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ABSTRACT

Background Depression and diet quality appear to be associated in the general population. Nevertheless, little is known about their relationship among pregnant females.

Objective The aims of this study were first, to investigate longitudinally whether or not diet quality is associated with depressive symptoms during pregnancy; second, to examine whether or not variation in diet quality during pregnancy predicts variation in depressive symptoms; and third, to explore how individual dietary components are associated with depressive symptoms.

Design A longitudinal secondary analysis of the Kuopio Birth Cohort Study in eastern Finland was conducted. Data were collected from pregnant females during the first and third trimesters of pregnancy.

Participants/setting The participants were 1,362 pregnant females who entered the study between 2012 and 2017.

Main outcome measures Depressive symptoms, as measured with the Edinburgh Postnatal Depressive Scale during the first and third trimesters of pregnancy were used as continuous variables.

Statistical analyses performed The main analyses consisted of linear mixed model analyses adjusted for potential confounders to longitudinally assess the association between diet quality as measured by the Healthy Eating Index-2015, calculated using data from a food frequency questionnaire completed during the first trimester and third trimester, and depressive symptoms during the study period. An exploratory set of linear mixed models was also used to longitudinally assess the associations between selected individual food frequency questionnaire food groups and depressive symptoms.

Results Descriptive analyses revealed that 12.3% of the participants had clinically relevant levels of depressive symptoms (ie, Edinburgh Postnatal Depressive Scale score $\geq$10) during either the first or third trimester. Longitudinal modeling suggested that depressive symptoms in pregnant females tend to remain stable throughout pregnancy. Females with a poorer quality diet already displayed higher levels of depressive symptoms during the first trimester of pregnancy ($\beta = -.038 \pm .016$; $P = 0.022$). Variation in diet quality did not predict variation in depressive symptoms over the course of pregnancy ($\beta = -9.741 \times 10^{-5} \pm .001$; $P = 0.869$).

Conclusions Females entering pregnancy with a poorer quality diet also displayed higher levels of depressive symptoms compared with females with a higher quality diet at the beginning of pregnancy, and this association remained constant throughout pregnancy. Further research is needed to assess the direction and the potential causality of the observed associations between diet quality and depressive symptoms.
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DEPRESSION, THE LARGEST CONTRIBUTOR TO disability globally alongside back and neck pain,[1,2] is both common and underrecognized during pregnancy,[3] affecting 9.2% to 19.2% of females, depending on the country and ethnicity.[4] About half of pregnant females experiencing major depression have no previous history of depression.[5]

The identification, prognosis, and treatment of prenatal depression and its risk factors are of utmost importance in current psychiatry and obstetrics care because prenatal

depression can lead to potentially devastating effects on both the mother and the developing child, such as maternal postpartum depression,[6] an increased risk of maternal suicide during the perinatal period,[7-9] preterm birth, low birth weight,[10] and higher levels of internalizing, externalizing, and general psychopathology during childhood.[11]

The risk factors identified for prenatal depression include the lack of a partner, a history of abuse or domestic violence, high perceived stress, previous pregnancy loss and pregnancy complications, a low education level, and smoking.[12] Diet, on the other hand, is currently considered a modifiable risk factor for depression in the general population.[13-15] Nevertheless, little is known of the relationship between depression and diet among pregnant females. To date, seven investigations have demonstrated significant associations between a lower quality diet and higher levels of depressive symptoms during pregnancy,[16-22] whereas four other studies have yielded less clear findings, including both significant and nonsignificant findings, depending on the dietary aspect investigated.[23-26]

Due to the heterogeneity of designs in previous studies focusing on depression and diet during pregnancy, the poor availability of longitudinal data (only four of the previous studies were longitudinal[20,21,23,26]), and the inconsistent results, further investigations are essential. To this end, a longitudinal prospective cohort study was conducted to investigate, first, the association between diet quality and depressive symptoms during pregnancy, as measured during the first (T1) and third (T3) trimesters. It was hypothesized that a lower quality diet is associated with a higher level of depressive symptoms, irrespective of the measurement point during pregnancy. The second aim of this study was to investigate whether or not variation in diet quality during pregnancy predicts variation in depressive symptoms. It was hypothesized that changes in diet quality are associated with variation in depressive symptoms during pregnancy. Third, if the first and second hypotheses were supported by the results of the main analyses, a more explorative analysis of the associations between individual dietary components and depressive symptoms would be conducted.

MATERIALS AND METHODS

Study Population

This study was a secondary analysis of data from the Kuopio Birth Cohort (KuBiCo) (www.kubico.fi) Study. KuBiCo, a Finnish birth cohort study aimed at examining the effects of genetics and pregnancy-related stress factors on the health of the mother and her child, is an ongoing joint effort between the University of Eastern Finland, Kuopio University Hospital (KUH), and the National Institute for Health and Welfare. A detailed description of KuBiCo has been given elsewhere.[27] In brief, KuBiCo is an epidemiological study initiated during 2012 with an aim to collect data from a total of 10,000 mother–child pairs. All pregnant females in the KUH catchment area are eligible and invited to participate. KUH provides tertiary care services for a population of nearly 1 million people (ie, approximately one-fifth of the Finnish population) in eastern and central Finland. The participation rate in KuBiCo was approximately 37% of all pregnant females in the KUH catchment area during 2012 to 2017, when the data used in this study were gathered. A descriptive analysis by Huuskonen and

RESEARCH SNAPSHOT

Research Question: Is diet quality, as measured by the Healthy Eating Index 2015, associated with depressive symptoms, as measured by the Edinburgh Postnatal Depression Scale, during pregnancy? Is variation in diet quality associated with variation in depressive symptoms between the first and third trimesters of pregnancy? What is the role of individual dietary components in the aforementioned associations, in the case that such are detected?

Key Findings: In this prospective cohort that included 1,362 pregnant Finnish females from the Kuopio Birth Cohort Study, lower diet quality was associated with a higher level of depressive symptoms in both the first and third trimesters. Variation in diet quality did not predict variation in the level of depressive symptoms.

colleagues[27] demonstrated that KuBiCo is representative of Finnish pregnant females. Participants gave their written informed consent after receiving a full explanation of the study. The protocol of KuBiCo has been approved by the research ethics committee of the Central Finland Health Care District (8.12.2011, K-S SHP Dnro 18U/2011).

An initial sample of 4,144 pregnant females was retrieved from the KuBiCo database during January 2017, the time frame of the data collection thus being from 2012 to 2017. Information on the sex of the study participants was obtained from personal data stored in the Finnish Population Information System. For each mother, only the first pregnancy recorded in the KuBiCo database was included, and any later pregnancies were disregarded. Multiembryonic and anembryonic pregnancies (n = 94), as well as cases with missing information on the number of fetuses (n = 61), were excluded. Mothers who had completed a depression questionnaire after the delivery or had missing completion dates in depression questionnaires were excluded (n = 43). Among the remaining sample, data on depressive symptoms were available from 1,414 females between gestational weeks 5 and 12 (T1), and from 1,867 between gestational weeks 28 and 44 (T3). Similarly, data on diet quality were available for 1,169 and 2,149 females in T1 and T3, respectively. The final study population consisted of 1,362 mothers with background information on all the covariates of interest and data on both depression and nutrition from at least one evaluation time point during pregnancy, whereas mothers not meeting these criteria were excluded (n = 2,223) (see the Figure).

Depressive Symptoms

Depressive symptoms during pregnancy were assessed using the Finnish translation of the Edinburgh Postnatal Depression Scale (EPDS) questionnaire[28] through an online survey. The EPDS has been shown to be valid and reliable for screening depression during pregnancy.[29,30] The Finnish translation of the EPDS has not been validated in the Finnish population. However, it is used as a routine screening method for depressive symptoms in Finnish prenatal care clinics[31] and has also been extensively used in previous research.[32-34] Beyond Finland, for example, the American College of
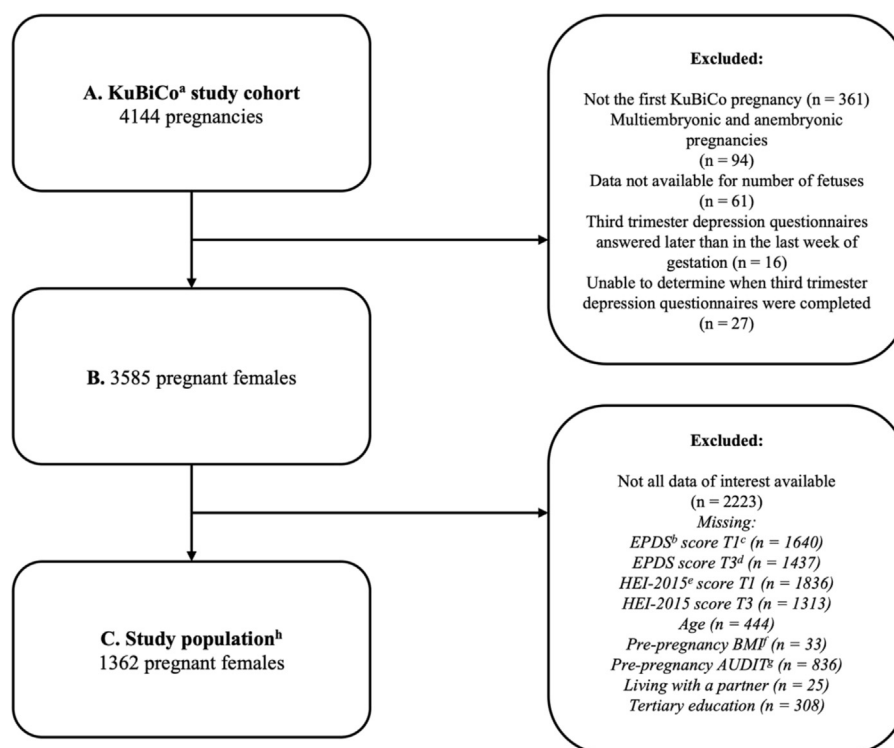
Figure. Flow diagram illustrating the selection of study participants from the Kuopio Birth Cohort database, with the number of persons excluded in each step in parentheses. The study assessed the association between maternal diet quality and depressive symptoms during pregnancy in the participants of the Kuopio Birth Cohort Study, with data gathered between 2012 and 2017 at Kuopio University Hospital, Kuopio, Finland. [a]KuBiCo = Kuopio Birth Cohort Study. [b]EPDS = Edinburgh Postnatal Depression Scale. [c]T1 = first trimester. [d]T3 = third trimester. [e]HEI-2015 = Healthy Eating Index 2015. [f]BMI = body mass index. [g]AUDIT = Alcohol Use Disorders Identification Test questionnaire. [h]To be included in the study population, the participant was required to have valid data available for EPDS in T1 and/or T3, and valid data available for HEI-2015 in T1 and/or T3, in addition to valid data available for all the covariates.

Obstetricians and Gynecologists recommends screening for depression during pregnancy and points out the EPDS as the most frequently used instrument.[35]

Invitations to participate in the survey, with individualized encryption keys together with information regarding the survey and how to respond, were sent to participants' e-mail addresses, with a reminder sent 2 weeks after the initial invitation in case the survey was not confirmed to be completed in this time. Participants could access the survey from any Internet-compatible device located in Finland. The survey automatically closed after 8 weeks if it had not been completed.

The EPDS is calculated based on a 10-item questionnaire with four response options for each question. The total range of the EPDS is zero to 30 points, with each question providing zero to three points. A cutoff value ≥10 or more suggests that a mother presents a clinically relevant level of depressive symptoms.[28] The EPDS score was used as the primary outcome variable of this study, and more specifically as a continuous variable in the linear mixed models, whereas grouping based on a cutoff value ≥10 was utilized in descriptive statistics. Cronbach alpha calculations evaluating the consistency of the EPDS scores within the sample were 0.85 for T1 and 0.93 for T3, which are acceptable and in line with the previously reported consistencies for the questionnaire.[28]

Diet Quality

Dietary data during pregnancy were collected in T1 and T3 using a food frequency questionnaire (FFQ) through an online-based survey in Finnish. The FFQ was part of the same online survey that contained the EPDS questionnaire. This FFQ was a version of the FFQ used in the Kuopio Breast Cancer Study, for which the validity and reliability have been described earlier.[36] The FFQ was modified by the addition of food items to reflect the increased selection of contemporary food items available (eg, probiotic yogurts). The modified FFQ included 163 food items, with a predefined portion size for each item and with nine frequency response options, over the previous 3 months. Only fully completed FFQs were entered into the KuBiCo database. Food consumption and nutrient intakes were calculated by multiplying the frequency of food consumption by the portion size (in grams) to obtain the estimated intake of each listed food item as an average daily intake.

Average daily food, nutrient, and energy intakes were calculated in 2018 using the National Food Composition (Fineli) database.[37] The output provided more than 60 nutrients and 100 food groups.

The Healthy Eating Index 2015 (HEI-2015) was calculated based on the FFQ data for each participant at both time points; that is, in T1 and T3.[38] The HEI-2015 is a measure of diet quality, independent of quantity, aligning with the 2015-2020 Dietary

Guidelines for Americans.[38,39] Both the Nordic Nutrition Recommendations[40] and the Finnish Nutrition Recommendations[41] align well with the Dietary Guidelines for Americans,[39] and the use of the HEI-2015 in a Finnish study population can therefore be considered justified. In calculating HEI-2015 scores, 13 key dietary components and nutrient groups (ie, total fruits, whole fruits, total vegetables, greens and beans, whole grains, dairy, total protein foods, seafood and plant proteins, fatty acids, refined grains, sodium, added sugars, and saturated fats) are assigned a score based on the quantity consumed. The HEI-2015, the latest version of the index[42,43] was used with one modification made necessary by the available data: The category of total vegetables was combined with greens and beans into one category, summing the maximum points available for both categories. This was done due to the challenge of extracting the consumed amounts of the latter category from the FFQ used. Thus, the HEI-2015 used in this study included 12 components (instead of the original 13) with a maximum total score of 100. Sixteen key FFQ components were selected to be analyzed individually alongside the main analyses (ie, grouped fruits and berries; grouped vegetables, fruits, and berries; liquid dairy; cheese; total dairy; fish; whole grains; refined grains; total grains; proteins; sucrose; monounsaturated fatty acids; polyunsaturated fatty acids; saturated fatty acids; total fats; and total energy). FFQ components were chosen instead of the HEI-2015 subscore components to reflect actual daily intakes and proportions of the total energy consumption per food group instead of the calculated HEI-2015 subscores, thus making the results more easily interpretable. The computed HEI-2015 score and FFQ component values were used as continuous variables in this study, and the HEI-2015 score was used as the main predictor/independent variable. For descriptive statistics, quartiles were calculated for the HEI-2015 score in T1, and the descriptive statistics of the participants in the lowest (lowest quality diet) and the highest (highest quality diet) quartiles were compared.

Background Measures and Covariates

Relevant covariates were chosen as relevant descriptive variables and for inclusion as independent variables in the statistical models. The choices were based on previous research on the risk factors for depression and low diet quality, and included maternal age[5] (obtained from an electronic patient record system), pre-pregnancy body mass index, obtained from self-reported height (in centimeters) and weight (in kilograms) measured at the first routine prenatal care visit,[44] pre-pregnancy alcohol use based on the Alcohol Use Disorders Identification Test, as validated by Levola and Aalto,[45] and Lee and colleagues[46] the use of antidepressant medication for any indication, as obtained from the medication information in the electronic patient record system,[47] living with a partner,[47] and education level as defined by the completion of tertiary education, derived from the occupational title and based on the recommended mapping between the International Standard Classification of Education 1997 and the International Standard Classification of Occupation 08.[5,47-49]

Time

Given the prospective nature of this study setting, a time variable was also included in the models to evaluate the association between the EPDS and HEI-2015 scores in T1 and their changes during the study period. The time variable was formed as follows: the earliest time point when the EPDS questionnaire was completed by a participant in the entire dataset (ie, the earliest EPDS response of the sample in relation to the duration of the pregnancy) was treated as time = 0, and the value of time for all other EPDS responses within the sample was computed using this time point as a reference. Time was used as a continuous variable, with weeks as the measurement unit. This approach was chosen instead of utilizing pregnancy weeks as a measurement for time. Had the latter approach been used, pregnancy week = 0 would have described the situation before the actual pregnancy had occurred (ie, the state preceding conception), resulting in a speculative model due to the absence of any observed data gathered before the study enrollment.

Statistics

The statistical procedures were initiated by examining the representativeness of our study sample, by comparing possible differences in the background characteristics of females included in and excluded from the study through logistic regression analyses with study inclusion (yes/no) as the dependent variable. Subsequently, similar comparisons of background characteristics were only conducted among females included in this study, analyzing females with and without clinically relevant depressive symptoms (as defined by an EPDS score cutoff $\geq$10) and with the poorest and the healthiest diet in T1 (as defined by the lowest and highest quartiles of the HEI-2015 score).

The main analyses in this study comprised a set of linear mixed models[50] in two stages. In addition, an exploratory set of modeling was conducted as a secondary analysis. In stage 1, it was evaluated whether or not diet quality (ie, HEI-2015 score) was associated with depressive symptoms (ie, EPDS score) at study intake (T1) and whether changes in HEI-2015 and EPDS scores were associated across the study period (between T1 and T3). The analyses were conducted in three steps. First, a basic intercept-only model was fitted to the data (model 1A). Second, different hypothetical longitudinal models were used to investigate whether EPDS scores were best described by baseline levels and the linear rate of change in EPDS scores during pregnancy (model 1B, including the intercept and time terms) or the baseline level and linear rate of change in EPDS, and the baseline and linear rate of change in HEI-2015 (time-dependent trait) during the follow-up period (model 1C, including terms for intercept, time, HEI-2015, and time $\times$ HEI-2015 interaction). In all of these models, random effects were solely considered for the intercept. In statistical terms, this latest, more complex model can be described through the following three equations: for the fixed effects, $EPDS_{ti} = \beta_{0i} + \beta_{1i}(Time_{ti}) + \beta_{2i}(HEI\text{-}2015_{ti}) + \beta_{3i}(Time \times HEI\text{-}2015)_{ti} + \varepsilon_{ti}$; for the random effects, $\beta_{0i} = \beta_{00} + \mu_{0i}$; and the overall composite model, $EPDS_{ti} = \beta_{00} + \beta_{1i}(Time_{ti}) + \beta_{2i}(HEI\text{-}2015_{ti}) + \beta_{3i}(Time \times HEI\text{-}2015)_{ti} + \mu_{0i} + \varepsilon_{ti}$. In these equations, "$EPDS_{ti}$" is the dependent variable of individual "i" measured at time "t", "β_0" is the regression intercept, "β_1" is the coefficient for the time variable indicating the time point, "β_2" is the coefficient for HEI-2015, and "β_3" is the coefficient for the "Time x HEI-2015" interaction, describing the variation across time of HEI-2015 and EPDS. In addition, ε_{ti} and μ_{0i} are the error terms for the

fixed and random effects, respectively. In Stage 2, the best-fitting model found in stage 1 was corrected for the covariates described earlier (age, body mass index, alcohol use, living with a partner, tertiary education, and antidepressant use). These covariates were sequentially removed to achieve a possibly better fit with the least number of potential confounders.

In Stages 1 and 2, the assessments of model fit were based on likelihood ratio tests with respect to the base model (Model 1A in Stage 1, Model 2A in Stage 2), the estimators utilized being the Akaike Information Criteria (AIC) and Bayesian Information Criteria (BIC). Accordingly, models offering a P value < 0.05 in likelihood ratio tests with respect to the basic model were considered significantly different and would indicate that the predictor added (Stage 1) or removed (Stage 2) was relevant and in need of consideration. Models with lower AIC and BIC values are usually considered better, and the model with the lowest AIC and BIC across stages was considered the final best-fitting model in this study. If discrepancies between AIC and BIC were observed, BIC was chosen as the determining criterion for the best fit because it tends to perform better in complex models with a larger number of explanatory terms.[51,52]

To examine the role of individual dietary components because part of the exploratory analyses, a set of ancillary linear mixed models exploring the role of key dietary components (16 FFQ items) in longitudinally predicting depression (EPDS score) was computed. These exploratory models also included the covariates found relevant in the main analyses. Because the number of hypotheses tested in these incidental analyses was relatively large and the possibility of type-I error (ie, incorrectly rejecting the null hypothesis) therefore increased in this section of the study, the P value threshold was redefined for these exploratory analyses in a manner that took into account the family-wise error rate (Bonferroni method). This P value correction countered the increased risk of type-I error by adapting the alpha level of significance to the number of distinct hypotheses examined through dividing α by the number of independent tests. Nevertheless, as the measured dietary components were not independent of one another, the number of independent tests in this section of the study needed to be determined by the product of the minimum number of orthogonal linear (principal) components (the main property of which is that their correlation is zero) explaining 95% of the observed variance within the longitudinal FFQ dataset. Accordingly, there were 11 principal components explaining 95% of the variance in the FFQ items (or 11 independent tests), thus setting the Bonferroni-corrected P value threshold for statistical significance in the exploratory analyses at ≤ 0.004.

Two-tailed tests were used for all statistical analyses, and an $\alpha = .05$ was applied for testing the predefined main hypotheses. Model assumptions were tested at every level of modeling and were met reasonably well. All analyses were implemented in the packages "stats" and "LmerTest" in R-CRAN software.[53,54]

RESULTS

Comparison of the background characteristics of the participants in this study (n = 1,362) vs those excluded from it (n = 2,223) revealed that the participants were generally older, drank less alcohol, were more likely to have completed tertiary education and to be living with a partner, and had lower levels of depressive symptoms in both T1 and T3. The results are summarized in Table 1 (available at www.jandonline.org). Due to this slightly differential selection, stabilized inverse-probability-of-censoring weights (IPCWs)[55] were computed using the aforementioned time-invariant characteristics associated with participation (ie, age, alcohol intake, tertiary education, and living with a partner). These IPCWs were subsequently included in all statistical models to reduce the possibility of selection bias affecting the results. The assumptions of positivity and mis-specification of the IPCWs were checked as recommended.[56]

Clinically relevant depressive symptoms (EPDS score $\geq$10) were displayed by 66 participants in T1 and by 115 participants in T3. In total, approximately 12.3% of the participants (n = 168) had clinically relevant depressive symptoms in least at one of the trimesters. Among these 168 participants, valid values for the EPDS scores were available for 97 and 142 participants in T1 and T3, respectively. Background data inspections indicated that mothers with clinically relevant depressive symptoms consumed more alcohol, were less likely to have completed tertiary education, were more likely to use antidepressant medication, and had a poorer diet quality at the end of the pregnancy compared with mothers without clinically relevant depressive symptoms. Further details are presented in Table 2. Females with the poorest diet during T1 (n = 204 at the lowest quartile vs n = 189 at the highest quartile of the HEI-2015 score) consumed more alcohol, were less likely to have completed tertiary education, and had a higher level of depressive symptoms in both T1 and T3. These results are summarized in Table 3 (available at www.jandonline.org).

The results from Stage 1 of modeling indicated that EPDS was best described longitudinally by Model 1C (ie, including the terms for an intercept, time, HEI-2015, and time × HEI-2015 interaction). The $\beta \pm$ SE and P value were $-.045 \pm .017$ and 0.007 for the term for HEI-2015 and ($2.91 \times 10^{-6} \pm .001$ and 0.996) for the term for time × HEI-2015 interaction. Thus, this model suggested that depressive symptoms remained relatively stable during the study period, and that the majority of females who entered pregnancy in a depressive mood remained in a similar state throughout pregnancy. More importantly, pregnant females with a higher level of depressive symptoms already had a poorer diet at the beginning of pregnancy. Alterations in overall diet quality during the study period, as measured by the HEI-2015, were not related to changes in depressive symptoms. The model fit comparison statistics are summarized in Table 4.

Stage 2 of modeling, with sequential elimination of covariates, further confirmed the associations found in Model 1C after the correcting of model estimates for alcohol use, living with a partner, and antidepressant use (see final Model 2I in Table 4). For the final Model 2I, the $\beta \pm$ SE and P value were $-.038 \pm .016$ and 0.022 for the term for HEI-2015 and $-9.741 \times 10^{-5} \pm .001$ and 0.869 for the term for time × HEI-2015 interaction.

The exploratory modeling of dietary components was not able to firmly pinpoint any of the key FFQ dietary components as independently associated with EPDS during T1 or the change in EPDS from T1 to T3. These results are summarized in Tables 5 and 6 (both available at www.jandonline.org)

Table 2. Characteristics of participants from the Kuopio Birth Cohort Study, Kuopio, Finland, participating in a study assessing the association between maternal diet quality and depressive symptoms during pregnancy from 2012 to 2017 (n = 1,362), overall and grouped by a clinically relevant cutoff of depressive symptoms (ie, Edinburgh Postnatal Depression Scale [EPDS][a] score <10 points [n = 1194; 87.7%] vs EPDS score ≥10 points [n = 168; 12.3%] in either the first or third trimester of pregnancy)

Characteristic	Overall sample[b]	EPDS <10[b]	EPDS ≥10[b]	Z statistic[c]	P value[c]
Age (years)	30.2 (4.9); n = 1,362	30.3 (4.8); n = 1,194	29.8 (5.2); n = 168	−1.324	0.186
Prepregnancy BMI[d] (kg/m^2)	24.9 (5.1); n = 1,362	24.8 (5.0); n = 1,194	25.4 (5.9); n = 168	1.346	0.178
Prepregnancy AUDIT[e] score	3.4 (2.3); n = 1,362	3.2 (2.2); n = 1,194	4.3 (3.1); n = 168	5.176	2.26×10^{-7}
Living with a partner					
No	54 (0.04)	43 (0.04)	11 (0.07)	−1.937	0.053
Yes	1308 (0.96)	1151 (0.96)	157 (0.93)		
Tertiary education					
No	655 (0.48)	561 (0.47)	94 (0.56)	−2.181	0.029
Yes	707 (0.52)	633 (0.53)	74 (0.44)		
Antidepressant use					
No	1315 (0.96)	1161 (0.97)	154 (0.92)	3.577	3.48×10^{-4}
Yes	47 (0.04)	33 (0.03)	14 (0.08)		
EPDS score, T1[f]	3.9 (3.5); n = 831	3.1 (2.5); n = 734	10.3 (3.5); n = 97	10.967	5.52×10^{-28}
EPDS score, T3[g]	4.5 (3.9); n = 1,081	3.5 (2.6); n = 939	11.6 (3.6); n = 142	11.738	8.12×10^{-32}
HEI-2015[h] score, T1	61.8 (8.1); n = 782	62.0 (8.1); n = 691	60.6 (8.2); n = 91	−1.387	0.166
HEI-2015 score, T3	56.2 (11.3); n = 1,239	56.6 (11.3); n = 1,088	53.8 (10.8); n = 151	−2.861	0.004

[a]Total score ranges from zero to 30, with a higher score indicating a higher level of depressive symptoms.
[b]Values in cells presented as mean (SD) for quantitative traits, and as n (subsample %) for qualitative traits.
[c]Z statistic and P value from logistic regression tests for differences between groups utilizing EPDS ≥10 (no/yes) as the dependent variable.
[d]BMI = body mass index.
[e]AUDIT = Alcohol Use Disorders Identification Test questionnaire (total score ranges from zero to 40, with a higher score indicating a higher likelihood of alcohol dependency and harmful alcohol use).
[f]T1 = first trimester.
[g]T3 = third trimester.
[h]HEI-2015 = Healthy Eating Index 2015 (total score ranges from zero to 100, with a higher score indicating a higher quality diet).

DISCUSSION

This investigation provided a set of results that need to be highlighted. Firstly, it was observed that pregnant females with a poorer quality diet already had higher levels of depressive symptoms at the beginning of pregnancy compared with pregnant females with a higher quality diet. This finding is in line with previous results from comparable population-based settings in both middle-[20,25] and high-income countries[16,17,22,23,24] and also from lower-income settings,[18,19,21] although they still partially contradict findings from some previous studies.[21,23,24,26] The aforementioned studies include both longitudinal[17,20,21,23] and cross-sectional[16,18,19,22,24,25] study designs with regard to the measurements made during pregnancy. As an example of a partially contradictory finding, Miyake and colleagues[24] reported no association between a Western diet and depressive symptoms during pregnancy in a cross-sectional study design, although they did find a significant inverse association between a Japanese diet and depressive symptoms during pregnancy.

The observed inverse association between diet quality and depressive symptoms is likely to be bidirectional and multifactorial, and could be partially accounted for by certain physiological adaptations resulting from an unhealthy diet. For example, it has been suggested that poor dietary habits may lead to elevated depressive symptoms through changes in the composition of the gut microbiome,[57] adverse effects on the functioning of the gut–brain axis,[57,58] and reduced brain plasticity.[59] Furthermore, individuals with a lower intake of vegetables,[60] along with a higher intake of refined sugars and carbohydrates,[61] or saturated and *trans*-unsaturated fats,[62] often display higher systemic inflammation and oxidative stress, physiological characteristics associated with higher levels of depressive symptoms.[63,64]

Furthermore, it was found that changes in diet quality did not predict variations in depressive symptoms during pregnancy. This is a relatively novel finding because previous investigations have not considered this aspect, despite the possible availability of longitudinal data.[20,26]

Strengths and Limitations

Among the strengths of this study was the relatively large sample of females who were followed-up during pregnancy in terms of both dietary measures and depressive symptoms. These rich data gathered from the participants during this period, along with the sophisticated analyses implemented,

Table 4. Results from the model fit comparison of the main statistical models (linear mixed models) examining the longitudinal association of diet quality, as measured by Healthy Eating Index 2015 (HEI-2015) scores in the first and third trimesters, with depressive symptoms, as measured by Edinburgh Postnatal Depression Scale (EPDS) scores in the first and third trimesters, in a study assessing the association between maternal diet quality and depressive symptoms during pregnancy in participants from the Kuopio Birth Cohort Study, Kuopio, Finland, 2012-2017

Stage	Model	Description[a]	−2LL[b]	Df[c]	χ^{2d}	⊿Df[e]	P value[f]	AIC[g]	BIC[h]
1[i]	1A[j]	Basic intercept model	9,458.7	3	0	0	1	9,464.7	9,481.1
	1B[k]	… + Time[l]	9,449.3	4	9.4	1	0.002	9,457.3	9,479.2
	1C[m]	**… + Time + HEI-2015 +**	**9,423.0**	**6**	**35.7**	**3**	**8.67×10^{-8}**	**9,435.0**	**9,467.8**
		(Time ● HEI-2015)							
2[n]	2A[o]	Full longitudinal adjusted model	9,353.1	12	0	0	1	9,377.1	9,442.7
	2B[p]	… - age	9,353.5	11	0.5	1	0.496	9,375.5	9,435.7
	2C[q]	… - BMI[r]	9,354.2	11	1.1	1	0.293	9,376.2	9,436.4
	2D[s]	… - alcohol use	9,391.2	11	38.1	1	6.56×10^{-10}	9,413.2	9,473.4
	2E[t]	… - living with a partner	9,358.2	11	5.2	1	0.023	9,380.2	9,440.4
	2F[u]	… - tertiary education	9,356.1	11	3.1	1	0.081	9,378.1	9,438.3
	2G[v]	… - antidepressant use	9,364.3	11	11.3	1	7.91×10^{-4}	9,386.3	9,446.5
	2H[w]	… - age − BMI	9,354.5	10	1.4	2	0.493	9,374.5	9,429.2
	2I[x]	**… - age − BMI - tertiary education**	**9,358.6**	**9**	**5.5**	**3**	**0.139**	**9,376.6**	**9,425.8**

[a]Summary of the model contents, with denotations for variables added (+) or removed (-) compared with model 1A (in Stage 1) or model 2A (in Stage 2). All models utilized the EPDS score as the dependent variable.

[b]−2LL = likelihood ratio test: Test statistic.

[c]Df = degrees of freedom of the model.

[d]Likelihood ratio test: χ^2 statistic.

[e]Change in model Df compared with the base model of the stage (1A or 2A for Stage 1 and Stage 2, respectively).

[f]Likelihood ratio test: P value.

[g]AIC = Akaike information criterion statistic.

[h]BIC = Bayesian information criterion statistic.

[i]In Stage 1: models examining the longitudinal association without covariates (unadjusted longitudinal model). The best-fitting model of the stage in bold and shaded.

[j]Model 1A contains the following independent variable: intercept.

[k]Model 1B contains the following independent variables: intercept, time.

[l]Refers to "weeks from the earliest study intake with respect to the weeks of pregnancy."

[m]Model 1C contains the following independent variables: intercept, time, HEI, and time × HEI.

[n]In Stage 2: Models examining the best longitudinal association from stage 1, including covariates (adjusted best-fitting longitudinal model). The best-fitting model of the stage is in bold and shaded.

[o]Model 2A contains the following independent variables: intercept, time, HEI, Time × HEI, age, BMI, alcohol use, living with a partner, tertiary education, antidepressant use.

[p]Model 2B contains the following independent variables: intercept, time, HEI, Time × HEI, BMI, alcohol use, living with a partner, tertiary education, antidepressant use.

[q]Model 2C contains the following independent variables: intercept, time, HEI, Time × HEI, age, alcohol use, living with a partner, tertiary education, antidepressant use.

[r]BMI = body mass index.

[s]Model 2D contains the following independent variables: intercept, time, HEI, Time × HEI, age, BMI, living with a partner, tertiary education, antidepressant use.

[t]Model 2E contains the following independent variables: intercept, time, HEI, Time × HEI, age, BMI, alcohol use, tertiary education, antidepressant use.

[u]Model 2F contains the following independent variables: intercept, time, HEI, Time × HEI, age, BMI, alcohol use, living with a partner, antidepressant use.

[v]Model 2G contains the following independent variables: intercept, time, HEI, Time × HEI, age, BMI, alcohol use, living with a partner, tertiary education.

[w]Model 2H contains the following independent variables: intercept, Time, HEI, Time × HEI, alcohol use, living with a partner, tertiary education, and antidepressant use.

[x]Model 2I contains the following independent variables: intercept, Time, HEI, Time × HEI, alcohol use, living with a partner, and antidepressant use.

allowed us to gain a more refined understanding of variation over time across multiple diet characteristics in relation to depressive symptoms. This type of analysis and the results gathered are novel and of relevance for understanding lifestyle factors associated with maternal prenatal depression.

Some limitations also need to be taken into consideration when examining the findings from the current study. First, the observational nature of this study does not allow the assessment of causality, and consequently the findings cannot be used to determine the direction of the observed associations or the nature of the mechanisms underlying the findings. Second, the measurements of both diet quality and depressive symptoms were based on self-administered questionnaires, which introduces a degree of uncertainty compared with clinical methods of assessment. Nevertheless, the utilized questionnaires have been deemed highly reliable and valid. In addition, it should be noted that some participants only provided data once during the study period. However, considering the large number of participants with information available from both T1 and T3, and the robust methodological approach in the statistical analyses (mainly the utilization of linear mixed models and their ability to handle unbalanced datasets), this should not present a problem concerning the reliability of the results. Third, the

study sample was to some degree selected because by study design, the focus was on each participant's first single-fetus pregnancy included in the KuBiCo study. Furthermore, as a result of the attrition process summarized in the Figure, the participants included in the final study population were older, drank less alcohol, were more likely to have completed tertiary education and to be living with a partner, and had lower levels of depressive symptoms in both the first and third trimesters. This could have influenced the results had the IPCWs not been included to counter the selection bias. In addition, in the case that the findings had not been corrected for selection bias, the bias would most likely have been toward attenuating the results that we observed because the included population was less influenced by depressive symptoms and factors associated with these symptoms.[5,45-47,49] Finally, it is possible that the examination of other potential confounders, such as the history of depressive symptoms before pregnancy, or more refined socioeconomic factors than those considered here would have further enhanced the analyses and conclusions. Unfortunately, such data were unavailable and further investigations including these aspects are therefore warranted.

CONCLUSIONS

This study demonstrated that pregnant females with poorer diet quality displayed higher levels of depressive symptoms compared with pregnant females with higher diet quality. Changes in overall diet quality were not related to any variation in depressive symptoms during pregnancy. Further research, including nutrition intervention trials involving pregnant females, is needed to replicate the results and to build upon the findings of this study.

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Table 1. Characteristics of participants from the Kuopio Birth Cohort Study, Kuopio, Finland, participating in a study assessing the association between maternal diet quality and depressive symptoms during pregnancy (n = 1,362) compared with participants excluded due to missing data (n = 2,223), 2012-2017

Characteristic	Excluded from the study[a]	Included in the study[a]	Z statistic[b]	P value[b]
Age (years)	29.7 (5.3); n = 1,779	30.2 (4.9); n = 1,362	2.995	0.003
Prepregnancy BMI[c] (kg/m^2)	24.9 (5.2); n = 2,190	24.9 (5.1); n = 1,362	0.031	0.975
Prepregnancy AUDIT[d] score	3.6 (2.8); n = 1,387	3.4 (2.3); n = 1,362	−2.219	0.026
EPDS[e] score, T1[f]	4.7 (3.9); n = 583	3.9 (3.5); n = 831	−3.758	1.72×10^{-4}
EPDS score, T3[g]	5.2 (4.2); n = 786	4.5 (3.9); n = 1081	−3.657	2.55×10^{-4}
HEI-2015[h] score, T1	60.9 (8.4); n = 387	61.8 (8.1); n = 782	1.726	0.084
HEI-2015 score, T3	56.2 (11.9); n = 910	56.2 (11.3); n = 1,239	0.042	0.967
Living with a partner				
No	124 (0.06)	54 (0.04)	2.272	0.023
Yes	2074 (0.94)	1308 (0.96)		
Tertiary education				
No	1074 (0.56)	655 (0.48)	4.628	3.70×10^{-6}
Yes	841 (0.44)	707 (0.52)		
Antidepressant use				
No	2143 (0.96)	1315 (0.96)	0.093	0.93
Yes	80 (0.04)	47 (0.04)		

[a]Values in cells presented as mean (SD) for quantitative traits, and as n (subsample proportion) for qualitative traits.

[b]Z statistic and P value from logistic regression tests for differences between groups utilizing participation (included/excluded) as the dependent variable.

[c]BMI = body mass index.

[d]AUDIT = Alcohol Use Disorders Identification Test questionnaire (total score ranges from zero to 40, with a higher score indicating a higher likelihood of alcohol dependency and harmful alcohol use).

[e]EPDS = Edinburgh Postnatal Depression Scale (total score ranges from zero to 30, with a higher score indicating a higher level of depressive symptoms).

[f]T1 = first trimester.

[g]T3 = third trimester.

[h]HEI-2015 = Healthy Eating Index 2015 (total score ranges from zero to 100, with a higher score indicating a higher quality diet).

Table 3. Characteristics of participants from the Kuopio Birth Cohort Study, Kuopio, Finland, participating in a study assessing the association between maternal diet quality and depressive symptoms during pregnancy from 2012 to 2017 within the lowest (n = 204) and highest (n = 189) quartiles of the Healthy Eating Index 2015 (HEI-2015)[a] score in the first trimester

Characteristic	HEI-2015 lowest quartile[b]	HEI-2015 highest quartile[b]	Z statistic[c]	P value[c]
Age (years)	30.5 (5.5); n = 204	29.4 (4.6); n = 189	−2.011	0.044
Prepregnancy BMI[d] (kg/m^2)	25.2 (5.4); n = 204	24.4 (5.1); n = 189	−1.288	0.198
Prepregnancy AUDIT[e] score	3.7 (2.3); n = 204	3.1 (2.5); n = 189	−2.177	0.029
Living with a partner				
No	8 (0.04)	9 (0.05)	−0.378	0.705
Yes	196 (0.96)	180 (0.95)		
Tertiary education				
No	121 (0.59)	86 (0.46)	2.717	0.007
Yes	83 (0.41)	103 (0.54)		
Antidepressant use				
No	198 (0.97)	188 (0.99)	−1.605	0.108
Yes	6 (0.03)	1 (0.005)		
EPDS[f] score, T1[g]	4.5 (3.8); n = 189	3.4 (3.2); n = 176	−2.946	0.003
EPDS score, T3[h]	4.5 (3.6); n = 134	3.7 (3.6); n = 122	−1.75	0.08
HEI-2015 score, T1	51.6 (3.7); n = 204	72.4 (3.8); n = 189	0.002	0.998
HEI-2015 score, T3	49.1 (9.2); n = 170	64.7 (10.3); n = 165	9.372	7.11 × 10^{-21}

[a]Total score ranges from zero to 100, with a higher score indicating a higher quality diet.

[b]Values in cells presented as mean (SD) for quantitative traits, and as n (subsample %) for qualitative traits.

[c]Z statistic and P value from logistic regression tests for differences between groups utilizing HEI quartile (lowest/highest) as the dependent variable.

[d]BMI = body mass index.

[e]AUDIT = Alcohol Use Disorders Identification Test questionnaire (total score ranges from zero to 40, with a higher score indicating a higher likelihood of alcohol dependency and harmful alcohol use).

[f]EPDS = Edinburgh Postnatal Depression Scale (total score ranges from zero to 30, with a higher score indicating a higher level of depressive symptoms).

[g]T1 = first trimester.

[h]T3 = third trimester.

Table 5. Results of an exploratory dietary component analysis in participants from the Kuopio Birth Cohort Study, Kuopio, Finland, participating in a study assessing the association between maternal diet quality and depressive symptoms during pregnancy from 2012 to 2017 (n = 1,362), overall and grouped by a clinically relevant cutoff of depressive symptoms: Edinburgh Postnatal Depression Scale (EPDS)[a] score <10 points (n = 1,194 [87.7%]) vs EPDS score ≥10 points (n = 168 [12.3%]) in either the first or third trimester of pregnancy

Characteristic	Overall sample[b]	EPDS <10[b]	EPDS ≥10[b]	Z statistic[c]	P value[c]
Trimester 1					
Fruits and berries (g/day)	352.9 (259.3); n = 786	354.7 (259.0); n = 695	339.4 (262.8); n = 91	−0.513	0.608
Whole grains (g/day)	160.7 (109.5); n = 786	161.4 (109.5); n = 695	155.3 (110.4); n = 91	−0.514	0.607
Vegetables, fruits, and berries (g/day)	619.5 (381.7); n = 786	620.7 (381.1); n = 695	610.7 (388.8); n = 91	−0.206	0.837
Total dairy (g/day)	599.8 (339.9); n = 786	595.7 (339.1); n = 695	631.0 (346.2); n = 91	0.960	0.337
Liquid dairy (g/day)	564.2 (332.5); n = 786	560.1 (331.8); n = 695	595.4 (337.6); n = 91	0.983	0.326
Cheese (g/day)	35.6 (26.0); n = 786	35.6 (25.2); n = 695	35.7 (31.3); n = 91	−0.022	0.983
Fish (g/day)	37.2 (25.4); n = 786	37.1 (25.2); n = 695	38.3 (26.8); n = 91	0.419	0.675
Refined grains (g/day)	21.2 (19.6); n = 786	21.1 (20.3); n = 695	21.7 (14.1); n = 91	0.309	0.758
Total grains (g/day)	196.8 (117.5); n = 786	197.5 (117.9); n = 695	191.9 (115.3); n = 91	−0.424	0.672
Proteins (%E[d])	18.7 (2.8); n = 786	18.7 (2.8); n = 695	18.3 (2.7); n = 91	−1.278	0.201
Sucrose (%E)	8.0 (2.8); n = 786	8.0 (2.8); n = 695	7.9 (2.8); n = 91	−0.308	0.758
MUFA[e] (%E)	9.8 (1.8); n = 786	9.7 (1.7); n = 695	9.9 (2.0); n = 91	0.769	0.442
PUFA[f] (%E)	4.1 (1.0); n = 786	4.1 (0.9); n = 695	4.1 (1.2); n = 91	−0.323	0.746
SAFA[g] (%E)	10.8 (2.3); n = 786	10.8 (2.2); n = 695	11.2 (2.6); n = 91	1.568	0.117
Total fat (%E)	23.5 (3.5); n = 786	23.4 (3.4); n = 695	23.9 (3.8); n = 91	1.117	0.264
Total energy (kcal/day)	2103 (625); n = 786	2091 (612); n = 695	2196 (713); n = 91	1.514	0.130
Trimester 3					
Fruits and berries (g/day)	371.2 (278.1); n = 1242	371.0 (276.9); n = 1091	372.5 (288.0); n = 151	−0.016	0.988
Whole grains (g/day)	167.9 (106.2); n = 1242	170.0 (107.2); n = 1091	152.7 (97.7); n = 151	−1.928	0.054
Vegetables, fruits, and berries (g/day)	649.9 (377.0); n = 1242	647.6 (374.8); n = 1091	666.3 (393.8); n = 151	0.498	0.619
Total dairy (g/day)	691.3 (335.4); n = 1242	695.4 (335.9); n = 1091	661.4 (331.9); n = 151	−1.202	0.229
Liquid dairy (g/day)	584.7 (326.5); n = 1242	588.8 (327.6); n = 1091	555.3 (317.6); n = 151	−1.229	0.219
Cheese (g/day)	36.7 (27.6); n = 1242	37.3 (28.0); n = 1091	33.9 (24.6); n = 151	−1.415	0.157
Fish (g/day)	38.7 (26.8); n = 1242	38.8 (27.0); n = 1091	37.7 (25.5); n = 151	−0.562	0.574
Refined grains (g/day)	25.8 (25.0); n = 1242	25.1 (20.5); n = 1091	30.4 (45.7); n = 151	2.149	0.032
Total grains (g/day)	208.4 (112.7); n = 1242	209.7 (112.1); n = 1091	198.7 (117.3); n = 151	−1.141	0.254
Proteins (%E)	18.6 (2.8); n = 1242	18.7 (2.8); n = 1091	18.1 (2.8); n = 151	−2.509	0.012
Sucrose (%E)	7.9 (2.9); n = 1242	7.9 (2.9); n = 1091	8.2 (2.7); n = 151	1.195	0.232
MUFA (%E)	9.9 (1.8); n = 1242	9.9 (1.8); n = 1091	10.1 (1.7); n = 151	1.414	0.158
PUFA (%E)	4.1 (1.0); n = 1242	4.1 (1.0); n = 1091	4.1 (1.0); n = 151	−0.817	0.414
SAFA (%E)	11.2 (2.4); n = 1242	11.2 (2.4); n = 1091	11.6 (2.4); n = 151	1.995	0.046
Total fat (%E)	30.8 (4.7); n = 1242	30.8 (4.7); n = 1091	31.3 (4.6); n = 151	1.391	0.164
Total energy (kcal/day)	2195 (614); n = 1242	2179 (587); n = 1091	2311 (773); n = 151	2.435	0.015

[a]Total score ranges from zero to 30, with a higher score indicating a higher level of depressive symptoms.
[b]Values in cells presented as mean (SD) for quantitative traits, and as n (subsample %) for qualitative traits.
[c]Z statistic and P value from logistic regression tests for differences between groups utilizing EPDS ≥10 (no/yes) as the dependent variable.
[d]%E = percent energy.
[e]MUFA = monounsaturated fatty acids.
[f]PUFA = polyunsaturated fatty acids.
[g]SAFA = saturated fatty acids.

Table 6. Results from linear mixed models examining the longitudinal associations of 16 dietary components, as measured by a food frequency questionnaire during the first and third trimesters, and depressive symptoms, as measured by Edinburgh Postnatal Depression Scale (EPDS)[a] scores in the first and third trimesters, in participants from the Kuopio Birth Cohort Study, Kuopio, Finland, participating in a study assessing the association between maternal diet quality and depressive symptoms during pregnancy from 2012 to 2017

Dietary component name[b]	Dietary component[c]	Time[d] × Dietary component[c]
Fruits and berries (g/day)	1.79×10^{-5} (5.179×10^{-4}) 0.972	5.561×10^{-6} (2.106×10^{-5}) 0.792
Vegetables, fruits and berries (g/day)	-4.601×10^{-4} (0.005) 0.928	-1.141×10^{-4} (2.06×10^{-4}) 0.580
Liquid dairy (g/day)	-0.002 (0.005) 0.67	1.035×10^{-4} (2.042×10^{-4}) 0.612
Cheese (g/day)	3.019×10^{-4} (2.11×10^{-4}) 0.153	4.47×10^{-6} (8.489×10^{-6}) 0.599
Total dairy (g/day)	-7.797×10^{-4} (0.001) 0.523	-1.693×10^{-5} (5.103×10^{-5}) 0.740
Fish (g/day)	0.089 (0.037) 0.016	-0.002 (0.001) 0.224
Whole grains (g/day)	1.673×10^{-4} (4.077×10^{-4}) 0.682	-3.788×10^{-5} (1.648×10^{-5}) 0.022
Refined grains (g/day)	1.611×10^{-4} (3.969×10^{-4}) 0.685	-3.554×10^{-5} (1.606×10^{-5}) 0.027
Total grains (g/day)	0.131 (0.078) 0.094	-5.31×10^{-4} (0.003) 0.865
Proteins (%E[e])	-0.04 (0.047) 0.393	-0.003 (0.002) 0.153
Sucrose (%E)	0.089 (0.141) 0.530	-0.004 (0.006) 0.472
MUFA[f] (%E)	0.141 (0.060) 0.018	-9.027×10^{-4} (0.002) 0.704
PUFA[g] (%E)	-0.034 (0.047) 0.478	0.004 (0.002) 0.060
SAFA[h] (%E)	-2.241×10^{-4} (3.536×10^{-4}) 0.526	8.781×10^{-6} (1.446×10^{-5}) 0.544
Total fats (%E)	0.009 (0.007) 0.196	1.86×10^{-4} (2.411×10^{-4}) 0.441
Total energy (kcal/day)	-3.103×10^{-4} (0.001) 0.783	-7.784×10^{-6} (4.752×10^{-5}) 0.870

[a]Total score ranges from zero to 30, with a higher score indicating a higher level of depressive symptoms.

[b]The description of the food group, as measured by the food frequency questionnaire that was used as an independent variable in the model. In each model the dependent variable was the EPDS score, and the independent variables were as follows: intercept, time, dietary component, time × dietary component, alcohol use, living with a partner, and antidepressant use.

[c]Values are presented as β (SE) P value. Due to the multiple tests conducted, Bonferroni correction was applied to the significance threshold of the P value ($\alpha \leq .004545$).

[d]Time = weeks from the earliest study intake with respect to the weeks of pregnancy.

[e]%E = percent energy.

[f]MUFA = monounsaturated fatty acids.

[g]PUFA = polyunsaturated fatty acids.

[h]SAFA = saturated fatty acids.