30.6; weight 91.7 and 86.2 kg.

Outcomes assessed in the review
The outcomes to be assessed were measures of body mass (weight in kg), BMI, lipid levels (total cholesterol, low-density lipoprotein, high-density lipoprotein and serum triglycerides), measures of glycaemic control (fasting serum glucose and insulin levels) and systolic blood-pressure.

Articles were excluded if they did not report data for at least one of the clinical outcomes of interest.

How were decisions on the relevance of primary studies made?
One author reviewed the search results for potentially relevant studies.
Assessment of study quality
The authors do not report the method used to assess validity, or how the validity assessment was performed.

Data extraction
Two authors independently abstracted data onto pre-tested abstraction forms. Any discrepancies were resolved by repeated review and discussion. The data extracted included dietary intervention, participants studied and clinical outcomes.

Methods of synthesis
How were the studies combined?
Individual study results (from bivariate analyses) were combined using a fixed-effect meta-analytic model (for continuous data), i.e. differences in means were combined. Since four non-independent outcomes were analysed, alpha (p) was set at 0.0125 based on a standard Bonferroni adjustment. The effect size and 95% confidence intervals (CI) were reported.

How were differences between studies investigated?
Differences between the studies were discussed, including the variety of diets (carbohydrate content and caloric value) used; the tables listed studies by study design. The homogeneity of the summary effect sizes was calculated using the Q statistic.

Results of the review
Ninety-four studies (3,268 participants) were included: 24 parallel RCTs (1,778 participants), 19 crossover RCTs (347 participants), 17 studies with comparison groups (602 participants), 9 sequential studies (144 participants) and 25 pre-test post-test studies (749 participants). In total, 38 studies (663 participants) evaluated lower-carbohydrate diets (60 g/day or below) and, of these, 13 studies (71 participants) evaluated the lowest carbohydrate diets (20 g/day or below).

The studies were highly heterogeneous in respect of design, carbohydrate content, total calorie content, diet duration and participant characteristics. At the end of both the lower and higher carbohydrate diets, the participants’ weight, BMI and percentage of body fat had decreased. In general, the greatest weight loss occurred with the lowest carbohydrate diets and in participants with the highest baseline weight. When only the RCTs and crossover RCTs of lower-carbohydrate diets were analysed, the studies appeared homogeneous and the mean weight loss was 3.6 kg (standard deviation, SD=1.2; 95% CI: 1.2, 6.0). For all higher-carbohydrate diets, for these study designs, the mean weight loss was 2.1 kg (SD=0.3; 95% CI: 1.6, 2.7). The diets with the greatest weight loss were those of longer duration, restricted calorie intake and those that included participants who were significantly overweight at baseline.

For all studies combined, no significant change was found in any serum lipid levels, but amongst the more homogeneous group of studies of higher-carbohydrate diets there was a significant reduction in cholesterol levels (-0.21 mmol/L, SD=0.04; 95% CI: -0.14, -0.28).

There were no significant changes in fasting serum glucose, insulin levels or systolic blood-pressure for either the lower- or higher-carbohydrate diets.

Authors’ conclusions
There is insufficient evidence to make recommendations for or against the use of low-carbohydrate diets, particularly among participants older than 50 years, for use longer than 90 days or for diets with a carbohydrate content of 20 g/day or less. Among the published studies, participant weight loss while using low-carbohydrate diets was principally associated with decreased caloric intake and increased diet duration, but not with reduced carbohydrate content.

CRD commentary
The aims of this review are not entirely clear. In particular, the authors do not give a definition of a low-carbohydrate
diet and seem to have included widely differing diets. The search was somewhat limited since only one database was searched, and this was restricted to English language publications. It is possible that studies were missed. The methods of the review (e.g. study selection, quality assessment) are not well reported. The authors summarised information from a variety of study designs and very disparate dietary interventions. It may have been useful to have more restrictive inclusion criteria, or to have included some grouping by such variables as study duration, percentage of carbohydrates in total diet, or calorific content.

The results do not appear to have been reported on an intention-to-treat basis. Although the authors set alpha at 0.0125, they reported a 95% CI when it would have been more appropriate to give a 98.75% CI. Some of the numbers in the tables (e.g. numbers of diets) appear inconsistent. It would have been interesting to see a meta-analysis of direct comparisons between lower- and higher-carbohydrate diets. Low-carbohydrate diets have become more popular and, as there is some controversy concerning the clinical side-effects and quality of life of these diets, it would have been useful to include these as outcomes (although it is possible that this information may not have been available).

**Implications of the review for practice and research**

**Practice:** The authors state that there is insufficient evidence to make recommendations for or against low-calorie diets.

**Research:** The authors state that there is a need for studies of isocaloric diets with different carbohydrate contents to specifically assess symptoms of hunger and tolerability of the diet. In addition, there is a need for (good quality) studies assessing long-term follow-up data including lipid levels and blood-pressure levels, studies on different racial or ethnic groups, as well as studies in older and younger participants with and without diabetes, hyperlipidaemia and hyperkalaemia.

**Bibliographic details**


**PubMedID**

12684364

**DOI**

10.1001/jama.289.14.1837

**Original Paper URL**

http://jama.ama-assn.org/

**Indexing Status**

Subject indexing assigned by NLM

**MeSH**

Blood Glucose /metabolism; Blood Pressure; Body Mass Index; Caloric Restriction; Diet, Reducing; Dietary Carbohydrates /administration & dosage; Dietary Fats; Dietary Proteins; Humans; Insulin /blood; Lipids /blood; Obesity /blood /diet therapy; Weight Loss /physiology

**AccessionNumber**

12003008214

**Date bibliographic record published**

30/11/2003

**Date abstract record published**

30/11/2003
Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.