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# Management of Type 1 Diabetes With a Very Low-Carbohydrate Diet

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### **Abstract**

**OBJECTIVES:** To evaluate glycemic control among children and adults with type 1 diabetes mellitus (T1DM) who consume a very low-carbohydrate diet (VLCD).

**METHODS:** We conducted an online survey of an international social media group for people with T1DM who follow a VLCD. Respondents included adults and parents of children with T1DM. We assessed current hemoglobin A1c (HbA1c) (primary measure), change in HbA1c after the self-reported beginning of the VLCD, total daily insulin dose, and adverse events. We obtained confirmatory data from diabetes care providers and medical records.

RESULTS: Of 316 respondents, 131 (42%) were parents of children with T1DM, and 57% were of female sex. Suggestive evidence of T1DM (based on a 3-tier scoring system in which researchers took into consideration age and weight at diagnosis, pancreatic autoimmunity, insulin requirement, and clinical presentation) was obtained for 273 (86%) respondents. The mean age at diagnosis was  $16 \pm 14$  years, the duration of diabetes was  $11 \pm 13$  years, and the time following a VLCD was  $2.2 \pm 3.9$  years. Participants had a mean daily carbohydrate intake of  $36 \pm 15$  g. Reported mean HbA1c was  $5.67\% \pm 0.66\%$ . Only 7 (2%) respondents reported diabetes-related hospitalizations in the past year, including 4 (1%) for ketoacidosis and 2 (1%) for hypoglycemia.

**CONCLUSIONS:** Exceptional glycemic control of T1DM with low rates of adverse events was reported by a community of children and adults who consume a VLCD. The generalizability of these findings requires further studies, including high-quality randomized controlled trials.

#### Abbreviations:

ADA — American Diabetes Association

CGM — continuous glucose monitor

DKA — diabetic ketoacidosis

HbA1c — hemoglobin A1c

HDLc — high-density lipoprotein cholesterol

LDLc — low-density lipoprotein cholesterol

MODY — maturity onset diabetes of the young

SDS — standard deviation score

TG — triglycerides

T1DM — type 1 diabetes mellitus

VLCD — very low-carbohydrate diet

#### What's Known on This Subject:

Despite pharmacological and technological advances, optimal glycemic control of type 1 diabetes remains elusive, putting millions of people worldwide at increased risk of micro- and macrovascular complications. One conceptually promising but poorly studied approach is dietary carbohydrate restriction.

### What This Study Adds:

Exceptional glycemic control of type 1 diabetes without high rates of acute complications may be achievable among children and adults with a very low-carbohydrate diet. However, the generalizability of these findings and long-term safety of carbohydrate restriction remain unknown.

Before the discovery of insulin, the lives of children with type 1 diabetes mellitus (T1DM) were extended, sometimes for years, by severe carbohydrate restriction. After the advent of insulin treatment, the recommended carbohydrate intake was increased without clinical trial proof of superiority. By the 1980s, a low-fat diet containing up to 60% of energy from carbohydrates became

the standard of care. More recently, the American Diabetes Association (ADA) has emphasized the individualization of diet rather than focusing on macronutrients.<sup>3</sup>

Despite major medical and technological advances, the management of T1DM remains suboptimal. With an average overall hemoglobin A1c (HbA1c) of 8.2%, only 20% of children and 30% of adults achieve the glycemic targets of HbA1c <7% for adults and <7.5% for children as set forth by the ADA to reduce long-term complications. The greatest challenge in this regard involves difficulty controlling postprandial glycemia, which is a major determinant of HbA1c.<sup>5</sup> Even with modern insulin analogs and technical advances, a mismatch between carbohydrate absorption and insulin action typically exists after meals. Beyond a point, measures to lower postprandial hyperglycemia inevitably increase risk for hypoglycemia, with potentially life-threatening consequences.6-9

The source and amount of carbohydrates consumed affect postprandial hyperglycemia and glycemic variability more than any other dietary factor, 3,10-12 providing a conceptual basis for interest in carbohydrate-modified diets for T1DM. Regarding carbohydrate source, a diet with a low versus high glycemic index can be used to reduce HbA1c moderately (by  $\sim 0.5\%$ ). <sup>13</sup> Case series and pilot studies reveal more substantial improvements in HbA1c and other benefits (less hypoglycemia and reduced glycemic variability) with a very low-carbohydrate diet (VLCD). 14-21 Although varying to some degree among studies, a VLCD is typically defined as  $\leq 20$  to 50 g per day of carbohydrates or  $\leq 5\%$  to 10% carbohydrates as a proportion of calories.  $^{22-24}$  In T1DM, small sample sizes and methodological issues limit the significance of VLCD benefits, and little is known about prevalence, practice, and sustainability. In the absence of larger studies in pragmatic settings, a VLCD is generally discouraged out of concern for potential diabetic ketoacidosis (DKA), hypoglycemia, dyslipidemia, nutrient deficiency, growth failure in children, and sustainability, 25,26 Our aim in this study was to characterize glycemic control and acute adverse events among children and adults who have adopted this approach for the long-term self-management of T1DM.

### Methods

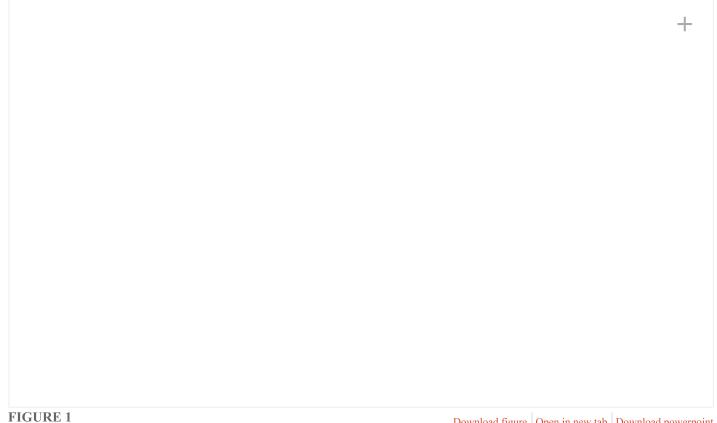
#### Design

Using an online survey, we collected primary data from respondents and confirmatory medical information from a secondary survey of health care providers or a review of medical records. Our goals were to (1) establish that adult respondents and children for whom an adult respondent completed the survey (both henceforth referred to as participants) were formally and accurately diagnosed with T1DM, (2) characterize glycemic control (ie, HbA1c, total daily insulin dose, average blood glucose concentrations and SD as measured by a continuous glucose monitor [CGM] or glucose meter), (3) determine adverse event rates (eg, DKA, hypoglycemia, diabetes-related hospitalizations and emergency department visits), (4) assess anthropometrics (eg, weight, height, and BMI) and metabolic health parameters (eg, serum lipids), (5) compare longitudinal changes in glycemic control (pre- to post-VLCD), and (6) characterize participants' satisfaction with their diabetes management and relationship with the health care system. The study was approved by the Boston Children's Hospital Institutional Review Board and is registered at www.clinicaltrials.gov (identifier NCT02839174). Electronic consent was obtained from the respondents.

#### **Participants and Enrollment**

A volunteer sample was recruited from TypeOneGrit, an online Facebook community for people with T1DM who follow a VLCD and diabetes management method as recommended in the book Dr Bernstein's Diabetes Solution. 20,27 This method comprises a VLCD with weight-based carbohydrate prescription of up to 30 g per day derived from fibrous vegetables and nuts with a low glycemic index. High-protein foods with associated fat are substituted for carbohydrates and adjusted on the basis of outcomes, including glycemic control and weight. Participants adhere to a structured meal plan and adjust bolus insulin empirically according to postprandial glycemia. Basal insulin is adjusted according to fasting glycemia. The group was established in April 2014, with ~1900 members at the time of the survey.

We used an eligibility survey of community members between September 2016 and November 2016. Members aged ≥18 years were eligible if they or a child in their care satisfied these 3 self-reported criteria: having T1DM, receiving insulin therapy, and consuming a carbohydrate-restricted diet for at least 3 months. Women who were pregnant or breastfeeding were excluded. Of 493 eligibility survey responses, 414 (84%) individuals were eligible to participate and 316 (76%) provided sufficient information to be included in the study (Fig 1). With respondent permission, we contacted 182 providers; 97 (53%) completed the full or short provider survey. Of 238 participants who agreed to provide medical records, 101 records were received. Primary data acquisition continued until January 2017. Confirmatory medical information was collected until March 2017.



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Enrollment. <sup>a</sup> The primary end point, current HbA1c, was available in the appropriate time frame (at least 3 months after starting the VLCD) for 300 participants. Data from all 316 eligible participants are included in the other analyses.

#### **Data Collection and Categorization**

When possible, survey questions were modified from the T1D Exchange Clinic Registry

(https://tldexchange.org/pages/resources/our-data/studies-with-data)<sup>28</sup> and covered several domains: (1) diabetes diagnosis and treatment, (2) diet, (3) insulin regimen, (4) other diabetes-related care, (5) glycemic control, (6) diabetes complications, (7) general health and health care, (8) interactions between the patient and the diabetes care provider, and (9) sociodemographic data. Survey instruments are avalable at https://osf.io/d6wrj/. Respondents were asked to provide consent so that their or their children's primary diabetes care providers could be contacted or to provide confirmatory medical records themselves. Data were collected and managed by using research electronic data capture (version 7.3.5; Vanderbilt University, Nashville, TN) tools hosted at Boston Children's Hospital.<sup>29</sup>

### **Ascertainment of T1DM Diagnosis**

We created a 3-tiered scoring system to ascertain T1DM diagnosis with varying levels of confidence using participant-reported and confirmatory medical information. Participants were classified as having diagnostic evidence of T1DM if they had a diabetes diagnosis at age <20 years, a nonobese body weight (BMI <30 in adults or BMI standard deviation score [SDS] <1.645 [~95th percentile] in children), and positive diabetes antibody test results. A classification of strong evidence was assigned to participants with a diabetes diagnosis at age <10 years; a diagnosis between ages  $\geq$ 10 and <20 years, immediate insulin requirement, and a nonobese body weight; or a diagnosis between ages  $\geq 20$  and  $\leq 40$  years, immediate insulin requirement, positive diabetes antibody test results, and a nonobese body weight. A classification of suggestive evidence was assigned to participants with a diagnosis at ages ≥20 and <40 years, immediate insulin requirement, a nonobese body weight, and 1 additional factor (including low C-peptide level at diagnosis, physician-specified diagnosis of T1DM, or other evidence [abrupt onset with consistent symptoms, history of DKA, or negative genetic test results for maturity onset diabetes of the young (MODY)]); or diagnosis at age >40 years, immediate insulin requirement, a nonobese body weight, and positive diabetes antibody test results or 1 of the aforementioned additional factors.

#### Statistical Analysis

Analyses were performed by using SAS version 9.3 (SAS Institute, Inc, Cary, NC). Statistical significance was defined as P < .01, which is a conservative threshold chosen to take into account multiple secondary outcomes. Exact P values are reported. To assess agreement among data sources, we performed Lin's concordance correlation between patient-provider pairs of each clinical measurement. The following statistical comparisons were made according to an a priori analysis plan. Comparisons between participants were made by independent sample t test or  $\chi^2$  test for participants with versus without confirmatory medical information and adults versus children. A within-subject, paired, 2-tailed t test was used for pre- and postdiet data and height SDS comparison. Multiple comparisons for diagnostic evidence groups were made by analysis of variance. We performed a linear regression of current, self-reported HbA1c on age, years with diabetes, years on VLCD, carbohydrate intake goal, educational status, and income class.

Post hoc analyses were performed with Pearson's correlation between pediatric height SDS and carbohydrate intake and by Wilcoxon signed-rank test and McNemar's test to compare participant- and provider-satisfaction data.

### Results

#### **Participants**

Descriptive characteristics are listed in Table 1. Most participants were from the United States, Canada, Europe, or Australia; 57% were of female sex, 42% were children, 88% were white and non-Hispanic, and 84% of all respondents (adults or parents of children with T1DM) completed college or the equivalent. The mean age at diabetes diagnosis was  $16 \pm 14$  years, the duration of diabetes was  $11 \pm 13$  years, and the time following a VLCD was  $2.2 \pm 3.9$  years.

TABLE 1 View inline

Participant-Reported Descriptive Characteristics

#### Validation of Participant-Reported Data

Confirmatory medical information (from providers and/or medical records) was available for 148 (47%) participants (Fig 1, Supplemental Table 4). Participant- and provider-reported data revealed good agreement for relevant clinical variables. Participants with and without confirmatory medical information did not differ (Supplemental Table 5). Therefore, only participant-reported information is reported below.

#### Ascertainment of T1DM

At least suggestive evidence for T1DM was reported by participants or providers in 273 (86%) patients, at least strong evidence was reported in 238 (75%) patients, and diagnostic evidence was reported in 85 (27%) patients. Evidence was unavailable for 36 (10%) patients, and 7 (2%) did not meet criteria only because of obesity (Table 1). Apart from expected differences related to the scoring system (eg., age, age at diagnosis, and obesity), participants with and without supportive evidence of T1DM did not differ (Supplemental Table 6). Therefore, data for all participants regardless of evidence category are presented together.

#### **Clinical Outcomes**

Participants reported a mean daily carbohydrate intake of  $36 \pm 15$  g (n = 223). The mean participant-reported current HbA1c was  $5.67\% \pm 0.66\%$  among the 300 participants who provided this information in the acceptable time frame (Table 2, Fig 2), and 97% of participants achieved the ADA glycemic targets. The participant-reported change in HbA1c from pre- to post-VLCD was  $-1.45\% \pm 1.04\%$  (n = 127; P < .001). Of the 137 respondents who reported CGM mean blood glucose values and the 115 who reported CGM blood glucose SD, average blood glucose was  $104 \pm 16$  mg/dL and SD was  $28 \pm 12$  mg/dL. In the regression analysis, a priori covariates explained little of the variation in HbA1c ( $r^2 = 0.06$ ). Carbohydrate intake goal was the only significant predictor (F = 10.4; P = .001), with an increase in HbA1c of 0.1% per 10 g of carbohydrate consumed (Supplemental Table 9). The mean daily insulin dose was  $0.40 \pm 0.19$  U/kg per day.

**TABLE 2** View inline

Participant-Reported Clinical Variables

FIGURE 2

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HbA1c distribution. The adult (light gray) and pediatric (dark gray) age groups are shown (n = 300).

Participant-reported rates of adverse events were low, and many declined after the initiation of a VLCD (Supplemental Table 7). Of 300 participants, 7 (2%) reported hospitalizations in the past 12 months (14 separate occurrences; 0.05 hospitalizations per person per year), 4 (1%) had 4 (0.01 per person per year) hospitalizations for DKA, and 6 (2%) had 9 hospitalizations (0.03 per person per year) for other reasons. Symptomatic hypoglycemia within the past month was reported by 205 (69%) participants, with the majority (112; 55%) having few (1–5) episodes per month. Likewise, rates of severe hypoglycemia were low, with 7 (2%) reporting hypoglycemia with seizure or coma and 11 (4%) requiring glucagon in the past year. Conventional chronic disease risk factors revealed a mixed profile, with low triglycerides (TG) and elevated high-density lipoprotein cholesterol (HDLc) but high total and low-density lipoprotein cholesterol (LDLc) (Table 2).

### Pediatric Age Group and Growth

Children, compared with adults, had similar participant-reported HbA1c and other clinical parameters (Supplemental Table 8). Participant- and provider-reported height SDSs were  $0.26 \pm 1.21$  (n = 107; 82% of children) and  $0.25 \pm 1.00$  (n = 49; 37%), respectively. There was no correlation of height SDS with carbohydrate intake goal (r = 0.15; P = .20) or diet duration (r = 0.14; P = .20)= .16). Provider-reported, current height SDS compared with height SDS at diagnosis was  $0.20 \pm 1.02$  vs  $0.41 \pm 1.27$  (P = .05) among the small subset of children for whom data were available (n = 34; 26%). Of the interval of 2.3 ± 2.0 years since diagnosis, these children had followed a VLCD for  $1.2 \pm 0.8$  years.

#### **Health and Health Care Satisfaction**

Participants reported high levels of overall health and satisfaction with diabetes management but not with their professional diabetes care (Table 3), and 27% did not discuss their adherence to a VLCD with their diabetes care providers. Of those who did discuss their diet, only 49% agreed or strongly agreed that their diabetes care providers were supportive. Narrative explanations by participants for not discussing their diet included disagreement on treatment goals and approach, perceived provider disinterest or unfamiliarity with a VLCD, a desire to avoid conflicts with the provider, and (for parents) fear of being accused of child abuse. Participating providers corroborated the overall health ratings and reported even greater satisfaction with diabetes control compared with participants (Z -4.09; P < .001). The therapeutic relationship was perceived as very good or excellent by 82% of providers. Interestingly, providers perceived themselves as more supportive of the VLCD compared with participant perception (Z -2.69; P.007).

TABLE 3 View inline

Participant- and Provider-Reported Health, Satisfaction With Diabetes Control and Care

# Discussion

In this survey of children and adults who follow a VLCD for the long-term treatment of T1DM, we observed measures of glycemic control in the near-normal range, low rates of hypoglycemia and other adverse events, and generally high levels of satisfaction with health and diabetes control. These findings are without precedent among people with T1DM, revealing a novel approach to the prevention of long-term diabetes complications.

Researchers in the Diabetes Control and Complications Trial achieved an average HbA1c of 7.2% in the intensively treated group but with increased rates of hypoglycemia. <sup>6,7,30</sup> In a recent survey of 3 international pediatric registries, an HbA1c < 7% was not associated with higher rates of hypoglycemia.<sup>31</sup> Nevertheless, targeting a near-normal HbA1c is generally not recommended because of concern for hypoglycemia. The participants in our survey had an average HbA1c in the normal range and low rates of hypoglycemia compared with those in other surveys. 32,33 Likewise, hospitalizations for DKA or all diabetes-related causes compared favorably with prevailing rates.<sup>32–34</sup>

The effect of a VLCD on cardiovascular disease risk has been subject to debate. Consistent with the known effects of low carbohydrate and (presumed) associated higher saturated fat intakes, participants had low TG and high HDLc and LDLc levels. The remarkably low ratio of TG to HDLc of 1:1, together with the low total daily insulin requirement, indicate high insulin sensitivity and good cardiometabolic health. 35 In contrast, total LDLc is considered a conventional cardiovascular risk factor. However, total LDLc elevation on a VLCD (associated with low TG) may reflect large, buoyant lipoprotein particles, which is a relatively low-risk subtype. 36 Furthermore, in the Diabetes Control and Complications Trial cohort of 1441 adolescents and young adults, HbA1c had the largest effects on cardiovascular risk, followed by TG and LDLc.<sup>37</sup> Postprandial hyperglycemia has been proposed as an independent cardiovascular disease risk factor<sup>38</sup> for which a VLCD would plausibly provide benefit. Another major cardiovascular risk factor, BMI, was significantly below population averages for study participants, possibly reflecting another benefit of a VLCD.39

Children generally did as well as adults, which is a promising finding in view of the adverse effects of diabetes-related hyper- and hypoglycemia on brain development 40,41 and growth. 42-46 The commonly reported growth deceleration in T1DM is generally ascribed to poor glycemic control. 42-46 Concerns have also been raised that a VLCD or chronic ketosis may adversely affect growth and pubertal development.<sup>25</sup> Although pubertal development was not assessed in this survey, we obtained children's height data from parents and medical providers. Participant-reported, current mean height was modestly above average for age and sex (SDS 0.26). Provider-reported data were used to corroborate this finding and also revealed a marginal decrease in height SDS since diabetes diagnosis. This possible growth deceleration may have preceded or occurred during the diet and is comparable in magnitude to the previously described decreases in height SDS in T1DM. Taken together, these data do not reveal an adverse effect of a VLCD on growth, but additional research into this possibility is warranted.

Although participants reported high levels of satisfaction with health and diabetes control, relationships with diabetes care providers were often fraught. A minority of participants did not disclose their adherence to a VLCD to their providers, citing concerns for being criticized, pressured to change behavior, or accused of child abuse. This distrust may increase the risk for a catastrophic adverse event if patients feel unable to seek medical support at times of need (eg, impending DKA) and instead make diabetes management decisions beyond their competencies. Notably, most providers described the therapeutic relationship as very good or excellent and perceived themselves as more supportive of a VLCD than how they were described by the participants. This discrepancy warrants follow-up in qualitative research.

Strengths of this study include verification of self-reported information by independent sources (diabetes care providers and medical records), a rigorous approach to establish T1DM diagnosis, and the pragmatic setting. Our study has 3 main limitations. First, we cannot prove that all participants had T1DM. However, we found no important discrepancies between those who did and did not have diagnostic evidence (eg, childhood onset, diabetes antibodies, and nonobese body weight). Second, the generalizability of the findings is unknown. We cannot determine how many of the members of the online group are active, have T1DM (versus being health care providers, family members, or others with general interest), and would be eligible to participate in the study. In addition, children and adults adhering to a VLCD and remaining in this online community may represent a special subpopulation with high levels of motivation and other health-related behaviors (eg, physical activity), presenting another source of selection bias. Therefore, the study sample may not be representative of all people with T1DM in the social media group and may differ from the general T1DM population in ways that could influence the safety, effectiveness, and practicality of a VLCD. Third, we did not obtain detailed information on participants' diet and other components of this diabetes management approach, nor did we assess factors contributing to glycemic control before the self-reported start of the VLCD.

# Conclusions

We suggest that a VLCD may allow for exceptional control of T1DM without increased risk of adverse events. This possibility is mechanistically plausible because of the dominant effects of dietary carbohydrates on postprandial glycemia and the lower insulin doses required with a VLCD. The results, if confirmed in clinical trials, indicate that the chronic complications of T1DM might be prevented by diet. In light of study limitations, these findings by themselves should not be interpreted as sufficient to justify a change in diabetes management. Additional research is needed to determine the degree of carbohydrate restriction (and other

dietary aspects) necessary to achieve these benefits, optimal insulin regimen to accompany a VLCD (specifically, with regard to avoiding severe hypoglycemia), safety and efficacy (in randomized controlled trials). If this work is a success, trials to evaluate effectiveness in preventing long-term diabetes complications should be conducted.

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### **Footnotes**

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**POTENTIAL CONFLICT OF INTEREST:** Dr Bernstein reported receiving royalties for books on the management of diabetes (which were used by members of the online social media group surveyed in this study). Dr Hallberg reported stock options and research support from Virta Health, a company that provides health care services for type 2 diabetes, and consulting fees from Atkins. Dr Rhodes is the site principal investigator in clinical trials for pediatric type 2 diabetes that are sponsored by Merck and AstraZeneca. Dr. Westman has ownership interest in companies using low-carbohydrate principles, and he receives royalties for books related to low-carbohydrate diets. Dr Ludwig reported receiving royalties from books on nutrition and obesity; the other authors have indicated they have no potential conflicts of interest to disclose.

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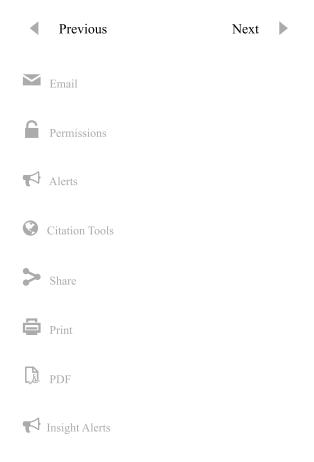
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