Are Low-Carbohydrate Diets Safe and Effective?
Heather Fields, MD; Barbara Ruddy, MD; Mark R. Wallace, MD; Amit Shah, MD; and Denise Millstine, MD

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 Bantering’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.8 Notwithstanding, a high intake of red meat, especially processed meat, is associated with increased cardiovascular and all-cause mortality4,9-10 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-
tosis 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 crossover 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
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,\textsuperscript{18} which found no difference in systolic blood pressure between VLCKD and 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.\textsuperscript{19}

The effects of LCDs may be different in women. An RCT\textsuperscript{19} 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,\textsuperscript{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

#### Table 1. Popular Low-Carbohydrate Diets

<table>
<thead>
<tr>
<th>Diet Name</th>
<th>Carbohydrate Content</th>
<th>Key Features*</th>
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<tbody>
<tr>
<td>Ketogenic</td>
<td>&lt;50 g/d</td>
<td>Patients may check urine for ketones or ask for blood work to confirm ketotic states (elevated β-hydroxybutyrate); diet emphasizes &quot;keto-adaptation,&quot; with the body switching from using glucose to fat as main energy source</td>
</tr>
<tr>
<td>Atkins</td>
<td>Induction phase: 20 g/d; later phases: 80-100 g/d</td>
<td>4 phases with more restriction in the beginning; the &quot;New Atkins&quot; diet offers a 40-g/d induction phase option for those &lt;40 lb overweight</td>
</tr>
<tr>
<td>Eco-Atkins</td>
<td>130 g/d</td>
<td>Vegan diet with 31% protein, 43% fat, 26% carbohydrate</td>
</tr>
<tr>
<td>South Beach</td>
<td>Phase 1: exclude most carbohydrates; phases 2 and 3: ≤140 g/d</td>
<td>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</td>
</tr>
<tr>
<td>Zone</td>
<td>40%</td>
<td>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</td>
</tr>
<tr>
<td>Paleo</td>
<td>Varies based on food choices</td>
<td>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</td>
</tr>
<tr>
<td>Dr Bernstein's Diabetes Solution</td>
<td>30 g/d</td>
<td>One of the original diets emphasizing glycemic index by restricting foods that cause rapid rise in blood sugar</td>
</tr>
<tr>
<td>Sugar Busters</td>
<td>2-3 servings per d</td>
<td>Emphasizes glycemic index by minimizing refined sugar, white flour, and starches</td>
</tr>
<tr>
<td>LCHF</td>
<td>&lt;20-100 g/d</td>
<td>Emphasizes fats for satiety; popular in Sweden</td>
</tr>
<tr>
<td>Protein Power</td>
<td>28-40 g/d</td>
<td>Emphasizes adequate protein and limited carbohydrates divided into 4-6 meals/snacks per d</td>
</tr>
<tr>
<td>Sonoma</td>
<td>Varies based on food choices</td>
<td>3 phases emphasize portion control; combines Mediterranean and low-carbohydrate diets; minimizes saturated fat, starches, and sugar</td>
</tr>
</tbody>
</table>

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

Abbreviation: LCHF, low carbohydrate, high fat.
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 Bazzano\(^1\)\(^2\) and Nordmann et al\(^1\)\(^5\) 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\(^1\)\(^8\),\(^2\)\(^1\)\(^8\) found no difference in fasting blood glucose or hemoglobin A\(_1c\) levels between LCDs and other diets. In 2 separate studies,\(^2\)\(^2\),\(^2\)\(^3\) a VLCKD and an LCD demonstrated short-term decreases of hemoglobin A\(_1c\) in people with type 2 diabetes. In the latter study,\(^2\)\(^3\) 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,\(^2\)\(^2\),\(^2\)\(^3\) but several showed no difference from the comparison diet.\(^2\)\(^2\),\(^2\)\(^4\)-\(^2\)\(^8\) One study with a VLCKD group\(^2\)\(^2\) 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\(^1\)\(^2\),\(^1\)\(^5\),\(^1\)\(^8\) 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\(^1\)\(^2\),\(^1\)\(^5\),\(^1\)\(^8\) 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.\(^8\),\(^2\)\(^9\)-\(^3\)\(^1\) One main concern is that certain meats have been implicated in worsened all-cause mortality\(^8\)-\(^1\)\(^0\) and increased cancer risk,\(^1\)\(^1\) 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

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

Abbreviations: HbA\textsubscript{1c}, hemoglobin A\textsubscript{1c}; LCD, low-carbohydrate diet; LDL, low-density lipoprotein; VLCD, very-low-carbohydrate diet.


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