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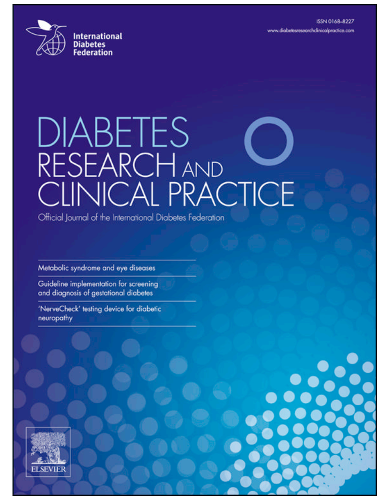

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Association between depressive symptoms and dietary intake in patients with type 1 diabetes

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Abstract

Aims: Depressive mood negatively affects self-care practices, and thereby increases the risk of long-term complications. Not much is known about the association between depressive symptoms and dietary intake in patients with type 1 diabetes, a population with high risk of cardiovascular disease.

Methods: Subjects (n=976, 41% men, age 48±14 years) were participants in the Finnish Diabetic Nephropathy Study. Depressive symptomatology was assessed with the Beck Depression Inventory (BDI). Dietary patterns were derived from food frequency questionnaire-entries by exploratory factor analysis. Energy and macronutrient intakes were calculated from food records. In the same record, participants also reported the results of their daily blood glucose monitoring. Associations between BDI score and self-care variables were analysed using generalized linear regression. For macronutrients, a substitution model was applied.

Results: Two dietary patterns ("Fish and vegetables", and "Traditional") negatively associated with the BDI score. Instead, an increase in the "Sweet" pattern score was positively associated with depressive symptomatology. Of the macronutrients, favouring protein over carbohydrates or fats associated with lower depression scores. Higher blood glucose self-monitoring frequency and higher variability of the measurements were positively associated with the BDI score. However, no association was observed between depressive symptoms and the mean of the blood glucose measurements.

Conclusions: Depressive symptoms are reflected in the dietary intake and the self-monitoring of blood glucose, in type 1 diabetes. Whether depression, via compromised self-care practices, negatively affect long-term outcomes in this patient group has to be the subject of future studies.

Keywords: Depressive symptoms; Dietary intake; Type 1 diabetes

1. Introduction

Diabetes is a major risk factor for various cardiovascular complications [1], and the emergence of these complications is associated with poor prognosis and high risk of premature mortality [2,3]. In addition to cardiovascular morbidity and mortality, diabetes is also frequently burdened by depression [4,5]. Importantly, depression in patients with diabetes is associated with greater non-adherence to various self-care practices [6,7], and may thereby further increase the risk of adverse long-term outcomes [8].

Of the self-care practices diet has the potential to, amongst others, modulate gut microbiota and inflammation [9], oxidative stress [10], cell membrane plasticity [11], and body composition [12]. These physiological phenomena may, on the other hand, be related to both cardiovascular health and depression [13]. A number of studies have been conducted to reveal an association between dietary intake and depression [14–17]. Many of these studies suggest that a diet rich in fruits, vegetables, and fish is associated with lower odds of depression [14,15], while a Western dietary pattern, with high intake of processed meats, refined grains and sugary products, are more typically associated with increased rates of depression [15,16]. The current literature is not consistent, however, as Prudent or Western dietary patterns are not unambiguously associated with the risk of depression [17].

As opposed to the food-based approach, taken in the above-mentioned studies, some studies have focused on the association between macronutrient intake and depression [18–20]. While a positive connection between carbohydrate intake and depression have been reported in some of these studies [18], the results are far from consistent [19]. In one study, neither carbohydrate nor fat intake showed any relation to depressive mood [20]. In the same study low protein intake, instead, was associated with higher prevalence of depressive symptoms.

Despite the emerging body of knowledge regarding the association between depression and dietary intake, such reports are practically non-existent in the type 1 diabetes population, a population with high risk of both depression and cardiovascular complications. There is some indication that depression in this patient group is associated with higher odds of disturbed eating behaviour [21], but the remaining observations in this field have been largely obtained from individuals with type 2 diabetes or mixed populations of subjects with type 1 and type 2 diabetes. While this is most likely explained by the fact that type 2 diabetes is the more prevalent diabetes type, these two diseases have important distinctions, such as different aetiologies and often also different treatment regimens, which warrant separate investigations.

In order to fill in the gaps in the knowledge, we aimed to study the association between dietary intake and symptoms of depression in a large population of individuals with type 1 diabetes. To this end, our approach was twofold. First, we looked at the association between mood and food intake at the level of dietary patterns. Second, we investigated the association between depressive symptoms and macronutrient intake, using the macronutrient substitution model. Finally, we looked at the association between depressive symptoms and self-monitoring of blood glucose (SMBG) practices.

2. Research design and methods

2.1. Study subjects

Study subjects were participants in the Finnish Diabetic Nephropathy (FinnDiane) Study. The FinnDiane Study is an ongoing endeavour to identify risk factors for diabetic complications in individuals with type 1 diabetes. In the current study, type 1 diabetes was assumed if diabetes was diagnosed before the age of 35 years, and permanent insulin treatment initiated within one year of the diagnosis. We included, in the current cross-sectional analyses, those who had completed both the Beck Depression Inventory and the diet questionnaire by the end of July 2017 (n=976, 41% men, mean ± standard deviation age 48 ± 14 years). The study protocol was approved by the Ethics Committee of the Helsinki and Uusimaa Hospital District as well as by the local ethics committees at each centre. Written informed consent was obtained prior to participation from each participant.

2.2. Clinical characteristics and laboratory tests

Participants' height and weight were measured in light clothing. Based on these measurements, body mass index (kg/m^2) was calculated. Following a minimum ten-minute rest, blood pressure was measured while seated. A second measurement was taken after a two-minute interval, and the mean of the two measurements was calculated. On a standardised questionnaire, patient's attending physician recorded cardiovascular hard events (acute myocardial infarction, coronary bypass procedures, stroke, amputation, and peripheral vascular disease). Smoking was self-reported. Blood samples were collected and HbA_{1c} was determined locally using standardised assays. Serum lipid and lipoprotein concentrations were measured as previously described [5].

2.3. Depressive symptomatology

Symptoms of depression were evaluated by using the self-reported, 21-item Beck Depression Inventory (BDI) [22]. A score ranging from 0 to 63 was calculated for each participant. In the multivariable analyses, the score was used as a continuous variable. However, for the purpose of describing the study population (Tables 1 and 4), we used a BDI score cut-off value of ≥16 to identify individuals with symptoms of depression.

2.4. Dietary patterns and macronutrient intake

Information on the subjects' dietary intake was collected using two separate methods, as previously described [23]. First, participants completed a validated diet questionnaire [24]. With this self-reported questionnaire, we aimed at capturing information on the participants' habitual dietary intake. As part of this form was embedded a food frequency questionnaire (FFQ). Here, on a seven point response scale ranging from "multiple times per day" to "once a month or less frequently", participants reported their intakes of fish dishes, meat dishes, poultry, sausages and cold cuts, eggs, legumes, fresh vegetables, cooked vegetables, potatoes, pasta and rice, fruits and berries, high-fat cheese, low-fat cheese, yoghurt and curd, ice cream, soft drinks, sweet pastries, sweets and chocolate, and fried and grilled foods. For the analyses, the FFQ entries were transformed to pseudo continuous variables describing the consumption frequencies per month. Thus, for example, "once a day" was recoded as 28, and "once a week" as 4. These data were analysed using exploratory factor analysis to reveal dietary patterns, as described in the statistical analyses.

Upon returning the diet questionnaire, the participants were sent an allocated three-day (two weekdays and one weekend day) exercise and food record. In this record, data on food consumption, physical activity, insulin dosing, and blood glucose measurements were reported. The three-day record-keeping was repeated within 2-3 months with the aim to obtain data from a total of six days with some seasonal variation. From these entries, mean energy and macronutrient contents (in grams, and in percentages of total energy intake, E%) 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 estimated as the difference between total fat and the sum of saturated, monounsaturated, and polyunsaturated fatty acids. Accordingly, the trans-fatty acids were only used to adjust the models, and were not used as an independent variable.

2.5. Self-monitoring of blood glucose

Data on SMBG were extracted from the exercise and food record. For each individual, we calculated the number of reported SMBG measurements and divided the obtained figure with the number of days the record were kept. We additionally calculated the mean and standard deviation of the reported blood glucose values.

2.6. Statistical analyses

Data are presented as frequencies (%) for categorical variables, mean ± standard deviation (SD) for normally distributed continuous variables, and median (interquartile range) for non-normally distributed continuous variables. The respective between-group comparisons were performed using Chi-squared test, independent-sample t-test, and Mann-Whitney U-test.

Generalized linear model was used to investigate the independent associations between the self-care variables and the BDI score. From the FFQ-derived data, exploratory factor analysis (maximal likelihood and varimax rotation) was used to identify underlying dietary constructs. In this analysis, the number of factors identified was based on eigenvalues >1.0, and items with factor loading |≥0.20| with a particular factor, were included. The factor score was the sum of the scores for all items associated with that particular factor multiplied by its corresponding factor loading. When investigating the association between mood and macronutrient intake, we applied the multivariable nutrient density substitution models, as previously described [25]. Using this approach, we mathematically assessed how an isoenergetic (5 E%) substitution of a given macronutrient with another macronutrient is related to the outcome variable (BDI score). This was achieved by including, in each model at a time, all but one macronutrient (per 5 E%), total energy intake, and other potential confounders. For example, in an equation: BDI score = $\beta_0 + \beta_1$ (5 E% from carbohydrates) + β_2 (5 E% from fats) + β_3 (5 E% from alcohol) + β_4 (kcal), β_1 would be interpreted as the change in the BDI score when dietary carbohydrate intake is increased by 5 E% at the expense of proteins. All analyses were conducted 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.

3. Results

Data from a total of 976 individuals with type 1 diabetes were available for the analyses. Of these participants, 116 (12%) had symptoms of depression (BDI ≥16). The proportion of men was lower among these individuals, compared to those without depressive symptoms (Table 1). Furthermore, the proportion of smokers and those with a cardiovascular hard event, was higher among those with depressive mood.

3.1. FFQ-derived dietary patterns

Seven dietary factors with high degree of inter-correlation were formed from the factor analysis of the FFQ data (Table 2). The factors (or dietary patterns) were intuitively named based on the food items included. In the multivariable model, adjusted for age, sex, smoking, cardiovascular hard event status, and other dietary patterns, increased factor scores of “Fish and vegetables” and “Traditional” dietary patterns were associated with lower BDI scores (Table 3). Instead, higher factor scores in the “Sweet” pattern were associated with higher BDI scores.

3.2. Food record-derived macronutrient data

The participants with symptoms of depression reported lower total energy, carbohydrate, fat, and protein intake (Table 4). However, no differences were seen in the macronutrient distribution, calculated as percentages of total energy intake, between the two groups. Using the macronutrient substitution approach, increased carbohydrate intake, at the expense of protein was associated with higher BDI score (Table 5). Similarly, substituting fats for proteins was also associated with higher BDI scores. As a note, the results of these substitution models may also be interpreted reversely, thus, increased intake of protein at the expense of carbohydrates or fats, is associated with lower BDI scores. Isoenergetic substitution between other macronutrients, or between fatty acids, was not associated with the BDI score.

3.3. Self-monitoring of blood glucose

Those with symptoms of depression reported more frequent blood glucose monitoring (Table 4). However, no between-group difference was observed in the mean of the reported blood glucose values or in the variation of these measurements, over the record-keeping days, in the unadjusted models. In line with these observations, the measured HbA_{1c} was no different between the two groups (Table 1). In a generalized linear model, adjusted for age, sex, smoking, and cardiovascular hard event status, the SMBG frequency (B = 0.252, 95% Wald Confidence Interval = 0.022 – 0.482, $P = 0.032$), and the standard deviation of the reported blood glucose values (B = 0.398, 95% Wald CI = 0.049 – 0.746, $P = 0.025$) were positively associated with the BDI score. With respect to the association between the BDI score and the mean of the measured blood glucose values, only a trend toward a positive association was observed (B = 0.234, 95% Wald CI = -0.002 – 0.469, $P = 0.052$).

4. Discussion

In a large population of individuals with type 1 diabetes, we observed an association between depressive symptoms and dietary intake at the level of both dietary patterns and macronutrient intake. Of the dietary patterns, the “Fish and vegetables” pattern, rich in fresh and cooked vegetables, fruits and berries, fish, and legumes, but low in soft drinks, was associated with better mood. Similarly, the “Traditional” dietary pattern scores, high in meat dishes, potatoes, and sausages and cold cuts, were associated with lower levels of depressive symptoms. Instead, the “Sweet” dietary pattern, comprising of sweet pastry, sweets and chocolate, and ice cream, was associated with higher depression scores. Looking at the dietary intake at the macronutrient level, we observed that favouring protein over either carbohydrates or fat was associated with lower levels of depressive symptoms.

While the association between dietary patterns and depression in type 1 diabetes has not previously been investigated, our observations, especially those dealing with the “Fish and vegetables” dietary pattern (something that could also be called the “Healthy” dietary pattern), are well in concordance with those reported in other populations. Indeed, in a meta-analysis of 21 studies, a Healthy dietary pattern, with high intakes of fruits, vegetables, whole grains, poultry, fish, and low-fat dairy products, was associated with reduced odds of depression [14]. There seems to be some diversity between studies, however, in how potatoes, meat, refined grains, and sugar-containing products are pooled into the dietary patterns. When pooled together, to approximate a Western dietary pattern, such a pattern has either been associated with increased odds of depression [26] or, alternatively, no association has been observed [14,27]. In their “Western” dietary pattern, instead, Jacka et al. omitted meat and potatoes, but included refined grains and sugary products [28]. This pattern, which shares similarities to our “Sweet” pattern was associated with increased depression score. Instead, meat dishes, in their analyses, were included in the “Traditional” dietary pattern which, similar to ours, was beneficial with respect to mental health.

Looking at the association between the macronutrient intake and depression offers a different perspective from the one obtained when investigating dietary patterns. Importantly, in isoenergetic conditions, when analysing macronutrient intakes one has to consider that reduction in one of the macronutrients is simultaneously accompanied by an increase in other macronutrient(s). The macronutrient substitution model offers a means to mathematically investigate how such an isoenergetic substitution between macronutrients would affect the outcome variable of interest. Using this approach, we observed that favouring carbohydrates over proteins was associated with higher depression scores. This observation is in line with the ones previously made in other populations [29,30].

A number of mechanisms explaining the connection between carbohydrate indulgence and depression has been suggested. One is the metabolism related to insulin [29]. Insulin, required to process the ingested carbohydrates, also facilitates the transport of tryptophan in the brain. Tryptophan, on the other hand, is required for the synthesis of serotonin, the neurotransmitter with a potential role in modulating mood. Consumption of carbohydrates could, therefore, be seen as an unconscious attempt to self-treat depressed mood. Another mechanism, particularly important to the individuals with type 1 diabetes, is that carbohydrate consumption directly boosts blood glucose levels. Of note here is that, while carbohydrates are more abundantly consumed when hypoglycaemic, their excess consumption may also result in hyperglycaemia. Indeed, compared to individuals without depressive symptoms, those with depressive symptoms have more frequently both hypoglycaemic and hyperglycaemic episodes [31]. While worse glycaemic control, referring to higher HbA_{1c} levels, have sometimes been reported in depressive individuals [32], the depressive symptomatology was not, in the current study, related to the glycaemic control. Instead, an independent positive association between the variability in the measured blood glucose levels and the depressive symptom scores was observed.

Yet another mechanism related to the association between carbohydrate intake and depression may not be due to the carbohydrates *per se*, but rather to what the carbohydrate-rich foods are lacking. Notably, abundant intake of sweet foods may result in reduction of the consumption of more nutrient-dense foods. Such poor quality diets may compromise the intake of nutrients important for mental well-being, including folate and other B vitamins, vitamin D, calcium, chromium, zinc, and magnesium [33]. Moreover, constituents of a healthy diet may influence the mental state indirectly, via supporting the growth and well-being of mood-enhancing gut microbiota [34]. Taken together, these factors could also explain why the "Fish and vegetables" and "Traditional" dietary patterns, that are high in nutrient-rich food items, were associated with lower levels of depressive symptoms. Finally, the convenience related to the consumption of carbohydrate-rich ready-made food products may serve as a practical explanation connecting depressive mood and high carbohydrate intake. Loss of interest in various activities, frequently related to depression may, after all, also extend to cooking.

We additionally observed that substituting fats for proteins was associated with increased levels of depressive symptoms. As was the case for carbohydrates, abundant consumption of fats may be a proxy for an overall poor diet quality. Indeed, such a diet may either be low in nutrients sufficient to support mental health or be secondary to poor food choices associated with depression-related anhedonia. Importantly, fats should not be looked at as one large entity, however, since different types of fats have different health effects. For example, the beneficial roles of omega-3 fatty acids, naturally found in fatty fish, and the detrimental effects of trans-fatty acids are often distinguished. The consumption of the former has been positively associated with mood [35], while the consumption of the latter is related to increased levels of depression [36,37]. The anti-inflammatory properties of polyunsaturated and monounsaturated fatty acids, more commonly associated with cardiovascular health, could also explain the relation between these fatty acids and the reduced odds of depression [36]. The case for the saturated fatty acids seems to be less clear, however, as no association [36], lower odds [38], and higher odds of depression [39] have been reported. In the current study, the relative distribution of different fatty acids was not associated with the depression scores.

There are a number of limitations related to the current study that need to be taken into consideration when interpreting the results. First, the setting is cross-sectional which prevents us from drawing conclusions about the cause and effect between diet and depression. While it is plausible that the quality of diet affects the mood, it is also likely that depression has an effect on the dietary choices an individual makes. Thus, the current results do not imply that healthy diet and intake of sweets are causal of good mental health and depression, respectively. Longitudinal studies are needed to reveal the causality between diet and depression. In due time, these data will serve as baseline for the subsequent analyses where the longitudinal associations will be investigated. Importantly, the current observations may be used to help identify individuals with special needs for enhanced dietary guidance. Second, data on both the dietary intake and the symptoms of depression were collected using self-reported questionnaires. While the use of self-report methods is convenient in large epidemiological studies, the collected data may also be subject to misreporting. With respect to the dietary data, for example, the intake of food items generally considered healthy may likely be overestimated, while those of non-healthy may be underestimated. Moreover, in the current study, the reported total energy intake was low both in the depressed and the non-depressed individuals. This may not be a major limitation, however, as instead of focusing on the total energy intake, we were rather interested in the macronutrient distribution. Importantly, the affective status has previously not been shown to be associated with major misreporting of macronutrients [40], suggesting that no systematic bias should be evident. With respect to the self-reported questionnaire used to study the depressive symptoms, some level of under-reporting of symptoms may be expected [41]. Should such under-reporting have taken place, it has most likely diluted the current results. Third, some selection bias may have taken place, as individuals more interested in health-related issues more likely volunteer in trials. Such selection bias, we argue, has rather the potential to dilute the current observations. Fourth, it is likely that depression, in men and women, is displayed in distinct eating behaviours. It has, for example, previously been shown that lower rates of depression are positively associated with

Healthy dietary pattern [42], and closer adherence to the dietary guidelines [43] in women but not in men. Moreover emotional eating has, in some studies [44] but not all [45], been associated with female sex. The current study was, however, underpowered to investigate the sex-specific differences in depression and dietary intake. These associations will need to be investigated in the future in a larger population. Finally, the possibility of residual confounding due to variables not taken into account, cannot be excluded. Importantly, dietary habits may be a component of an overall lifestyle, which may influence mood and mental wellbeing. Amongst the strengths of the current study are the use of validated questionnaires, and a large, well-defined study population. Moreover the dual approach taken, covering the association of symptoms of depression both with dietary patterns and macronutrient intake, is a valuable addition to the obvious knowledge gap in this high risk patient population.

In conclusion, two dietary patterns were observed to be positively associated with mood, “Fish and vegetables” and “Traditional”. While differing in the actual food items included, those included in both dietary patterns are more nutrient-rich, compared to the “Sweet” pattern which was associated with higher depression scores. Macronutrient-wise we observed that favouring proteins over carbohydrates or fats was associated with better mental health. In the future, the longitudinal associations between dietary intake and mood will be evaluated. These cross-sectional data will also help assessing whether depressed mood, via compromised self-care practices, negatively affects the long-term health outcomes in this patient group.

Conflict of interest statement 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, 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 conflicts of interest.

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Table 1 Basic characteristics divided by presence or absence of depressive symptoms

	No symptoms of depression n = 860 (88%)	Symptoms of depression n = 116 (12%)	*P*
Men, %	43	27	0.001
Age, years	48 (37 – 58)	50 (36 – 60)	0.675
BDI score	4 (1 – 7)	20 (18 – 25)	<0.001
BMI, kg/m^2	25.3 (23.2 – 28.1)	26.0 (23.0 – 30.1)	0.145
Systolic blood pressure	136 (125 – 151)	135 (122 – 149)	0.562
Diastolic blood pressure	76 (70 – 83)	77 (73 – 83)	0.349
HbA_{1c}, mmol/mol	64 (56 – 73)	64 (57 – 70)	0.895
HbA_{1c}, %	8.0 (7.3 – 8.8)	8.0 (7.4 – 8.6)	0.895
Total cholesterol, mmol/l	4.4 (3.9 – 5.0)	4.4 (4.0 – 5.2)	0.344
HDL cholesterol, mmol/l	1.7 (1.4 – 2.0)	1.7 (1.4 – 2.0)	0.900
Triglyceride, mmol/l	0.9 (0.7 – 1.2)	1.0 (0.6 – 1.4)	0.085
Current smoking, %	10.9	17.5	0.044
Cardiovascular hard event, %	15	23	0.020

Data are presented as frequencies (%) for categorical variables, and median (interquartile range) for continuous non-normally distributed variables. Between-group differences have been analysed with Chi-squared test, and Mann-Whitney U-test, respectively. Symptoms of depression, BDI score ≥16; BDI, Beck Depression Inventory; BMI, body mass index.

Table 2 Factor analysis-derived dietary patterns

Dietary pattern	Eigenvalue	% of variance	Included food items	Factor loadings
Fish and vegetables	2.26	11.89	Fresh vegetables	0.548
			Cooked vegetables	0.533
			Fruits and berries	0.509
			Fish dishes	0.286
			Legumes	0.250
			Soft drinks	-0.228
Sweet	1.92	10.09	Sweet pastry	0.663
			Sweets and chocolate	0.582
			Ice cream	0.352
Modern	1.59	8.36	Poultry	0.544
			Pasta and rice	0.533
			Meat dishes	0.376
			Fried foods	0.366
			Fresh vegetables	0.239
Legumes and vegetables	1.41	7.43	Legumes	0.959
			Cooked vegetables	0.243
Traditional	1.37	7.22	Meat dishes	0.788
			Potatoes	0.424
			Sausages and cold cuts	0.334
High-fat cheese and eggs	1.09	5.71	High-fat cheese	0.826
			Eggs	0.236
			Low-fat cheese	-0.379
Healthy snack	1.00	5.29	Yoghurt and curd	0.648
			Fruits and berries	0.303
			Low-fat cheese	0.238

Eigenvalues are the variances of the factors; % of variance represent the per cent of total variance accounted by each factor; factor loadings show the correlation of each food item with the given dietary pattern.

Table 3 The associations between Beck Depression Inventory score and dietary patterns

Dietary pattern	Model	B	95% Wald Confidence Interval	*P*
Fish and vegetables	1	-0.824	-1.484 – -0.164	0.014
	2	-0.795	-1.470 – -0.120	0.021
Sweet	1	0.649	0.058 – 1.239	0.031
	2	0.698	0.091 – 1.305	0.024
Modern	1	0.531	-0.113 – 1.175	0.106
	2	0.670	-0.004 – 1.345	0.051
Legumes and vegetables	1	0.268	-0.208 – 0.744	0.270
	2	0.269	-0.212 – 0.750	0.274
Traditional	1	-0.631	-1.191 – 0.071	0.027
	2	-0.713	-1.285 – -0.141	0.015
High-fat cheese and eggs	1	-0.066	-0.608 – 0.476	0.812
	2	-0.011	-0.564 – 0.543	0.970
Healthy snack	1	-0.360	-1.039 – 0.319	0.298
	2	-0.284	-0.977 – 0.409	0.422

Model 1 is adjusted for age, sex, and the other dietary patterns. Model 2 is further adjusted for smoking and cardiovascular hard event status. Generalized linear regression.

Table 4 Self-monitoring of blood glucose, energy, and macronutrient intake divided by presence or absence of depressive symptoms

	No symptoms of depression n = 860 (88%)	Symptoms of depression n = 116 (12%)	*P*
Daily SMBG frequency, n	3.7 (2.2 – 4.8)	4.0 (3.0 – 5.3)	0.011
Mean SMBG, mmol/l	8.1 (6.9 – 9.4)	8.3 (7.0 . 9.7)	0.248
SD of SMBG values	3.3 (2.5 – 4.1)	3.5 (2.9 – 4.3)	0.083
Energy, kcal	1842 (1526 – 2164)	1633 (1389 – 1915)	<0.001
Carbohydrate, g	196 (155 – 238)	171 (144 – 210)	0.001
Carbohydrate, E%	42.9 (38.3 – 47.1)	43.3 (39.3 – 46.9)	0.470
Fat, g	73.2 (58.7 – 90.7)	63.9 (51.9 – 81.0)	0.001
Fat, E%	36.3 (31.7 – 40.3)	36.4 (32.3 – 39.9)	0.812
SAFA, E%	12.6 (10.6 – 14.7)	13.0 (10.7 – 14.6)	0.895
MUFA, E%	12.0 (10.6 – 13.9)	12.3 (10.6 – 13.9)	0.464
PUFA, E%	6.0 (5.1 – 7.0)	6.0 (5.1 – 6.8)	0.949
Protein, g	75.7 (62.9 – 92.3)	68.6 (56.1 – 85.6)	<0.001
Protein, E%	16.6 (14.8 – 18.7)	16.5 (14.4 – 18.8)	0.486
Alcohol, g	1.9 (0 – 7.5)	0.4 (0 – 7.7)	0.342
Alcohol, E%	0.7 (0 – 2.9)	0.2 (0 – 2.7)	0.458

Data are presented as median (interquartile range). Between-group comparisons are done with Mann-Whitney U-test. Symptoms of depression, BDI score ≥16; SMBG, self-monitoring of blood glucose; SD, standard deviation; E%, percentage of total energy intake; SAFA, saturated fatty acids; MUFA, monounsaturated fatty acids; PUFA, polyunsaturated fatty acids.

Table 5 The association between Beck Depression Inventory score and macronutrient intake (substitution model)

Macronutrient intake increased (decreased)	B	95% Wald Confidence Interval	*P*
Carbohydrate (fat)	0.153	-0.219 – 0.525	0.420
Carbohydrate (protein)	1.086	0.381 – 1.791	0.003
Carbohydrate (alcohol)	0.362	-0.317 – 1.041	0.296
Fat (protein)	0.912	0.178 – 1.645	0.015
Fat (alcohol)	0.226	-0.486 – 0.937	0.534
SAFA (MUFA)	0.511	-1.330 – 2.352	0.587
SAFA (PUFA)	0.744	-0.556 – 2.044	0.262
MUFA (PUFA)	1.220	-1.139 – 3.578	0.311
Protein (alcohol)	-0.726	-1.686 – 0.234	0.138

SAFA, saturated fatty acids; MUFA, monounsaturated fatty acids; PUFA, polyunsaturated fatty acids. All models are adjusted for age, sex, smoking, and cardiovascular hard event status. Models with fatty acid have been additionally adjusted for trans-fatty acids. Generalized linear regression. In each model, a given macronutrient is included as an independent variable, while one of the macronutrients (shown in the parentheses) is excluded from the model. The remaining macronutrients and total energy intake are included as covariates. The B (95% Wald Confidence Interval) represent the increase (if positive) or decrease (if negative) in the Beck Depression Inventory score when the intake of the independent macronutrient is increased by 5% of total energy at the expense of the excluded macronutrient.