Supplementary Figures and Tables

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Supplementary Figures

1. Age
2. Gender: Male/ Female
3. Date of birth
4. Country of birth (if born outside of Israel, year of immigration to Israel)
5. Family member's country of birth: mother, father, grandparents
6. Mark the average appetite level you feel during the day and in the morning, noontime and evening (a scale of 5 levels, from very low to very high)
7. Specify the types of foods you do not eat
8. Specify the types of foods you are allergic to
9. Do you have lactose intolerance? If so, is it congenital, primary, secondary
10. Are you on a diet at the moment?
11. How many meals do you consume on average per day?
12. Do you consume dietary supplements? If so, please specify each type of supplement and the frequency in which you consume it (1-2/week, 3-4/week, 5-7/week, 1-3/month, less than 1/month, other)
13. Do you consume probiotic probiotic yogurt? If so, what is the frequency in which you consume it (every day, every week, every month, rarely or never), how many servings? (per day/week/months)
14. How would you define the general health status? Very good/good/ not so well/ not well
15. Were you diagnosed during the last year with any of the following diagnosis? (Iron deficiency anemia, jaundice or other liver or biliary disease, helicobacter pylori infection)
16. Have you ever been diagnosed with medical conditions (apart for T1D)? If so please specify
17. Have you ever had a gastrointestinal surgical procedure or appendectomy?
18. Have you parents ever been diagnosed with medical conditions? If so please specify
19. Have any members of your family been diagnosed with T1D? If so please specify if siblings, parents, cousins or grandparents
20. Were you sick during the last 6 months?
21. Did you consume antibiotics in the last 6 months? If so, when was the last date in which you were treated?
22. When were you diagnosed with T1D?
23. Which type of insulin do you use?
24. Please specify your daily medications. For each medication, please specify the underlying medical condition and the daily dosage
25. Do you have any additional comments regarding your health status?
26. Do you know what your blood type is? If so, please specify
27. What is your delivery mode? (Vaginal delivery, cesarean section, unknown)
28. Where were you born? (Hospital/clinic, home delivery, unknown)
29. Were you breastfed? (yes, no, unknown)
30. For women - when was your last menstrual period? (for girls: did you get your first menstrual period? If so, when was the last menstrual period?
31. How many hours a day do you usually sleep? How many during daytime?
32. Do you suffer from sleep disorders? If so, please specify
33. How do you define your sleep quality? (4 levels from very good to not well)
34. Have you exercised regularly during the last year? If so, in what frequency (1-2/week, 3/week, 4-7/week, 2-3/month, less than 1/month)
35. What is your average daily screen time? (the amount of time spent using a device with a screen such as a smartphone, computer, television, or video game console)
36. What is your stool frequency? (1-2/day, 3-5/day, >5/day, 1-2/ week, 3-4/week, 5-6/week), How would you define your regular bowel habits? (normal, diarrhea, constipation, unknown), is it usually in a constant hour of the day? yes/no
37. Do you suffer from flatulence? (yes- often, yes - occasionally, no, unknown)
38. Do you use any means to alter your bowel movements (e.g. laxatives, enema) ?

Figure S1: Baseline questionnaire. The original survey was distributed in Hebrew. Parents were requests to answer the questions on behalf of their children in cases in which they were not able to answer the questions themselves, and the questions were modified accordingly.

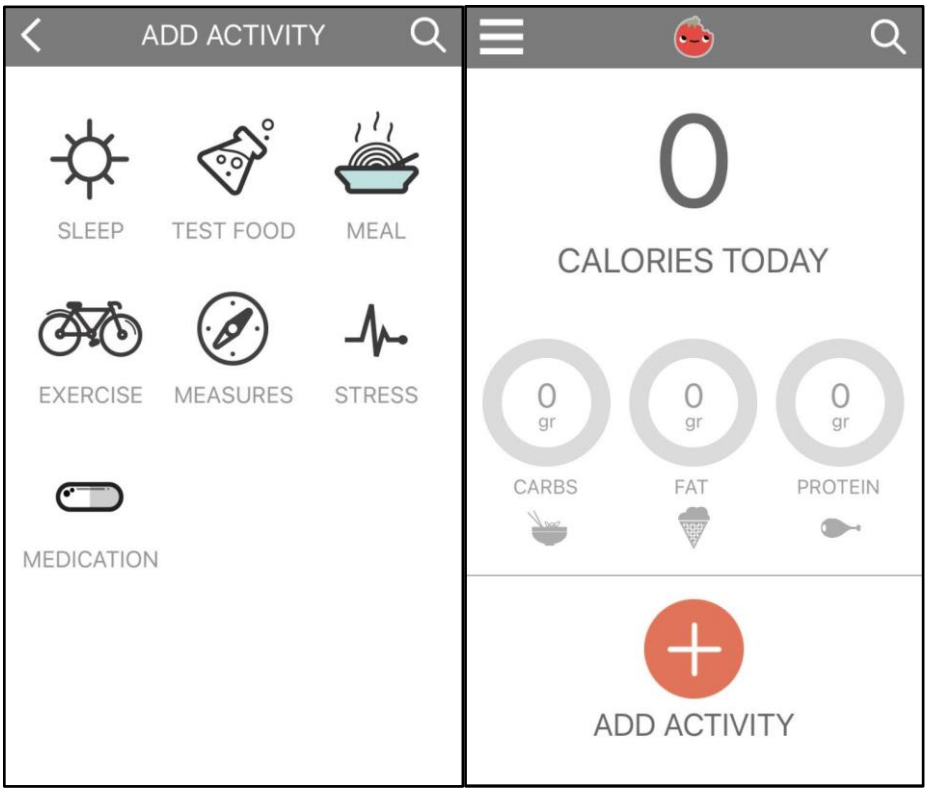

Figure S2: Smartphone App for real time activity logging. Participants were instructed to record in real-time their daily activities during study participation using a proprietary smartphone application that was developed for this purpose and was already used in a previous study. Participants were asked to record, for each meal, exact components and component weights. Meal components were searched against a database of 6,401 foods components. In addition, participants were asked to record the consumption of standardized meals, sleep times, physical activity, stress levels, hunger levels, and drug consumption (with the exception of insulin). Participants were instructed on how to perform correct logging in the App during the initiation meeting and unclarities were personally resolved with each participant.

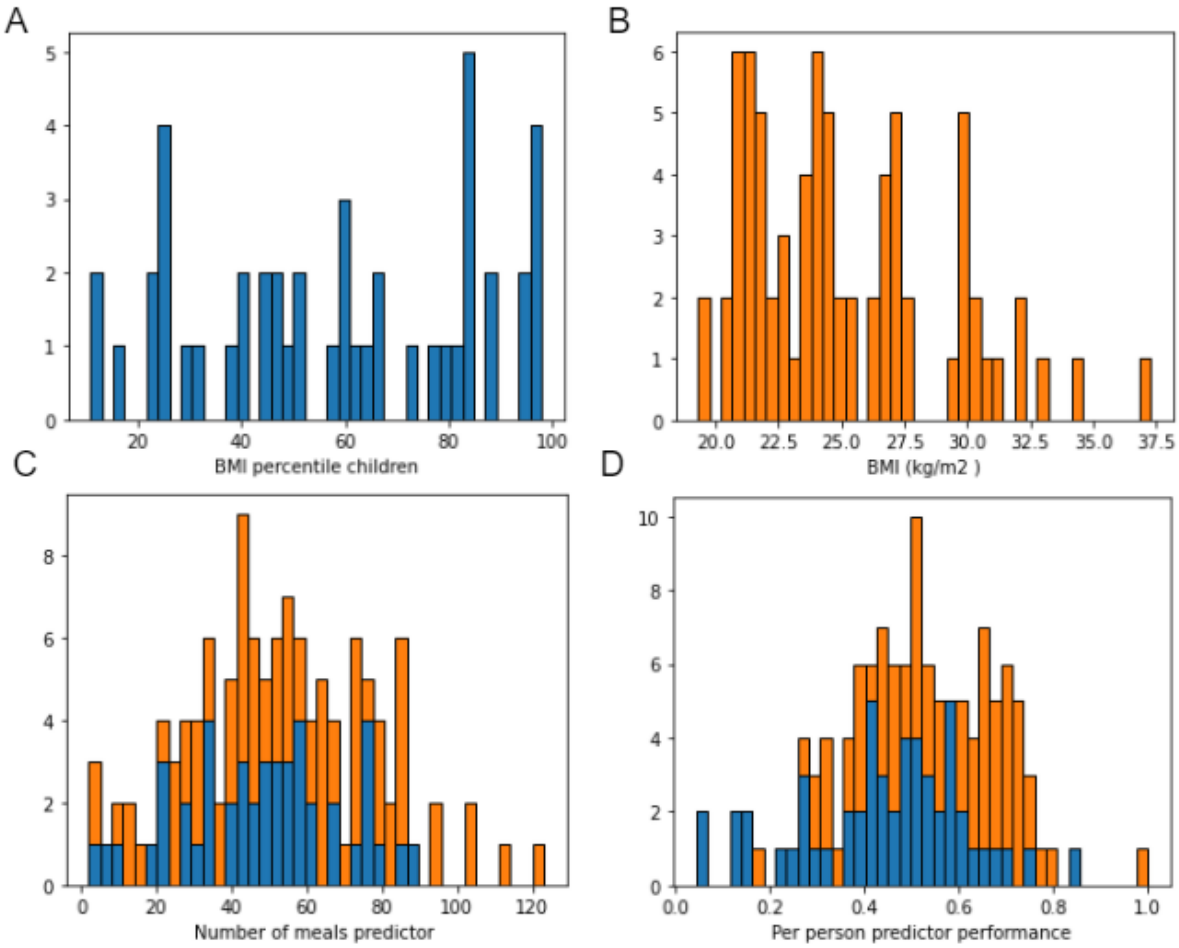

Figure S3: Distribution of BMI, meal logging and variability in the prediction results. Adults are marked in orange and children in blue (A) BMI percentiles of children participated in the study. BMI values were converted to reference percentiles provided by the Center for Disease Control and Prevention (CDC). (B) BMI values of adult participants. (C) Number of meals logged and included in the prediction model per participants (D) Pearson correlation for predicted and measured PPGR per participant.

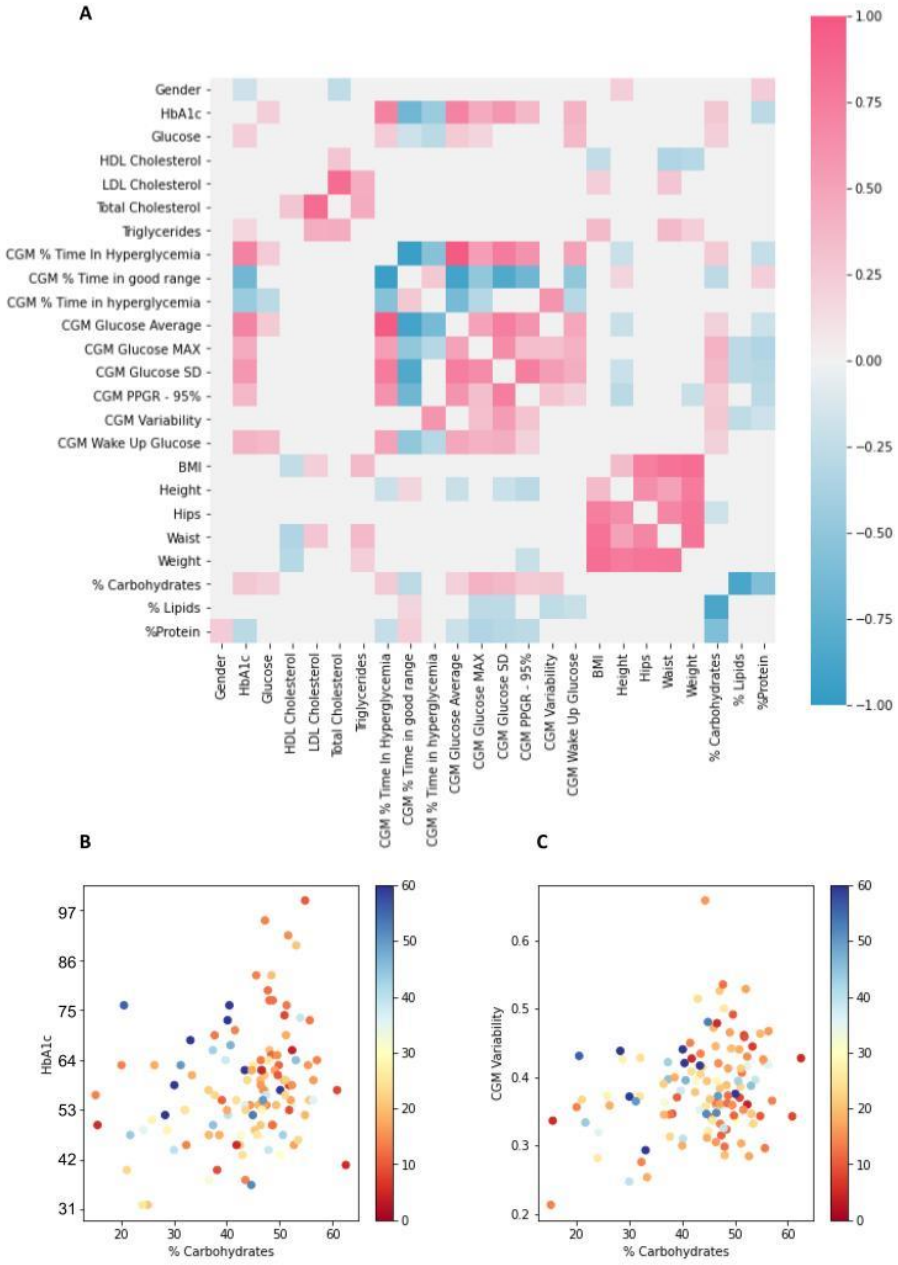
A
Gender
HbA1c
Glucose
HDL Cholesterol
LDL Cholesterol
Total Cholesterol
Triglycerides
CGM % Time In Hyperglycemia
CGM % Time in good range
CGM % Time in hyperglycemia
CGM Glucose Average
CGM Glucose MAX
CGM Glucose SD
CGM PPGR - 95%
CGM Variability
CGM Wake Up Glucose
BMI
Height
Hips
Waist
Weight
% Carbohydrates
% Lipids
%Protein
1.00
0.75
0.50
0.25
0.00
−0.25
−0.50
−0.75
−1.00
B
HbA1c
% Carbohydrates
C
CGM Variability
% Carbohydrates

Figure S4: Correlation of clinical parameters. (A) Time in hypoglycemia is considered as the percentage of time in which glucose level is less than 70 mg/dl (3.9 mmol/L), time in range is considered as the percentage of time spent in glucose values which are more than 70 mg/dl and less the 180 mg/dl (3.9-10 mmol/L), time in hyperglycemia is considered as the percentage of time spent in glucose level above 180 mg/dl (10 mmol/L), PPGR- 95p is considered as the 95 percentile of postprandial glucose responses, %lipid and %carbs are considered as the percentage of lipids and carbohydrates from the total energy intake respectively (B) Correlation between the level of HbA1C (mmol / mol) measured in by a blood test at study initiation and the percentage of carbohydrates from the total energy intake per day during the study ($r = 0.25$, $p<0.05$). The dots are colored by age. (C) Correlation between CGM variability and the percentage of carbohydrates from the total energy intake per day during the study ($r = 0.27$, $p<0.05$). The dots are colored by age as specified in the colour legend.

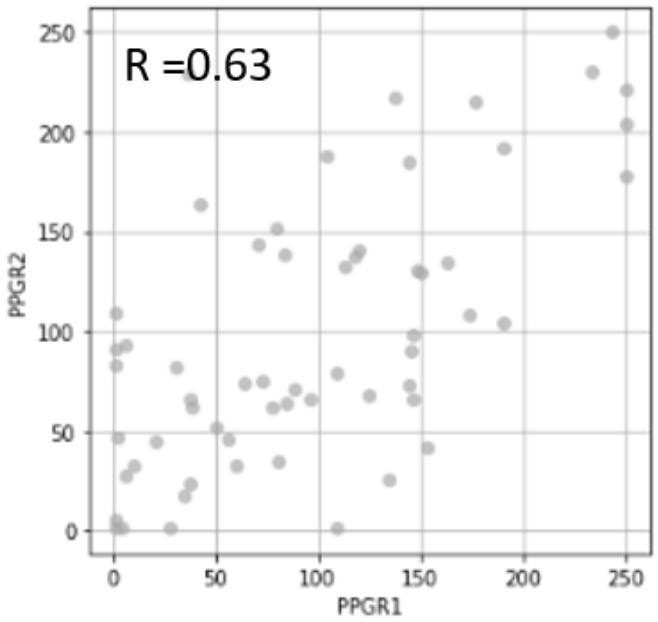

Figure S5: Agreement between PPGR values of the same test meal for the same person. PPGR1 and PPGR2 represent CGM-measured PPGR to test meals in the same person with T1D. 118 test meals were included for 59 individuals. Pearson correlation between the PPGR to the two test meals is indicated. p-value<0.0001 for all correlations.

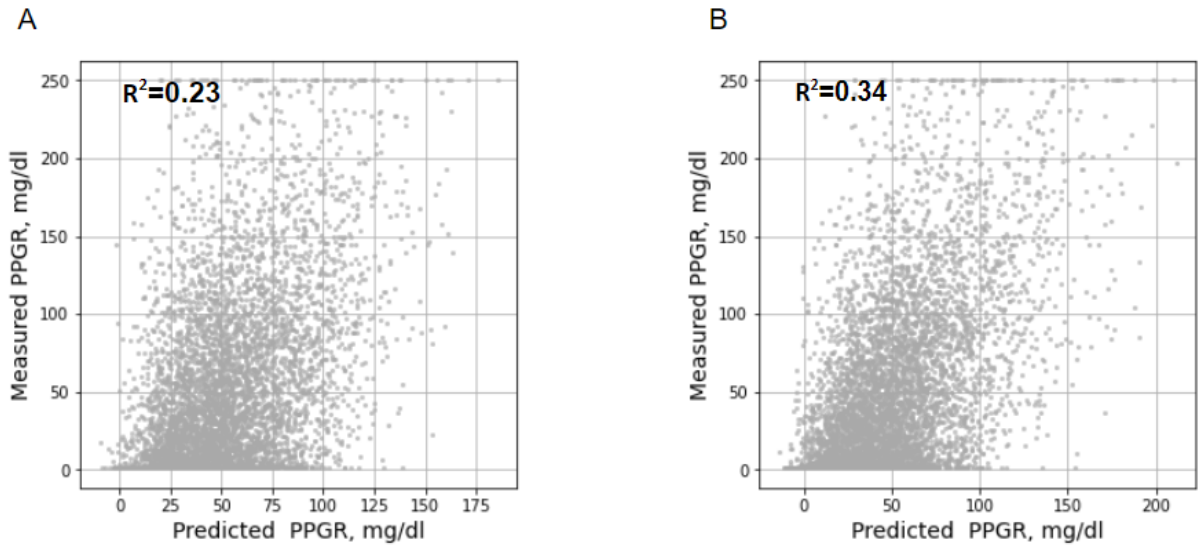

Figure S6: Correlations achieved by utilizing the PPGR prediction model tested in different cross- validation schemes. Dots represent predicted (x axis) and CGM-measured PPGR (y axis) in (A) Cross validation by individuals: the model was trained on 90% of individuals in the cohort, and the remaining 10% were used as validation (Pearson R = 0.48). (B) Cross validation by groups of meals: for every participant, the meals were divided into two seperate groups in which carbohydrate content was similar. Cross validation was then performed on held-out groups (Pearson R = 0.58). explained variance values are indicated.p-value<0.0001 for all correlations.

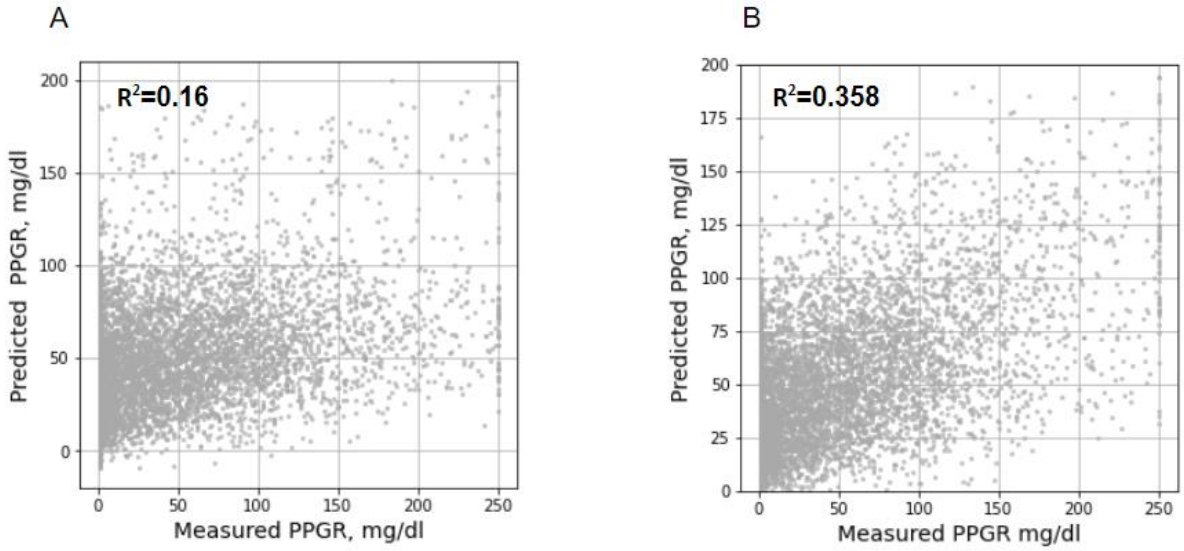

Figure S7: Integration of data from healthy individuals to the PPGR prediction model. Dots represent predicted (x axis) and CGM-measured PPGR (y axis) in (A) A model trained solely on the data from the healthy individuals cohort on tested on T1D (Pearson R = 0.40) and (B) A model trained on data of individuals with T1D

but take the output of a model trained on data that originates from healthy individuals as an additional feature (Pearson R = 0.59). Explained variance values are indicated.p-value<0.0001 for all correlations.

Supplementary Tables

Category	Features
Meal content	kcal, meal total weight, time of meal consumption rounded to an hour, water content, macronutrients (proteins, fats and carbohydrates), carbohydrate/fat ratio, micronutrients (dietary fiber, cholesterol, fatty acids, total saturated fatty acids, total monounsaturated fatty acids, total polyunsaturated fatty acids, total trans fatty acids, zinc, vitamin E, vitamin C,vitamin D, magnesium, sodium, niacin, sugars total, caffeine, calcium)
Blood tests results	HbA1c, thyroid stimulating hormone (TSH), free thyroxine (FT4), creatinine, glucose, total cholesterol, HDL, LDL, triglycerides, albumin, total bilirubin, total protein, aspartate transaminase (AST), alanine transaminase (ALT), sodium, calcium, potassium, uric acid, alkaline phosphatase
Anthropometric measurements	Weight, height, waist and hips circumference, BMI
CGM-derived features	Features obtained from the CGM records included: 1,2,5,10,50,90,95 and 98 percentiles of glucose values during study participation, value of average wake-up glucose, glucose values during the 4 hours prior to the meal, glucose value at meal initiation, glucose trends calculated by subtraction of glucose value at meal initiation from the glucose values at 30, 60 and 120 minutes prior to the meal start.
Insulin dosages, 4 hours prior to the meal	Features were obtained from the CSII records, 1 hour, 1.5 hours, 4 hours prior to the meal and included: Bolus insulin, basal insulin, total insulin, total insulin in the 4 hours prior to the meal per Kg
Survey- derived features	Age, gender, time from T1D diagnosis
Microbiome	Metagenomic RAs, log transformed
Physical activity	Time from the most recent physical activity performed by the participant

Table S1: Features included in the model. A total of 296 features were included in the prediction model. A window of 4 hours prior to the meal for the glycemic and insulinemic profile was chosen since the short-acting insulin analogs which are being used in the insulin pumps begin to exert their effects within 15 minutes of subcutaneous administration, with a peak levels that occur 30 to 90 minutes after administration and total duration of activity less than 4 hours (34)

Blood test result	Mean	Standard deviation
HbA1c* (%), (mmol / mol)	7.5, 58.5	1.1, 12.1
Glucose (mmol/L), (mg/dl)	8.6, 155.6	3.4, 60
Creatinine (μmol/L)	70.7	70.7
Sodium (mmol/L)	138	2.4
Potassium (mmol/L)	4.3	0.3
Chloride (mmol/L)	104	2.5
Calcium (mmol/L)	2.4	0.1
Total bilirubin (μmol/L)	12	8.6
Uric acid (μmol/L)	237.9	65.4
ALT (IU/L)	18.5	12.1
AST (IU/L)	22.6	7.1
Alkaline Phosphatase (IU/L)	122.4	86.2
Protein, total (g/L)	208	266
Albumin (g/L)	43	4
Cholesterol, total (mmol/L)	4.3	0.7
HDL Cholesterol (mmol/L)	1.6	0.35
LDL Cholesterol (mmol/L)	2.4	0.7
Triglycerides (mmol/L)	1.8	0.9
TSH (mIU/L)	2.2	1.2

Table S2: Blood test results. Mean values of blood test results at study initiation are presented. AST- aspartate transaminase, ALT- alanine transaminase, HbA1c - Hemoglobin A1C, TSH- thyroid stimulating hormone.

Medical diagnosis	N	%
Hypothyroidism	17	14.05%
Hyperlipidemia	13	10.74%
Celiac	7	5.79%
Helicobacter pylori carrier	5	4.13%
Anemia	4	3.31%
Asthma	3	2.48%

Gastro-Esophageal reflux	3	2.48%
Attention Deficit Hyperactivity Disorder	3	2.48%
PCOS	2	1.65%
Allergy	2	1.65%
Endometriosis	2	1.65%
Anxiety	2	1.65%
Hypertension	1	0.83%
Osteoporosis	1	0.83%
Irritable bowel syndrome	1	0.83%
Fibromyalgia	1	0.83%
Epilepsy	1	0.83%
Depression	1	0.83%
Alopecia areata	1	0.83%
Recurrent urinary tract infection	1	0.83%
Vitamin B12 and Folic acid deficiency	1	0.83%
Diverticulosis	1	0.83%
Graves' disease	1	0.83%
S/P Acute coronary syndrome	3	2.48%
S/P Appendectomy	2	1.65%
S/P Malignancy	2	1.65%
Medications	**N**	**%**
Levothyroxine	12	9.92%
Oral contraceptives	9	7.44%
Antilipidemic drug	9	7.44%
Antihypertensive drug	7	5.79%
Anti-anxiety or antidepressants drugs	4	3.31%
Methylphenidate	4	3.31%
Aspirin	3	2.48%
Metformin	3	2.48%
GLP-1 agonist	2	1.65%

Antihistamine	2	1.65%
Proton pump inhibitor	2	1.65%
Ticagrelor	1	0.83%
Atomoxetine	1	0.83%

Table S3: Medical conditions and medications consumed by study participants. Number and percentage of individuals reported as suffering from a medical condition or consuming drugs apart from insulin on a daily basis are presented. Medical conditions and medication were reported in the survey and medications were also logged in the smartphone application. GLP-1 -Glucagon-like peptide-1, IBS- Irritable bowel syndrome, PCOS- Polycystic ovary syndrome, SSRI - Selective Serotonin Reuptake Inhibitor, S/P - status post

Group	**Subgroup**	**N**	**Pearson correlation**
Age	Children (less than 12 years of age)	17	0.56
	Adolescents (between 12-18 years of age)	32	0.53
	Adults (above 18 years of age)	68	0.62
HbA1c%	< 7% (53 mmol/mol)	42	0.56
	7-8% (53-63.9 mmol/mol)	49	0.57
	>8% (63.9 mmol/mol)	25	0.64
Time spent in hypoglycemia	Low (less than 3.5% of the time in hypoglycemia)	41	0.64
	Medium (between 3.5% and 7.8% of the time in hypoglycemia)	40	0.59
	High (more than 7.8% of the time in hypoglycemia)	40	0.54
Insulin pump manufacture*	Omnipod	24	0.61
	Medtronic	78	0.59
	Animas	18	0.55
CGM device†	Dexcom	26	0.56
	Navigator	8	0.56
	Libre	43	0.60
	Medtronic	42	0.57

Table S4: Subgroup analysis. Pearson correlation of predicted versus measured PPGR are presented, p-value<0.001 for all correlations . *One participant used an insulin pump manufactured by Accu-Chek and was not included in this

analysis. † Two participants have used two different types of CGM devices during the study and were not included in this analysis CV- coefficient of variation

Mean	Individuals with a high correlation (upper thirtile) between predicted and observed PPGR	Individuals with a low correlation (lower thirtile) between predicted and observed PPGR	MW p-value	FDR p-value
Age (years)	26.86	23.51	0.04	0.11
Gender - Male %	39%	30%	0.20	0.26
Glucose level at meal initiation (mg/dl), (mmol/L)	141.81, 7.9	141.26, 7.8	0.36	0.42
HbA1c (%), (mmol/mol)	7.45, 57.9	7.49, 58.40	0.45	0.49
BMI (kg/m^2)	24.37	22.32	0.04	0.12
Total number of meals logged during the trial*	54.68	42.81	0.01	0.08
Number of meals logged per day during the trial*	4.36	3.58	0.01	0.07
Percentage of carbohydrate from total energy intake	0.42	0.45	0.19	0.26
Percentage of fat from total energy intake	0.39	0.37	0.15	0.23
Percentage of protein from total energy intake	0.17	0.16	0.49	0.49
Glucose variability*	0.36	0.39	0.02	0.06
Mean glucose value during the trial	159.32	147.83	0.07	0.14
Number of meals that were excluded in the meal exclusion process	3.32	7.00	0.12	0.22
Percentage of meals that were excluded in the meal exclusion process*	0.07	0.13	0.01	0.08
Number of test meals consumed during the study	5.63	5.31	0.12	0.21

Table S5: Comparison between the characteristics of individuals who had a high versus low correlation between predicted and observed PPGR. Individuals with a correlation in the upper thirtile of the cohort (average Pearson R- 0.68) were compared to individuals who had a correlation in the lower thirtile of the cohort (average Pearson R- 0.3). Mean glucose value was calculated from glucose measurements obtained from the CGM device during the study. CV-

coefficient of variation. P-values were calculated by Mann-Whitney (MW) U test. *statistically significant following FDR employed at the rate of 0.1