

Are Low-Carbohydrate Diets Safe and Effective?

Heather Fields, MD; Barbara Ruddy, MD; Mark R. Wallace, MD; Amit Shah, MD; and Denise Millstine, MD

From the Mayo Clinic
in Scottsdale, Arizona.

Financial Disclosures:
None reported.

Support: None reported.

Address correspondence to
Heather Fields, MD,
13400 E Shea Blvd,
Division of Community
Internal Medicine,
Mayo Clinic, Scottsdale, AZ
85259-5452.

E-mail:
fields.heather@mayo.edu

Submitted
January 14, 2016;
final revision received
August 17, 2016; accepted
September 6, 2016.

The rate of obesity has dramatically increased since the 1970s and is the second leading preventive cause of death in the United States.¹ In 2014 alone, the US weight loss market totaled \$64 billion, with approximately 20% of adults attempting weight loss through various diets.² One such diet, the low-carbohydrate diet (LCD), was advocated as early as 1869 in William Banting's *Letter on Corpulence*.³ The LCD regained popularity with the 1972 publication of *Dr. Atkins' Diet Revolution: The High Calorie Way to Stay Thin Forever*.⁴ Notably, Atkins did not publish safety or efficacy findings in a peer-reviewed, scientific journal. Since then, many variations of LCDs have been popularized.

The public is likely confused about dietary recommendations and restrictions because of changing guidelines. The 2015 revised US Department of Agriculture Dietary Guidelines adjusted some long-held tenets of healthful eating, including the removal of the cholesterol intake limitation (previously, 300 mg/d).^{5,6} The low-fat philosophy of the past several decades has been called into question, with publications included in a meta-analysis⁷ dismissing the link between saturated fat intake and cardiovascular disease. Patients might change their diets based on these new guidelines and reports and increase their consumption of red or processed meats, for example, despite the consistent, unchanged recommendation to limit these foods.⁵ Notwithstanding, a high intake of red meat, especially processed meat, is associated with increased cardiovascular and all-cause mortality⁸⁻¹⁰ and is recognized as carcinogenic.¹¹ In this review, we analyzed LCDs, which are inherently higher in cholesterol, saturated fats, and animal products, to assess their effects on weight loss, glucose metabolism, blood pressure, and lipid levels.

Clinical Question: Are low-carbohydrate diets (LCDs) safe and effective for weight loss and cardiovascular and metabolic health?

Evidence: In the short-term, LCDs may be slightly better than low-fat diets for weight and triglycerides management but not superior for the management of blood glucose, blood pressure, or cholesterol levels.

Recommendation: Physicians should be aware that available evidence for LCDs is limited because of variable definitions, lack of long-term studies, and lack of patient adherence. However, patients who follow LCDs may see modest benefits in short-term weight loss compared with those who follow low-fat diets.

How Do We Define and Classify LCDs?

The definition of LCD is highly variable. Some LCDs restrict carbohydrate intake to a percentage of calories consumed, and others restrict absolute grams of carbohydrates. For example, a 2014 systematic review of randomized controlled trials (RCTs) defined LCD as having less than 45% of energy intake from carbohydrates¹²; by comparison, the typical Western diet has more than 50%, which is minimally different. *Table 1* lists the popular names and key features of several LCDs.

In general, most LCDs allow 20 to 60 g/d of carbohydrates (<20% of total daily calorie intake), and very-low-carbohydrate ketogenic diets (VLCKDs) typically restrict carbohydrates to less than 20 g/d. Some less-restrictive diets allow up to 130 g/d of carbohydrates (26% of total calories).¹³ Most LCDs we reviewed fit these parameters, although some authors designated diets as LCD up to a maximum of 46% of total calories from carbohydrate calories. Other nutrition experts, however, disregard these LCDs based on the lack of ketosis, which is another inconsistent parameter in the definition of LCD. Unlike conventional weight loss diets, most LCDs do not restrict caloric intake, which may increase their allure. Many popular LCDs include a 10- to 14-day induction phase, with Atkins placing the strictest limits on carbohydrate intake to 20 g/d, inducing ke-

tositis and rapid weight loss, followed by a subsequent less-restrictive phase. The lack of a consistent definition makes comparison among LCDs difficult.

Review of the Literature

Our literature search was originally designed to find articles that addressed potential adverse effects and overall safety of LCDs. We used the Ovid MEDLINE online database, searching January 2005 through April 2016 with key search terms: *Atkins, diet, ketogenic diet, ketosis, low carbohydrate, nutrition, risk, paleo, safe, South Beach, and Zone*. We limited our search to RCTs, meta-analyses, and systematic reviews in English. After duplicates were removed, the titles and abstracts of 72 articles were screened to identify potentially eligible studies for subsequent full review.

The majority of the articles addressed implications of LCDs in weight loss or obesity and cardiovascular parameters, such as glucose metabolism, blood pressure, and cholesterol levels, which became the focus of our review. Nonhuman studies, non-English studies, and observational studies were excluded. Studies that did not specifically address weight loss, glucose metabolism, blood pressure, or cholesterol were also excluded, as were studies involving pediatric or pregnant populations. We did not exclude studies on the basis of trial length or number of participants. References of the included studies were scanned, and pertinent articles were added to the review.

The Evidence

Included studies were RCTs of either parallel or cross-over design and systematic reviews. The majority of studies required participants to be overweight or obese, often with 1 cardiovascular risk factor, but some studies had healthy adult samples. The number of participants in the trials ranged from 9 to several hundred. The authors defined LCDs according to carbohydrate restriction, which ranged from 4% of total calories (<20 g) to 46%. The comparison diets were usually low-fat diets (LFDs)

or restricted in calories (variably defined) and, in some, LCDs were compared with a Mediterranean diet or other diets or programs, such as Weight Watchers, a high fiber diet, or a diet or program recommended by the American Dietetic Association. Calories were usually not equal between the intervention diets and the comparison diets. Diets were tracked by participant self-recordings and nutrition software. Some studies used urine ketone levels to track the progress of VLCKDs. A few studies provided meals to participants, and some implemented short-term inpatient stays.

Effect of LCDs on Health

Weight Loss

Forty-one trials that evaluated the effects of LCDs on weight loss were reviewed. Two meta-analyses demonstrated greater weight loss with LCDs compared with LFDs at 6 months, but they had comparable weight loss results at 12 months.^{14,15} In a third meta-analysis of long-term (at least 1 year) weight loss, LCDs had a statistically significant 1.15-kg weighted mean difference compared with LFDs.¹⁶

In addition, a 2-year, prospective RCT¹⁷ of overweight or obese, mostly male (86%), middle-aged participants reported a 4.7-kg vs 2.9-kg weight loss with a non-calorie-restricted LCD compared with a calorie-restricted LFD, respectively. Further, at the 2-year conclusion, a 5.5-kg mean weight loss was found in participants who still adhered to the diets compared with 3.3 kg in those who had not adhered to the diets.¹⁷

Greater weight loss may be promoted by VLCKDs than by moderate LCDs. When carbohydrate intake was restricted to 10% of total calories, a meta-analysis of 13 trials found a weighted mean difference weight loss of 0.91 kg with VLCKDs at end points of 12 months or longer compared with LFDs. The clinical significance of this small weight loss is questionable, and adherence to VLCKDs beyond 6 months is nearly nonexistent.¹⁸

Compared with LFDs, LCDs have not been shown to result in greater long-term weight loss in people with type 2 diabetes mellitus. In a large trial¹⁹ restricted to

Table 1.
Popular Low-Carbohydrate Diets

Diet Name	Carbohydrate Content	Key Features ^a
Ketogenic	<50 g/d	Patients may check urine for ketones or ask for blood work to confirm ketotic states (elevated β -hydroxybutyrate); diet emphasizes "keto-adaptation," with the body switching from using glucose to fat as main energy source
Atkins	Induction phase: 20 g/d; later phases: 80-100 g/d	4 phases with more restriction in the beginning; the "New Atkins" diet offers a 40-g/d induction phase option for those <40 lb overweight
Eco-Atkins	130 g/d	Vegan diet with 31% protein, 43% fat, 26% carbohydrate
South Beach	Phase 1: exclude most carbohydrates; phases 2 and 3: ≤ 140 g/d	Created in response to concerns about increased saturated fat content of Atkins diet; emphasizes restriction of carbohydrates and saturated fats; 3 meals and 3 snacks per d
Zone	40%	Emphasizes proper proportions of carbohydrates, protein (30%), and fat (30%) to help satiety and metabolism; diet emphasizes small, frequent meals and snacks, totaling 7 per d
Paleo	Varies based on food choices	Limited to foods that early humans ate, including meat, fish, eggs, vegetables, fruits, and nuts; minimal whole grains; no processed food, foods with added sugar, dairy, legumes, or potatoes
Dr Bernstein's Diabetes Solution	30 g/d	One of the original diets emphasizing glycemic index by restricting foods that cause rapid rise in blood sugar
Sugar Busters	2-3 servings per d	Emphasizes glycemic index by minimizing refined sugar, white flour, and starches
LCHF	<20-100 g/d	Emphasizes fats for satiety; popular in Sweden
Protein Power	28-40 g/d	Emphasizes adequate protein and limited carbohydrates divided into 4-5 meals/snacks per d
Sonoma	Varies based on food choices	3 phases emphasize portion control; combines Mediterranean and low-carbohydrate diets; minimizes saturated fat, starches, and sugar

^a Most of these diets focus on content of diet and are not strictly calorie limited.

Abbreviation: LCHF, low carbohydrate, high fat.

overweight adults with a diagnosis of type 2 diabetes mellitus for at least 6 months, the LCD resulted in a faster weight loss at 3 months compared with the LFD, but at 12 months, both groups had lost a mean of 3.1 kg.¹⁹

The effects of LCDs may be different in women. An RCT²⁰ compared the Atkins and Zone LCDs with the LEARN and Ornish LFDs among premenopausal women, and they found that the participants' weight loss with the Atkins LCD was statistically significantly greater (4.7 kg) compared with the others. In a subgroup analysis of the Shai et al trial,¹⁷ women reported a 2.4-kg weight loss with LCDs compared with a 4.7-kg weight loss in all participants with LCD.

Blood Pressure

Twenty-nine trials that evaluated the effects of LCDs on blood pressure were reviewed. Studies that compared more than 2 types of diets (eg, LCD vs LFD vs Mediterranean diet) were separated into individual components for a total of 38 comparisons. More than half of the comparisons (63%) showed a statistically significant improvement in blood pressure from baseline (systolic, diastolic, or both) with both the LCD and comparison diets. Most (76%) showed no statistically significant difference in participants' blood pressure between the diets at the end of the studies. This finding is consistent with the meta-analysis by Bueno et al,¹⁸ which found no difference in systolic blood pressure between VLCKD and

comparison groups, though a small (-1.43 mm Hg) significant reduction in diastolic blood pressure was observed with the VLCKD ($P=.008$). The reviews by Hu and Bazzano¹² and Nordmann et al¹⁵ also found no difference in participants' blood pressure between LCDs and comparison diets.

Glucose Metabolism

Low-carbohydrate diets have little known effect on long-term glycemic control. Eleven trials evaluating the effects of LCDs on glucose metabolism were reviewed. Two meta-analyses^{18,21} found no difference in fasting blood glucose or hemoglobin A_{1c} levels between LCDs and other diets. In 2 separate studies,^{22,23} a VLCKD and an LCD demonstrated short-term decreases of hemoglobin A_{1c} in people with type 2 diabetes. In the latter study,²³ the improvements in hemoglobin A_{1c} at 6 months were not sustained at 24 months. Glycemic effects of LCDs compared with LFDs have varied, including improved outcomes with LCDs from baseline in 2 studies,^{24,25} but several showed no difference from the comparison diet.^{22,24-28} One study with a VLCKD group²² demonstrated decreased need for pharmacotherapy.

Cholesterol and Triglyceride Levels

Forty-four trials that evaluated lipids, including triglyceride, high-density lipoprotein (HDL), low-density lipoprotein (LDL), and total cholesterol levels had mixed results. Trials that compared more than 2 diets were separated into individual components for clarity. Triglycerides were evaluated in 50 comparisons. An LCD was favored in 48% of the comparisons, the comparison diet in 4%, and 48% showed no statistically significant difference between the 2 diets. Three systematic reviews^{12,15,18} favored the LCDs or VLCKDs in lowering triglycerides. In 53 trial comparisons of HDL, LDL, and total cholesterol levels, 43% showed no difference between the 2 diets, 6% favored LCDs, 6% favored the comparison diet, and 45% had discordant results (sometimes LCD improved HDL but not LDL or total cholesterol levels). However, the 3 systematic reviews^{12,15,18} showed discordant results for nontriglyceride lipids.

Discussion

Low-carbohydrate diets may be appealing to patients because of their simplicity and lack of calorie restriction in most. Physicians should be familiar with the popular names of LCDs and their key features, because patients often refer to their LCD by its popular name. Physicians seeking to advise patients can conclude that short-term (eg, 6 months) adherence to an LCD with high-quality protein may be associated with weight reduction, but the amount of weight loss is small and of questionable clinical significance. These diets may lead to improved blood pressure reduction and glycemic control and are not inferior to comparators, such as LFDs and calorie-restricted diets. Low-carbohydrate diets were often favorable over comparators in the reduction of triglyceride levels, but they were not consistently favorable in their effects on HDL, LDL, or total cholesterol levels (*Table 2*).

Physicians must keep in mind that the literature is surprisingly limited, considering the popularity of these diets and the claims of health benefits in the public press. The variable definition of LCDs and VLCKDs makes it difficult to interpret results, and studies do not consistently address the source or quality of the protein and fat that are consumed in LCDs. To the authors' knowledge, no long-term epidemiologic studies have evaluated primary cardiovascular outcomes or all-cause mortality with LCDs as there are for other diets, such as the vegetarian diet.^{8,29-31} One main concern is that certain meats have been implicated in worsened all-cause mortality⁸⁻¹⁰ and increased cancer risk,¹¹ and strict LCDs may be difficult to follow without intake of substantial amounts of meat. Our review found no safety issues identified in the current literature, but patients considering LCDs should be advised of the paucity of data on long-term safety and efficacy.

The RCTs assessing LCDs are small and of short duration, making it difficult to draw conclusions about overall health effects. Other limitations include several sources of heterogeneity, such as diversity of participants (nondiabetic, prediabetic, and diabetic partici-

Table 2.
Effect of Low-Carbohydrate Diets on Weight, Glucose Levels, Blood Pressure, and Lipid Levels

Health Outcome	Effects of LCDs
Weight	Minimally consequential weight loss between LCDs and comparator diets, with possible greater initial (<6 mo) loss. VLCDs may result in greater weight loss in adherent patients
Glucose levels	Noninferior lowering of glucose and HbA _{1c} between LCDs and comparators, although trials have reported conflicting results
Blood pressure	Noninferior lowering of blood pressure between LCDs and comparator diets
Lipid levels	Noninferior reductions in total cholesterol and LDL cholesterol between LCDs and comparators, with some trials reporting greater lowering of triglycerides with LCDs

Abbreviations: HbA_{1c}, hemoglobin A_{1c}; LCD, low-carbohydrate diet; LDL, low-density lipoprotein; VLCD, very-low-carbohydrate diet.

pants; normal weight, overweight, and obese participants) and variety of interventions (macronutrient content, calorie restriction, LCD, VLCKD, counselling, medication). The studies did not consistently address the source or quality of the protein and fat, nor did they address the type of weight lost (ie, muscle, water, fat). Furthermore, the phase of evaluation (eg, induction, maintenance) in LCD studies convolutes the evidence. Another limitation common to most nutrition research is the reliance on dietary recall, which is highly susceptible to error.

Low-carbohydrate diets seem to have short-term efficacy in weight loss without negatively affecting blood pressure, glucose, and cholesterol compared with other diets. Conclusions about long-term efficacy and safety cannot be made, however. (doi:10.7556/jaoa.2016.154)

References

- Wang Y, Beydoun MA. The obesity epidemic in the United States—gender, age, socioeconomic, racial/ethnic, and geographic characteristics: a systematic review and meta-regression analysis. *Epidemiol Rev*. 2007;29:6-28.
- Kell J. Lean time for the diet industry. *Fortune*. May 22, 2015.
- Banting W. Letter on corpulence, addressed to the public: third edition [reprint]. *Obes Res*. 1993;1(2):153-163.
- Atkins RC. *Dr. Atkins' Diet Revolution: The High Calorie Way to Stay Thin Forever*. New York, NY: D. McKay Co; 1972.
- Scientific Report of the 2015 Dietary Guidelines Advisory Committee*. Washington, DC: US Dept of Agriculture; 2015.
- de Souza RJ, Mente A, Maroleanu A, et al. Intake of saturated and trans unsaturated fatty acids and risk of all cause mortality, cardiovascular disease, and type 2 diabetes: systematic review and meta-analysis of observational studies. *BMJ*. 2015;351:h3978. doi:10.1136/bmj.h3978
- Chowdhury R, Warnakula S, Kunutsor S, et al. Association of dietary, circulating, and supplement fatty acids with coronary risk: a systematic review and meta-analysis [published correction appears in *Ann Intern Med*. 2014;160(9):658]. *Ann Intern Med*. 2014;160(6):398-406. doi:10.7326/M13-1788
- Fields H, Millstine D, Agrwal N, Marks L. Is meat killing us [review]? *J Am Osteopath Assoc*. 2016;116(5):296-300. doi:10.7556/jaoa.2016.059
- Larsson SC, Orsini N. Red meat and processed meat consumption and all-cause mortality: a meta-analysis. *Am J Epidemiol*. 2014;179(3):282-289. doi:10.1093/aje/kwt261
- Abete I, Romaguera D, Vieira AR, Lopez de Munain A, Norat T. Association between total, processed, red and white meat consumption and all-cause, CVD and IHD mortality: a meta-analysis of cohort studies. *Br J Nutr*. 2014;112(5):762-775. doi:10.1017/S000711451400124X
- Consumption of Red Meat and Processed Meat*. Lyon, France: International Agency for Research on Cancer; 2015:6-13.
- Hu T, Bazzano LA. The low-carbohydrate diet and cardiovascular risk factors: evidence from epidemiologic studies. *Nutr Metab Cardiovasc Dis*. 2014;24(4):337-343. doi:10.1016/j.numecd.2013.12.008
- Best D, Grainger P. Low-fat or low-carbohydrate diet for cardiovascular health. *Can J Cardiovasc Nurs*. 2007;17(3):19-26.
- Hession M, Rolland C, Kulkarni U, Wise A, Broom J. Systematic review of randomized controlled trials of low-carbohydrate vs. low-fat/low-calorie diets in the management of obesity and its comorbidities. *Obes Rev*. 2009;10(1):36-50. doi:10.1111/j.1467-789X.2008.00518.x
- Nordmann AJ, Nordmann A, Briel M, et al. Effects of low-carbohydrate vs low-fat diets on weight loss and cardiovascular risk factors: a meta-analysis of randomized controlled trials. *Arch Intern Med*. 2006;166(3):285-293.
- Tobias DK, Chen M, Manson JE, Ludwig DS, Willett W, Hu FB. Effect of low-fat diet interventions versus other diet interventions on long-term weight change in adults: a systematic review and meta-analysis. *Lancet Diabetes Endocrinol*. 2015;3(12):968-979. doi:10.1016/S2213-8587(15)00367-8
- Shai I, Schwarzfuchs D, Henkin Y, et al. Weight loss with a low-carbohydrate, Mediterranean, or low-fat diet [published correction appears in *N Engl J Med*. 2009;361(27):2681]. *N Engl J Med*. 2008;359(3):229-241. doi:10.1056/NEJMoa0708681

18. Bueno NB, de Melo ISV, de Oliveira SL, da Rocha Ataide T. Very-low-carbohydrate ketogenic diet v. low-fat diet for long-term weight loss: a meta-analysis of randomised controlled trials. *Br J Nutr*. 2013;110(7):1178-1187. doi:10.1017/S0007114513000548
19. Davis NJ, Tomuta N, Schechter C, et al. Comparative study of the effects of a 1-year dietary intervention of a low-carbohydrate diet versus a low-fat diet on weight and glycemic control in type 2 diabetes. *Diabetes Care*. 2009;32(7):1147-1152. doi:10.2337/dc08-2108
20. Gardner CD, Kiazand A, Alhassan S, et al. Comparison of the Atkins, Zone, Ornish, and LEARN diets for change in weight and related risk factors among overweight premenopausal women: the A to Z weight loss study: a randomized trial [published correction appears in *JAMA*. 2007;298(2):178]. *JAMA*. 2007;297(9):969-977. doi:10.1001/jama.297.9.969
21. Naude CE, Schoonees A, Senekal M, Young T, Garner P, Volmink J. Low carbohydrate versus isoenergetic balanced diets for reducing weight and cardiovascular risk: a systematic review and meta-analysis. *PLoS One*. 2014;9(7):e100652. doi:10.1371/journal.pone.0100652
22. Saslow LR, Kim S, Daubenmier JJ, et al. A randomized pilot trial of a moderate carbohydrate diet compared to a very low carbohydrate diet in overweight or obese individuals with type 2 diabetes mellitus or prediabetes. *PLoS One*. 2014;9(4):e91027. doi:10.1371/journal.pone.0091027
23. Iqbal N, Vetter ML, Moore RH, et al. Effects of a low-intensity intervention that prescribed a low-carbohydrate vs. a low-fat diet in obese, diabetic participants. *Obesity (Silver Spring)*. 2010;18(9):1733-1738. doi:10.1038/oby.2009.460
24. Jonasson L, Guldbrand H, Lundberg AK, Nystrom FH. Advice to follow a low-carbohydrate diet has a favourable impact on low-grade inflammation in type 2 diabetes compared with advice to follow a low-fat diet. *Ann Med*. 2014;46(3):182-187. doi:10.3109/07853890.2014.894286
25. Yancy WS Jr, Westman EC, McDuffie JR, et al. A randomized trial of a low-carbohydrate diet vs orlistat plus a low-fat diet for weight loss. *Arch Intern Med*. 2010;170(2):136-145. doi:10.1001/archinternmed.2009.492
26. Tonstad S, Malik N, Haddad E. A high-fibre bean-rich diet versus a low-carbohydrate diet for obesity. *J Hum Nutr Diet*. 2014;27(suppl 2):109-116. doi:10.1111/jhn.12118
27. Guldbrand H, Dizdar B, Bunjaku B, et al. In type 2 diabetes, randomisation to advice to follow a low-carbohydrate diet transiently improves glycaemic control compared with advice to follow a low-fat diet producing a similar weight loss. *Diabetologia*. 2012;55(8):2118-2127. doi:10.1007/s00125-012-2567-4
28. Lim SS, Noakes M, Keogh JB, Clifton PM. Long-term effects of a low carbohydrate, low fat or high unsaturated fat diet compared to a no-intervention control. *Nutr Metab Cardiovasc Dis*. 2010;20(8):599-607. doi:10.1016/j.numecd.2009.05.003
29. Le LT, Sabate J. Beyond meatless, the health effects of vegan diets: findings from the Adventist cohorts. *Nutrients*. 2014;6(6):2131-2147. doi:10.3390/nu6062131
30. Key TJ, Fraser GE, Thorogood M, et al. Mortality in vegetarians and non-vegetarians: a collaborative analysis of 8300 deaths among 76,000 men and women in five prospective studies. *Public Health Nutr*. 1998;1(1):33-41.
31. Huang T, Yang B, Zheng J, Li G, Wahlqvist ML, Li D. Cardiovascular disease mortality and cancer incidence in vegetarians: a meta-analysis and systematic review. *Ann Nutr Metab*. 2012;60(4):233-240. doi:10.1159/000337301

© 2016 American Osteopathic Association

Keywords: carbohydrate, diabetes, diet, low-carb diet, weight loss

Download JAOA PowerPoint Slides

Readers can download Microsoft PowerPoint slides of figures published in *The Journal of the American Osteopathic Association*. When viewing the figure in the full text article on JAOA.org, simply click on the link "Slide (.ppt)."