Associations of dietary macronutrient and fibre intake with glycaemia in individuals with Type 1 diabetes

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Dietary macronutrient and fibre intake and glycaemia in individuals with type 1 diabetes

Running title: Diet and glycaemia in type 1 diabetes

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Conflicts of interest disclosures

Professor Per-Henrik Groop has received research grants from Eli Lilly and Roche, is an advisory board member for AbbVie, Astra Zeneca, Boehringer-Ingelheim, Cebix, Eli Lilly, Janssen, MSD, Medscape, Novartis, Novo Nordisk, and Sanofi. He has received lecture fees from Astra Zeneca, Boehringer-Ingelheim, Eli Lilly, Elo Water, Genzyme, MSD, Novartis, Novo Nordisk, and Sanofi. All other authors declare no conflict of interest.

Novelty statement

- Data on the association between dietary intake and glycaemia, in type 1 diabetes, are mixed and fibre intake is not always accounted for, in the analyses.
- This is a large study among well-defined individuals with type 1 diabetes
- Reported fibre intake was associated with lower mean blood glucose measurements
- Reported protein intake, over any other macronutrients, was associated with lower glucose variability

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Abstract

Aims To study the association between dietary intake and glycaemia in type 1 diabetes.

Methods Data on energy and nutrient intakes, and mean and coefficient of variation of the self-monitored blood glucose (SMBG) measurements were obtained from records completed by 1000 adults. Associations between these measures of glycaemia and dietary intake were investigated using generalised linear regression with and without macronutrient substitution.

Results In the first set of analyses, fibre intake was associated with lower mean SMBG values (B=-0.428, 95% CI=-0.624 to -0.231, *P*<0.001). In these same analyses, carbohydrate (B=0.011, 95% CI=0.002 to 0.020, *P*=0.014), alcohol (B=0.013, 95% CI=0.003 to 0.023, *P*=0.009), and monounsaturated fatty acid (B=0.012, 95% CI=0.001 to 0.023, *P*=0.029) intakes were associated with higher variability in BG measurements. In the macronutrient substitution analyses, substituting proteins for either carbohydrates (B=-0.026, 95% CI=-0.040 to -0.013, *P*<0.001), fats (B=-0.018, 95% CI=-0.033 to -0.004, *P*=0.014), or alcohol (B=-0.026, 95% CI=-0.045 to -0.006, *P*=0.010), or fats for carbohydrates (B=-0.009, 95% CI=-0.017 to -0.001, *P*=0.030) were all associated with lower variability in the measured BG values. After adjusting for fibre intake, no significant results were observed in analyses of mean SMBG.

Conclusions This observational, cross-sectional study indicates that dietary fibre is associated with lower mean blood glucose concentrations in people with type 1 diabetes. Glycaemic excursions were reduced when protein was substituted for other macronutrients and when fat replaced carbohydrate, after adjusting for fibre intake.

Key words: Dietary intake; Fibre; Glycaemia; Macronutrients; Type 1 diabetes

Introduction

The role of glycaemic control in the prevention of diabetic complications was first illustrated by the Diabetes Control and Complications Trial (DCCT) [1], and people with type 1 diabetes are now recommended to achieve target HbA_{1c} levels of <53 mmol/mol (<7.0%) in order to reduce risk [2]. However, as frequently seen, not many individuals with type 1 diabetes achieve these recommendations. For example in two large cohorts of individuals with type 1 diabetes average concentrations at around 67 mmol/mol (8.3%) were reported [3, 4]. While HbA_{1c} represents long-term glycaemic control, and is therefore the primary indicator of diabetes control, levels of day-to-day glycemia and glycaemic variability contribute to this measure [5]. Moreover, in insulin-treated individuals, high glucose variability may increase the risk of severe hypoglycaemia [6].

Dietary intake plays an important role in the glycaemic control of people with type 1 diabetes. Current evidence in this field is, however, somewhat mixed. For example, analyses are frequently not adjusted for fibre intake [7–10]. Moreover, under isoenergetic conditions, increase in the intake of one macronutrient is accompanied by decrease in the intake of another macronutrient(s). Most of the published studies have not taken such macronutrient substitution into consideration [7, 9–13].

In the current study, we explored the association between dietary intake and glycamia in individuals with type 1 diabetes. In specific, we focused on the macronutrient and fibre intake, and their role in defining mean daily blood glucose values and the variability in these measurements.

Participants and Methods

Of the participants of the Finnish Diabetic Nephropathy (FinnDiane) Study, we included all with completed food record within 2 years from the study visit and with plausible reported energy intake (5.0–14.6 MJ/d). Individuals with end-stage renal disease were excluded. Type 1 diabetes was defined as onset of diabetes before the age of 35 years, permanent insulin treatment initiated within one year from the diagnosis, and C-peptide negativity. The study protocol was approved by the Ethics Committee of the Helsinki and Uusimaa Hospital District,

and by the local ethics committees at each centre. Written informed consent was obtained from the participants prior to the study participation.

At the FinnDiane Study visit participants' height and weight were measured in light clothing. Blood pressure was measured twice after a minimum of 10-minutes rest. Mean of the two blood pressure measurements was used in the analyses. Blood was drawn for subsequent central analyses of lipids and lipoproteins. HbA_{1c} was locally measured using standardized assays. Data on diabetic complications, including dialysis and renal transplantation (i.e. end-stage renal disease), were collected from medical records. Smoking was self-reported in a questionnaire, and current smoking refers to smoking at least one cigarette per day.

Dietary intake was measured using two separate questionnaires. First participants completed a validated [14] diet questionnaire, and after returning it, a 3-day food record (allocated two consecutive week-days and one week-end day) twice with a 2 to 3-month interval. Detailed instructions with a completed example page were provided. In brief, participants were instructed to report all food-items eaten or drunk during the record-keeping days. Continuation of habitual dietary practices was emphasised. Meticulous reporting of food-items (e.g. fat contents of liquid milk products, types of fats used for cooking and as spreads, and types of grains in breads) and cooking methods (e.g. boiled, grilled, fried) was encouraged. Brand names of ready-made meals, and recipes for atypical dishes were requested. Instructions were given to report the amounts in common household measures (e.g. spoons, decilitres, and glasses), pieces, centimeters, or grams. Along with reporting their food and beverage intakes in this record, participants also reported physical activity, insulin dosing, and self-monitored blood glucose (SMBG) values. In the current study, only data collected with the records were used. Included were data from participants who had completed at least one 3-day record. From the record entries, average (based on either 3 or 6 days' reported intake) daily energy, nutrient, and fibre (using the Association of Official Analytical Chemists method) intakes were calculated using the AivoDiet software (version 2.0.2.3, AIVO, Turku, Finland), which is based on the Finnish National Food Composition Database. The proportion of energy derived from trans-fatty acids was calculated by subtracting energy derived from saturated fatty acids, monounsaturated fatty acids, and polyunsaturated fatty acids from the total fat intake. Calculated trans-fatty acid intake was used as confounding factor in the analyses. The number of daily blood glucose measurements,

and mean and coefficient of variation (CV) of the reported SMBG concentrations were calculated for each participant. The calculated SMBG means and CVs were used as continuous variables in the analyses.

Statistical analyses were performed using IBM SPSS Statistics for Windows, Version 22.0 (IBM Corp, Armonk, NY, USA). A two-tailed *P* value <0.05 was considered statistically significant. Categorical variables are presented as frequencies (%), parametric data are presented as mean ± SD, and non-parametric data are presented as median (interquartile range). Spearman's correlation coefficient was calculated to study the unadjusted correlations between variables. The independent associations between dietary intake and the continuous mean SMBG concentrations and CVs were analysed with generalized linear regression. In the analyses, adjustments were made for age, sex, BMI, triglyceride concentration, insulin dose/kg, physical activity, fibre intake, and other macronutrients. Analyses were conducted with and without macronutrient substitution. In each of the macronutrient substitution models, we included all but one of the macronutrients (per 5 E%), total energy intake, and the above-mentioned cofactors. The emerging beta value may be interpreted as increase (when positive) or decrease (when negative) in the given outcome variable when 5 E% of the excluded macronutrient is substituted with 5 E% of the macronutrient in question. For example, in an equation: Mean SMBG concentration = β_0 + β_1 (5 E% from carbohydrates) + β_2 (5 E% from proteins) + β_3 (5 E% from alcohol) + β_4 (kcal), β_1 would be interpreted as the change in the mean SMBG concentration when dietary carbohydrate intake is increased by 5 E% at the expense of fats.

Results

Data on mean SMBG concentration were available from a total of 1000 individuals (42% men, median age 47 years), and the CV of the reported BG concentrations was calculated for 992 participants. Mean SMBG concentration correlated positively with insulin dose, use of insulin pump, body mass index (BMI), triglyceride concentration, and HbA_{1c} (Table 1). Instead, a negative correlation between the mean SMBG concentration and male sex, physical activity, age, and systolic blood pressure was observed. The number of BG measurements, insulin dose, and HDL-cholesterol concentration were positively correlated with the variability of the

SMBG concentrations, while a negative correlation was observed between the CV and age, systolic blood pressure, diastolic blood pressure, BMI, and triglyceride concentration.

Dietary intake of the population is shown in Table 2. Total fat, saturated fatty acid, and monounsaturated fatty acid intakes were positively associated with mean SMBG concentration. In contrast, carbohydrate, fibre, polyunsaturated fatty acid, and protein intakes were negatively associated with the mean SMBG concentrations. Positive correlations were observed between variability of the BG concentrations and total energy, carbohydrate, sucrose, fat, and alcohol intakes, while the intakes of polyunsaturated fatty acids, and proteins were negatively correlated with the measures of BG variability.

In generalised linear regression analysis where macronutrient substitution was not taken into consideration, fibre intake was negatively associated with mean SMBG concentration (Table 3). Instead, carbohydrate, alcohol, and monounsaturated fatty acid intakes were positively associated with the variability of the BG measurements.

We then investigated the association between macronutrient intake and the two continuous variables of blood glucose monitoring while taking macronutrient substitution into consideration (Table 4). Adjusted for age, sex, BMI, triglyceride concentration, insulin dose/kg, and physical activity, higher mean SMBG concentrations were observed when energy intake from fats was increased at the expense of proteins. Similarly, increased consumption of saturated fatty acids, in place of either monounsaturated or polyunsaturated fatty acids, was associated with higher mean SMBG concentration. After incorporating fibre intake into the model, however, these observations were no longer significant. In the fully adjusted models, favouring either carbohydrates or fats over proteins, was associated with higher variability in the measured BG values. In contrast, lower variability was observed when proteins were substituted for alcohol. Moreover, substituting carbohydrates for fats was associated with higher BG variability.

Discussion

Current obesrvations highlight the important role of dietary fibre in the management of glycaemia, in type 1 diabetes. Importantly, fibre intake was the only dietary variable

associated with lower mean SMBG concentrations. The suggested mechanisms through which dietary fibres are thought to exert their glycaemia-reducing effects include, but may not be restricted to, delayed gastric emptying, reduced accessibility of α-amylase to its substrates due to fibre-induced increase in the viscosity of the partly digested food mass, and increasing insulin sensitivity related to short-chain fatty acid production by the gut microbiota [15]. Of interest, the self-reported median fibre intake in the current study fell below the Finnish dietary recommendations (3 g/MJ) [16], suggesting that increase in fibre intake could be beneficial in this population.

A number of previous studies investigating the association between dietary intake and glycaemic control have been published. It should be noted, however, that many of these studies were conducted in children or adolescents, rather than in middle-aged adults, a population mainly represented in the current study. The observations made in such studies may not directly translate to the current population. Taking this into consideration, a number of studies have also made a connection between fibre intake and better glycaemic control. For example, in a cross-sectional study including 252 adolescents with type 1 diabetes, with the highest quartile as a reference, the lowest quartile of fibre intake had 3.6 times the odds of having an HbA_{1c} ≥69 mmol/mol (≥8.5%) [7]. In another cross-sectional study, adolescents with type 1 diabetes with optimal glycaemic control (HbA_{1c} ≤58 mmol/mol or ≤7.5%) had lower intake of added sugars, higher intake of fibre, and higher intake of fruits and vegetables compared to those with less optimal glycaemic control [17]. Of these dietary variables, however, only fibre remained significant after adjustment for potential confounders. A 24-week intervention with high-fibre diet (50 g/day), compared to low-fibre diet (15 g/day), significantly reduced mean daily blood glucose concentrations and the number of hypoglycaemic events [18]. In the 7-year prospective analyses of the EURODIAB study, baseline fibre intake below the median (<18 g/day) was associated with higher HbA_{1c} [4]. In addition to studies confirming the beneficial role of fibre, a number of studies were identified where no association between dietary fibre and glycaemia were observed. Amongst these was the prospective SEARCH Nutrition Ancillary Study [19], and a small intervention in children with type 1 diabetes, where addition of fibre into the habitual meal plan did not affect the mean blood glucose excursions after the meals, or the incidence of hypoglycaemia [20].

When we investigated the role of macronutrient substitutions for the mean blood glucose concentrations, inclusion of fibre abolished all significant associations observed in the previous models. However, in the analyses dealing with the variability of the measurements, a number of significant observations remained even after controlling for fibre intake. Indeed, substituting proteins for either carbohydrates, fats, or alcohol, as well as substituting fats for carbohydrates were all associated with more stable blood glucose measurements. The role of macronutrient substitutions in the glycaemic control of people with type 1 diabetes was also investigated in the prospective DCCT [8]. In their analyses no macronutrient was significantly associated with the level of glycaemia. Importantly, albeit non-significant observations, these analyses were not adjusted for fibre intake which, as seen in the current study, could play a major role in modifying glycaemia. Moreover, as energy derived from alcohol was also omitted from their analyses, the results have to be interpreted as the effect of substituting the index macronutrient for a combination of alcohol and the other excluded macronutrient.

While beyond the DCCT we are not aware of other reports of macronutrient substitutions and glycaemic control in people with type 1 diabetes, the role of macronutrients in modifying glycaemia has been investigated in various other settings. Dietary carbohydrates in particular, potentially due to their pronounced connection with the blood glucose concentrations, have gained substantial interest. The current evidence of the role of carbohydrates for the glycaemic control is, however, somewhat mixed. Over an 18-month behavioural nutrition intervention trial among 136 adolescents with type 1 diabetes, higher intake of carbohydrates was associated with lower HbA_{1c} [9]. In contrast, in a cross-sectional study of 46,010 children and adolescents with type 1 diabetes, lower carbohydrate intake was associated with lower HbA_{1c} [10]. To our knowledge, however, neither of these two analyses were corrected for other dietary variables such as fibre. Yet in another cross-sectional study, accounting for fibre intake, higher carbohydrate intake was positively associated with time spent in euglycaemia, and negatively with time spent in hyperglycaemia [11]. Furthermore, even when adjusted for fibre intake, the source of carbohydrates may be important, as was seen in cross-sectional analyses of the EURODIAB study where higher intakes of total carbohydrates and potato-derived carbohydrates, but lower intakes of vegetable-based carbohydrates, were associated with less optimal HbA_{1c} [12]. It has also been suggested that it is not the total amount of carbohydrates in the diet *per se* that determines the level of glycaemia, but rather the

consistency of carbohydrate and starch intake from meal to meal [21]. After all, consistency in the eating behaviours related to carbohydrate containing foods may improve the accuracy of carbohydrate counting. Considering the substantial errors observed in estimating carbohydrate contents of the meals [22] and with considerable intra-individual variability in the metabolic effect of the injected insulin [23], the potential of reduced carbohydrate intake in improving glycaemia has also been investigated. Indeed, in a number of low-carbohydrate diet interventions significant improvements in glycaemic control of individuals with type 1 diabetes have been reported [24, 25]. Moreover, in one short-term low-carbohydrate diet intervention, although mean glucose concentrations were not impacted, lower glucose variability, more time spent in euglycaemia, and less time in hypoglycaemia were observed [26]. However, more studies are needed to reveal the health effects of low-carbohdyrate diets, as there is currently insufficient evidence to support their use in type 1 diabetes [27].

As is the case for carbohydrates, the results obtained for the role of fats in glycaemic control are also mixed. While in three prospective studies baseline intake of total fat was not associated with glycaemic control measured at the end of the follow-up period [4, 8, 19], a number of cross-sectional studies have associated higher intakes of either total fats or saturated fatty acids with less optimal glycaemic control. Amongst these is a study in 33 adult individuals with type 1 diabetes, where higher fat intakes were correlated with less time in euglycemia, and more time in hyperglycaemia [11]. In another study in 252 adolescents with type 1 diabetes, the highest quartile of fat intake increased the risk of suboptimal glycaemic control 2.5-fold [7]. In children and adolescents with type 1 diabetes, intake of saturated fatty acids was associated with 53% increased risk of having HbA_{1c} concentrations above the recommended 58 mmol/mol (7.5%) [13]. In line with the above study, intake of saturated fatty acids when replacing polyunsaturated fatty acids was also in the current study associated with worse glycaemic control, measured both as higher mean SMBG concentrations and the variability of these measurements. These effects were, however, lost after further adjustment for fibre intake.

In the current analyses, higher intake of protein at the expence of any other macronutrient was associated with lower variability of the measured blood glucose concentrations. We are not aware of other studies reporting similar findings. In contrast, Nansel et al observed that lower protein intake was associated with better glycaemic control [9]. In another study, no

correlation between protein intake and time spent in hypoglycaemia, euglycaemia, or hyperglycaemia were observed [11]. The longitudinal analyses of the EURODIAB study revealed that, although baseline intakes of total protein did not determine glycaemia, intake of vegetable protein below median (<29 g/day) was associated with worse glycaemic control [4]. In the prospective SEARCH Nutrition Ancillary Study, instead, not only total protein intake but also vegetable and animal protein intakes predicted lower HbA_{1c} concentrations at the end of the mean 1.5 years of follow-up [19]. In the current study, the source of protein was not examined.

The mechanisms behind current observations relating protein intake to more stable blood glucose measurements is not known. It is possible, however, that the mechanism is not directly related to protein intake but rather to what they are replacing. Indeed, while carbohydrates are known to directly boost blood glucose concentrations, alcohol intake, via reduction in the hepatic gluconeogenesis, has the potential to reduce blood glucose concentrations over the following 10-12 hours [28]. Dietary fats, on the other hand, due to delayed gastric emptying, reduce early glucose response [29], and via free fatty acid-induced insulin resistance, cause delay in the emergence of the postpradial blood glucose peak [30, 31]. While also proteins are known to increase blood glucose concentrations in the late postprandial period [31], based on the current observations it may be speculated that compared to the other macronutrients, ingestion of proteins leads to less pronounced changes in the blood glucose fluctuations. Moreover, people with type 1 diabetes may be better able to take dietary proteins into account when estimating their prandial insulin dosing. Indeed, although estimating the required prandial insulin dose has traditionally been based on carbohydrate counting, there is increasing evidence that also fats and proteins may need to be taken into consideration. To this end, calculating the so-called fat-protein units has recently been introduced as a method to estimate the required bolus insulin to cover the glycaemic effects of these macronutrients [32]. In this method, each 100 kcal derived from the combination of ingested fats and proteins are considered to call for the same amount of insulin as 10 grams of carbohydrates. Importantly, the application of this method in a dual wave or square wave bolus mode, has shown to improve glycaemic control in individuals with type 1 diabetes [32, 33].

There are strengths and limitations related to the current study. Amongst the limitations is the use of self-reported data for both dietary intake and blood glucose monitoring. There may be a tendency to over-report the consumption of foods regarded as healthy and under-report those considered unhealthy. While it may be difficult to control for such a phenomenon we did, however, try to control for potential under- or over-reporting of total energy intake. Various cut-off values may be used to identify under- and over-reporters. According to Willett, for example, mean daily intakes between 500 and 4000 kcal (2.1 MJ and 16.7 MJ) may be considered appropriate [34]. Taking into consideration the characteristics of the current study population (type 1 diabetes, average age and BMI) we, however, chose to use more conservative cut-off levels of 5 MJ and 14.6 MJ, as intakes closer to 500 kcal and 4000 kcal may not be plausible in the long-term. The self-reported blood glucose measurements are a mixture of pre- and post-prandial values. Variation in the timing of measurements has likely taken place, and may be a source of bias in the current study. Importantly, studies taking advantage of continuous glucose monitoring devices have, amongst others, shown that fibre intake is associated with more optimal glycaemic control [9]. In contrast, the results related to protein intake, in these studies, have been mixed as increased postprandial glucose excursions [31], increased hypoglycaemic events [35], as well as no effect on postprandial, overnight, or late night glucose concentrations [36] have been reported. Furthermore, whether self-reporting of blood glucose measurements were subject to misreporting, in the current study, is not known. Due to issues related to social desirability it is possible that extremely high or low values are less frequently reported. If such misreporting has taken place, it has most likely attenuated the current observations. The participants included in the FinnDiane Study have been carefully assessed regarding their type of diabetes. Key features are onset of diabetes before the age of 35 years, initiation of insulin treatment within a year of the diagnosis, and C-peptide negativity. These features are all typical of type 1 diabetes and we are therefore confident that misclassification is not an issue in this cohort. Finally, the potential for residual confounding cannot be excluded. In particular, smoking and socioeconomic status were not accounted for, in the analyses, as multicollinearity between these variables and a number of variables included in the model were observed. A large population of well-defined individuals is one of the strengths of the current study. Moreover, the cross-sectional study design is suitable for the current study, considering that our aim was to look at the relationship between dietary intake and the concomitant glycaemia. Using the

record method ensured that the measures of dietary intake did not reflect dietary history, but were the intakes that also covered the period when blood glucose concentrations were monitored.

In conclusion, based on the observations made in this cross-sectional study, dietary fibre plays a major role in the successful management of glycaemia in type 1 diabetes. Moreover, even when adjusted for fibre intake, proteins, when replacing excess carbohydrates, fats, or alcohol, may reduce glycaemic excursions. In the future, long-term effects of dietary intake in the risk of diabetic complications will be investigated.

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Conflicts of Interest

Professor Per-Henrik Groop has received research grants from Eli Lilly and Roche, is an advisory board member for AbbVie, Astra Zeneca, Boehringer-Ingelheim, Cebix, Eli Lilly, Janssen, MSD, Medscape, Novartis, Novo Nordisk, and Sanofi. He has received lecture fees from Astra Zeneca, Boehringer-Ingelheim, Eli Lilly, Elo Water, Genzyme, MSD, Novartis, Novo Nordisk, and Sanofi. All other authors declare no conflict of interest.

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Table 1 Basic characteristics of the population, and correlations between the basic characteristics and measures of glycaemia

	Total population	Mean SMBG		CV of SMBG	
		r	*P*	*r*	*P*
Mean SMBG	8.1 (6.8 – 9.4)			0.093	0.003
CV of SMBG	0.42 (0.34 – 0.49)	0.093	0.003		
Measurements/day, n	3.8 (2.7 – 5.0)	0.039	0.223	0.078	0.014
Men, %	42.4	-0.084	0.008	-0.061	0.056
Insulin dose, IU/kg	0.56 (0.43 – 0.71)	0.128	<0.001	0.079	0.013
Insulin pump, %	16	0.069	0.029	-0.029	0.360
Physical activity, METh/d	19 (9 – 34)	-0.134	<0.001	0.045	0.207
Age, years	47 (37 – 58)	-0.146	<0.001	-0.091	0.004
SBP, mmHg	136 (124 – 149)	-0.098	0.002	-0.078	0.015
DBP, mmHg	76 ± 9	0.054	0.089	-0.077	0.015
BMI, kg/m^2	25.5 (23.2 – 28.3)	0.106	0.001	-0.073	0.022
Total cholesterol, mmol/l	4.6 (4.0 – 5.1)	-0.028	0.400	-0.009	0.785
HDL cholesterol, mmol/l	1.57 (1.32 – 1.90)	-0.057	0.085	0.114	0.001
Triglycerides, mmol/l	0.94 (0.71 – 1.27)	0.140	<0.001	-0.099	0.003
HbA_{1c}, mmol/mol	63 (55 – 71)	0.451	<0.001	0.029	0.366
HbA_{1c}, %	7.9 (7.2 – 8.6)	0.451	<0.001	0.029	0.366
Current smoker, %	10.4	0.024	0.451	-0.032	0.317

Data are presented as median (interquartile range) for continuous variables that were skewed, mean ± standard deviation for continuous variables with normal distribution, frequency (%) for categorical variables, and Spearman's correlation coefficients with respective *P*-values. SMBG, self-monitored blood glucose; CV, coefficient of variation; IU, international unit; METh, metabolic equivalent of task hours; SBP, systolic blood pressure; DBP, diastolic blood pressure; BMI, body mass index.

Table 2 Reported energy, macronutrient, sucrose, and fibre intakes of the population, and correlations between dietary intake and measures of glycaemia

	Total population	Mean SMBG		CV of SMBG	
		r	*P*	*r*	*P*
Energy, MJ	7.8 (6.6 – 9.1)	-0.015	0.629	0.123	<0.001
Carbohydrates, g	196 (161 – 236)	-0.045	0.152	0.157	<0.001
Carbohydrates, E%	42.8 (38.3 – 47.1)	-0.072	0.023	0.104	0.001
Sucrose, g	32 (21 – 47)	0.050	0.115	0.194	<0.001
Fibre, g	21 (17 – 27)	-0.204	<0.001	0.027	0.402
Fibre, g/MJ	2.7 (2.2 – 3.4)	-0.210	<0.001	-0.052	0.101
Fats, g	74 (60 – 91)	0.037	0.238	0.064	0.043
Fats, E%	36.2 (31.9 – 40.2)	0.097	0.002	-0.059	0.065
SAFA, E%	12.7 (10.7 – 14.6)	0.156	<0.001	0.002	0.954
MUFA, E%	12.1 (10.6 – 13.8)	0.064	0.043	-0.053	0.093
PUFA, E%	5.9 (5.1 – 7.0)	-0.082	0.009	-0.080	0.012
Proteins, g	77 (65 – 94)	-0.049	0.124	-0.011	0.740
Proteins, E%	16.6 (14.8 – 18.7)	-0.062	0.051	-0.176	<0.001
Proteins, g/kg	1.05 (0.87 – 1.27)	-0.091	0.004	0.036	0.253
Alcohol, E%	0.8 (0 – 3.0)	-0.021	0.515	0.083	0.009

Data are presented as median (interquartile range), and Spearman correlation coefficient with respective *P*-value. SMBG, self-monitored blood glucose; CV, coefficient of variation; SAFA, saturated fatty acids; MUFA, monounsaturated fatty acids; PUFA, polyunsaturated fatty acids.

Table 3 The association between SMBG and CV and energy-adjusted reported macronutrient and fibre intakes

	Mean SMBG			CV of SMBG		
	B	95% Wald Confidence Interval	*P*	B	95% Wald Confidence Interval	*P*
Carbohydrates, E%	0.045	-0.084 to 0.175	0.493	0.011	0.002 to 0.020	0.014
Proteins, E%	0.034	-0.105 to 0.173	0.631	0.006	-0.003 to 0.016	0.190
Alcohol, E%	0.017	-0.121 to 0.155	0.810	0.013	0.003 to 0.023	0.009
SAFA, E%	0.069	-0.072 to 0.210	0.338	0.009	-0.001 to 0.019	0.081
MUFA, E%	-0.016	-0.170 to 0.137	0.834	0.012	0.001 to 0.023	0.029
PUFA, E%	0.034	-0.130 to 0.198	0.683	0.007	-0.004 to 0.018	0.233
Fibre, g/MJ	-0.428	-0.624 to -0.231	<0.001	-0.011	-0.024 to 0.003	0.121

SMBG, self-monitored blood glucose; CV, coefficient of variation; β, regression coefficient; SAFA, saturated fatty acids; MUFA, monounsaturated fatty acids; PUFA, polyunsaturated fatty acids. The model, including all dietary variables, is adjusted for age, sex, BMI, triglyceride concentration, trans fatty acids, insulin dose/kg, and physical activity. Generalised linear regression.

Table 4 The association between mean and coefficient of variation of blood glucose measurements and reported macronutrient intake (substitution model)

		Mean SMBG			CV of SMBG		
Macronutrient intake increased (decreased)	Model	B	95% Wald Confidence Interval	*P*	B	95% Wald Confidence Interval	*P*
Carbohydrate (fat)	1	-0.106	-0.220 to 0.008	0.067	0.005	-0.002 to 0.013	0.181
	2	-0.007	-0.123 to 0.109	0.911	0.009	0.001 to 0.017	0.030
Carbohydrate (protein)	1	0.100	-0.097 to 0.296	0.320	0.028	0.015 to 0.041	<0.001
	2	0.065	-0.122 to 0.253	0.496	0.026	0.013 to 0.040	<0.001
Carbohydrate (alcohol)	1	0.026	-0.187 to 0.239	0.810	-0.006	-0.021 to 0.008	0.410
	2	0.156	-0.053 to 0.365	0.143	-0.002	-0.016 to 0.013	0.824
Fat (protein)	1	0.215	0.009 to 0.421	0.041	0.023	0.009 to 0.037	0.001
	2	0.076	-0.129 to 0.282	0.467	0.018	0.004 to 0.033	0.014
Fat (alcohol)	1	0.148	-0.078 to 0.374	0.200	-0.009	-0.024 to 0.007	0.264
	2	0.164	-0.053 to 0.382	0.138	-0.009	-0.024 to 0.006	0.235
SAFA (MUFA)	1	0.681	0.131 to 1.231	0.015	0.027	-0.011 to 0.064	0.161
	2	0.387	-0.162 to 0.936	0.167	0.015	-0.024 to 0.054	0.445
SAFA (PUFA)	1	0.717	0.331 to 1.103	<0.001	0.034	0.008 to 0.060	0.011
	2	0.229	-0.207 to 0.665	0.303	0.022	-0.009 to 0.052	0.166
MUFA (PUFA)	1	0.372	-0.319 to 1.062	0.291	0.058	0.011 to 0.105	0.015
	2	-0.149	-0.860 to 0.562	0.681	0.045	-0.005 to 0.095	0.078
Protein (alcohol)	1	-0.022	-0.307 to 0.263	0.880	-0.031	-0.050 to -0.011	0.002
	2	0.108	-0.167 to 0.383	0.441	-0.026	-0.045 to -0.006	0.010

SMBG, self-monitored blood glucose; CV, coefficient of variation; SAFA, saturated fatty acids; MUFA, monounsaturated fatty acids; PUFA, polyunsaturated fatty acids. Model 1 is adjusted for age, sex, BMI, triglyceride concentration, insulin dose/kg, and physical activity. Models with fatty acid have been additionally adjusted for trans-fatty acids. Model 2 is further adjusted for fibre intake. Generalized linear regression. In these substitution models, one macronutrient at the time is considered as an independent variable, while one of the macronutrients (in the parentheses) is excluded from the model. The remaining macronutrients and total energy intake remain as covariates. The obtained results represent an increase (when positive) or a decrease (when negative) in the dependent variable when the intake of the independent macronutrient is increased by 5% of total energy at the expense of the excluded macronutrient.