Published in final edited form as:
Curr Obes Rep. 2021 September ; 10(3): 409–422. doi:10.1007/s13679-021-00451-z.

Benefits of Low Carbohydrate Diets: a Settled Question or Still Controversial?

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Abstract

Purpose of Review—The purpose of this review was to provide an update on the available data on the benefits of low-carbohydrate (low-carb) diets for weight management and type 2 diabetes (T2DM) and determine if low-carb diets were a settled question or still controversial.

Recent Findings—Most of the recent published literature in this area consists of reviews of past trials, with a relatively smaller number of recent trials. Low-carb is most commonly compared to low-fat, with problematically inconsistent definitions of both. There are numerous challenges in trying to draw clear conclusions about efficacy and effectiveness. Short-term vs. long-term effects can differ, which is likely impacted by adherence. Adherence is very different between metabolic chamber or feeding studies vs. free-living. Body weight alone is a crude measure that fails to capture potentially important differences in lean-mass, fat-mass, and body water. Benefits for glycemic control need to be balanced with impacts on non-glycemic outcomes such as LDL-cholesterol, the microbiome, and inflammation. It is important to differentiate between low-carb and very-low carbohydrate diets (VLCD). To date no large-scale long-term clinical trials have been conducted testing whether low-carb diets can prevent T2DM.

Summary—Many issues regarding benefits and risks of low-carb diets remain controversial or unresolved, particularly for VLCD. Some of the recent, better studies highlighted in this review suggest strategies for resolving these controversies.

Keywords

Low carbohydrate; Very low carbohydrate; Ketogenic; Narrative review; Weight management; Type 2 diabetes

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Conflict of Interest The authors report no conflicts of interest.

Compliance with Ethical Standards
Ethics Approval Not applicable.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

Introduction

Low-carbohydrate diets have been promoted for over half a century, with a primary focus on weight loss (e.g., The Atkins Diet, 1972). However, a significant rise in popularity for low-carbohydrate diets resulted after decades of focus from public health professionals on low-fat diets and a parallel rise in national obesity rates [1]. Low-carbohydrate diets were fueled and promoted by a series of popular weight loss diet books (e.g., Zone, South Beach, Paleo) and under the claim that they are healthier than current recommended dietary patterns [2, 3]. One rationale for a low-carbohydrate or very-low-carbohydrate diets stems from the idea that excessive carbohydrate intake may promote weight gain through the stimulation of insulin release and hunger [4•]. Glycemic load (the product of glycemic index and carbohydrate content) is associated with adverse long-term health effects, and consumption of easily digestible carbohydrates (e.g., sugar) promotes obesity [4•, 5, 6]. As a result, there has been increased enthusiasm for the use of low-carbohydrate and very-low-carbohydrate diets for weight management and glycemic control, particularly in regard to lowering added sugars and refined grains [5, 7, 8]. There have also been reports of positive psychosocial effects of carbohydrate reduction, although, in controlled trials, these effects have not been substantiated [9]. In recent years, such diets have now been used in broader therapeutic applications [10]. Emerging research has examined the association between use of low-carbohydrate and very-low-carbohydrate diets in cancer [11–13], polycystic ovary syndrome[14], cardiovascular disease risk parameters [15••, 16], nonalcoholic fatty liver disease [17–19], and neurological diseases [20, 21] with some evidence of benefit, but further research is needed.

Despite the current popularity of low-carbohydrate or very-low-carbohydrate diets among the general public, and its diverse applications for health, some researchers have suggested that the enthusiasm outpaces the evidence [7, 22]. The purpose of this review is to examine recent literature on the potential benefits of low-carbohydrate diets for obesity and weight management and type 2 diabetes mellitus (T2DM), with a focus on the last 5 years of publications. Many of the other potential therapeutic uses of low-carbohydrate or very-low-carbohydrate diets have a limited evidence base and were considered beyond the scope of this review.

Defining Low- and Very-Low Carbohydrate Diets

There is substantial variability in definitions of “low-carbohydrate” diets in the literature in terms of percentage from energy intake or total daily grams of carbohydrate, anywhere from 5 up to 40% [23, 24]. There are dozens of dietary patterns and diets ranging in ratio of carbohydrates to other macronutrients or in the foods to include and/or exclude that have been tauted as being the ideal low-carbohydrate diet. The Zone diet, which rose to popularity in the 1990s, is an example of a moderately low carbohydrate diet, encouraging about 40% of daily energy from carbohydrates [25]. The Paleo diet, also referred to as the “Caveman” or “Stone-Age” diet, encourages followers to eat the way Paleolithic era humans ate. Overall, the diet is high in protein, moderate in fat, and moderate in carbohydrates (~40% of energy intake), specifically restricting high-glycemic carbohydrates [26, 27]. The South Beach Diet emerged in the early 2000s as a phased low-carbohydrate diet. The diet starts with cutting out nearly all carbohydrates for 2 weeks and then progresses towards a maintenance phase which is moderately low in carbohydrates, allowing for ~30% of daily energy from carbohydrates. The diet also heavily focuses on foods with lower glycemic index and glycemic load [28]. The Mediterranean diet, that has been around for centuries, promotes the consumption of high fat sources such as olive oil, nuts, seeds, avocados, and fatty fish. As a consequence, the Mediterranean diet is a moderately low-carbohydrate diet pattern, in the range of 35–40% energy from carbohydrates [29].

Very-low-carbohydrate diets, also referred to as ketogenic diets, are the most restrictive, generally containing < 50g and often as few as 20g of total carbohydrates per day (<10% of calories, on a 2000 kcal/day diet) [30]. The goal of very-low-carbohydrate diets in particular is to induce nutritional ketosis (blood ketone bodies > 0.5mM) where fatty acid oxidation is diverted to ketone production (ketogenesis). In the absence or scarcity of circulating blood glucose from foods, ketone bodies are used to generate energy [31]. To achieve ketosis, very-low-carbohydrate diets, and to some extent low-carbohydrate diets, require the elimination or severe restriction of legumes, fruits, starchy vegetables, and grains (including whole grains), despite the established general health benefits of these foods and food groups [30, 32, 33]. Eliminated carbohydrate-rich foods are replaced with foods that are high in fat and protein. These dietary patterns and practices tend to be high in saturated fat consumption which can increase plasma LDL-C and risk for premature cardiovascular disease [34, 35]. Ketogenic diets have also been found to consistently lower triglycerides and raise HDL-C concentrations, both of which are considered beneficial for cardiovascular health [15, 36, 37]. Individuals in ketosis may feel more full or satiated, as evidence suggests that ketosis may provide a mechanism for appetite suppression and resultingly may decrease food consumption [38, 39]. However, they may also experience symptoms/side effects (nausea, headache, fatigability) from initiating a ketogenic diet, commonly referred to as the “keto flu” which may lead people to discontinue the diet early on [40]. For some individuals with certain chronic diseases (e.g., type 1 diabetes, chronic kidney disease, liver failure) or comorbidities, very-low-carbohydrate diets are discouraged or require evaluation and close medical monitoring from a disease specialist to assess contraindication [41•].

Trends in Low-Carbohydrate Diet Research

A notable increase in published research into low-carbohydrate diets began in 2003 following a study by Foster et al which examined a low-carbohydrate, high-protein, high-fat Atkins diet compared to a low-calorie, high-carbohydrate, low-fat, health professional’s diet for weight loss [42]. During the decade that followed, researchers continued to compare different levels of carbohydrate restriction to low-fat/high-carbohydrate diets [43–50]. Typically this involved defining a target amount of daily carbohydrates (e.g., <40% of total daily calories) throughout the intervention or utilizing the original Atkins protocol by initially starting with < 20g of carbohydrate per day for a few months and then adding back some grams of daily carbohydrates to diminish cravings but maintain weight loss. Early studies reported that low-carbohydrate diets resulted in greater weight loss, glycemic control, and improvements in cardiometabolic risk factors (primarily decreases in triglycerides and increases in HDL-C cholesterol). More recent studies have indicated that weight loss is often similar to comparison diets in the long term, but low-carbohydrate diets may have advantages in reducing diabetic medication and reducing triglycerides, while increasing HDL cholesterol [51–53, 54••, 55, 56••].

Given the strong interest and growing popularity of low-carbohydrate diets, one would expect there to be numerous high-quality trials that properly control for dietary adherence and comprehensively explain the potential changes in energy metabolism that result from restricting carbohydrates on weight loss and glycemic control (e.g., increased energy expenditure [EE], decreased hunger, reduced insulin concentrations, increased fat oxidation and gluconeogenesis, and more). Yet, recent publications on low-carbohydrate or very-low-carbohydrate diets results are more likely to be review articles than randomized controlled trials (RCTs) (Table 1). Most of the reviews report the same general conclusions: the majority of RCTs on low-carbohydrate vs. low-fat diets indicate effective weight loss, glycemic control, and some improvements on metabolic risk factors in the short term (i.e., 6 months or less) [15••, 57–60]. However, those benefits are observed to diminish over time, and beyond a year or two of intervention follow-up, the long-term low-carbohydrate diets are not superior to comparison diets, particularly low-fat diets for the aforementioned benefits.

Low-Carbohydrate Diets for Weight Management

After reviewing the evidence base for a comprehensive set of different weight loss diets, the 2014 guidelines from the American Heart Association (AHA), American College of Cardiology (ACC), and the Obesity Society (TOS) on the management of overweight and obesity in adults state that the level of *certainty of evidence* for low-carbohydrate approaches to weight loss is *low* [61]. The guidelines recommend a comprehensive approach for reducing overall daily energy intake, which includes (1) reducing energy intake by ~500 kcals/day, (2) increasing physical activity, and (3) sustaining behavioral changes, such as routine self-monitoring of food intake or frequent monitoring of body weight.

Due to the fact that most clinical trials assessing low-carbohydrate diets versus low-fat diets, or comparison diets, are short in duration (< 1 year) and/or involve significant design limitations, it is not surprising that many of the meta-analyses and systematic reviews report little to no differences in long-term weight loss between diet types [7]. For example, a summary of 62 randomized trials comparing low-carbohydrate diets to low-fat diets indicated greater weight loss for the low-carbohydrate diets for 31 studies [59]. However, among studies that were 12 months or longer, only 4 out of 18 studies reported greater weight loss for the low-carbohydrate diets [59]. An umbrella review (i.e., a meta-analysis of meta-analyses) indicated that lower quality studies did report overall superiority in weight loss for low-carbohydrate diets, but among the subset of higher quality studies, there were little or no differences between diets [60]. However, there are overall metabolic and physiological benefits that were reported for utilizing a low-carbohydrate approach to weight loss and management, including increased EE, reduced appetite, and better insulin control.

One rationale for restricting carbohydrates is based on the carbohydrate-insulin model (CIM) [4•]. The CIM asserts that the increased consumption of high-glycemic foods produces hormonal changes that promote calorie deposition in adipose tissue, increases in hunger, lowers EE, and results in weight gain [4•]. Therefore, restricting carbohydrate intake would improve weight loss. Results from two well-controlled metabolic ward studies also support this conclusion, in terms of the substitution of fat in place of carbohydrates resulting in higher EE [55, 56••]. One study involved comparing 17 men with overweight or obesity consuming either an isocaloric high-carbohydrate diet (50% CHO, 15% protein, 35% fat) or a very-low-carbohydrate diet (5% CHO, 15% protein, 80% fat) for 4 weeks to assess changes in EE and body composition [55]. The results indicated EE was 151 kcal/d higher for the very-low-carbohydrate diet as measured by the doubly labeled water (DLW) method. The other study by the same investigators randomized 20 adults to a very low-carbohydrate diet (10.0% CHO, 14.2% protein, 75.8% fat) or a plant-based diet (75.2% CHO, 14.5% protein, 10.3% fat) for 2 weeks followed by the alternate diet for another 2 weeks to determine if ad libitum energy intake would be different between the two diets [56••]. The EE was 153 kcal/d higher during the low-carbohydrate phase. However, the plant-based diet led to less daily energy intake (689 ± 73 kcal/d) than the low-carbohydrate diet. In both studies, the low-carbohydrate diets initially resulted in faster total weight loss than the low-fat diets, but results assessed from DXA scans indicated that most of the weight loss was actually fat-free mass. This is most likely due to the loss of water weight, since during the first few weeks of extreme carbohydrate restriction glycogen stores get depleted and water loss follows [56••]. In contrast, the weight loss from the low-fat diets in these studies did not result in significant lean body mass loss. Other analyses have reported greater EE from low-carbohydrate diets [62, 63]. This could contribute to weight loss, if energy intake remained constant, although in the study by Hall et al., noted above, the decrease in energy intake for the low-fat diet substantially exceeded the increase in EE with the low-carb diet [56••]. Additionally, there is dispute about the accuracy of measuring EE with the DLW method for individuals on low-carbohydrate diets [64, 65].

Another reason why low-carbohydrate diets may help with weight loss is that they may reduce appetite through nutritional ketosis or influence various hormones that affect hunger [38, 51, 66]. The decreased appetite may also be due to decreases in ghrelin, leptin, and cholecystokinin [38, 51, 66]. However, reports on these effects are mixed. One trial that assessed ghrelin levels and self-reported appetite reported no differences in either measures from a very low-carbohydrate diet (< 40g/d) compared to a low-fat diet (<30% from energy intake) [67]. Another trial indicated that participants that consumed a calorie-restricted, high-carbohydrate diet resulted in greater daily overall fullness than participants on the calorie-restricted, very-low-carbohydrate diet [68]. Finally, one of the metabolic ward studies by Hall et al. challenges the notion that restricting carbohydrate intake reduces hunger, since the participants actually ate less energy during the low-fat (plant-based) diet phase of the study [56].

Some trials have suggested that individuals with higher insulin secretion respond well to restricting carbohydrate intake for weight loss [50, 69]. Yet the 2018 DIETFITS Trial, which included more than 600 participants, concluded that baseline insulin-30 (insulin level 30 minutes into an oral glucose tolerance test, a proxy used for insulin resistance) was not a significant effect modifier of weight loss for those randomized to a healthy low-carbohydrate vs. a healthy a low-fat diet [54]. Both groups lost a similar amount of weight at 12 months despite substantial differences in the balance of fat and carbohydrate intake. The differences noted above may be related to different study settings—more controlled efficacy studies vs. free-living effectiveness studies.

Another important variable involved in assessing low-carbohydrate diets' effectiveness on weight loss is the degree of carbohydrate restriction. A study by Ebbeling et al. assessed EE during the 20-week weight maintenance phase of the study after participants' initially lost 12% of their bodyweight over 9–10 weeks on an energy-restricted diet (45% CHO, 25% protein, 30% fat) and then were randomized to varying degrees of isocaloric carbohydrate intake (high = 60%, moderate = 40%, low = 20) [51]. Total EE was greatest in the lowest-carbohydrate group, and there was a linear trend of 52 kcal/d per 10% reduction in dietary carbohydrates. Improvements in triglycerides, HDL-C cholesterol, and lipoprotein insulin resistance were reported to parallel the degree of restriction of carbohydrates [52]. However, in contrast to these findings, a recent review on different degrees of carbohydrate restriction [(1) moderate-carbohydrate diets (40–45% of energy intake, n = 13 trials), (2) low-carbohydrate diets (30–40% of energy intake, n = 16 trials), and (3) very-low-carbohydrate diets (3–30% of energy intake; n = 8 trials)] concluded that the effects of weight loss were not related to the degree of carbohydrate restriction [70].

An alternative to carbohydrate restriction is the low glycemic index (GI) or low glycemic load (GL) diet that focuses on the quantity and type of carbohydrate-rich foods consumed and their overall effects on postprandial glycemia [71]. Systematic reviews comparing low-GI/GL dietary patterns lead to improvements in weight loss, glycemic control, blood lipids, and blood pressure [72–75]. However, the findings reported by some meta-analyses are limited by various issues, such as studies being pooled with different definitions for the range of exposures (e.g., tertiles, quartiles, and quintiles), including studies that used inadequately validated dietary instruments, and a lack of clear inclusion and exclusion criteria for selected studies [76••]. Nevertheless, given that >40% of energy in the US diet comes from low-quality carbohydrates (e.g., added sugars and refined grains [77] that are, in general, high GI foods contributing to a higher GL, a low GI, or low GL approach that significantly restricts those foods has substantial overlap with a low-carb diet for improving weight or glycemic control.

In summary, the results from clinical trials and meta-analyses on low-carbohydrate diets versus comparison diets indicate that in long-term weight loss is similar for either diet. There remain questions and issues to resolve regarding the efficacy and effectiveness of low-carbohydrate diets for weight loss.

Low-Carbohydrate Diets for Diabetes

Type 2 diabetes is characterized by carbohydrate intolerance due to insulin resistance. Prior to medication, carbohydrate restriction can be used as a first approach for diabetes management [78, 79]. Numerous studies have attempted to identify the optimal mix of macronutrients for people with T2DM to improve glycemic control [80]. Current American Diabetes Association recommendations suggest an individualized approach to macronutrient proportions based on assessment of current dietary patterns and practices, preferences, and metabolic and health goals [30, 78]. Low-carbohydrate eating patterns, especially very low-carbohydrate ketogenic dietary patterns, have been suggested as a way to reduce HbA1c and the need for antihyperglycemic medications in people with T2DM and insulin resistance [30, 81•]. Suggested mechanisms for the therapeutic use of low-carbohydrate diets for persons with T2DM or insulin resistance include reduction of blood insulin levels and reversal of hepatic insulin resistance [82, 83].

There is conflicting evidence to suggest that low-carbohydrate diets compared to low-fat diets elicit superior benefits. Studies examining low-carbohydrate diets compared to low-fat diets on glycemic control outcomes range from as short as 4 weeks to 2 years [84]. To date most studies examine durations <1 year, and few studies to date have examined study durations across multiple years [85–87]. A 2018 systematic review included 33 RCTs comparing the effects of low-carbohydrate (≤ 40% of energy) to a low-fat (≤ 30% of energy) diet over at least 4 weeks in people with T2DM using the GRADE assessment [84]. The review reported that a low-carbohydrate diet compared to a low-fat diet may result in a clinically important reduction in HbA1c (low certainty of evidence) and that a low-carbohydrate diet results in a small effect that may not lead to an important reduction in fasting glucose in studies lasting < 16 weeks (moderate level of certainty in the evidence). In studies lasting > 26 weeks, the conclusion was that a low-carbohydrate diet may result in a small effect that may not be an important reduction in HbA1c compared with a low-fat diet (low certainty of evidence). For fasting glucose outcomes in studies lasting > 26 weeks, both diets have a potentially important impact on glucose concentrations, but neither diet resulted in more substantial changes compared to the other (moderate certainty of evidence). Similarly, a recent review by Ross et al. reported that in the 8 studies reviewed, diabetes markers (fasting blood glucose, Hb1Ac, and insulin) were generally improved regardless if individuals were on a very-low-carbohydrate or low-fat diet [88]. Differences between arms were limited to two studies, one favoring the very-low-carbohydrate diet and the other favoring the low-fat diet.

Recent trials have also examined differing amounts of carbohydrate and the associations with improvements in glycemic outcomes. A 2017 RCT by Saslow et al. examined very-low-carbohydrate diets versus moderate-carbohydrate diets in 34 adults with T2DM or prediabetes [53]. Individuals assigned to the very-low-carbohydrate diet had greater reductions in HbA1c and reduced medications more than those on the moderate-carbohydrate diet [53]. Within recent meta-analyses, the findings have been mixed. A 2016 review including 12 RCTs reported that a low-carbohydrate diet appeared to have no different effect compared to a high-carbohydrate diet in terms of glycemic control [89]. In contrast, a 2017 meta-analysis of 9 RCTs comparing low-carbohydrate diets to intermediate or high-carbohydrate diets reported a beneficial effect of carbohydrate restriction on glucose control [90].

Two recent trials have included durations of at least 2 years. The non-randomized Virta trial comparing an individualized low-carbohydrate diet to a convenience sample of usual care adults with T2DM reported that participants in the low-carbohydrate diet group demonstrated improved HbA1c, fasting glucose and insulin, and HOMA-IR after 2 years [81]. More than half (53.5%) of the patients in the treatment group experienced a reversal of diabetes with substantial reductions in the use of diabetic medications [81]. It is worth mentioning that the Virta trial is being conducted by for-profit company, Virta Health. Similarly, a 2-year parallel designed study by Tay et al included 115 adults with T2DM randomized participants to a low-carbohydrate (<50g/day) (14% CHO, 28% protein, and 58% total fat) or to a high-carbohydrate diet (53% CHO, 17% protein, and 30% fat) reported that both diets achieved comparable weight loss and glycosylated hemoglobin (HbA1c) reductions [85]. Compared to participants on a high carbohydrate diet, the low-carbohydrate diet participants sustained greater reductions in diabetes medication requirements and in improvements in diurnal blood glucose stability.

There has also been interest in examining the type of dietary carbohydrate within the diets, as some carbohydrate-rich foods have a greater effect than others on blood glucose. Low-GI foods lower peak postprandial blood glucose excursions and have been suggested to have a positive effect on glucose control [91]. The seminal OmniCarb examined four differing levels of glycemic diets within a 5-week controlled feeding study [92]. Findings from the study suggested that low glycemic compared to high-glycemic index foods did not improve insulin sensitivity. A recent systemic review and meta-analysis reported that low-GI diets in people with impaired glucose tolerance, type 1 diabetes, or type 2 diabetes were effective at reducing HbA1c, BMI, total and LDL cholesterol, and fasting glucose [74]. The greatest reductions in blood glucose were observed in studies of the longest duration. Strikingly, low-GI diets were only found to be effective for weight loss in people with normal glucose tolerance and were not found to be effective in people with glucose tolerance, type 1 diabetes, or type 2 diabetes [74, 93].

It should be noted that very-low-carbohydrate diets compared to more moderate levels have been suggested to be unrealistic for long-term adherence in people with T2DM [89, 94]. Further research is needed as adherence to study diets were generally poor and often the carbohydrate intake between the two diets deviated substantially from prescribed protocol amounts, often converging towards a moderate intake [89, 94]. Unlike other dietary patterns such as the Mediterranean diet for which long-term efficacy and safety have been observed [95, 96], low-carbohydrate and very-low-carbohydrate diets lack data on long-term safety, adherence, and efficacy [97]. Long-term adherence is consistently reported as a limitation of low-carbohydrate and very-low-carbohydrate diets, particularly in the latter [84, 88, 89, 94]. Individuals with T2DM must also balance the potential mixed impacts of very low carbohydrate diets on cardiovascular risk factors—adverse increases in LDL-C levels, improvement of glycemic control, positive changes in triglyceride and HDL-C levels, and potential weight change benefits as described above [98, 99]. Further research is also needed to examine the influence of low-carbohydrate and very-low-carbohydrate diets on non-glycemic outcomes, such as the microbiota and inflammation. Research has found that the ketogenic diet can modulate and reshape gut microbiota; however, some initial human studies have reported lowered microbiome diversity and an increased amount of pro-inflammatory bacterial species when consuming a very-low-carbohydrate diet [100•, 101].

Programs such as the Diabetes Prevention Program (DPP) or similarly modeled intensive lifestyle intervention programs provide the strongest evidence for T2DM prevention [102–104]. The most recent guidelines for nutrition therapy in adults with diabetes or prediabetes by Evert et al. reviewed 9 different eating patterns (e.g., Mediterranean, vegetarian/vegan, low-fat, low-carbohydrate, very-low-carbohydrate) and their potential benefits for the prevention and management of diabetes [30]. There is evidence for the benefit of low-fat diets and the prevention of T2DM [102, 105]. For low-carbohydrate and very-low-carbohydrate diets evidence was not available regarding reduced incidence of T2DM. However, this is not evidence of *absence of effect*, but rather this is due to an *absence of evidence*. To resolve the issue of whether low-carbohydrate or very-low-carbohydrate is effective in the prevention of diabetes, a trial of the size and scope of DPP would be needed.

Challenging Methodological Issues in Studies

Limitations of many of the studies highlighted in this review involve study design issues that create challenges for interpretation and comparison between studies [106]. First, although the studies included in this review typically use the same descriptive names or terms (i.e., low-carbohydrate, very-low-carbohydrate, or ketogenic) for describing restricted-carbohydrate diets, they should not be assumed to be equivalent. As there is no consensus on cutoffs for low-carbohydrate and very-low-carbohydrate, definitions of these dietary patterns can vary from study to study [15]. Further, many studies do not report on the specific types of carbohydrate sources or their quality (e.g., whole intact grains vs. refined grains, dietary fiber, GI, or GL) [76••]. Another factor to consider when interpreting studies included in this review was how well the participants adhered to the original definition of their assigned diets. Unfortunately, many studies fail to include assessments of dietary adherence making it challenging to determine the actual carbohydrate intake of participants compared to the prescribed carbohydrate intake. Additionally, long-term adherence to highly restrictive carbohydrate diets is a challenge. The most well-controlled in-patient studies, where adherence to study diets is the highest, are typically of very short durations and are therefore limited in terms of real-world generalizability regarding long-term adherence outside of a study's controlled setting [55, 56]. People in free-living conditions may find it difficult to eliminate or strictly limit a number of foods that they have been accustomed to eating for years when preparing and cooking foods on their own. Lastly, many of the studies compared a low-carbohydrate diet to a diet with a different macronutrient composition; however, in some cases the comparison diet was of lower quality, or had no dietary intervention at all, resulting in a worse chance of success than the low-carbohydrate diet [107–109]. Future RCTs examining low- and very-low-carbohydrate diets should use designs including fair comparisons between other types of diets and should transparently report achieved levels of dietary adherence.

Conclusions

This narrative review assessed recent literature on the effectiveness of low-carbohydrate diets for obesity and T2DM. The review focused on a large number of recent reviews and meta-analyses focusing on trials published between 2000 and 2021 and a smaller number of recent trials. In general, results from RCTs that assessed low-carbohydrate diets report better weight loss than comparison or control diets in the short term (i.e., 6 months or less), but beyond 6 months, those benefits diminish [59, 60]. The more rapid total weight loss in the first few weeks observed from low-carbohydrate diets compared to low-fat diets likely involves loss of water weight and lean body mass, as evidenced from two well-controlled metabolic ward studies [55, 56]. For long-term weight loss or weight management, low-carbohydrate diets, as they have been defined and studied, are not superior to other dietary patterns. Other major reviews have made similar conclusions [15, 57, 58].

For diabetes management, there is increasing evidence that adults with prediabetes or diabetes benefit from reduced carbohydrate diets by improving glycemia and some cardiometabolic risk factors [30, 78]. Low-carbohydrate diets may have advantages for reducing appetite, triglycerides, and diabetic medications but with potential adverse effects raising LDL-C cholesterol levels [23, 38, 39] and possible detrimental effects on the microbiome and inflammation [100, 101]. There is also increasing evidence that low-carbohydrate diets are more effective at lowering HbA1c levels than other dietary patterns even after controlling for body weight [81, 90, 94]. However, the National Lipid Association Nutrition and Lifestyle Task Force state in their report that after 2 years, there are no differences in most metabolic markers between low-carbohydrate diets or other dietary patterns.[23]

What is settled in this area is that further trials of low-carbohydrate vs. low-fat, as have been conducted in general for the last two decades, are not needed. Similarly, further reviews and meta-analyses of these trials are also not needed; there are apparently more reviews of the existing trials, than there are trials. Low-carbohydrate diets, as has been studied in general, are neither superior nor inferior to low-fat or other dietary approaches that offer a reasonable alternative (e.g., Mediterranean, healthy low-fat diet). As studied, most dietary approaches in general have been negligibly to nominally effective. If any of the current dietary approaches was strikingly more effective than others, the entire field would have shifted to adopt and promote that approach.

Further research is needed in at least five domains. One of these involves direct head-to-head comparison between *lower* carbohydrate diets that differ clearly in degree of carbohydrate restriction—moderate-low-carbohydrate vs. very-low-carbohydrate. While there is widespread agreement in the public health community that low quality carbohydrates (e.g., added sugars, refined grains) should be substantially reduced, what added benefit or risks come from further restricting carbohydrates to the very low carbohydrate level that requires avoidance of legumes, fruits, whole intact grains, and starchy vegetables? This leads to a second area of opportunity in future studies, regarding a more comprehensive assessment of benefits and risks. In addition to the outcomes of weight, glucose control, and lipid profiles, important additional outcomes of interest include the microbiome and inflammation. Third, future studies should also increase the rigor involved in addressing the challenges of adherence and assessment of adherence in these studies. It is difficult to interpret studies of "low-carbohydrate" diets when definitions are inconsistent, adherence is poor, and documentation of adherence is inadequate. Fourth, sustainability of these diets cannot be addressed in studies of less than 1 year in duration; more longer-term studies are needed, provided they are designed to address the first three issues noted above. Lastly, there is an absence of evidence to determine whether low- or very-low carbohydrate diets could prevent the onset of incident diabetes. To resolve this, major trials on the scale of the DPP will be required.

With these suggestions for future research, some of the more recent trials identified in this review provide good examples of what is needed. The efficacy trials conducted by Hall, Ebbeling, and Ludwig et al. [51, 56] are examples of rigorous trials focused on very specific research questions. The results of the Virta trial are to be welcomed for their attention to long-term follow-up, but in future work, an appropriate comparison group is needed and preferably funding from a source free of potential conflict of interest [81]. The DIETFITS trial was important for its relatively large sample size, 1-year duration, attention to adherence and assessment of adherence, assessment of a comprehensive set of potential benefits and risks, and perhaps most importantly, its focus on potential effect modifiers (insulin secretion and genotype pattern) [54, 110–113]. And finally, a pilot study recently completed by our group, comparing a Ketogenic to a Mediterranean Diet, combines many of the suggestions outlined above (design and adherence paper published [114•], main paper in process). More research in line with these recent studies and the recommendations of this review are warranted.

Funding

This work was supported by a training grant from the NIH National Heart, Lung, and Blood Institute [T32 HL007034] and by the Stanford Diabetes Research Center [NIH P30DK116074].

Availability of Data and Material

Not applicable.

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Table 1

Recent review articles of low-carbohydrate diets for weight management or diabetes

Article	Nunrber of articles reviewed	Comparison diets	Focus of review	Key findings
Meta-analyses				
Chawla et al. (2020) [57]	38 randomized controlled trials	Low-fat diets	Compare the effects of low-carbohydrate diets and low-fat diets on weight loss and CVD risk factors	Improvements in weight loss, HDL cholesterol, and triglycerides favored the low-carbohydrate diets, while improvements in LDL cholesterol favored the low-fat diets
Dong et al. (2020) [115]	12 randomized controlled trials	Moderate or high-carbohydrate diets	To assess the relationship between low-carbohydrate diets and CVD risk factors	Low-carbohydrate diets were significantly related to reductions in body weight, CVD risk factors, and glucose (particularly within the first 6 months)
Fechner et al. (2020) [70]	37 randomized controlled trials	(1) Moderate-low-carbohydrate diets: 45–40% carbohydrate from energy intake (2) Low-carbohydrate diets: 40–30% carbohydrate from energy intake (3) Very-low-carbohydrate diets: 30–3% carbohydrate from energy intake	A review of 37 low-carbohydrate trials that aimed to compare the effects of different degrees of carbohydrate (CHO) restriction on cardiometabolic risk markers in humans	Other than LDL cholesterol and triglycerides, the degree of carbohydrate restriction was not related to weight loss or other variables
Goldenberg al. (2021)[11–6••]	23 randomized controlled trials	Primarily low-fat diets (18/23 studies)	To determine the efficacy and safety of low-carbohydrate diets and very low-carbohydrate diets for people with type-2 diabetes	Patients adhering to a low-carbohydrate diet for 6 months may experience remission of diabetes based on the significant reductions in HbA1c levels
Huntriss et al. (2018)[94]	18 randomized controlled trials (6 included in meta-analy sis)	Primarily low-fat diets (14/18 studies)	Assess the effects of low-carbohydrate diets on weight loss and CVD risk factors among type-2 diabetics	There were no significant differences for weight loss, total cholesterol, LDL-cholesterol, or diastolic blood pressure between the low-carbohydrate diets or control diets. But there were significant improvements in HbA1c, HDL cholesterol, triglycerides, and systolic blood pressure in favor of the low-carbohydrate diets
Mansoor et al. (2016)[98]	11 randomized controlled trials	Low-fat diets	Assess the effects of low-carbohydrate diets compared to low-fat diets on weight loss and CVD risk factors	The low-carbohydrate diets elicited greater reductions in body weight and triglycerides, but greater increases in HDL and LDL cholesterol levels
Meng et al. (2017) [90]	9 randomized controlled trials	High-carbohydrate diets	Compare low-carbohydrate diets (≤ 26% of total energy intake/< 130g of carbohydrate/day) to normal or high carbohydrate diets on weight loss and CVD risk markers among type-2 diabetics	There were no significant differences in weight loss between low-carbohydrate diets and other diets. For CVD risk factors, the low-carbohydrate diets significantly reduced triglycerides and increased HDL cholesterol levels
Sainsbury et al. (2018)[97]	25 randomized controlled trials	High-carbohydrate diets	Systematic review and meta-analysis were performed to assess the effects of carbohydrate-restricted diets (≤ 45% of total energy intake) compared to high carbohydrate diets (> 45% of total energy intake) on glycemic control in adults with diabetes mellitus	The low-carbohydrate diets produced greater reductions in HbA1c for 3–6 months. But there were no differences at 12 or 24 months

Article	Nunrber of articles reviewed	Comparison diets	Focus of review	Key findings
Silverii et al. (2020)[117]	37 randomized clinical trials	(1) Balanced-carbohydrate diets: 45–60% carbohydrate from energy intake (2) Moderate-carbohydrate diets: 26–15% carbohydrate from energy intake (3) Very low-carbohydrate diets: < 26% carbohydrate from energy intake	To assess whether low-carbohydrate diets are associated with long-term improvement in glycemic control and weight loss among people with type-2 diabetes	Low-carbohydrate diets were associated with modest reductions in body weight and HbA1c levels within the first 6 months compared to other diets. But at 24 months balanced-diets resulted in superior weight control than the low-carbohydrate diets
Snorgaard et al. (2017)[118]	10 randomized controlled trials	High-carbohydrate diets	To examine the effects of low to moderate-carbohydrate diets in comparison to high-carbohydrate diets on glycemic control, weight loss, and CVD risk factors among participants with type 2 diabetes	Low to moderate-carbohydrate diets had a greater effect on glycemic control in the short term ($\leq$ 1 year). The greater the carbohydrate restriction was the greater glucose was reduced. There was no superiority of low-carbohydrate diets on weight loss or lipids
Non-systematic reviews				
Batch et al. (2020)[99]	N/A	N/A	Review of ketogenic diets on the benefits and risks associated with metabolic, endocrinological, and CVD risk factors	Within the first 6–12 months of initiating a ketogenic diet there are improvements in blood pressure, triglycerides, and glycosylated hemoglobin, as well as increases in HDL and weight loss. However, beyond 12 months the aforementioned effects are generally not observed
Churuangsuk et al. (2020)[119]	N/A	N/A	To review the current evidence that supports or challenges the use of low-carbohydrate diets for type-2 diabetes management	Clinical trials demonstrate the efficacy of low-carbohydrate diets for weight loss and glycemic improvement among people with type-2 diabetes or obesity in the short term
Kelly et al. (2020)[120]	N/A	N/A	Assess the role of low-carbohydrate diets for treating obesity and type-2 diabetes	The current guidelines support the use of low-carbohydrate diets as an alternative to low-fat diets for managing obesity and type-2 diabetes
Kirkpatrick et al. (2019)[15]	N/A	N/A	To provide a scientific statement and comprehensive review of the current evidence on the effects of low-carbohydrate diets and very low-carbohydrate diets on body weight, lipoprotein lipids, glycemic control, and other cardiometabolic risk factors	Low-carbohydrate and very-low-carbohydrate diets are not superior to weight loss than other diets. But they have advantages on appetite, some CVD risk factors, and diabetes compared to other diets
Merrill et al. (2020)[121]	N/A	N/A	To review the differences between various low-carbohydrate eating plans for promoting weight loss in overweight and obese individuals and preventing and treating type 2 diabetes	Low-carbohydrate and very low-carbohydrate diets are just as effective at weight loss as other dietary strategies, but also have the added benefit of reducing the need for using diabetic medications
Mooradian et al. (2020)[6]	N/A	N/A	To review the potential short-term benefits from consuming a low-carbohydrate and adverse health effects from long-term consumption	Low-carbohydrate diets are effective for short-term weight loss and glycemic control for patients with diabetes. However, there are potential adverse effects, such as nausea, fatigue, and water or electrolyte loss
O'Neill (2020)[122]	N/A	N/A	To review recent findings on the role of low-carbohydrate diets preventing or reversing components of metabolic syndrome or type-2 diabetes	There is substantial evidence that low-carbohydrate diets can reverse various metabolic abnormalities and inflammation related to metabolic syndrome or diabetes

Article	Nunrber of articles reviewed	Comparison diets	Focus of review	Key findings
Seid et al. (2019) [58]	N/A	N/A	To evaluate whether or not there is sufficient evidence to conclude whether a low carbohydrate or low-fat diet can be recommended for sustained weight loss and improved health	There was no evidence that the degree of weight loss or the duration of reduced weight maintenance are significantly affected by dietary macronutrient quantity beyond effects attributable to caloric intake
Sievenpiper (2020)[76••]	N/A	N/A	To assess the evidence for the role of carbohydrate quantity vs. quality in cardiometabolic health	Reviews of the best available evidence on carbohydrate quality indicate that the highest markers of carbohydrate quality (e.g., high dietary fiber or low glycemic index foods) are associated with weight loss and decreased incidence and mortality of diabetes and CVD
West and Yancy (2020)[123]	N/A	N/A	To review the history of utilizing low-carbohydrate diets for clinical use and providing recommendations implementing them for addressing obesity, type-2 diabetes, or metabolic syndrome	Low-carbohydrate diets can be implemented to improve weight loss andmetabolic abnormalities from patients with obesity, type-2 diabetes, or metabolic syndrome, but medical monitoring is needed
Systematic reviews				
Ross et al. (2020) [88]	8 randomized controlled trials	Low-fat diets	Compare very low-carbohydrate diets (≤ 25% of total energy intake) to low-fat diets (≤ 30% of total energy intake) on weight loss, diabetes, and CVD risk factors	All groups achieved significant weight loss and improvements in blood pressure and blood glucose. Reductions in LDL cholesterol favored the low-fat diets; while increases in HDL cholesterol and reductions in triglyceride levels favored the very low-carbohydrate diets
Van Wyk et al. (2016)[89]	9 meta-analyses and 12 randomized controlled trials	High-carbohydrate diets	Compare low-carbohydrate diets (≤ 45% of total energy intake) and high carbohydrate diets (> 45% of total energy intake) on weight loss and CVD risk among type-2 diabetics	For body weight, total energy intake was predictive of weight loss. The low-carbohydrate diets did not appear any different than high-carbohydrate diets on metabolic markers or glycemic control
van Zuuren et al. (2018)[84]	36 clinical trials (33 were randomized controlled trials)	Low-fat diets	Assess the effects of low-carbohydrate diets compared to low-fat diets on HbA1c, CVD risk factors among, and weight loss among type-2 diabetics	HbA1c levels declined more for people consuming the low-carbohydrate diets in the short term (< 1 year), but there were no differences after 2 years. There were moderate improvements in glucose, triglycerides, and HDL levels favoring the low-carbohydrate diets. While there were no differences in LDL cholesterol levels or body weight from either diet
Umbrella reviews				
Churuangsuk et al. (2018)[60]	12 systematic reviews	Low-fat diets	A review of published systematic reviews on RCTs between low-carbohydrate vs. control (low-fat/energy-restricted) diets in adults with overweight and obesity	Overall review quality among the studies was high in 2, moderate in 3, and critically low in 7. Among reviews with meta-analyses (n = 10), 4/5 with critically low quality showed low-carbohydrate diets' superiority for weight loss, while high quality meta-analyses reported little or no difference between diets