

Adherence to Low-Carbohydrate Diets in Patients with Diabetes: A Narrative Review

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Abstract: Evidence suggests that low carbohydrate (<130 g/day of carbohydrate) (LCD) and very low carbohydrate, ketogenic diets (typically <50 g/day of carbohydrate) (VLCKD) can be effective tools for managing diabetes given their beneficial effects on weight loss and glycemic control. VLCKD also result in favorable lipid profile changes. However, these beneficial effects can be limited by poor dietary adherence. Cultural, religious, and economic barriers pose unique challenges to achieving nutritional compliance with LCD and VLCKD. We review the various methods for assessing adherence in clinical studies and obstacles posed, as well as potential solutions to these challenges.

Keywords: low carbohydrate diet, ketogenic diet, adherence, type 2 diabetes

Introduction

The number of people with type 2 diabetes has nearly quadrupled from 1980 to 2014 with the prevalence now estimated to be 8.5% of the global population.¹ Diabetes is associated with increased morbidity and mortality, but the development and progression of weight-related type 2 diabetes can be delayed with exercise, diet, and weight loss of 5–10%.^{2–5} Guidelines from the American Diabetes Association and Academy of Nutrition and Dietetics therefore recommend that overweight adults with type 2 diabetes reduce energy intake to promote weight loss.^{6–9} However, the optimal dietary approach to weight loss is widely debated, among both health professionals and the lay public. A preponderance of data suggests that low carbohydrate diets (LCD) and very low carbohydrate, ketogenic diets (VLCKD) can be effective tools for weight loss, A1c reduction, blood pressure lowering, and improving triglycerides and HDL-C in trial settings.^{7,10} An emerging body of evidence, however, suggests that better adherence to a weight-reducing diet, rather than the diet composition itself is an important factor for weight loss success.^{11,12}

Dietary predictors of adherence vary based on the type of diet. In one study examining both qualitative and quantitative methods among adults following a restrictive dietary pattern, adherence varied significantly between dietary groups, with those following a vegan and vegetarian-based diet demonstrating particularly high adherence and gluten-free and weight loss dieters being comparably low. Four consistent predictors of adherence were noted. Self-efficacy and social identification with one's dietary group positively predicting adherence, whereas mood or weight control as motivation for dietary choice had negative effects.¹³ Personality characteristics have also been linked to dietary adherence, with conscientiousness, lower levels of emotional eating, and openness to experience being associated with better adherence in weight-loss intervention programs.^{13–15} Mental health is known to play an important role as well. For those with celiac disease, depression and anxiety were associated with poor adherence to a gluten-free diet.¹³

There is no consensus on the amount of carbohydrates permitted for a LCD or VLCKD. Whether carbohydrates should include total carbohydrates versus net carbohydrates also remains debatable. Net carbohydrates are calculated as total carbohydrates after excluding fiber and sugar alcohols (if applicable). For this review, studies were eligible for

inclusion if they were randomized control trials including adults diagnosed with Type 2 diabetes, had a minimum intervention duration of 24 weeks, and if the intervention restricted the proportion or quantity of dietary carbohydrate to at least less than 50 grams of carbohydrate per day. Studies using active control diets were included. All forms of comparison diet that did not include carbohydrate restriction were permitted, including low-fat, high-carbohydrate, low-glycemic index, high-protein, Mediterranean and “healthy eating”. Included studies also needed to report actual (self-reported or measured) carbohydrate intake during or at the end of the intervention. All countries were eligible but language was restricted to English. Studies that did not meet these criteria were excluded. Included studies did not differentiate between total versus net carbohydrates. This article seeks to review the literature related to adherence to LCD and VLCKD in people with type 2 diabetes based on the aforementioned criteria.

A Brief History of Low Carbohydrate and Very Low Carbohydrate Diets

The development of the VLCKD as a treatment for diabetes mirrors its use as a treatment for epilepsy. VLCKD was the standard of care for both diabetes and epilepsy prior to the development antidiabetic and antiepileptic drugs, respectively^{16–18} After the development of pharmacologic treatments, interest in dietary modification waned. However, medications failed to yield a universal cure, prompting a resurgence in research and clinical interest in LCD and VLCKD for the management of diabetes and epilepsy.

In 1921, the Mayo Clinic treated a series of epilepsy patients with a ketone-producing diet. This “ketogenic diet” was an effective alternative to fasting.¹⁸ First reported in 1925, the macronutrient distribution of the ketogenic diet for pediatric epilepsy consisted of 1 g protein per kilogram of body weight, 10–15 g of carbohydrates per day, and the remainder of the calories from fat.¹⁹ In these earliest reports of the diet in the treatment of epilepsy, dietary adherence played a significant role in seizure control.¹⁹

In the 1910s, Drs. Frederick Madison Allen and Elliot Proctor Joslin studied low carbohydrate, high-fat diets for the treatment of diabetes mellitus.¹⁷ Decreased urinary glucose output was a marker of efficacy. These diets consisted roughly of 70% fat and 10% carbohydrates.¹⁷ Prior to 1920, poor dietary adherence in patients with diabetes was noted to result in recurrent admission and poor outcomes.²⁰

The Atkins’ diet, popularized in 1972, was the first ketogenic diet to gain widespread appeal for obesity management. Variants of the classical ketogenic diet (CKD) were developed to improve tolerability. These include the modified Atkins’ diet (MAD)^{21,22} the medium-chain triglyceride diet, and the low glycemic index treatment.²³ The MAD does not require an initial fasting period and is meant to be easy to follow. Fats are encouraged and carbohydrates limited to less than 20 grams per day.^{22,24} A meta-analysis evaluated the 15 studies of ketogenic diets for epilepsy in adults.²³ The studies had a combined dropout rate of 45%, with fewer patients completing the trials of the CKD (38%) and better completion rates with the MAD (56%).²³ Of the patients who dropped out of the classical ketogenic diet studies, about 60% did so due to inability to adhere which was attributed to psychosocial reasons, fatigue and weight loss.^{25–28} Among the participants who failed to complete the MAD studies, about half discontinued the diet due to inability to adhere. When ketogenic diets are used to control epilepsy, adherence appears to be inversely related to the degree of dietary restriction. Side effects and psychosocial stressors also appear to impact dietary adherence in this setting.

Defining Low Carbohydrate and Very Low Carbohydrate Diets and Their Clinical Benefits

Dietary approaches for weight loss typically emphasize either decreasing carbohydrate intake, decreasing fat intake or decreasing calories/portions.²⁹ A typical American diet consists of 2200 calories per day, with roughly 36–40% from fat, 16–18% from protein, and 45% from carbohydrates.^{30–32} Traditional dietary guidelines for people with diabetes recommended that individuals consume 45–65% of daily energy intake from carbohydrates high in fiber.³³ Randomized control trials generally define low carbohydrate diets as <40–45% of calories from carbohydrate.⁷ However, more recently, studies have examined carbohydrate restricted eating patterns and found them to be safe. Some studies have also demonstrated metabolic benefits with LCDs and VLCKDs including weight loss,^{34,35} improved lipid profiles,^{7,36} better glycemic control,³⁶ and reduced medication dependence in persons with diabetes.^{34,37}

Although there are no accepted definitions for LCD or VLCKD, a selection of these eating patterns is reviewed herein based on the aforementioned criteria.

Low Carbohydrate Diets (LCDs)

These diets typically limit carbohydrate intake to 26–45% of daily caloric intake but do not seek to promote ketosis.^{7,38} These eating plans emphasize vegetables low in carbohydrate, fat from plant and animal foods, and protein from meat, poultry, fish, shellfish, eggs, cheese, plant-based sources like tofu and tempeh, and nuts. They avoid starchy and sugary foods such as pasta, rice, potatoes, bread, couscous, barley, polenta, cereal, crackers, and sweets. Popular LCDs include the South Beach and the Zone Diets.^{39,40} A meta-analysis of 9 studies showed significant weight loss in patients with type 2 diabetes on LCDs (less than 130g/day of carbohydrate) compared to control groups over long durations, and greater weight loss than control diets (typically low fat diets) at 6 months but not statistically greater at 12 months, possibly due to declining adherence over time.^{41,42} LCDs are associated with an increase in serum HDL-cholesterol and a decrease in fasting triglycerides when compared to low fat eating patterns.^{7,36} In an analysis of nine studies of dietary patterns each using a <130 g/day from three months to two years, triglycerides were reduced and HDL was increased. LDL and total cholesterol changes were not statistically significant.⁴¹ Kirkpatrick analyzed eight meta-analyses of studies involving LCD and VLCKD in overweight or obese patients with prediabetes or type 2 diabetes and found a reduction in triglyceride levels, but no consistent changes in HDL, LDL, or total cholesterol though this was thought to be likely due to low adherence in all but one of the studies included.⁴³ Fechner's meta-analysis compared the effects of varying degrees of carbohydrate reduction in LCDs on metabolic markers. Though only four of 37 included trials involved those with type 2 diabetes, the authors found that the degree of carbohydrate restriction was proportional to triglyceride reduction.⁴⁴

In meta-analyses, there is a significant A1c reduction in people adhering to LCD compared to a high carb (fat restricted) diet with 2 years of follow-up.^{36,45} However, the A1c reduction appears to be due to the studies with carbohydrate restriction to less than 26% of energy, so this may not be generalizable.⁴⁵ LCDs are associated with greater reductions in the number and dose of diabetes medications compared to other diets.^{45,46}

Very Low Carbohydrate Ketogenic Diets (VLCKDs)

Ketogenic diets adapted for weight management and general wellness differ from those used to treat epilepsy. Although there is no standardized definition, these eating patterns are typically characterized by reducing dietary carbohydrates to 20–50 g per day but sometimes are defined for study purposes as <26% of daily calories.^{7,47} This goal is based on the level of carbohydrate reduction required to produce ketosis, which is typically <50 g/day.⁴⁸ Many of these eating plans consist of an induction phase and most do not advocate for calorie restriction, based on the premise that the higher protein and fat in the diet, and potentially the circulating ketones, promote satiety.^{48–50} In research and clinical practice, ketosis can be measured as BHB in blood on fingerstick or acetoacetate in urine.⁵¹ Ketone meters are available to monitor for home use and have also been used to follow adherence in studies.^{52,53}

These eating patterns have been shown in meta-analysis to cause greater A1c reduction and weight loss than diets without carbohydrate restriction at 3 and 6 months, but this advantage is no longer seen at 12 months.⁴⁵ VLCKDs have shown superior weight loss to other eating plans in some studies^{54,55} and no difference in others.^{56,57} Guldbrand's study compared a low fat diet to a VLCKD and weight loss was similar for the two groups (LFD -3.99 ± 4.1 kg; LCD -4.31 ± 3.6 kg).⁵⁸

Lipid profile changes induced by LCDs can occur in a relatively short time. Additionally, Choi's meta-analysis found that the VLCKD has cardiovascular disease risk reducing effects in patients with diabetes and obesity or overweight, with serum HDL significantly increased and serum triglycerides decreased in those on VLCKD.⁵⁹ Similarly, Westman's 6-month trial showed that VLCKD reduced triglycerides and increased HDL, with improvements significantly more than those seen with LFD.⁶⁰

VLCKDs have an immediate impact on glycemic control. Over 3–6 month study periods, Yancy, Saslow, and Westman demonstrated HbA1c improvements in patients on VLCKDs compared to other dietary interventions.^{34,61,62} The success of longer-term interventions has been more modest, but also more difficult to interpret as adherence wanes over time and most studies relied on dietary recall and self-reporting to monitor adherence.

Medication reductions are a prominent benefit of very low carbohydrate eating patterns. A majority of patients in three to six month VLCKD studies by Yancy and Westman were able to either eliminate or reduce their diabetes medications.^{34,62} Though HbA1c reductions were often modest in studies more than a year in duration, many of these studies still demonstrated significant reductions in insulin and diabetes medication requirements, and it is likely that medication reduction blunted the A1c response.^{53,54,63,64}

Diabetes remission has been defined as achieving an HbA1c of 6.5% or less in the context of either complete medication cessation or cessation of all medications except metformin.⁶⁵ A systematic review and meta-analysis of studies comparing LCDs to other diets or control arms by Goldenberg identified studies that reported on diabetes remission rates at 6 months (8 studies) and 12 months (3 studies). When complete medication independence was not factored in, LCDs achieved greater remission compared to controls at 6 months (an additional 32 per 100 subjects) and more modest remission rates at 12 months (an additional 10 per 100 subjects). When complete medication cessation was used as the definition for diabetes remission, rates were reduced and results were no longer statistically significant. Subgroup analyses showed more significant remission rates at six months among patients on non-insulin agents.⁴²

Dietary Adherence Methods and Results in Low Carbohydrate Diet Trials

Adherence is defined by the World Health Organization as “the extent to which a person’s behavior – taking medication, following a diet and/or executing lifestyle changes – corresponds with agreed recommendations from a health care provider”.⁶⁶ Assessing dietary adherence remains a challenge due to inconsistencies in how it is measured in studies. One common method is self-reporting using tools such as food records, food frequency questionnaires, or 24-hour dietary recalls. Other measurements include biomarkers, attendance at counseling sessions, and completion rates of the study intervention.

Dietary Recall

Though dietary recall is commonly used to assess adherence in LCD studies, the validity of self-reported food diaries is widely debated. Kipnis compared biomarkers with dietary recall using Food Frequency Questionnaires and showed that relying on dietary recall can dramatically underestimate intake.⁶⁷ It is not surprising that underreporting is common given that food records are reactive by nature, 24h dietary recall relies on memory, and food frequency questionnaires have a finite list of foods. In addition to this, a societal stigma against obesity often creates a social desirability bias that potentially exacerbates underreporting. Still, self-reported data can be useful in understanding food behaviors and eating patterns beyond the information provided by biomarkers alone.⁶⁸

Some of the studies already reviewed relied on dietary records to assess adherence. Guldbrand’s randomized two-year intervention compared a LFD to VLCKD (Table 1). Diet records were conducted during three consecutive days including one weekend day at 3, 6, 12, and 24 months, and participants were given dedicated scales to weigh foods. During the first 6 months, adherence to their respective diet was similar between the groups based on mean macronutrient intake, with an increase in energy from fat in the LCD group. The study was unable to conclude that VLCKD caused greater weight reduction. This finding differs from many other studies, but the authors also noted that they used fewer resources to achieve adherence.⁵⁸ Iqbal’s randomized two year study of patients with obesity and type 2 diabetes compared an LCD of <30g/day with an LFD. Participants were given educational nutrition sessions carbohydrate counting applications to help maintain their target intake, which was estimated using 24-hour recall. These were group sessions conducted as frequently as weekly in the first month and then gradually decreased to monthly for the study duration. Despite these interventions, adherence was low based on these metrics. Additionally, the VLCKD group had a 60% attrition rate and participants in both groups appeared to consume similar diets with moderate restriction in carbohydrates at the study’s conclusion.⁶⁹ Hu’s clinical trial compared a VLCKD with a LFD (<30% fat, <7% saturated fat) over 12-months (Table 1). Overall adherence was measured using a composite score composed of attendance at counselling sessions, deviation from nutrient goals, and urinary ketone presence. Four weekly one-on-one dietician sessions were held in the first month, followed by 10 group sessions every other week for 5 months and 6 monthly group sessions thereafter. Attendance between groups did not vary significantly with over 50% participating. The study also had a relatively low attrition rate of 21% in the VLCKD group. However, composite scores for adherence were similar between the groups. A

Table 1 Summary of Trials on Adherence to LCKD in Patients with Type 2 Diabetes

Study	Year	Trial Design	Study Duration	Arm	Goal Macronutrient Intake	Dietary Records	Actual Reported Macronutrient Intake at Study Conclusion	Educational Sessions	Attendance at Counseling Session	Attrition	Biomarker Results
Guldbrand	2012	Randomized trial	2 years	VLCKD (n=30)	1800kcal for men; 1600 kcal for women with 50% of energy from fat, 20% energy from carbohydrates and 30% energy from protein.	Obtained at baseline, 2, 3, 6, and 12 months. Records conducted during three consecutive days including one weekend day and the participants were provided with dedicated scales and notebooks to weigh and record all food items consumed during these periods (no food frequency questionnaires)	1251 ± 425 kcal; 31% from carbohydrates; 44% from fat; 24% from protein	Group meetings about which food items to choose given at baseline, at 2, 6 and 12 months by physicians; no individual sessions with nutritionist		4 did not attend sessions and expressed difficulty with adherence; 10 did not complete study	significant reduction in A1c from baseline at 6 months but not at study conclusion
				Low-fat diet (n=31)	1800kcal for men; 1600 kcal for women with 30% energy from fat (< 10% from saturated fat), 55–60% of energy from carbohydrates and 10–15% energy from protein.		1458±451 kcal; 47% from carbohydrates; 31% from fat; 20% from protein			3 did not attend sessions and expressed difficulty with adherence; 4 did not complete study	
Iqbal	2010	Randomized trial	2 years	VLCKD (n=70)	<30g carbohydrates per day	24 hour self reported dietary intake at baseline and 6, 12, and 24 months	Self-reported caloric intake did not differ significantly between groups at any time. At month 24, participants in the low-carbohydrate and low-fat groups reduced their caloric intake over time by 397 and 571 cal, respectively. Macronutrient intake did not differ significantly between groups at any point.	Both diet groups were invited to attend separate weekly 2h nutrition classes for the first month then every 4 weeks for the study duration. Sessions included up to 10 participants and were led by a registered dietitian with expertise in weight-loss counseling. Information was presented by lecture and handouts during the first 30min of the session, followed by reinforcement of concepts using interactive games and quizzes.	Participants attended a mean (s.d.) of 9.9 (9.5) sessions, with a mode of three sessions and a median of six sessions (interquartile range 4–12).	60% did not complete study	At month 6, the low-carbohydrate group had a clinically significant reduction in HbA1c of –0.5% (compared to –0.1% in the low-fat condition), but this was not sustained over time
				Low-fat diet (n=74)	(≤30% of calories from fat with a deficit of 500 kcal/day)					46% did not complete study	

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Table I (Continued).

Study	Year	Trial Design	Study Duration	Arm	Goal Macronutrient Intake	Dietary Records	Actual Reported Macronutrient Intake at Study Conclusion	Educational Sessions	Attendance at Counseling Session	Attrition	Biomarker Results
Tay	2017	Randomized trial	2 years	VLCKD (n=58)	Diet plans were individualized and energy-matched, with moderate (~30%) (500–1000 kcal/day deficit). 14% energy as carbohydrate (< 50 g per day), 28% as protein, 58% as fat (<10% saturated fat)	Foods were listed in a semi-quantitative food record that participants completed daily	1707 kcal/day with a mean of 19% daily energy from carbohydrates; 25% from protein; 50% from fat	During the first 12 weeks, participants were provided with 30% of total energy requirement in key foods. Participants met individually with a dietitian for diet instruction and support every 2 weeks for 12 weeks and monthly thereafter	Exercise session attendance was similar between the two groups	44% did not complete the study	initial 3 fold increase in plasma beta hydroxybutyrate with levels decreasing back to baseline over time. VLCKD group also had greater increases in 24 hour urinary urea/creatinine excretion ratio throughout the study period
				Low-fat, high-carbohydrate, low-glycaemic index diet (n = 57)	Diet plans were individualized and energy-matched, with moderate (~30%) (500–1000kcal/day deficit) 53% as CHO, 17% as protein, 30% as fat (<10% saturated fat); (processed carbohydrates and high glycaemic index foods were discouraged.		1757 kcal/day with a mean of 48% from carbohydrates; 18% from protein; 27% from fat			51% did not complete the study	

Yancy	2004	Randomized trial	6 months	VLCKD (n=59)	<20g carbohydrates per day	24-hour recall of food intake at baseline and take-home food records (5 consecutive days + weekend) twice monthly for 3 months, then monthly for 3 months	1461.0 ± 325.7 kcal; 8% from carbohydrates (8% of daily intake), 68% from fat; 26% from protein	Group meetings took place at an outpatient research clinic twice monthly for 3 months, then monthly for 3 months. These 1hr meetings consisted of diet instruction, supportive counseling, questionnaires, and biomedical measurements		24% did not complete the study	86% of VLCKD had trace or greater urinary ketones at 2 weeks and decreased to 42% at 24 weeks. 64% of VLCKD had moderate or greater ketones and decreased to 18% at 24 weeks. VLCKD had statistically greater changes in TG, HDL, and ratio of TG to HDL.
				Low-fat diet (n=60)	<30% energy from fat, <200 mg of cholesterol daily, and deficit of 500–1000 kcal/d		1502.0 ± 162.1 kcal; 52% from carbohydrates, 29% from fat, 19% from protein			43% did not complete the study	
Westman	2008	Randomized trial	6 months	VLCKD (n=48)	<20g carbohydrates per day	Food records (5 consecutive days, including a weekend) at baseline and weeks 4, 12, and 24	1550 ± 440 kcal; 13% from carbohydrates, 59% from fat, 28% from protein	Group meetings took place every week for 3 months, then every other week for 3 months. These consisted of physician review of BP and BG medications if applicable.		56% did not complete the study	Mean change in HbA1c for LCKD group was –1.5%, significantly more than LGID with HbA1c change of –0.5%.
				Low glycemic index diet (n=49)	55% of daily energy intake from carbohydrate with –500 kcal less than calculated energy intake for weight maintenance		1335 ± 372 kcal per day; 44% from carbohydrates, 36% from fat, 20% from protein			37% did not complete the study	

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Table I (Continued).

Study	Year	Trial Design	Study Duration	Arm	Goal Macronutrient Intake	Dietary Records	Actual Reported Macronutrient Intake at Study Conclusion	Educational Sessions	Attendance at Counseling Session	Attrition	Biomarker Results
Hu	2016	Randomized trial	12 months	VLCKD (n=75)	<40g carbohydrates per day	Two 24h dietary recalls, one on a week day and the other on a weekend day, were obtained from each participant by a certified dietician at 0, 3, 6, and 12 months	73.9%, 59.7%, and 44.8% met carbohydrate goals at 3, 6, and 12 months. Those who did not had mean deviations of 145% (representing a carbohydrate intake of approximately 98 g d ⁻¹), 104% (82 g d ⁻¹) and 198% (119 g d ⁻¹), respectively	20 regular dietary counselling sessions including four weekly individual sessions for the first month followed by 10 group sessions every other week for 5 months and 6 monthly group sessions after.	There was no significant difference in attendance between groups. 56.7% of VLCKD and 52.3% of low-fat diet group attended counselling sessions.	21% did not complete the study	VLCKD group had higher cumulative percentage urine ketones at 3, 6, and 12 months compared to low-fat diet group. This was associated with greater reductions in body weight and percent fat mass and increase in percent lean mass. No associations were identified in the low-fat group.
				Low-fat diet (n=73)	Total fat <30% of daily energy and saturated fat <7% of daily energy		59.4% and 42.2% of individuals met total and saturated fat goals at 3 months, 64.8% and 33.3% did at 6 months and 55.6% and 27.8% did at 12 months, respectively. Those who consumed more than the goal had mean deviations of 19.1% (representing an intake of about 35.7% of daily energy from total fat) and 40.6% (9.8% saturated fat) at 3 months, 17.4% (35.2% total fat) and 39.8% (9.8% saturated fat) at 6 months and 23.3% (37.0% total fat) and 46.2% (10.2% saturated fat) at 12 months, respectively			18% did not complete the study	

Saslow	2017	Randomized trial	12 months	VLCKD (n=16)	Carbohydrate intake reduced over 7–10 days to between 20–50 grams of carbohydrates a day, not including fiber, with the goal of achieving nutritional ketosis as measured by blood beta-hydroxybutyrate level 0.5–3 mM twice a week at home. Protein intake prior to the study was maintained and the rest of the calories were derived from fat.	Food intake was assessed with an online 24- hour food recall questionnaire. Timing of questionnaire administration not reported.	1693.7 kcal; 57.8g from carbohydrates; 24.2% of daily calorie intake from protein; 58.0% of dietary intake from fat	Participants attended 19 classes over 12 months including twelve 2-hour classes that met weekly initially and gradually tapered to 1.5-h every 2 months. One hour was devoted to instruction on the assigned diet, with three classes also discussing the importance of sleep and exercise. Each class session included a break with snacks appropriate to the assigned diet. Participants were encouraged to change their diet gradually; ideally, by the fourth class, participants were to have changed all of their meals to be in alignment with the new recommendations. Those on VLCKD were given a goal of B-OH between 0.5 and 3 mmol measured twice weekly at home. Half of each two-hour class in both groups was focused on learning skills to support behavior change and diet maintenance.	Not reported	14/16 (87.5%); similar between groups	HbA1c in VLCKD group improved from baseline 6.6% to 6.0% and 6.1% at 6 and 12 months, respectively. HbA1c in MCCR group improved from 6.9% at baseline to 6.7% at 6 and 12m. Body weight (kg) decreased 7 kg (from 99.9 kg to 92.0 kg) in VLCKD group compared to a decrease of 2 kg (from 97.5 to 95.8 kg) in MCCR group at 12m. With regards to lipids, TG improved from 102.6 to 92.7 mg/dL in VLCKD vs an increase from 158.9 to 173.4 mg/dL in MCCR group. Changes in HDL were not significant.
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Table 1 (Continued).

Study	Year	Trial Design	Study Duration	Arm	Goal Macronutrient Intake	Dietary Records	Actual Reported Macronutrient Intake at Study Conclusion	Educational Sessions	Attendance at Counseling Session	Attrition	Biomarker Results
				Medium carbohydrate, low fat, calorie restricted, carbohydrate counting diet (n=18)	45–50% of calories from carbohydrates; carbohydrates counted using 15 grams as a unit. Most participants were asked to eat 3 carbohydrate units per meal and 1 per snack, or 165 grams of carbohydrates a day. Protein intake was kept the same as before the study and fat consumption was lowered. Participants ate 500 fewer kilocalories (kcal) per day than their calculated maintenance needs based on their age, weight, height, and physical activity level, using the formula from the Institute of Medicine Dietary Reference Guidelines		1380.8 kcal per day; 138.5 g carbohydrates; 20.5% from protein; 35.1% from fat			15/18 (83.3%); similar between groups	There was no statistically significant change in blood glucose.

Mayer	2014	Randomized trial	48 weeks	VLCKD (n=22)	Daily carbohydrate intake limited to less than 20 g, but calories were not restricted. Carbohydrate intake was slowly liberalized if participants approached their goal weight or cravings threatened adherence.	Diet adherence was measured using 4-day food records (including 2 weekend days) at baseline and weeks 2, 12, 24, 36, and 48	Mean daily carbohydrate intake was 75.9 g, total fat 103.2 g, and energy 1707.9 kcal/day	Small group meetings (6 to 12 participants) every 2 weeks for 24 weeks, then every 4 weeks for 24 weeks. Meetings lasted 1 to 2 hours and consisted of study measurements followed by group counseling that were parallel between the 2 interventions but specific to diet.	Not reported	50% of patients did not have food records at the end of the study period	Fasting glucose declined from mean 152.6 to 133.7 (p=0.2)
				Low Fat Diet + Orlistat (n=24)	Daily intake of fat limited to <30% energy, saturated fat to <10% energy, cholesterol to <300mg, and calories (500–1000 kcal deficit). Orlistat 120mg was taken three times per day.		Mean daily carbohydrate intake was 155.8 g, total fat 55.5 g, and energy 1419.6 kcal/day			50% of patients did not have food records at the end of the study period	Fasting glucose declined from mean 149.0 to 146.8
Davis	2009	Randomized trial	12 months	VLCKD (n=55)	Initially 20–25 g of carbohydrate x 2 weeks. As weight reduced, carbohydrate intake was increased at 5 g per week.	Single-day 24h recall by in-person interviews were obtained at baseline, 6, and 12 months. At 3 months, food diaries were reviewed for the day prior.	1642 ± 600 kcal; 33% of calories from carbohydrates; 44% from fat, 23% from protein	All received 45 min dietary instruction of registered dietician and were given a specific gram allowance of carbohydrates or fat to achieve a 1-pound weight loss each week. They also had a total of six scheduled, 30-min visits with the dietician for additional counseling over 12 months. Participants also had study visits 1–2x weekly for the 1st month followed by every 6 weeks in addition to this to review dietary adherence and adjust medications.	Not reported	No difference between arms. 8 withdrew.	Decreased adherence noted based on macronutrient intake over 12 months. Weight reduction was the same in both groups at 1 year. There was no significant differences in A1c or lipids at 1 year.
				Low-fat diet (n=50)	Fat intake <25% of energy needs, based on baseline weight.		1810 ± 590 kcal; 50% of calories from carbohydrates; 31% from fat, 19% from protein			6 withdrew.	

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Table 1 (Continued).

Study	Year	Trial Design	Study Duration	Arm	Goal Macronutrient Intake	Dietary Records	Actual Reported Macronutrient Intake at Study Conclusion	Educational Sessions	Attendance at Counseling Session	Attrition	Biomarker Results
Yancy	2020	Randomized trial	48 weeks	VLCKD weight management (n= 127)	<20–30 g of carbohydrate/d initially followed by an increase in carbohydrates based on individual	Food records were collected at baseline and every 16 weeks by 3-day food records.	Not reported.	Every 2 weeks x 16 weeks followed by every 8 weeks thereafter. More comprehensive classes including low-carbohydrate nutrition, physical activity, and weight management counseling, as well as dietician-led nutritional counseling.	60.6% of VLCKD weight management group and 55.2% of medication intensification arm attended at least 75% of counseling sessions.	14.2% did not complete HbA1c measurements at study conclusion.	VLCKD group was noninferior but not superior compared to medication intensification group. VLCKD group had greater mean reduction in A1c at 16 weeks but not at 48 weeks.
				Medication intensification arm (n=136)	Not specified.		Not reported.	Every 4 weeks x 16 weeks followed by every 8 weeks thereafter. Nurse-led classes focused on DM management.		14% did not complete HbA1c measurements at study conclusion.	

Goldstein	2011	Randomized trial	52 weeks	VLCKD weight management (n= 26)	25gm of carbohydrate/d for first 6 weeks followed by max 40gm of carbohydrate/d	3-day records obtained at 1.5, 3, 6, and 12 months.	1725 ± 600 kcal; 85 gm ± 35 from carbohydrates; 111 gm ± 45 from fat; 102 gm ± 37 from protein	Weekly nutritional counseling during initial 12 weeks followed by monthly for a total of 25 sessions.	There was a small non-significant advantage in the ATK group with regards to keeping dietician appointments over the first 3 months (p=0.27).	20 participants in each group persisted for 6 months in their respective diets. 46% of VLCKD did not complete 1 year f/u.	Poor adherence in the VLCKD was observed after the initial 6 weeks, with mean carbohydrate intake more than double the goal at 3, 6, and 12 months. Only 7% of participants in VLCKD group had ketogenic effect of diet apparent at 12 months, from 61% at 6 weeks. There was no statistically significant difference in weight loss between the trial groups over the 12 month period. There was a statistically significant decrease in HbA1c level in both groups at 1 year, with no significant between-group differences.
				American Diabetes Assn (ADA) diet (n=26)	Calorie-restricted with 10–20% of daily energy intake from protein and the other 80% divided between fats, carbohydrates, and 35 gm of fiber. Men were allowed up to 1500 kcal/day and women 1200 kcal/day.		1937 ± 376 kcal; 208 gm ± 61 from carbohydrates; 85 gm ± 24 from fat; 90 gm ± 12 from protein			38% did not complete the 1 year follow up	

one-interquartile-range increase in composite score suggested better adherence to VLCKD and was associated with greater weight loss and improved body composition with increased lean mass. Indicators of adherence in the LFD were not associated with weight loss.⁷⁰

The results of these studies demonstrate the challenges of dietary adherence and of measuring adherence with dietary recall.

Biomarkers

Other studies have used a combination of biomarkers with self-reporting to address these limitations. Tay assessed dietary intake using daily weighed food records with software to calculate average quarterly nutrient intake between VLCKD and LFD (Table 1). Biomarkers were used to confirm adherence: protein intake was measured using 24-hour urinary urea to creatinine ratio and carbohydrate reduction by using monthly plasma BHB concentrations. Plasma BHB concentrations and the ratio of urinary urea to creatinine excretion increased and remained higher over the 52-week period than with the high carbohydrate diet, consistent with lower carbohydrate and higher protein intake in LCD patients. In addition to individualized dietary plans, this study involved one-on-one sessions with a dietician for dietary instruction and support every 2 weeks for the first 12 weeks and monthly thereafter. The use of individualized dietary sessions may have played a part in the high adherence rate noted.⁷¹ Yancy's unblinded study compared VLCKD versus orlistat plus LFD (Table 1). As participants approached their goal weight or if cravings threatened dietary adherence, 5g of carbohydrates were added to their daily intake each week until weight was maintained or cravings diminished.⁵⁵ Dietary adherence was measured using urinary ketones in combination with 4-day food records at baseline and at 2, 12, 24, 36, and 48 weeks. The proportion of VLCKD participants with urinary ketones present (≥ 5 mg/dL [≥ 0.9 mmol/L]) at two weeks was 72%. This declined to a low of 13% at 48 weeks; the decline could have been due to decreased adherence, increased carbohydrate intake for weight maintenance or increased use of ketones for energy leading to lower urinary levels. Participants had one-hour group meetings for dietary instruction and counseling twice monthly for 3 months then monthly for 3 months. The frequency of these sessions may have contributed to the relatively low attrition rate of 24% in the VLCKD group.⁶³

Similarly, Goldstein's study comparing a VLCKD with the calorie restricted ADA diet used urinary ketones measured at 6 weeks and 3, 6, and 12 months to compliment the information obtained by 3 day dietary recall. The authors noted that mean carbohydrate intake at 3, 6 and 12 months was more than double the goal. This correlated with urinary ketone elevation in 61% of the VLCKD diet at 6 week after diet initiation, but in only 7% at the conclusion of the study 12 months later (Goldstein et al, 2011).

Westman's study randomized individuals with obesity and type 2 diabetes to either a VLCKD or a low-glycemic, reduced calorie diet (500 kcal/day deficit from weight maintenance diet) (Table 1). Adherence to diet and exercise was measured using a combination of self-report, food records, and urinary ketones. All participants completed food records (on 5 consecutive days, including a weekend) at baseline and at weeks 4, 12, and 24. Though group rather than individual meetings were held, these were conducted as frequently as weekly for 3 months and included a physician. After that, regular meetings were held every other week for 3 months. Though only 58% of participants completed the study, both groups had good adherence based on self reported dietary intake and interventions led to improvements in hemoglobin A_{1c}, fasting glucose, fasting insulin, and weight loss, though the VLCKD group had greater improvements in hemoglobin A_{1c}, body weight, and HDL.³⁷

Challenges Affecting LCD Adherence in Patients with Diabetes

Cultural Barriers

Although it is well-established that genetics influences the development and degree of complications associated with type 2 diabetes, it is also known that behavioral factors including diet and physical activity are directly associated with diabetes diagnosis and progression. Dietary habits are shaped early in life and are influenced by an individual's knowledge and experiences which are often shaped by their culture.⁷² Today, there is increased recognition for the impact of culture on health.⁷³ Culture refers to shared values, beliefs and social behaviors that collectively shape a

group's identity and interaction in and with their environment.⁷³ When prescribing diabetes management plans, it is important that clinicians are sensitive to their patients' cultural traditions so that counseling and interventions are appropriate and more likely to have meaningful outcomes.⁷⁴

East Asian diets are typically white rice-based with less consumption of whole grains and fat. Excess consumption of white rice has been associated with higher risk of type 2 diabetes due to its⁷⁵ high glycemic index and load, leading to postprandial blood glucose excursions and hyperinsulinemia.⁷⁶ Zhao et al recently analyzed gender difference in dietary energy of Chinese adults and found that the intake of carbohydrates was 282.4g/day in males and 242 g/day in females, respectively.⁷⁷ Data from the 2013–2015 Korean National Health and Nutrition Examination Survey found that a significant part of the population exceeded recommended ranges of carbohydrates. A higher carbohydrate diet was associated with lower intake of energy and saturated fats, including more grains and fruit but less meat, fish, eggs, beans, and dairy.⁷⁸ Noodles are often used as the main ingredient in Korean meals and are additionally noted to have high glycemic loads and are usually eaten in larger than recommend serving sizes.⁷⁹ Similarly, a typical Thai meal involves many complementary dishes, which are served together with rice.⁸⁰ The importance of rice is reflected by one of the most common greetings, “kin khaao reuu yang?” (Have you consumed rice yet?).⁸¹

Traditional South Asian diets are often high in starchy foods such as potatoes, flatbread (roti and chapati), rice and fried snacks.^{82,83} The STARCH study, a cross-sectional multicenter survey of 796 patients, demonstrated carbohydrates made up over 60% of energy intake for Indian patients with T2DM.⁸⁴ Due to globalization, industrialization and socioeconomic changes, dietary patterns in South Asia have generally shifted to consumption of high fat, less nutrient-dense foods with increased intake of sugar and dairy, particularly among urban and higher income rural dwellers.⁸⁵ Both the traditional eating patterns and modern eating patterns can make adherence to dietary patterns difficult in South Asian countries. This is of particular importance given that South Asians develop type 2 diabetes at younger ages and at lower BMI and have increased rates of complications.⁸² A systematic review noted that for individuals of South Asian descent, food plays a key role in maintaining relationships. This often resulted in⁷⁴ social pressure to not adhere to diabetic diets when at social events.⁷⁴

Traditional Hispanic diets among Dominican, Mexican and Puerto Rican communities include staples such as rice, beans and tortillas.⁸⁶ As seen in other cultures, migration is associated with changes in dietary habits. Mexican Americans are one of the largest growing minority groups in the USA. Higher acculturation among adults of Mexican descent living in the USA has been associated with lower intake of the healthy foods in a traditional Mexican diet, including fruits, vegetables, legumes, and whole grains. Instead, adoption of a Western diet is common, which is usually low in fruits and vegetables and high in refined grains and added sugar.^{87–89} The 2017–2018 prevalence of diagnosed diabetes in adults aged 18 years or older living in the US was highest among people of Hispanic origin (12.5%), and non-Hispanic blacks (11.7%). Among adults of Hispanic origin, Mexicans (14.4%) and Puerto Ricans (12.4%) had the highest prevalence, followed by Central/South Americans (8.3%) and Cubans (6.5%) (Prevalence of Diagnosed Diabetes | Diabetes | CDC).

In the US, non-Hispanic blacks (NHBs) are comprised of heterogeneous groups including those from African and Caribbean ancestry. Despite differences in ethnicity, both groups of NHBs in the US are more likely to be diagnosed with diabetes and experience higher rates of complications and mortality compared to their Caucasian counterparts.⁹⁰ Eating patterns of NHBs are shaped by historical factors such as the transatlantic slave trade, and the common social belief that “more shapely” body types are deemed more desirable compared to other cultures' value of “ideal thinness”.⁹¹ Traditional African America cuisine, often referred to as “soul food” includes starchy vegetables and legumes (black-eyed peas, pinto beans, lima beans), grains (rice, grits, cornbread, biscuits), a variety of green leafy vegetables (collards, mustard and turnip greens) in addition to meats that are often breaded and fried. It is not uncommon to see combinations of foods such as rice paired with black eyed peas (“hopping john”) or red beans and rice. It is also common to see smoked meats added to vegetables to increase flavor.⁸⁶ A common theme of qualitative and ethnographic studies investigating eating practices of African Americans is the importance of taste and concerns that healthier options did not taste as satisfying as traditional foods.^{92–95} Social events with more attendees usually translated to more traditional cultural foods being present and increased the likelihood of choosing less healthy options and overeating.⁹²

Because of vast similarities in culture such as religion and language, the Middle Eastern and North African (MENA) Region are often grouped together when describing health outcomes. Traditionally, this region's diet was felt to be one of the healthiest as it is the basis of the well-studied "Mediterranean diet" that is high in vegetable proteins, fibers, minerals and vitamins. The cultural emphasis on these foods makes it challenging for patients to adhere to ketogenic diets. The authors of the Goldstein study noted difficulty involved in prescribing the Atkins diet over an extended period in the Mediterranean area, where fruit and vegetable intake is high. Patients were able to avoid eating "pure carbohydrates" (bread, rice, etc.), but continued to consume vegetables and dairy products.⁹⁶ Over the past few decades,⁹⁷ many countries in this region continue to experience a socioeconomic transition due to urbanization, and this has impacted nutritional choices. There has been a shift away from tradition to a diet heavier in processed foods,⁹⁸ sugar sweetened beverages, and often lacking in vegetables, fruits, and whole grains.⁹⁹ Mean energy intake in most countries in this region is higher than the global average, with Turkey and Yemen ranking among the highest.⁹⁸ In countries like Saudi Arabia, female gender is believed to be a barrier to optimal diabetes management due to limitations of health education. Women also have lower levels of physical activity compared to men due to time-consuming domestic responsibilities as well as a lack of culturally appropriate outdoor facilities.¹⁰⁰

Traditional Italian cuisine is that of the Mediterranean diet, including controlled quantities of fats, a low percentage of carbohydrates, a low glycemic index and a high content in dietary fiber.¹⁰¹ Pasta, traditionally an Italian dish, has expanded to many countries and has become a major dietary source of energy globally. Somewhat counterintuitively, several studies have found the glycemic index of pasta to be low to moderate compared to other starchy foods such as white bread and potatoes. Cross sectional analysis demonstrated that higher pasta intake was associated with better adherence to the Mediterranean diet.¹⁰² However, over the years there has been a decrease in adherence to the Mediterranean dietary pattern. This is thought to be secondary to several factors, including changes in socio-cultural, intergenerational, and economic factors, such as increased income. Poor adherence is also believed to be a consequence of the evolving female gender role, different organization of working hours, urbanization and globalization.¹⁰³

Religious Barriers

Similar to cultural traditions, dietary patterns and adherence to specific diets can be influenced by religion. For example, studies have shown a short-term increase in caloric intake with corresponding weight increase and an increase in glycemic and lipid markers due to Christmas festivities.¹⁰⁴

Several recent publications have shown that the nutritional changes observed during Ramadan are associated with unhealthy dietary changes. During observance, individuals will consume a predawn meal, to obtain requirements of water, carbohydrates and energy needed for daytime hours. This meal varies slightly by region but typically consists of bread/cereal, couscous, eggs, cheese, and/or rice. The sunset meal that breaks the fast can average up to 150 g of carbohydrates and over 1200 kcal and usually includes dates, meat or cheese pastries and rice.^{105,106} This is traditionally followed by an additional meal eaten a few hours later or nocturnal grazing.¹⁰⁶ One food survey of 340 Moroccan households found significant increases in energy intake, carbohydrate intake, sucrose intake, sodium intake, and calcium intake and a significant decrease in protein and lipid intake. Carbohydrates increased from 312 g/day before Ramadan to 360 g/day during Ramadan. This was possibly due to increased consumption of cereal products, which are popular in this period. An atmosphere of festive solidarity and family grouping is also thought to contribute to the changes in dietary habits.¹⁰⁷

Yom Kippur (Jewish Day of Atonement) is considered the holiest day of the Jewish calendar and is one of two times of the year that people of Jewish faith abstain from food and water for 25 hours (from sunset on day 1 to one hour after sunset the following day). The other day long fast is Tish B'Av, also known as Ninth of Av, but there are 4 additional periods of potential fasting of shorter duration within the Jewish faith.¹⁰⁸

The religious group Seventh-day Adventists promotes vegetarianism, which may be advantageous as several studies have shown that vegetarianism is associated with lower prevalence of type 2 diabetes.¹⁰⁹ However, the diet of Seventh-day Adventists is characterized by a large intake of carbohydrates in the form of fruits and vegetables, as well as high content of fatty acids, dietary fiber, folic acid, vitamin C, vitamin E and Mg.¹¹⁰ Vegetarianism is also practiced in Hinduism and Buddhism.^{111,112} Though dietary practices vary, the traditional diets of Hindu families include

carbohydrates as a staple, usually rice and or chapatis (form of bread).¹¹³ Lin et al investigated vegetarian practices of Hindus and Buddhist in Malaysia and found that rice was a major dietary staple and was consumed daily by majority of participants. Other carbohydrates consumed included porridge, rice noodles and bread. Buddhism participants consumed higher daily intake of carbs compared to Hindu ones with a carbohydrate intake of 67.7% of total energy intake and 63.55%, respectively.¹¹⁴

Economic Barriers

People of lower socioeconomic status often face unique challenges in adhering to planned dietary changes. One barrier unique to people with lower economic security is food insecurity – the disruption of food intake or eating patterns due to the cost of food items exceeding an individual's or family's financial circumstances.¹¹⁵ Food insecurity is associated with a higher hemoglobin A1c.¹¹⁶ Low carbohydrate eating patterns are potentially more expensive than higher carbohydrate plans, although one study regarded the potential increased cost as negligible.^{117,118} This could potentially limit access (or perceived access) to this eating pattern for people with inadequate financial resources.

Patient Preference

A potential component of adherence that is difficult to quantify is patient buy in. In studies of low carbohydrate dietary interventions, randomized trials such as those by Guldbrand and Iqbal,^{58,69} tend to have poorer rates of adherence than non-randomized trials such as those by Hussein and Hallberg.^{35,53} In a 24-week study by Hussain in which obese participants chose between a VLCKD and a low-calorie diet, participants with diabetes who chose a VLCKD lost 12% of their body weight, whereas those who chose a low-calorie eating plan lost 7%.³⁵ In a year-long intervention, Hallberg found that patients with type 2 diabetes on a VLCKD experienced a 12% mean weight loss and 17% reduction in hemoglobin A1c. Health coaches monitored ketones and adjusted diet as needed to achieve ketosis. Participants received education either on-site or via web-based recorded content and also received remote care from health coaches. The study had a very low attrition rate of 16.8% from the VLCKD group.⁵³ Two-year follow-up showed more modest improvements in glycemic control with HbA1c reductions of 0.6–0.9% observed in those on VLCKDs, which may be in part due to the higher attrition rate over longer observation periods.^{64,119,120} This suggests that there may be an element of patient “buy-in” to the dietary strategy that promotes adherence.

Potential Solutions

Overcoming barriers to dietary adherence in patients with diabetes is critical to reducing disease burden and preventing its progression. Objective self-monitoring of carbohydrate intake can help maintain dietary adherence. Validated examples include the use of home biomarkers such as urinary ketone levels and blood or breath ketone meters.^{121–123} Urbain et al examined serum and urine ketones during the 6th week of a VLCKD. Urine ketones were measured using over-the-counter reagent strips that determined the presence of acetoacetate. The levels of blood and urine ketone bodies correlated throughout the 24-hour period. The best time for urine testing for ketosis was early morning and several hours after dinner.⁵¹ Hand-held ketone sensors using a fingerstick obtained capillary blood sample accurately measure BHB in starvation-induced ketonemia when compared with the gold standard, venous whole blood by an enzymatic laboratory reference method.¹²⁴ More affordable meters have also shown good correlation. Moore compared the Precision Xtra meter with the more affordable Meter 2- Keto-Mojo in a double-blind cross-over study. Ketone and glucose levels were measured before and twice after ingesting racemic ketone, natural ketone, or maltodextrin supplement. Both meters had excellent agreement between each other for measuring ketone measurement, including the more affordable Meter 2.¹²⁵

In office monitoring of other biochemical markers is also helpful. As described above, significant improvements in blood glucose, HbA1c, HDL cholesterol and triglyceride levels are consistently noted in those who following a VLCKD and therefore could be used as markers of adherence. Weight loss and improvements in blood pressure have also been noted but are less specific to an LCD.

Accuracy issues notwithstanding, another potential tool to improve adherence may be through self-monitoring of food intake, eg, using a food diary. Burke's systematic review of self-monitoring in weight management found significant associations between monitoring frequency and weight loss consistently in the 15 studies assessing dietary self-

monitoring. However, the level of evidence was weak due to methodologic limitations.¹²⁶ Though a food diary has the limitations previously discussed, when used as the sole tool for assessing adherence, it may play a role in improving the mindfulness of the types and amounts of foods consumed, thereby indirectly helping adherence.

Educational interventions may also be a means of improving adherence. In a Swedish study, an educational course on carbohydrate restricted diet (75 g/day or less) and corresponding insulin dose reduction was used to enhance adherence among patients with type 1 diabetes over four years. After 2 years, about 50% achieved stable lowering of HbA1c.¹²⁷ In addition, continuous care models integrating telemedicine are a novel approach that has been effective at guiding nutritional ketosis and assisting with adherence.¹²⁰

Future Research Directions

Research has identified multiple methods to measure and improve dietary adherence to LCD. Given the bias associated with self-reported dietary intake, studies comparing various objective measures of dietary adherence are needed to determine the optimal metric. More research is also needed to better understand the potential role for weight loss medications as adjunct therapy to assist adherence to an LCD, as well as the myriad of cultural, psychological, and economic factors that play a role in adherence. Additionally, the long-term effects of VLCKD on biochemical parameters requires further investigation to help individualize therapy.

Disclosure

Dr William S Yancy Jr reports personal fees from [dietdoctor.com](https://www.dietdoctor.com). The authors report no other conflicts of interest in this work.

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