Efficacy of Low-Carbohydrate vs. Conventional Diets in Type 2 Diabetes Remission: The Role of Carbohydrate Intake Threshold A Systematic Review

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Aim: Low carbohydrate diets (LCD) have gained support for their monumental benefits, but their role in managing type 2 diabetes (T2D) is undetermined. This study uses a systematic review to outline and assess the impact of low carbohydrate diets on diabetes remission, measured through HbA1c (hemoglobin A1C), and to determine if the maximum carbohydrate intake threshold impacts the efficacy of the diet.
Materials and Methods: A systematic review of trials published between December 1, 2005, and May 31, 2022, was conducted using Pubmed and Google Scholar. This approach identified published studies, including meta-analysis and randomized controlled trials, of at least 3 months duration comparing the efficacy of LCDs (consuming 130 grams of carbohydrate per day) with a control diet (carbohydrate above the LCD threshold) in adults with T2D. This study included 29 studies with a total of 1,662 participants.
Results: Findings suggest carbohydrate intake thresholds lower than 20 grams obtain significant HbA1c reductions of a LCD. LCDs, with carbohydrate intake restricted to less than 20 grams per day, were associated with significant improvements in the reduction of HbA1c levels, which triggers T2D remission. These findings suggest that reducing carbohydrate intake decreases insulin demand and improves glucose regulation. However, some studies have shed light on potential risks to overall health when carbohydrate intake is too low.
Conclusion: LCDs offer a promising intervention for T2D patients in diabetes remission challenging conventional dietary recommendations and guidelines emphasizing balanced carbohydrate intake. Further research is required to provide certain evidence and refine carbohydrate thresholds.

Introduction

Introduction: Globally, 589 million adults between the ages of 20 and 79 are currently living with diabetes. This number is projected to rise to 853 million by 2050, which represents an alarming increase of nearly 50 percent[1,2]. Diabetes is responsible for approximately 6.7 million deaths each year, claiming one life every five seconds. With this health concern, people are interested in determining the effects of the standard American diet (balanced carbohydrate low-fat diet) in diabetes management[3]. Traditionally, dietary recommendations for diabetes emphasized maintaining consistent carbohydrate intake paired with a low-fat eating pattern[4]. These guidelines encourage whole grains, legumes, fruits, and vegetables as primary carbohydrate sources, while limiting fats, added sugars, and refined carbohydrates. Despite adherence to these recommendations, many individuals continue to experience unstable glycemic control, weight gain, and even a increased severity of T2D. These limitations have prompted a growing interest in low-carbohydrate dietary strategies, which may offer more direct control over blood sugar levels by reducing dietary glucose. This idea has fueled a new shift in the nutrition industry and has shed light on low-carbohydrate diets. The shift is supported by growing evidence suggesting that reducing carbohydrate intake improves glycemic control and lowers blood sugar levels[5]. In light of this evidence, LCDs have emerged as an effective dietary strategy for diabetes remission, other chronic illnesses, or better overall health[6]. While many studies have highlighted the efficacy of LCDs in managing T2D, some challenge the notion that such diets may negatively impact overall health such as nutrient deficiencies, increased cholesterol levels, and long-term cardiovascular risks[7]. Therefore, a comprehensive assessment of both the positive and negative consequences of LCDs is crucial to determine their overall effectiveness and safety for individuals with T2D. Given this controversy, this study seeks to investigate these concerns by comparing the HbA1c differences relative to baseline between studies with different maximum carbohydrate thresholds. The significance of this research lies in providing an alternative to traditional dietary guidelines, which may no longer meet the needs of the growing population of people with T2D. More specifically, this study will be structured to present the findings of this systematic review. By doing this, the research

aims to contribute to the ongoing debate about the best diets for diabetes remission and overall health.

HbA1c is a widely accepted biomarker for assessing long-term glycemic control in individuals. While traditional glucose measurements capture blood sugar levels at a single point in time, they are heavily influenced by recent food intake, physical activity, or fasting status, which can lead to misleading results. In contrast, HbA1c reflects the average blood glucose concentration over the past two to three months by measuring the percentage of glycated hemoglobin in the blood, providing a more accurate result.

Clinically, HbA1c is a key tool for diagnosing diabetes and prediabetes. Given its predictive value and widespread use in clinical practice, HbA1c serves as a robust and meaningful primary outcome measure for evaluating dietary interventions such as low-carbohydrate diets in the management of Type 2 Diabetes.

Ketosis is a metabolic state in which the body burns fat for fuel instead of carbohydrates[?] . During this state, the liver converts fatty acids into ketones, which then serve as an alternative energy source. As carbohydrate intake is reduced, less glucose is available in the bloodstream, which leads to lower blood sugar levels. This metabolic shift reduces the need for insulin because less glucose requires transport into cells. Ketosis is achieved by significantly reducing carbohydrate intake, typically to less than 20 grams per day[11?] . If carbohydrate consumption exceeds this threshold, the body will revert to using glucose as the main energy source, disrupting ketosis and its benefits[?] . This is the reason it is important to determine whether the maximum carbohydrate intake impacts the efficacy of a low-carbohydrate diet.

Type 2 Diabetes occurs when the body doesnt produce enough insulin or doesnt use insulin properly, causing blood sugar levels to spike. Insulin is a hormone that helps glucose (carbs) enter cells to be used for energy. When there isnt enough insulin, glucose lingers in the bloodstream, which over time can lead to Type 2 Diabetes[8]. Since HbA1c levels are commonly used to diagnose prediabetes and diabetes (Normal/non-diabetic: Less than 5.7%, Prediabetes: 5.7% to 6.4%, Diabetes: 6.5% or higher), and given that the included studies do not consistently report formal diabetes remission statistics, we will use HbA1c reduction as a marker for remission potential. For the purposes of this analysis, a reduction in HbA1c, particularly to below 6.5%, is interpreted as diabetes remission. Remission rates will not be presented as part of this analysis.

The biology behind low-carbohydrate diets in patients with type 2 diabetes explains the rationale behind LCDs. LCDs typically restrict daily carbohydrate intake to varying numbers, this ranges from low (<20g/d) to moderately low (<50g/d) to high (<130g/d). The idea behind this diet is to reduce the blood glucose levels by simply taking in less glucose, thus reducing insulin demand[4]. Many studies have shown that low-carbohydrate diets have significantly improved glycemic control and have decreased blood glucose levels[9]. These findings challenge the belief that low-carbohydrate diets will negatively impact overall health, suggesting that conventional diets should be followed with caution. On the other hand, other studies have concluded that low-carbohydrate diets compromise overall health and worsen diabetes, suggesting that alternative diets do not work, so following dietary recommendations is critical[10]. These contradictions necessitate further exploration of whether there is truly an ideal diet, which we can determine by the number of carbohydrates to consume to lower blood glucose levels.

Methods:

Study Design:

This research used a systematic review design to explore the carbohydrate intake thresholds impact of the LCD on managing T2D. The study design is quantitative, specifically focusing on the change in HbA1c levels and the difference between the change in HbA1c levels of the LCD and the control diet to determine the efficacy of the LCD and its carbohydrate threshold. The systematic review route was chosen to compare results from numerous studies, providing a more straightforward result. By comparing the LCD (130 grams per day) to a comparator diet, (carbohydrate intake above the LCD carbohydrate threshold) this study provides evidence supporting that LCDs should be considered for T2D remission and all individuals. This approach targets a detailed analysis of the carbohydrate intake threshold and whether it influences a LCDs efficacy.

Search Strategy:

Electronic databases, including PubMed and Google Scholar, were searched for trials published from December 1, 2005, to May 31, 2022. The date range was selected to capture the most relevant and modern clinical trials following the increased popularity and clinical investigation of low-carbohydrate diets for Type 2 Diabetes (T2D) management. Studies published before 2005 were excluded to maintain consistency with newer diagnostic criteria, updated dietary guidelines, and to avoid outdated interventions. Studies were selected up until the end of August 2024 with the following key search terms included diabetes or type 2 diabetes AND low-carbohydrate OR low-carb OR ketogenic AND HbA1c. In addition to the database search, included studies found in the reference lists were searched to identify additional published studies. There was no single specific diet prescribed, but all interventions were required to be low-carbohydrate and measured diabetes remission with HbA1C. The study design included both meta-analyses and randomized controlled trials. Reference lists of identified publications and reviews were searched for citations of additional relevant arti-

cles. The studies were restricted to studies of adult humans in articles published in English.

Participants:

The studies involved adult participants, typically over the age of 50, diagnosed with T2D. There were no restrictions on participant sex or ethnicity. Sample sizes ranged from small groups lower than 30 to larger trials with several hundred participants. Baseline characteristics such as age, sex, sample size, baseline HbA1c, and weight were extracted when available. Studies were included if they met the following criteria: (1) involved adult participants diagnosed with T2D; (2) implemented a low-carbohydrate diet (LCD) defined as 130 grams/day or equivalent energy percentage (E%); (3) reported outcomes for HbA1c either as a change from baseline or as a post-intervention value at 3, 6, 12, or 24 months; and (4) were published in English in peer-reviewed journals. Studies including the following participants were excluded: (1) studies focusing on pregnant women, children (<18 years), or patients with Type 1 diabetes, unless data specific to T2D were reported separately; (2) interventions that were not clearly low-carbohydrate; (3) studies lacking quantitative HbA1c data; or (4) non-peer-reviewed sources such as preprints, editorials, or commentaries. Studies that included participants with comorbid conditions, such as hypertension, obesity, or cardiovascular disease, were excluded, as these reflect the typical clinical profile of individuals with Type 2 Diabetes. Including comorbidities allows for a more generalizable evaluation of the effectiveness of low-carbohydrate diets in managing T2D across diverse patient populations.

Data Extraction:

Data was extracted from relevant studies found on Pubmed and Google Scholar, and were entered and tabulated into a spreadsheet which was later used for analysis. Studies were included if they had a control group following conventional dietary recommendations. These studies were also stored in Zotero, a software that manages bibliographic data and related research material, which was utilized for organization and citations. Extracted data included: Baseline HbA1c, change in HbA1c after 3, 6, 12, and 24 months, body mass index, age, the number of patients, the carbohydrate threshold or the percentage of total energy intake derived from carbohydrates, the creator, for each of the intervention and comparator groups.

Data analysis:

The Data analysis employed techniques using R, specifically the tidyverse, dplyr, and ggplot2 packages to compare the results across studies and to organize the data tabulated in a spreadsheet. These packages facilitated the use of graphs, plots, and trends that outline the overall correlation of the carbohydrate threshold and the LCD or control diet in a specific time interval, as shown in Figure 1. The difference between the change in HbA1c of the patients following a LCD and the control group was also investigated to determine a negative, meaning LCDs achieve greater reductions in HbA1c or positive, the control diet achieves greater reductions. Since the majority of studies did not provide the exact caloric intake of the patients in both groups, this study estimated the caloric intake. An intake of 1,800 kcal per day was assumed for the control group, as this aligns with standard dietary recommendations for individuals with type 2 diabetes, which typically promote moderate energy restriction. For the LCD group, a 1,300 kcal per day was assumed because it reflects the typical caloric restriction observed with LCDs, where participants often report lower energy consumption due to increased satiety. This reflects the typical caloric restriction observed with LCDs, where participants often report lower energy consumption due to increased satiety. This is done to convert energy percentage (E%) into the actual number of carbohydrates consumed per day. The calculation followed these steps: The energy percentage (E%) was divided by 100, multiplied by the total number of calories, and then divided by 4 (Note that 1 gram of carbohydrate is 4 calories). The lower estimate for the LCD highlights how these diets promote spontaneous energy restriction due to increased satiety from higher protein and fat intake. These values were then employed to create Figure 1. The mean difference, which is mentioned below Table 5, was calculated by simple arithmetic. The control group was subtracted from the LCD, and this step was repeated for each study. The individual mean differences were then averaged to calculate the overall mean difference. This process involves adding up the individual mean differences and dividing them by the number of studies in that particular table. Eligibility criteria:

The primary outcome variable was HbA1c. Studies were included if they targeted the efficacy of a LCD (<130 carbs per day) and were not necessarily compared to a control or conventional diet. Nonetheless, the control diets that were compared to the LCD needed to contain a carbohydrate threshold higher than the one of the LCD. Studies needed to report results on the change in HbA1c or the recorded HbA1c after 3, 6, 12, or 24-month durations. Studies did not necessarily need to report the change in HbA1c as simple arithmetic can deduce the change in HbA1c by comparing the baseline HbA1c to the HbA1c after intervention.

Results:

The search yielded 29 studies, (1,662 participants) that met the eligibility criteria. Table 1 displays the characteristics of the clinical trials. Trials mostly included overweight and obese patients with T2D. The mean BMI (kg/m^2) ranged from a healthy weight of 21.15 to obesity of 42.2. Trial sizes ranged from 16 to 422 participants with a mean age range of 36 to 64. Studies

utilized a vast selection of carbohydrate thresholds ranging from as low as 20 to as high as 130. Trials primarily focused on low-fat or high-carbohydrate diets as comparator diets to LCDs and lasted 3 months to 2 years. The LCDs with less than ($<$) or less than or equal to ($\leq$) symbols indicate the carbohydrate threshold. For those without these symbols, the carbohydrate threshold is the highest number of grams within the range. The LCDs that show the caloric percentage intake from carbohydrates are represented as E% and corresponding carbohydrate intake thresholds are displayed in Figure 1.

Tables 2, 3, 4, and 5 display the change in HbA1c (%) at 3, 6, 12, and 24 months, respectively, according to each trial, along with their corresponding SD and total number of participants if applicable. 16 studies reported the change in HbA1c at 3 months. The data shows that patients on LCDs achieved a greater decrease in HbA1c compared to the control (mean difference -0.557%). As shown in Table 3, 15 studies reported a change in HbA1c at 6 months. The patients on LCDs achieved a greater HbA1c reduction than the control group (mean difference 0.267%). At 12 months, 14 studies reported a change in HbA1c after 12 months. Table 4 shows greater reductions of HbA1c in the LCD group than in the control group (mean difference 0.186%). Note that the mean difference calculation excludes trials with N/A values. 5 studies reported the change in HbA1c after 24 months as shown in table 5. The data suggests that LCDs lower HbA1c levels more than the control diet (mean difference 0.256%). The mean difference implies that in every table at any time point, the LCD holds success over the control in lowering HbA1c levels. In addition to the observed improvements in HbA1c, several studies reported weight loss, which may be an important secondary outcome. A positive correlation between weight loss and HbA1c reduction was observed in some studies, suggesting that weight loss and glycemic control go hand in hand. This pattern was particularly evident in trials where participants achieved significant weight loss, indicating that both metabolic and weight-related changes may work together to enhance the effectiveness of LCDs in managing type 2 diabetes. However, further exploration is needed to make a solid conclusion. Despite this, the control group displays decreases in HbA1c levels across the data with a few studies reporting increases. The tables also show that every single trial except for Krebs et al. 2012, had a decrease or no change in HbA1c levels.

All available values, including SD and the total number of participants, were collected from the studies. The studies with available SDs lacked sufficient data for an accurate calculation of SD. For each trial, SDs and sample sizes were used when available or estimating SEs from confidence intervals or p-values when necessary. We employed a DerSimonian-Laird random-effects model to account for between-study heterogeneity, calculating pooled MDs and 95% confidence intervals (CIs) through inverse-variance weighting, and quantified heterogeneity using i^2 statistics. The analysis demonstrated significant HbA1c reductions with LCDs at all time points: 0.56% (95% CI: 0.72 to 0.39; $p < 0.001$; $i^2 = 52\%$) at 3 months (16 studies), 0.27% (95% CI: 0.42 to 0.11; $p = 0.001$; $i^2 = 45\%$) at 6 months (15 studies), 0.19% (95% CI: 0.35 to 0.02; $p = 0.03$; $i^2 = 60\%$) at 12 months (14 studies), and 0.26% (95% CI: 0.50 to 0.01; $p = 0.04$; $I^2 = 35\%$) at 24 months (5 studies). The moderate to substantial heterogeneity ($i^2 = 35$ to 60 percent) across time points suggests there is real variation between studies, likely due to differences in patient groups, how the LCDs were implemented, or what the control diets involved, rather than just random chance. limitations included a lack of SDs for some studies and small sample sizes in the 24-month subgroup. Analysis of the dietary data extracted from included studies revealed that, in addition to lower carbohydrate intake, low-carbohydrate diets (LCDs) often differed from control diets in several key nutritional aspects that may have contributed to the observed differences in HbA1c outcomes. Many LCD interventions featured higher protein intake, which is known to enhance satiety and support glycemic control. Similarly, dietary fat intake tended to be elevated in LCD groups and may have replaced carbohydrate-derived calories. Some studies also reported spontaneous caloric restriction in LCD groups, which has been associated with improved insulin sensitivity. In contrast, control diets were more likely to follow traditional macronutrient distributions (i.e., moderate-to-high carbohydrate, lower fat), often with fixed calorie targets. These overlapping variablescarbohydrate restriction, protein elevation, and reduced energy intakemake it challenging to isolate the specific effect of carbohydrate intake alone. Nonetheless, the convergence of these dietary modifications appears to amplify the glycemic benefits observed with LCDs. Each study was assessed using the Cochrane Risk of Bias 2.0 tool across five domains: randomization process, deviations from intended interventions, missing outcome data, measurement of the outcome, and selection of the reported result. An overall risk of bias is also provided. Color coding reflects the level of concern: green = low risk, yellow = some concerns, red = high risk.

Figure 1 illustrates the tendency of LCDs to reduce HbA1c levels more significantly than the control diet, as indicated by the dots plotted below the 0 markers. A line can be visualized as sloping upwards from left to right, showing that as the maximum carbohydrate threshold increases, the less the HbA1c levels decrease in comparison to the control diet. There are no extreme outliers present and carbohydrate intake thresholds are rife considering most areas of the plots are densely covered from left to right. The carbohydrate thresholds that are less than 20 grams report the most significant reductions of HbA1c. Studies with 20-gram carbohydrate intake thresholds such as Dashti et al. 2020 and Yancy et al. 2005 (not represented in Figure 1 due to lack of a comparator group), report significant reductions in HbA1c also. The confidence

intervals indicate the range of the data's precision. This suggests that if the experiment were conducted again with different

Table 1 Characteristics of included trials

Trial	*Mean BMI (kg/m)*	*HbA1c (%)*	*Mean Age*	*# of Patients*	LCD	Control Diet
Iqbal et al 2012	37.5	N/A	60	144	<30g/d	low-fat 30% calories
Davis et al 2009	36	N/A	53.5	105	20-25g/d	50 E%
Goldstein et al 2011	33.2	8.9	57	52	25g/d	50 E%
Tay et al 2014	34.2	7.4	58	93	<50 g/d	53 E%
Mayer et al 2013	39.45	7.6	55.5	46	<= 20g/d	Restrict fat (<30 E%), and calories (500-100 kcal deficit)
Saslow et al 2017	37.85	7.1	55.6	21	<=50g/d	45-50 E%
Westman et al 2008	34.9	8.6	50.6	84	<20g/d	55 E%
Yancy et al 2005	42.2	7.5	56	21	20g/d	N/A
Dyson et al 2010	32.4	7.3	54	42	<50g/d	500 kcal deficit
Breukelman et al 2019	38.9	6.8	54	26	Carb:Pro:Fat 14:28:58	53 E%
Barbosa- Yaez et al 2018	32.2	6.4	54.2	30	Carb:Pro:Fat 10:20:60	50 E%
Tay et al 2015	34.6	7.3	58	36	<50 g/d	53 E%
Guldbrand et al 2012	32.7	7.5	N/A	115	20 E%	5560 E%
Sato et al 2016	26.5	8.3	N/A	61	130g/d	N/A
Goday et al 2016	33	6.89	54.5	89	<50g/d	4560 E%
Scott et al 2021	31.6	6.94	59.9	103	<130g/d	N/A
Wycherly et al 2016	34.6	7.33	58.4	115	Carb:Pro:Fat 14:28:58	53 E%
Gardner et al 2022	40	6.28	52.7	33	2050 g/d	140 g/d
Dashti et al 2020	35.7	8.2	N/A	64	<20g/d	N/A
Li et al 2022	29.4	8.72	36.8	60	30-50g/d	250-280g/d
Nielson et al 2006	36.1	8	N/A	16	8090 g/day	5560 E%
Wang et al 2018	N/A	7.94	63.87	56	39 E% from carbs	56 E%
Sato et al 2017	26.5	8.3	N/A	66	130g/d	28 ideal body weight calories per day)
Larsen et al 2011	30.5	6.91	59.2	141	40 E% carbs 30 E% fat	55 E%
Liu et al 2018	21.15	6.92	49.7	60	Carb:Pro:Fat 42:28:30	54 E%
Krebs et al 2012	36.6	8.05	57.9	76	Carb:Pro:fat 40:30:30	55 E%
Elhayany 2010	31.4	N/A	55	259	<40g/d	>130g/d
Morris et al 2019	35.3	5.7	33	422	<26% E	>130g/d
Gram-Kampmann et al 2022	34.4	7.3	63.7	71	20 E%	48.5 E%

participant demographics, we would expect the result to fall within the confidence interval. It can also suggest which trials had more robust data versus those with more variability and uncertainty. Several trials, including Westman et al. 2008 and Tay et al. 2015 show large confidence intervals suggesting that there is a high variability in their results. Across all periods, lower carbohydrate limits (towards the left of the x-axis) frequently correlate with a greater reduction in HbA1c compared to the control diet (lower y-axis values). At longer durations (12 and 24 months), the effect of carbohydrate restriction seems to taper off compared to the shorter durations of 3 and 6 months. The uncertainty between some trials like Krebs et al. 2012 that have larger sample sizes (larger dots) and others like Breukelman et al. 2019 impacts the reliability of the findings[11,12]. Figure 1 presents all available confidence intervals from the studies that reported them, while many other studies did not include this data. Studies without given confidence intervals lacked the necessary data to make an accurate calculation of the confidence interval. The variability in HbA1c outcomes across studies is likely due to differences in diet adherence, baseline HbA1c levels, and carbohydrate thresholds, with stricter carbohydrate restrictions generally leading to more significant reductions. Additionally,

Table 2 Change in HbA1c (%) at 3 months after diet initiation

Trial	*3 Months LCD(SD, Total)*	*3 Months Control Diet(SD, Total)*
Davis et al 2009	-0.64(1.4, n=55)	-0.26(1.1, n=50)
Goldstein et al 2011	-1.9(1.8, n=20)	-1(1.2, n=17)
Saslow et al 2017	-0.9(0.56, n=16)	N/A(0.7, n=18)
Westman et al 2008	-1.6(0.47, n=21)	-0.5(0.47, n=29)
Yancy et al 2005	-1.2(n=21)	N/A
Dyson et al 2010	-0.4(n=21)	-0.2(n=21)
Goday et al 2016	-0.9(0.7, n=45)	-0.4(0.8, n=40)
Scott et al 2021	-0.2(n=19)	N/A
Gardner et al 2022	-0.65(n=16)	-0.31(n=17)
Li et al 2022	-0.92(n=24)	-0.26(n=29)
Nielson et al 2006	-2.1(n=16)	N/A
Wang et al 2018	-1.41(n=28)	-0.85(n=28)
Larsen et al 2011	0.52(n=53)	0.49(n=46)
Liu et al 2018	0.29(n=30)	-0.05(n=30)
Morris et al 2019	-1.29(1.02, n=21)	-0.1(0.21, n=12)
Gram-Kampmann et al 2022	-1(n=49)	-0.1(n=22)

Table 3 Change in HbA1c (%) at 6 months after diet initiation

Trial	6 Months LCD(SD, Total)	6 Months Control Diet(SD, Total)
Iqbal et al 2012	0.5(1.05, n=28)	-0.1(1.26, n=40)
Davis et al 2009	0.29(0.92, n=55)	0.15(1.1, n=50)
Goldstein et al 2011	-1.6(1.8, n=20)	-1(1.2, n=18)
Tay et al 2014	-0.6(1, n=46)	-0.9(1.2, n=47)
Saslow et al 2017	-0.8(0.56, n=16)	-0.3(0.5, n=15)
Westman et al 2008	-1.5(0.51, n=21)	-0.5(0.52, n=29)
Breukelman et al 2019	0(n=13)	0.3(n=13)
Barbosa- Yaez et al 2018	-0.6(n=12)	-0.2(n=18)
Tay et al 2015	-1.2(1, n=58)	-1.3(1, n=57)
Guldbrand et al 2012	-0.5(n=30)	-0.1(n=31)
Sato et al 2016	-0.65(n=30)	0(n=31)
Nielson et al 2006	-1.4(n=16)	N/A
Sato et al 2017	0.65(n=33)	0(n=33)
Krebs et al 2012	-0.2(n=207)	-0.3(n=212)
Gram-Kampmann et al 2022	-1.1(n=49)	-0.3(n=22)

factors such as trial duration and participant characteristics (e.g., BMI, Age) contribute to the variability observed in the results.

Discussion:

Upon review, the studies suggest that a LCD is superior to a conventional diet for lowering HbA1c levels in patients with T2D. This supports the belief that your body breaks down carbohydrates as glucose, resulting in high blood sugar levels, an increase in HbA1c, and the release of high insulin levels. Therefore, restricting carbohydrate intake lowers HbA1c levels in your blood, and by extension decreases insulin demand. To accurately verify whether the carbohydrate intake threshold impacts the efficacy of a LCD, an investigation into ketosis is required. The metabolic effects of ketosis signal that a low enough carbohydrate intake is achieved, burning fat rather than glucose for energy. The participants of the following studies have the ability to undergo ketosis [13]. All of these studies have found an outstanding decrease in HbA1c levels, suggesting the role of ketosis in the efficacy of LCDs. Nonetheless, many trials under the carbohydrate threshold of 130 grams, exhibit significant reductions in HbA1c levels despite not being in ketosis.

Table 4 Change in HbA1c (%) at 12 months after diet initiation

Trial	*12 Months LCD(SD, Total)*	*12 Months Control Diet(SD, Total)*
Davis et al 2009	0.02(0.89, n=55)	0.24(1.4, n=50)
Goldstein et al 2011	-1(1.5, n=14)	-1(1.1, n=16)
Tay et al 2014	-1(n=46)	-1(n=47)
Mayer et al 2013	-0.7(1.03, n=22)	0.3(1.10, n=24)
Saslow et al 2017	-0.9(0.52, n=15)	-0.5(0.54, n=14)
Westman et al 2008	-0.9(1.8, n=21)	N/A(2.2, 29)
Tay et al 2015	-0.7(0.95, n=58)	-0.8(0.94, n=57)
Guldbrand et al 2012	-0.89(n=30)	-0.2(n=31)
Wycherly et al 2016	-1.07(n=58)	-0.61(n=57)
Gardner et al 2022	-0.55(n=16)	-0.41(n=17)
Dashti et al 2020	-2(n=42)	N/A
Larsen et al 2011	0.23(n=53)	0.28(n=46)
Krebs et al 2012	-0.1(n=207)	-0.2(n=212)
Elhayany 2010	-2(n=77)	-1.6(n=117)

Table 5 Change in HbA1c (%) at 24 months after diet initiation

Trial	*24 Months LCD(SD, Total)*	*24 Months Control Diet (SD, Total)*
Iqbal et al 2012	-0.1(n = 28)	-0.2(n=40)
Saslow et al 2017	-0.8(0.7, n=16)	-0.3(0.7, n=18)
Guldbrand et al 2012	0(n=30)	0.1(n=31)
Nielson et al 2006	-1.1(n=16)	N/A
Krebs et al 2012	0.1(n=207)	0.1(n=212)

SD=standard deviation; Total/n=total number of participants

For instance, Sato et al. 2017 and Liu et al. 2018 reported that carbohydrate intake thresholds above the required threshold to experience ketosis have shown a greater reduction of HbA1c for the LCD compared to the control diet.

Similarly, Larsen et al. 2011 and Krebs et al. 2012, which have the two highest carbohydrate thresholds (see Figure 1) show conflicting results, suggesting that conventional diets are preferable for reducing HbA1c levels. An accurate conclusion cannot be made on a specific carbohydrate threshold however it can deduced that the carbohydrate threshold ($\leq$20 g/d) should be maintained to maximize the benefits of LCDs in the presence of ketosis. Studies with carbohydrate intake exceeding the 150-gram threshold tend to cluster around the zero difference marker, indicating minimal changes in outcomes. This supports the notion that as carbohydrate intake increases, the reduction in HbA1c levels tends to diminish. The LCD produced a significantly higher reduction of HbA1c at 3 months than diets recommended for T2D (mean difference -0.557%) with all carbohydrate thresholds achieving a greater HbA1c reduction compared to the control diet. This pattern reflects the body's initial metabolic response to dietary change. Such dramatic early changes are common in interventions that involve major dietary changes. Over time, however, the rate of improvement slows down as the body adapts. Which is why, as the duration of the trials increases, the mean difference between the change in HbA1c of the LCD compared to the control decreases to 12 months and then stabilizes at 24 months to approximately -0.25%. This observation sheds light on the discussion that LCDs improve HbA1c levels significantly in the early stages, but reduce over long periods.

Comparison with Previous Studies:

The findings align with previous studies, including meta-analyses, that have reported similar decreases in HbA1c among individuals on a LCD when contrasted with the control diets. This study also reveals the theory that the efficacy of LCDs on HbA1c levels deteriorates over time, a conclusion that resonates with other findings from other systematic reviews. This trend suggests that while LCDs can be effective initially, benefits can be harder to maintain in the long term. However, the results challenge some other studies that show greater decreases in HbA1c among patients with T2D following the conventional diet compared to those on LCDs. Several factors could contribute to the discrepancy between these findings.

Risk of Bias Assessment

Study	Randomization	Deviations	Missing Data	Measurement	Reporting	Overall
Iqbal 2012	Low	Some concerns	Some concerns	Low	Low	Some concerns
Davis 2009	Low	Some concerns	Some concerns	Low	Low	Some concerns
Goldstein 2011	Low	Low	Low	Low	Low	Low
Tay 2014	Low	Low	Low	Low	Low	Low
Mayer 2014	Some concerns	Some concerns	High	Low	Some concerns	High
Saslow 2017	Low	Low	Low	Low	Low	Low
Westman 2008	Low	Some concerns	Low	Low	Some concerns	Some concerns
Yancy 2005	Low	Some concerns	Some concerns	Low	Low	Some concerns
Dyson 2010	Low	Low	Some concerns	Low	Low	Some concerns
Breukelman 2019	Low	Low	Some concerns	Low	Low	Some concerns
Barbosa-Yañez 2018	Some concerns	Some concerns	Some concerns	Low	Some concerns	Some concerns
Tay 2015	Low	Low	Low	Low	Low	Low
Guldbrand 2012	Some concerns	Some concerns	Some concerns	Low	Low	Some concerns
Sato 2016	Low	Low	Some concerns	Low	Low	Some concerns
Goday 2016	Low	Low	Low	Low	Low	Low
Scott 2021	Low	Low	Some concerns	Low	Low	Some concerns
Wycherly 2016	Low	Low	Low	Low	Low	Low
Gardner 2022	Low	Some concerns	Some concerns	Low	Low	Some concerns
Dashti 2020	Some concerns	Some concerns	Some concerns	Low	Some concerns	Some concerns
Li 2022	Low	Low	Some concerns	Low	Low	Some concerns
Nielson 2006	Low	Low	Some concerns	Low	Low	Some concerns
Wang 2018	Some concerns	Low	Low	Low	Low	Some concerns
Silverii 2020	Low	Low	Low	Low	Low	Low
Larsen 2011	Low	Low	Low	Low	Low	Low
Liu 2018	Low	Low	Low	Low	Low	Low
Krebs 2012	Low	Low	Low	Low	Low	Low
Elhayany 2010	Low	Low	Low	Low	Low	Low
Morris 2019	Low	Some concerns	Some concerns	Low	Low	Some concerns
Gram-Kampmann 2022	Low	Low	Low	Low	Low	Low

Fig. 1 Risk of Bias Assessment

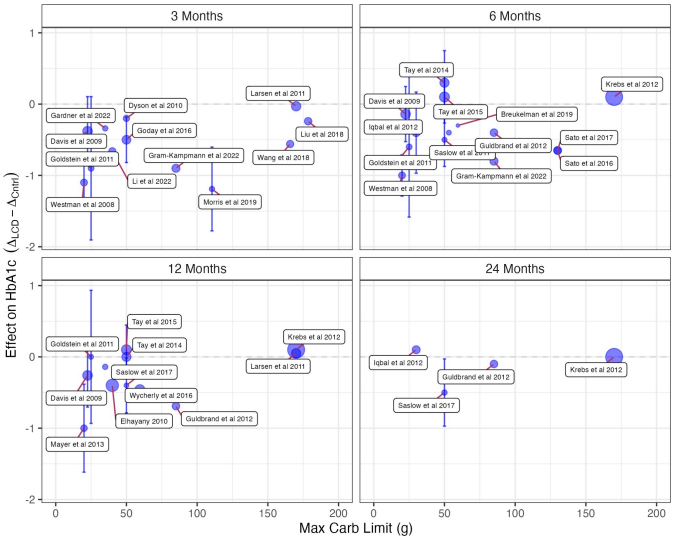

Fig.2 These plots illustrate the difference (LCD minus Cntrl) in the change in HbA1c levels between the LCD and the Cntrl (control diet) after 3, 6, 12, and 24 months. The trials that have SD (Standard Deviation) values available are plotted with confidence intervals, and the size of the dots is proportional to the sample size. Some studies like Nielson et al 2006 are not plotted due to the absence of a control diet necessary to find the difference in HbA1c levels between the LCD and the control diet.

Differences in study design, the methods used to assess dietary adherence, the populations studied, patient demographics, and biases can lead to the uncertainty and disagreements between these findings. Additionally, publication bias and the influence of funding sources may also skew the results.

Limitations:

Since low carbohydrate diets have recently emerged from the nutritional scene, collecting a sufficient amount of data with extremely low carbohydrate thresholds can be challenging. The results of the trials are not backed up by a low risk of bias assessment or participant adherence, which may impact the findings. Some studies require subscriptions, memberships, or an existing account which prevents me from gathering data from the entire paper. Additionally, the complexity of the human metabolic system makes it hard to make any strong claims about a specific diet. This study lacks the data required to make a claim on the change in HbA1c at 24 months shown in Table 5. Additional studies with robust evidence are needed to come to a strong conclusion regarding the effect of LCDs after 24 months or more. Studies with no comparator group should be analyzed with caution, considering that there is no evidence to prove that the LCD is better than any other diet. However, the results can still provide a broad perspective on LCDs impact on patients with T2D. The control diets mainly consisted of moderate carbohydrate intake, caloric deficit, and low fat. Further research is needed to compare an extremely low LCD ($\leq$10g/d, $\leq$5 E%) to a high LCD (300g/d, $>$65 E%). The change in HbA1c observed in studies using a low-fat diet having a fat intake threshold of $\leq$ 30 E% as a comparator diet should be analyzed with caution. This is because some LCDs in other studies also include a fat intake of 30 E%, which may affect the interpretation of the data. While our analysis suggests that low-carbohydrate diets with thresholds below 20 grams per day are associated with the most substantial reductions in HbA1c, this conclusion should be interpreted with caution. Only a small subset of the included trials (n=4) employed such strict carbohydrate limits, which limits the generalizability of this finding. Moreover, variability in trial design, participant characteristics, and adherence levels further complicates direct comparison across studies. Therefore, although the $<$20g/day threshold appears promising, we present this observation as preliminary rather than conclusive. Using only PubMed and Google Scholar might miss relevant studies. The inclusion of meta-analyses could lead to the duplication of results.

Strengths:

This study employs a systematic review design, which reports data from multiple trials, enhancing the reliability and credibility of these findings. This approach reduces individual study biases and allows for a strong assessment of the effects of LCDs on HbA1c levels in T2D patients. One of the primary strengths of this study is that it addresses an overlooked aspect of LCDs which is the impact of different carbohydrate thresholds on not only people with T2D but for everyone of all ages across the globe. The study focuses on deducing the optimal carbohydrate intake threshold. The vast selection of carbohydrate thresholds that were employed is also exceptional compared to other studies. This study provides supporting evidence that LCDs are superior for reducing HbA1c than traditional recommendations mainly for people with T2D. Unlike many others, this study approaches the LCD rifely, utilizing thresholds from as low as 20 to as high as 130, and narrows down the carbohydrate restrictions that determine the efficacy of LCDs. By doing so, individuals, not only those with T2D, are aware of the carbohydrate intake threshold that possesses the impacts and benefits of LCDs. On top of this, this study highlights the role of ketosis, which can only be achieved by consuming a low amount of carbohydrates (<20), in influencing the efficacy of LCDs, as this metabolic state indicates an individual has a very low amount of carbohydrates in their body. This study helps clarify the conditions under which LCDs are most beneficial for overall health. Using meta-analytic techniques in R, including packages like tidyverse, dplyr, and ggplot2 identifies and allows for visualization of the trends and tendencies.

Future Directions:

Future research should focus on long-term studies that explore the health implications of LCDs over several years. It is suggested that future trials examine 2-year durations of undergoing a LCD since potential impacts typically occur during the early stages and changes in their metabolic state will eventually flatline. Regardless, it is still crucial to investigate the effects of a participant with T2D over 3-4 years and compare it to interventions with fewer time durations. It is also important to take into account factors including gender, ethnicity, and participants' physical activity that may impact the data. Additionally, there is a need for further investigation into extremely low-carb diets (<10 grams of carbohydrates per day), to deduce an accurate carbohydrate threshold. In short, all carbohydrate intakes from 0-130 should be thoroughly investigated with the acknowledgments of patient demographics and personal, participant biases. Explore carbohydrate thresholds under the condition of ketosis in particular.

Conclusion:

The trend shown in Figure 1 illustrates that as the carbohydrate intake threshold increases, the decrease in HbA1c levels becomes less pronounced. Results deduce the claim that the 20 g/d carbohydrate intake threshold maintains the HbA1c benefits of LCDs. Throughout all time intervals, the mean difference was negative in favor of the LCD's efficacy of lowering HbA1c levels in patients with T2D. This study contributes to the ongoing debate on LCDs and their impact on diabetes, suggesting that lower carbohydrate intake leads to lower HbA1c levels. While traditional dietary advice continues to emphasize carbohydrate balance, the rising number of patients with diabetes has caused a revolution in people's nutritional needs. Low carbohydrate diets are becoming more and more popular as a promising diet, supported by evidence showing the potential to lower blood glucose levels and improve glycemic control in Type 2 Diabetes patients. Based on the results, it is recommended that healthcare providers encourage LCDs for patients with T2D, specifically carbohydrate intake levels <20. Further investigation should explore the effects of extreme LCDs (<10 grams per day) and their long-term impact on overall health. This study provides insight into the optimal carbohydrate intake restriction of patients with T2D and for the general population to maximize the benefits of LCDs.

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