Supplemental Information

METHODS

Surveys

A link to a participant survey (adult or pediatric version) was displayed and sent by e-mail, with up to 3 reminders provided over a 3-month period .

Demographics

Age, years with T1DM, and years on the diet were calculated on the basis of reported dates in relation to the survey date. Current age and age at diagnosis were also collected and used when dates were not reported. Highest educational attainment was categorized as primary (primary school or less), secondary (secondary school, including high school), postsecondary (intermediate between secondary and university [eg, some college and technical training]), or tertiary (completed college, university, graduate school, or equivalent). Participants were asked to self-identify their income category as lower, middle, or upper and report the subspecialty of their diabetes care providers. Race and ethnicity were self-identified.

Diabetes Diagnosis

Participants were asked whether they started insulin immediately after diagnosis, had positive diabetes antibody test results or low C-peptide levels around the time of diagnosis, or were told by a physician that they that had T1DM. If all answers were negative, they were prompted to provide a free-text answer: "Why do you think you have T1DM?" An analogous question to the provider asked about immediate insulin requirement, diabetes antibody

results, and C-peptide levels at diagnosis. Height and weight at diagnosis or suspicion for other types of diabetes was ascertained from providers or medical records only.

Diet

Participants who indicated a specific goal for total daily carbohydrate intake (n = 223; 71%) were asked to specify this goal and the number of days in the last week it was achieved.

Clinical Variables

HbA1c values at diagnosis, values before beginning the diet, current values, and the 2 most recent values before the current value; current lipid panels; and blood glucose meter and CGM averages were obtained from each participant and provider or extracted from the medical record. For recent HbA1c, the mean of the most recent HbA1c levels before the current value (up to 2 values) was calculated. Insulin daily dose was reported by the participant. Participants who did not know their insulin daily dose were prompted to provide 3-day pump review data (or basal insulin and average bolus doses for meals and snacks if not using a pump) for dose calculation.

Complications

Annual rates of diabetes-related hospitalizations, diabetes-related emergency encounters, severe hypoglycemia with seizure or coma, and hypoglycemia treated with glucagon were assessed for the 12 months before beginning the VLCD and for the most recent 12 months. Hypoglycemia requiring help by others was assessed only for adults because children generally require help by others. For participants

who had followed the VLCD for <12 months, annualized rates were extrapolated. Episodes of symptomatic hypoglycemia were assessed for the last month.

Health Care and Satisfaction

Likert scales were used to rate overall health, satisfaction with diabetes control, satisfaction with professional diabetes care, and perceived provider support of the dietary approach.

Confirmatory Data

For participants who consented to provider involvement, a link to a full provider survey was sent to the identified diabetes care providers, with up to 3 reminders in a 3-month period. On the third contact attempt, providers were offered an abbreviated short provider survey in electronic and paper formats. The paper survey was also mailed to participants to be taken to their next clinical encounter with the identified diabetes care provider. Participants who opted to provide confirmatory medical information themselves were instructed to submit reports of the most recent diabetes care encounter, the last clinical encounter before beginning the VLCD, and the clinical encounter at the time of diabetes diagnosis; and laboratory reports of the 3 most recent HbA1c tests, the last HbA1c test before beginning the VLCD, a HbA1c test at the time of diabetes diagnosis, and the most recent serum lipid test. Participants received up to 3 reminders to provide this information over a 3-month period. All medical records and paper surveys were reviewed by an endocrinologist, and extracted

data were entered in the database. The following information was extracted from the medical record: type of records available (eg, laboratory reports, clinic summaries, and CGM downloads), provider subspecialty, date of diabetes diagnosis, anthropometrics and results of diagnostic testing at the time of diagnosis (eg, fasting, random or 2-hour glucose, HbA1c, diabetes antibodies, and C-peptide levels), information on insulin requirement at diagnosis, any comments relating to the differential diagnoses of type 2 diabetes or MODY, glucometer or CGM averages, ranges and SDs, total daily insulin dose, glucose-lowering medications, reports of DKA or severe hypoglycemia with seizure or coma within the past year, current anthropometrics, and lipid profile results.

Data Cleaning and Categorization

Duplicate survey responses were identified on the basis of repeated e-mail addresses and removed. Participants who provided responses that were discrepant with eligibility criteria were excluded from the analysis. For dates, only the month and year were collected, and the day was set to the 15th of each month. The following data were removed: for current or recent HbA1c and lipid tests, values within 3 months of the start of the VLCD or the diabetes diagnoses; for pre-VLCD, HbA1c values within 3 months of the diabetes diagnosis; and physiologically implausible data.

Because all information was not available for all participants, the number is reported for every variable in the Results section.

Units of Measure

For this international study, data were collected in the local unit system indicated by the respondent (metric, imperial, international system of units, and conventional) and converted to metric and conventional units by using the following conversion factors: height (inches to centimeters – 2.54); weight (pounds to kilograms – 0.45); glucose (millimoles per liter to milligrams per deciliter – 18); total cholesterol, low-density lipoprotein (LDL), and high-density lipoprotein (HDL) (millimoles per liter to milligrams per deciliter – 38.67); and TG (millimoles per liter to milligrams per deciliter – 88.57). HbA1c was converted from millimoles per mole to percent by using the formula HbA1c (%) = $0.09148 \times$ HbA1c (mmol/mol) + 2.152, which was proposed by the International Federation of Clinical Chemistry and Laboratory Medicine for the standardization of HbA1c (http://www.ngsp.org/ifccngsp.asp).

Dyslipidemia was defined as having HDLc values <35 mg/dL, total cholesterol >200 mg/dL, LDLc >130 mg/dL, or TG >150 mg/dL. This definition has been used by researchers in large epidemiologic studies and allows for comparison across studies.[47,48]

Anthropometric Data

Because absolute weight and height change rapidly throughout childhood, age- and sex-specific BMI and height

SDS were calculated on the basis of the self-reported or medical record heights and weights according to World Health Organization references. Computations were performed by using the publicly available SPSS (version 23.0; IBM SPSS Statistics, IBM Corporation) syntax files (http://www.who.int/childgrowth/software/igrowup_SPSS.zip?ua=1) for children up to the age of 5 years and the World Health Organization 2007 files (http://www.who.int/growthref/tools/WHO2007_spss.zip?ua=1) for children aged 6 to 18 years.

For BMI SDS, female sex was used as the default if sex was not reported. Height SDS for participants >18 years of age was calculated by using the World Health Organization standard for age 19 years, assuming no relevant height attainment after that age.

Precision

For the prespecified primary outcome of current HbA1c, we estimated a precision of 0.045 in a sample of 500 participants, assuming an SD of 1.0. We obtained HbA1c values in 300 participants with an SD of 0.66, resulting in an attained precision (SE) of 0.038.

SUPPLEMENTAL TABLE 4 Participant- Versus Provider-Reported Clinical Variables ($n = 148$)

Variables	No. Response Pairs	Participant-Reported, Mean ± SD or No. (%)	Provider-Reported, Mean ± SD or No. (%)	Concordance Correlation[a] (95% CI)
BMI adult, kg/m^2	48	24 ± 3	24 ± 3	0.95 (0.92–0.97)
BMI SDS pediatric	51	0.46 ± 0.82	0.56 ± 0.82	0.61 (0.42–0.75)
HbA1c current	129	5.57% ± 0.59%	5.59% ± 0.59%	0.88 (0.84–0.92)
HbA1c prediet	45	7.01% ± 0.87%	6.89% ± 0.87%	0.90 (0.82–0.94)
HbA1c diagnosis	51	10.60% ± 2.45%	10.40% ± 2.45%	0.87 (0.78–0.92)
Age diagnosed, y	113	15 ± 13	15 ± 13	0.98 (0.98–0.99)
Insulin daily dose, U/kg per d	76	0.38 ± 0.22	0.40 ± 0.22	0.70 (0.57–0.80)
CGM average, mg/dL[b]	18	105 ± 16.36	106 ± 16.36	0.73 (0.38–0.90)
CGM SD, mg/dL[b]	11	34 ± 15	34 ± 15	0.79 (0.31–0.95)
Total cholesterol, mg/dL[c]	45	233 ± 87	233 ± 87	0.94 (0.90–0.97)
LDLc, mg/dL[c]	46	141 ± 77	134 ± 77	0.83 (0.72–0.91)
HDLc, mg/dL[c]	45	75 ± 23	76 ± 23	0.88 (0.80–0.94)
TG, mg/dL[c]	46	80 ± 44	79 ± 44	0.83 (0.71–0.90)
Hospitalizations for DKA, persons per y	92	1 (1)	1 (1)	—
Hypoglycemia with seizure and/or coma, persons per y	92	1 (1)	1 (1)	—

CI, confidence interval; —, not applicable.

[a] Patient-provider pairs of each clinical measurement characterized with Lin's concordance correlation coefficient and 95% CIs.

[b] Obtained over 20 ± 18 d.

[c] Fasting.

SUPPLEMENTAL TABLE 5 Characteristics and Clinical Variables of Participants With and Without Confirmatory Medical Information

Variables	Medical Information Available		Medical Information Not Available		P
	No. Responses	Finding, Mean ± SD or No. (%)	No. Responses	Finding, Mean ± SD or No. (%)	
Age, y	138	27 ± 18	178	28 ± 18	.47
Diagnostic information					
Age at diagnosis, y	138	15 ± 13	178	18 ± 14	.07
Diabetes antibodies	138	58 (42)	178	76 (43)	.91
Immediate insulin	138	121 (88)	178	159 (89)	.65
Years with T1DM	138	12 ± 13	178	11 ± 12	.37
Diet					
Years on VLCD	138	2.2 ± 3.3	175	2.1 ± 2.6	.67
Carbohydrate intake goal, g	91	33 ± 14	132	37 ± 16	.08
Goal achieved, d per wk	90	6.4 (1.0)	126	6.5 (0.9)	.55
Clinical variables					
HbA1c	132	5.58% ± 0.60%	168	5.74% ± 0.70%	.04[a]
CGM average, mg/dL[b]	68	104 ± 17	69	104 ± 16	.71
CGM SD, mg/dL[b]	61	29 ± 12	54	25 ± 11	.07
Insulin daily dose, U/kg per d	136	0.40 ± 0.20	146	0.41 ± 0.18	.86
Diabetes-related hospitalizations, persons per y	138	2 (1)	163	5 (3)	.35
Diabetes-related emergency encounters, persons per y	138	2 (1)	164	8 (5)	.10
Hospitalizations for DKA, persons per y	137	1 (1)	163	3 (2)	.40
Hypoglycemia with seizure and/or coma, persons per y	138	1 (1)	160	6 (4)	.09
Hypoglycemia requiring help from others, adults per y[c]	68	8 (11)	101	12 (12)	.85
Hypoglycemia requiring glucagon, persons per y	137	4 (3)	162	7 (4)	.52
Total cholesterol, mg/dL[d]	59	236 ± 84	37	225 ± 84	.51
LDLc, mg/dL[d]	61	144 ± 78	36	141 ± 81	.83
HDLc, mg/dL[d]	60	76 ± 23	36	71 ± 17	.25
TG, mg/dL[d]	61	77 ± 40	36	71 ± 29	.38

[a] Not significant after adjusting for covariates (5.62 ± 0.07; 5.76 ± 06; $P = .25$).

[b] Obtained over 20 ± 18 d.

[c] Assessed only in adults (children are assumed to require help).

[d] Fasting.

SUPPLEMENTAL TABLE 6 Characteristics and Clinical Variables by Diagnostic Evidence Group

Variables	No. Responses	Diagnostic (N = 85; 27%), Mean ± SD or No. (%)	No. Responses	Strong (N = 153; 48%), Mean ± SD or No. (%)	No. Responses	Suggestive (N = 38; 12%), Mean ± SD or No. (%)	No. Responses	Unascertained (N = 40; 13%), Mean ± SD or No. (%)	P
Anthropometrics									
Age, y	85	13 ± 11	153	27 ± 17	38	45 ± 11	40	44 ± 14	<.001
Obese	84	4 (5)	129	5 (4)	38	0 (0)	25	7 (28)	<.001
Diagnostic information									
Age at diagnosis, y	85	8 ± 4	153	12 ± 10	38	35 ± 11	40	31 ± 13	<.001
HbA1c diagnosis	64	10.87% ± 2.43%	76	11.62% ± 2.85%	21	11.69% ± 2.77%	12	9.41% ± 2.54%	.03
Diabetes antibodies	85	76 (89)	152	38 (25)	38	12 (32)	37	8 (20)	<.001
Immediate insulin requirement at diagnosis	85	82 (97)	152	143 (94)	38	36 (95)	37	19 (48)	<.001
Low C-peptide level	85	43 (51)	152	37 (24)	38	16 (42)	37	6 (15)	<.001
T1DM per physician	85	83 (98)	152	132 (86)	38	35 (92)	37	22 (55)	<.001
T1DM other criteria	85	0 (0)	152	2 (1)	38	1 (3)	37	10 (25)	<.001
Years with T1DM	85	5 ± 7	152	14 ± 15	38	10 ± 9	38	13 ± 12	<.001
Diet									
Years on VLCD	85	1.7 ± 1.8	152	2.3 ± 3.4	38	3.0 ± 3.5	38	1.9 ± 1.6	.11
Carbohydrate intake goal, g	57	34 ± 12	114	36 ± 15	27	40 ± 21	25	34 ± 11	.31
Carbohydrate intake goal achieved, d per wk	55	6.5 ± 1.1	111	6.4 ± 1.0	27	6.6 ± 0.8	23	6.4 ± 0.8	.64
Clinical variables									
HbA1c	80	5.61% ± 0.62%	147	5.64% ± 0.60%	36	5.67% ± 0.65%	37	5.89% ± 0.91%	.16
CGM average, mg/dL[a]	40	106 ± 17	70	102 ± 13	17	108 ± 25	10	101 ± 11	.45
CGM SD, mg/dL[a]	36	30 ± 11	57	26 ± 11	15	26 ± 15	7	25 ± 11	.36
Insulin daily dose, U/kg per d	85	0.41 ± 0.20	134	0.42 ± 0.19	38	0.34 ± 0.15	25	0.40 ± 0.16	.15
Diabetes-related hospitalizations, persons per y	85	2 (2)	146	3 (2)	38	2 (5)	32	0 (0)	.52
Diabetes-related emergency encounters, persons per y	85	5 (6)	146	5 (3)	38	0 (0)	33	0 (0)	.24
Hospitalizations for DKA, persons per y	85	1 (1)	145	3 (2)	38	0 (0)	32	0 (0)	.67
Hypoglycemia with seizure and/or coma, persons per y	83	0 (0)	145	4 (3)	38	1 (3)	32	2 (6)	.24
Hypoglycemia requiring help, adults per y[b]	20	3 (15)	86	9 (11)	37	4 (11)	31	4 (13)	.94
Hypoglycemia requiring glucagon, persons per y[c]	85	4 (5)	144	5 (4)	38	0 (0)	32	2 (6)	.51
Total cholesterol, mg/dL[c]	12	198 ± 62	59	242 ± 96	16	234 ± 59	9	205 ± 39	.29
LDLc, mg/dL[c]	14	120 ± 57	59	152 ± 90	15	144 ± 66	9	115 ± 35	.38
HDLc, mg/dL[c]	14	71 ± 21	58	74 ± 20	15	77 ± 28	9	78 ± 18	.81
TG, mg/dL[c]	14	75 ± 37	58	77 ± 38	16	69 ± 35	9	71 ± 38	.88

a Obtained over 20 ± 18 d.
b Assessed only in adults (children are assumed to require help).
c Fasting.

SUPPLEMENTAL TABLE 7 HbA1c and Adverse Events Compared With Prediet Reports

Clinical Variables	No. Response Pairs	Current, Mean ± SD or No. (%)	Prediet, Mean ± SD or No. (%)	P
Glycemic control				
HbA1c	127	5.69% ± 0.71%	7.15% ± 1.15%	<.001
Diabetes related hospitalizations, persons per y	300	7 (2)	25 (8)	<.001
DKA		4 (1)	13 (3)	.01
Hypoglycemia		2 (1)	8 (3)	.07
Other		4 (1)	8 (3)	.21
Diabetes-related emergency encounters, persons per y	301	10 (3)	25 (8)	.007
DKA		3 (1)	6 (2)	.45
Hypoglycemia		2 (1)	13 (4)	.001
Other		7 (2)	9 (3)	.75
Hypoglycemia with seizure and/or coma, persons per y	300	7 (2)	11 (4)	.34
Hypoglycemia requiring help from others, adults per y	176	12 (7)	23 (13)	<.001
Hypoglycemia requiring glucagon, persons per y	301	11 (4)	20 (7)	.04

SUPPLEMENTAL TABLE 8 Characteristics and Clinical Variables of the Adult Versus Pediatric Age Groups

Variables	No. Responses	Adult, Mean ± SD or No. (%)	No. Responses	Pediatric, Mean ± SD or No. (%)	P
Age, y	185	41 ± 12	131	9 ± 4	<.001
Diagnostic information					
Age at diagnosis, y	185	23 ± 14	131	6 ± 4	<.001
HbA1c at diagnosis	89	11% ± 3%	84	11% ± 2%	.69
Diabetes antibodies	185	63 (34)	131	71 (54)	<.001
Immediate insulin	185	154 (83)	131	126 (96)	<.001
Years with T1DM	182	17 ± 14	131	2 ± 2	<.001
Diet					
Years on VLCD	185	2.7 ± 3.6	131	1.4 ± 1.2	<.001
Carbohydrate intake goal, g	130	36 ± 16	93	36 ± 14	.91
Carbohydrate intake goal achieved, d per wk	126	6.4 (0.9)	90	6.5 (1.0)	.255
Clinical variables					
HbA1c	176	5.64% ± 0.71%	124	5.71% ± 0.58%	.39
CGM average, mg/dL[a]	79	102 ± 17	58	107 ± 15	.13
CGM SD, mg/dL[a]	64	26 ± 12	51	29 ± 12	.16
Insulin daily dose, U/kg per d	167	0.37 ± 0.14	15	0.46 ± 0.23	<.001
Diabetes-related hospitalizations, persons per y	176	6 (3)	125	1 (1)	.14
Diabetes-related emergency encounters, persons per y	177	3 (2)	125	7 (6)	.06
Hospitalizations for DKA, persons per y	175	4 (2)	125	0 (0)	.09
Hypoglycemia with seizure and/or coma, persons per y	174	5 (3)	124	2 (2)	.48
Hypoglycemia requiring glucagon, persons per y	174	6 (3)	125	5 (4)	.80
Total cholesterol, mg/dL[b]	68	238 ± 87	11	198 ± 52	.08
Total cholesterol ≥200 mg/dL	—	45 (66)	—	2 (18)	—
LDLc, mg/dL[b]	67	148 ± 85	14	124 ± 46	.24
LDLc >130 mg/dL	—	44 (49)	—	6 (43)	—
HDLc, mg/dL[b]	67	76 ± 20	13	65 ± 21	.03
HDLc <35 mg/dL	—	0 (0)	—	0 (0)	—
TG, mg/dL[b]	68	75 ± 38	10	68 ± 33	.90
TG >150 mg/dL	—	4 (6)	—	1 (8)	—
Dyslipidemia (TG >130 mg/dL, LDLc >130 mg/dL, or HDLc <35 mg/dL)	68	45 (66)	14	6 (43)	—

—, not applicable.

[a] Obtained over 20 ± 18 d.

[b] Fasting.

SUPPLEMENTAL TABLE 9 Linear Regression of HbA1c on A Priori Covariates

All Participants (n = 316)	β	F	P
Age	.06	0.36	.55
Years with T1DM	−.10	0.92	.34
Years on diet	−.03	0.13	.73
Carbohydrate intake	.23	10.40	.001
Educational status	.01	0.02	.90
Income class	−.08	1.03	.31

No collinearity observed, variance inflation factor (VIF) <2 for all variables.

SUPPLEMENTAL REFERENCES

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