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Descriptive Study of Perinatal Nutritional Markers and Maternal Mental Health: EDEN Cohort in France

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List of Acronyms:

Abbreviation	Definition
ACE	Adverse Childhood Event
CES-D	Center for Epidemiological Studies Depression Scale
BMI	Body Mass Index
EDEN	Etude sur les déterminants pré et post natals précoces du Développement psychomoteur et de la santé de l'Enfant
EPDS	Edinburgh Postnatal Depression Scale
HIC	High Income Countries
LMIC	Low and Middle Income Countries
MUFA	Monounsaturated Fatty Acids
PUFA	Polyunsaturated Fatty Acids
STAI	State-Trait Anxiety Inventory
SES	Socioeconomic Status
FFQ	Food Frequency Questionnaires

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Abstract:

Background: Perinatal depression and anxiety are associated with adverse child and maternal outcomes. The etiology of these mood disorders is a complex relationship between previous mental health problems, physiological changes and possibly, nutritional imbalances. This study aims to explore relationships between nutrition during pregnancy and maternal mental health status, specifically the occurrence of perinatal depression and anxiety, in participants of the French EDEN cohort.

Methods: The EDEN (Etude sur les déterminants pré et post natals précoces du Développement psychomoteur et de la santé de l'ENfant) study was set up to assess the pre- and postnatal nutritional, social and environmental determinants of infant and child development and health. We used data from a sample selected on maternal mental health outcomes (n=1438) to conduct a network analysis of nutritional markers collected from food frequency questionnaires and mental health surveys (CES-D, STAI and EPDS) during the perinatal period. Four networks were constructed and analyzed for structure, node centrality and node predictability.

Results: We found an association between the Western diet and the EPDS survey in both macronutrient and micronutrient networks. Education appeared as a central covariate associated with consumption of the Western diet. The nodes most explained by other nodes in both the micro and macronutrient models were the Healthy diet (R^2=0.855, micro) and Western diet (R^2=0.617) after adjustment. The EPDS and Western diet also had the highest betweenness in all models.

Conclusion: We determined that a Western diet is associated with increased postnatal depression scores and that this relationship may vary by years of education. The Western diet does not address maternal nutritional needs during pregnancy on the macro or micronutrient level. Adequate and appropriate nutrition benefits the mother and her fetus in many different ways, even though its impact on maternal mental health still needs further study to understand the precise associations with certain dietary patterns and their nutritional components. Because nutritional status is a modifiable, affordable, measurable, and feasible intervention, it could be a future mitigant of perinatal depression and anxiety prevention.

Introduction:

Perinatal Maternal Mental Health

Pregnancy is a psychologically and physically demanding time for a woman. Perinatal Maternal Mental Health refers to the mental wellness of mothers surrounding the time of pregnancy and the postpartum. The 'perinatal' period can be defined as anytime during gestation, up to one year after childbirth (O'Hara & Wisner, 2014); however, in the literature this period is sometime extended to two years postpartum. During this time period, some new mothers experience symptoms of anxiety or depression in a way that affects her self-care or the ability to care for her new baby. Perinatal anxiety and depression are more pervasive and longer lasting than the commonly known 'baby blues', which affect almost 70% of women after pregnancy and usually resolve within two weeks after birth (Marcus & Heringhausen 2009).

Perinatal Anxiety

'Prenatal anxiety' refers to a collection of symptoms related to an overwhelming worry about the health of the developing fetus, pregnancy, childbirth or a state of generalized anxiety during pregnancy. Other symptoms include fatigue, irritability, tension and insomnia. Most often these worrying thoughts are described as 'intrusive', with a quality of irrationality, and can prevent the mother from functioning properly in her daily life (Misri et al., 2015). Prevalence of clinical prenatal anxiety is estimated between 8.5% and 10.5% and self-reported symptoms of prenatal anxiety have been reported as high as 24.6% in a recent meta-analysis (Dennis et al., 2017). However, these estimations vary due to the methods associated with identifying cases in different populations (hospital patients versus epidemiological survey), difficulty with diagnosis (symptoms are hard to distinguish from common symptoms in pregnancy), or lack of clinical expertise and access to prenatal care (Dennis et al., 2017). 'Postpartum anxiety' has a similar prevalence (4.4% - 10.8%) however, for the purposes of the current study, only prenatal anxiety will be discussed (Misri et al., 2015).

Prenatal and Postnatal Depression

'Perinatal depression' refers to either prenatal depression or postnatal depression. Prenatal depression can occur during the same time period as prenatal anxiety but presents with different symptomology. Symptoms of prenatal depression include feelings of guilt, worthlessness, or helplessness, persistent sad mood, loss of interest or pleasure, difficulty concentrating and persistent doubts about ability to care for the new baby (National Institutes of Mental Health, 2015). Postnatal depression presents itself in the same manner; however, the onset period is any time after childbirth until the child is one year old. Prevalence of both prenatal and postnatal depression vary dependent upon the use of diagnostic tools or self-reported symptoms, and between higher and lower-and-middle-income countries. A 2018 systematic review of postnatal depression estimated a global prevalence range from 4.0% to 63.9% however, most commonly seen estimates are 10-15% (Arifin et al., 2018). Another recent systematic review and meta-analysis reported an overall pooled prevalence of 11.9% (95% CI 11.4–12.5) of perinatal depression in LMIC and HIC (Woody et al., 2017). Prevalence of postnatal depression varies widely between HIC and LMIC, 9.5% (CI 8.9–10.1) and 18.7% (CI 17.8–19.7) respectively, as did prevalence of prenatal depression, reported at 9.2% (CI 8.4–10.0) for HIC and 19.2% (CI 18.0–20.5) for LMIC (Woody et al., 2017). The wide variability in prevalence could be attributed to the complexity of diagnosis, the cultural or contextual understanding of mental health, and the significant lack of research in underserved populations.

The challenges in research on perinatal anxiety and depression are exacerbated by the fact that the pathogenesis is largely unknown and associated with exposures that are difficult to measure, such as genetic and social factors. Currently, the largest predictors of postnatal depression are depression during pregnancy with possible preconception origins (Kee et al., 2020). Other previously studied indicators of perinatal anxiety and depression comprise a lack of social support, lower socioeconomic status, and genetic polymorphism (Stewart and Vigod 2016, Parrigon and Stuart, 2014, Li et al., 2020). Biophysiological factors like the extreme fluctuations in progesterone, estrogen, and corticosteroids are also suspected to contribute to the risk (Yim et al., 2015). Lastly, it is possible that there is an epigenetic influence in the development of perinatal mental health problems. Environmental exposures such as extreme stress or adverse childhood events could change the expression of specific genes, and subsequently, the functionality of the Hypothalamic Pituitary Adrenal axis instigating perinatal mood disorders (Carnevali & Buoli 2020, Garfield et al., 2015). Because of the public health costs associated with poor perinatal mental health, it is paramount that research focuses on potential mitigatory factors.

Nutrition and Mental Health

One potential contributing factor to perinatal anxiety and depression can be found in the association between a person’s nutrition and her mental health. Because nutrition plays a large role in prevention of chronic disease and over-all health, it is likely that it is also a key feature of mental health. In recent years, a new field of study has emerged to address the potential effects of nutrition on mental health. Nutritional Psychiatry seeks to address the burden of disability brought on by mood disorders and neuropsychiatric conditions through improvement of nutrition and diet. Recently, several studies have demonstrated the association between a diet high in vegetables, fruits, whole grains and fish, and a decreased risk of depression in adults (Lai et al., 2014). Epidemiological studies of this type usually focus on ‘diet patterns’ to assess exposure. A *diet pattern* is the frequent consumption of specific food groups which then determine the nutritional profile of the person. While there is no standardized definition of specific diet patterns and they are usually defined within each study, specifically named diets such as ‘healthy’ or ‘western’ are often made up of similar food groups across studies. For example, the Mediterranean Diet has been shown to consistently include fresh vegetables, fruit, whole grains and olive oil (Davis et al., 2015). Within these defined diet patterns, nutritionists or dieticians refer to their components as macronutrients and micronutrients. *Macronutrients* refer to the chemical compounds that the human body is required to consume for energy in the largest amounts, such as carbohydrates, proteins, and fats. *Micronutrients* are those elements that are essential but in much smaller quantities, such as Vitamin C or calcium. Both macro and micronutrients are essential for growth, development, and daily function of the human body throughout life with certain time periods requiring higher demand. Specific to mental health, the availability of nutrients in the body affects the functionality of the neurons in the brain and has been linked to depression in the non-pregnant population (Rao et al., 2008). Biomedical research shows that deficiency of key nutrients, such as folic acid or omega-3 fatty acids, inhibits the workability of neurons in the brain. The composition of the phospholipid membrane surrounding neurons regulates the transmission of serotonin, dopamine and norepinephrine and decreased transmission of these vital neurochemicals is a component of perinatal depression (Rechenberg, & Humphries 2013). Lastly, extreme changes in pregnancy hormones (progesterone, estrogen, testosterone, and oxytocin) interact with the hypothalamic-pituitary-adrenal (HPA) axis which could lead to perinatal depression; however, the exact mechanism is not yet understood (Zonana 2005, Parry et al., 2003, Ressler & Nemeroff, 2000, Rechenberg, & Humphries 2013).

The Complexities of Perinatal Mental Health and Nutrition

The perinatal period is considered a time period of intense nutritional demands for the mother due to a multitude of factors, mainly the needs of the developing fetus and an increase in resting metabolic rate (Most et al., 2019). These high-demand pathophysiological changes in the mother’s body require an additional intake of up to an extra 450 kcal a day to account for the total daily energy expenditure (Most et al., 2019). However, it is paramount that the mother consumes nutrient dense foods of the most optimal proportions, not only an increase in brute caloric intake. Consumption of varying proportions of macro and micronutrients, as well as different diet patterns cause changes in functionality, both in the mother and in the developing fetus. The association between nutrition and mental health during pregnancy is a promising field of research and of recent interest. Nutrition has become a focal point, possibly because its quantifiable effects on a developing fetus are well established, and there is evidence to support the influence of nutrition on mental health in the general population. The potential association between nutrition and mood is magnified during pregnancy by the increase of nutritional demands and changes in hormones, both of which could suddenly affect the functionality of the nervous system. The nutritional demands during pregnancy place already deficient populations at risk for severe nutritional imbalance after pregnancy. Disrupted biophysiological processes coupled with environmental risk factors (adverse childhood events, genetics) could also increase the possibility of perinatal depression and anxiety.

The study of nutrition's role in perinatal mental health covers a broad scope of associations including sociodemographic, mental health history, diet patterns, macronutrients and micronutrients. Importantly, diet patterns determine the macro and micronutrient composition of a person's nutritional status, which in turn affects his/her biochemistry at the cellular level. These mechanisms become further complicated to understand when environmental factors such as stress are involved. One study examined whether stress and depression during pregnancy are associated with diet quality in a population of women consuming low quality diets before pregnancy. It found that stress, but not depression, was positively associated with higher consumption of refined grains and added sugars (Boutté et al., 2021). Even though stress may be involved, a healthy diet may act as a preventative measure. A systematic review of diet pattern studies indicated that a 'healthy' diet showed a protective affect against pre and post-natal depression (Khan et al., 2020). Another systematic review concluded a similar inverse relationship between a healthy diet and perinatal anxiety and depression when looking at diverse diet patterns across the globe, however, a direct link between poor diet and perinatal depression was not established (Silva et al., 2019). Diet patterns may serve as a window into consumption of macronutrients and their effects on perinatal mental health. Research has established that particular diet patterns provide or lack essential nutrients required during pregnancy (Bodnar & Wisner, 2005). For example, the Western diet is linked to an imbalance of polyunsaturated omega-6 fatty acids (found in vegetable oils) and omega-3 fatty acids (found in fish and seafood). This same imbalance of polyunsaturated fatty acids could be affiliated with perinatal depression as found in meta-analyses by Hsu et al., (2018) and Lin et al., (2017). Similar patterns in overconsumption of macronutrients such as sugar and saturated fat could also contribute to the disruption of neurochemistry in the brain. In animal studies, high fat and sugar intake cause a reduction in hippocampal growth and disrupt dopamine pathways in both mother and fetus (DeCapo et al., 2018). The research concerning the effects of overconsumption of macronutrients typical in the Western diet is still lacking but could be relevant to the etiology of perinatal depression and anxiety.

The quality and quantity of macronutrients in the maternal diet determine the availability of micronutrients for vital processes. While the Western diet provides a surplus of macronutrients such as refined grains and added sugars, it simultaneously lacks certain micronutrients often found in fresh fruits and vegetables. Pregnancy is a time in which specific micronutrients are of great importance. The lack of folic acid increases the risk of neural tube defects in the fetus and has been linked to anemia in the mother (Greenberg et al., 2011). Micronutrient imbalances in the mother may contribute to mood disturbances. Recent systematic reviews demonstrated that iron-deficient anemia, as well as deficiencies in trace minerals such as zinc and selenium are associated with an increased risk of post-partum depression (Azami et al., 2019, Ellsworth-Bowers et al., 2012), while higher levels of vitamin D, folic acid, and fatty acids showed a protective effect against perinatal depression and anxiety (Sparling et al 2017, Serati et al 2016, Trujillo et al 2018). Likewise, another systematic review of cohort, cross-sectional, and interventional studies demonstrated that a correction of nutritional deficiencies had a promising mitigatory effect on maternal depression in LMIC (Madeghe et al., 2021).

The complexity of how nutrients are absorbed, processed and utilized in the body during pregnancy make it difficult to make robust claims about the connection between nutrition and maternal mental health. While nutrition may play an important role in perinatal mental health, the specific mechanisms surrounding these associations is not yet clear. Previous research has mostly focused on studying one or two specific micronutrients or diet patterns, and many studies fail to account for important confounders, including social determinants or previous mental health history (Sparling et al., 2017). Socioeconomic status for example can influence diet, and thus also possibly disturb micronutrient balance (Alkerwi et al., 2015, Darmon & Drewnowski, 2008). Research that takes a more comprehensive approach enables us to disentangle the complexities that influence perinatal depression and anxiety. A more precise insight into these associations is paramount when investigating root causes and the feasibility of potential prevention strategies.

Overall Objective: This study aims to explore relationships between nutrition during pregnancy and maternal mental health status, specifically the occurrence of perinatal depression and anxiety, in participants of the French EDEN cohort.

Specific Objectives:

1. To study the association between prenatal dietary patterns and the occurrence of perinatal depression and anxiety in women of the EDEN cohort.
2. To visualize and explain the relationship of specific macro and micronutrients and their associations with perinatal depression and anxiety in women of the EDEN cohort.

Methods:

Study Design

Analysis will be based on data from the French EDEN Mother-Child cohort (Heude, 2016). The EDEN (Etude sur les déterminants pré et post natals précoces du Développement psychomoteur et de la santé de l'ENfant) study was set up to assess the pre- and postnatal nutritional, social and environmental determinants of infant and child development and health. Participants were pregnant women recruited between the 24th and 28th weeks' gestation at two university maternity clinics in Nancy and Poitiers, France. Recruitment took place between 2003 and 2006. Exclusion criteria were multiple pregnancies, a history of diabetes, intention to deliver outside the university hospital or move out of the study region within the next 3 years, and the inability to speak and read French. A total of 3758 women were invited to participate in the cohort study and 2002 (53%) were enrolled, on average during the 15th week of amenorrhea. Written consent was obtained from the mother for herself at inclusion and for her newborn child after delivery. Birth data were obtained from 1899 mother-infant pairs. During pregnancy and after birth (4, 8, 12, 24 months, 3, 4, 5 and 8 years) sociodemographic and biomedical data on the mother and child were gathered from obstetrical records, in face-to-face interviews with the mother, and by mother's self-completed questionnaires. The current study will only analyze sample data from pregnancy to the 4-month postnatal mark. Ethical approval for the collection and use of this data was approved by the ethics committee (CCPPRB) of Kremlin Bicêtre on 12 December 2002 and by the Commission Nationale Informatique et Liberté (CNIL).

Measures

Perinatal Mental Health

To assess *prenatal depression*, the Center for Epidemiological Studies-Depression Scale (CES-D Radloff, 1977) was self-completed between the 24th and 28th week of pregnancy. The CES-D questionnaire is a 20-item questionnaire measuring the number of symptoms over the preceding week (range 0-60) and addresses severity of those symptoms as different features of depression. It has high reliability and validity and is used in numerous epidemiological studies (Joiner 2005). Although not specifically designed to measure depression in pregnancy, the CES-D has been used previously in pregnant women (Canady 2009). *Prenatal anxiety symptoms* were measured with the State Trait Anxiety Inventory (the STAI state component) (Spielberger et al 1970). The State-Trait Anxiety Inventory (STAI) was used to assess prenatal anxiety current state in mothers (Spielberger, Gorsuch, Lushene, Vagg, & Jacobs, 1983). The 'state' portion of the STAI is a 20-question assessment (range 20-80) that can be used in clinical settings, specifically to distinguish between anxiety and depression, but more frequently it can indicate a state of anxiety in caregivers (e.g., Greene et al., 2017, Ugalde et al., 2014). Symptoms of *postnatal depression* were assessed at four months post-partum using the Edinburgh Postnatal Depression Scale (EDPS) (Cox, Holden, & Sagovsky, 1987). The EPDS is a 10-item questionnaire constructed to assess postnatal depression (range 0-30) and measures the frequency of statements concerning certain feelings (0 points for 'never', 3 points for 'most of the time'). All questionnaires have been translated and validated in French (Fuhrer 1989, Spielberger 1993, Guédeney and Fermanian 1998). Cronbach's alpha was tested for each mental health survey, and all had good or excellent internal consistency (CES-D: 0.861 STAI: 0.912 EPDS: 0.855). The scores of each test were treated as continuous variables in the analysis (with higher scores indicative of higher levels of depression/anxiety) thus no cut off points were determined to define 'depressed' versus 'non-depressed' or 'anxious' versus 'non-anxious' women.

Prenatal nutrition

Maternal nutrition during the last trimester of pregnancy was assessed retrospectively during the mother's time at the maternity ward. Each mother completed a French validated Food Frequency Questionnaire (FFQ) that comprised 137 items with frequency ranges between 'never' and 'more than once a day' on a scale of seven categories. Photographs of portion sizes and cup sizes measured the quantity of consumption (i.e., 330ml glass, 100g of steak). Each food item was grouped into a total of 44 food groups (Deschamps et al., 2009). Previously compiled nutrition composition tables from the SU.VI.MAX study (a large, French epidemiological study examining antioxidants and cancer) were used to determine the nutrient content of foods and beverages of all types: processed, prepared, packaged, and fresh. FFQ values were only calculated for those women in the study who had less than 3 missing responses on the survey (n=1599). Each value for a given nutrient (i.e., vitamin A) represents its daily average intake in grams/milligrams/micrograms.

In addition, using data from the FFQ, two distinct maternal Dietary Patterns during pregnancy were previously identified through Principal Component Analysis (Yuan et al, 2017) 'Healthy' (i.e. characterized by a high intake in fruits, vegetables, high fat dairy products, fish, legumes, and whole grains) and 'Western' (i.e. characterized by a high intake of cakes, snacks, processed meat, prepared meals, soda, and chocolate) (highest quartile vs. others). These two dietary patterns were responsible for 10.8% (Western) and 6.8% (Healthy) of total variance. Each participant was assigned a score corresponding to the appropriate diet pattern. The current study uses these scores in our estimated networks as a continuous variable.

Covariates:

Information regarding covariates was collected between the 24^{th} and 28^{th} week of gestation via a face-to-face interview, examination or medical record from the obstetrician's office. Covariates relating to health status, education, adverse childhood events, and previous mental health history were selected based on prior research (Hutchens and Kearney 2020, Urech et al., 2020, Jani et al., 2020) and our conceptual framework. Our conceptual framework attempts to reveal the relationships and patterns of nutrients that comprise the Western and Healthy diet and how they may in turn be associated with perinatal depression and anxiety. Education serves as a proxy for socio-economic level while BMI is meant to be a generalized measure of pregestational health. Four mental health related covariates were initially chosen. The selection was then refined after testing for collinearity. 'Mental health treatment during pregnancy' and 'life events during pregnancy' were removed. Covariates included in at least one or more models include: BMI before pregnancy (kg/m^2), educational level (years of formal education obtained), adverse childhood events (experienced yes vs.no), history of mental health problems (yes vs. no). All variables were kept as continuous scores except for adverse childhood events and history of mental health problems which are binary.

Statistical Analysis:

Descriptive Analysis

R (version 4.0.4) statistical software was used to complete the data analysis. Initially, a descriptive statistical analysis was performed on the entire cohort (n=2002) and a sample was selected based on the presence of both exposure and outcome variables (nutritional markers and mental health survey EPDS), with a corresponding sample size of n=1438. Sample selection was based on availability of data at the 4-month postnatal mark. Statistical tests (Student T-test or Chi2) were performed on all variables to examine the difference between the complete cohort and our sample. Each of the four networks were constructed based on the availability of mental health survey data (CES-D, STAI, and EPDS).

Network Analysis:

Network analysis provides a unique opportunity to view dynamic relationships between variables and the underlying structures that comprise a biological system or a psychological disorder (McNally 2016, Muzio et al., 2021). In psychopathology, latent variables are often not the cause of a mood disorder, but rather the disorder is comprised of symptoms and the interplay between them (McNally 2016). Based on this conceptual framework, we employ network analysis to describe the interplay of nutritional markers as they constitute diet patterns and relate to perinatal mental health. Our networks are built from weighted adjacency matrices. We have considered biological, mental health, and sociodemographic variables as 'nodes'. The 'edges' represent the relationships between the nodes and are considered conditionally dependent on the other existing nodes in the network. In network estimation, the weight of an edge is 'inversely proportional to the variance of the population from which that observation was sampled' (Wicklin et al., 2017).

All networks were estimated after preliminary linear modeling, literature review, and conceptual framework consideration of the study design. The following variables comprised one or more of our initial matrices: total energy (calories), proteins (total, vegetable, animal), total lipids (cholesterol), fats (poly, mono, saturated, unsaturated), omega 3, omega 6, total carbohydrates, added sugars, alcohol, vitamins A, B1, B2, B3, B5, B9, B12, C, D and E, calcium, iron, iodine, potassium, magnesium, sodium, phosphorus, STAI, CES-D, and EPDS scores. All missing data points were removed and the final sample for each network determined. Skewed data were then transformed using the non-paranormal Empirical Cumulative Distribution Function (Liu et al., 2009). This procedure follows the recommended and commonly utilized technique in psychological studies when estimating regularized partial correlation networks (Epskamp et al., 2018). After data preparation and visualization, we confirmed that our correlation matrix was positive definite using the *corpcor* package in R which implements a James-Stein-type shrinkage estimator (Schafer et al., 2017). Next, we addressed the possibility of collinearity using the *goldbricker* package in R to eliminate redundant variables. Finally, the matrices were used to estimate our four networks: *Un-adjusted macronutrients*, *adjusted macronutrients, un-adjusted micronutrients,* and *adjusted micronutrients.* Given that our study includes variables from different domains, a Mixed Graphical Model was used to estimate all networks (Haslbeck 2021, Sedgewick 2014). Networks were estimated using the R package *mgm* and plotted using the R package *qgraph* (Haslbeck 2021, Epskamp 2021). We calculated the predictability estimates for all nodes using *mgm* and included them in the graph indicated by the colored perimeter of each node.

Sensitivity Analysis

The *mgm* package uses the LASSO (least absolute shrinkage and selection operator) regularization technique to assess the most important relationships between nodes. However, given that the LASSO regression does not distinguish between the relationships by level of importance (it simply shrinks already small edges into non-existence) we set the gamma at 0 and 0.25. Thus, we were able to see these edges regardless of their capacity for shrinkage, which is recommended in the literature (Fried et al., 2020). For each network, sensitivity analysis was conducted by changing the gamma from 0 to 0.25, and then comparing both models using the Pearson's correlations test of the two pairwise weighted matrices and predictability estimates. The model with gamma 0.25 was selected (to be more conservative) in the case that there was significant change between models.

Accuracy, centrality, and predictability

Currently, many fields that use network analysis are facing the issue of replicability, therefore, we must consider the power and robustness of any estimated network (Borsboom et al., 2017). To do this we can explore various measures of stability and accuracy to provide confidence in our network results. In this study, we considered the network structure and accuracy, node centrality and node predictability. Accuracy, centrality, and predictability were assessed using the R package *bootnet* (Epskamp 2020).

First, to assess the accuracy and stability of our networks, we extracted confidence intervals for the model parameters using the program *bootnet* in R (Epskamp 2020). Bootstrapping allows us to make inferences from our networks and provides power when using parametric bootstrapping (sampling from a second parametric model). We re-estimated all models using *bootnet* (parametric) then bootstrapped each model 500 times to extract confidence intervals. The manner in which we interpret confidence intervals for estimated networks is of great importance. Because we used LASSO regularization, when an edge appears as different than zero in our bootstrapped model, we can say with 95% confidence that it is likely different from zero, even if the confidence interval of the bootstrap includes zero. This is because using regularization in the estimation of our model already biases edge estimates towards zero. For example, if the point estimate for an edge in the bootstrapped model is 0.76 (CI: -0.1 to 0.45), the edge was estimated as non-zero 76% of the time (Fried et al., 2018). However, we must continue to interpret edge weights with caution in regard to network *inference* because the model treats all nodes the same within the network (e.g., there is no 'dependent' variable).

Node Centrality identifies the most important nodes in a network (also known as centrality indices). We can examine the *strength*, *betweenness*, *closeness*, and *expected influence* of a node to better understands its role in the network. We have plotted centrality measures as z-scores, higher scores signify higher importance in the network. Node strength reflects the absolute sum of the edge weights that are directly connected a node. Similarly, closeness relates the connectedness to other nodes via the sum of the distances to all other nodes in the network. And betweenness counts the frequency of which a node is on the shortest path connecting it to other nodes. Lastly, expected influence calculates the total amount of influence a node has in the network.

Node Predictability is graphically represented by rings of color around the nodes. Predictability refers to the extent to which a node is predicted by all other nodes to which it is connected within the network. It is akin to R^2, thus implies the degree of explained variance of the node due to the other nodes. If the predictability of a node is very low, we can imagine that other variables not included in the network would be important to consider. Predictability involving categorical nodes 'adverse childhood events' and 'history of mental health problems' is calculated as a *normalized accuracy* and thus must be interpreted differently than R^2 (Haslbeck & Waldorp, 2018).

Results:

Demographics

Table 1 presents the characteristics of our 1438 study participants according to those who responded to the EPDS survey at 4 months. Respondents to the EPDS survey, when compared to the initial cohort, tended to be slightly more educated (college vs. two-year diploma), have a higher income, were married or in a legal partnership, and experienced fewer adverse childhood events. There were no differences in the means of the prenatal mental health survey scores (see *Supplementary Table 1*). The average age of our study sample was 29.6 years (SD=4.8). The majority of women were of French nationality with French parents (87.6%) or second-generation migrants (9.6%). A small fraction were migrants to France (2.8%). More than half of the women were in a legal partnership to the father (55.2%) or cohabitated with the father of the baby (40.0%), while 4.7% were single/divorced/widowed. The majority reported an income level of between 1501-3000€/month (57%). Our sample was relatively healthy before and during pregnancy. Pre-pregnancy body mass index for our sample was 'normal' or 'not overweight' (mean BMI = 23 m^2/kg) as defined by the WHO (World Health Organization, 2021). Almost 25% of participants were considered above normal BMI before pregnancy. Average daily caloric intake was 2203 calories. 61% of participants reported giving up certain foods during pregnancy and 15.6% reported being diagnosed with anemia prior to pregnancy. Many women reported a history of mental health problems (22.4%) and/or experiencing adverse childhood events (35.9%). 14.3% of women reported receiving mental health treatment during pregnancy and almost all participants reported having social support of some kind (99.7%). In our sample, 23.8% of women reported clinical symptoms of prenatal depression (CES-D score ≥16), 20.2% clinical symptoms of prenatal anxiety (STAI ≥17), and 14.9% clinical symptoms of post-natal depression (EPDS score ≥11).

Table 1: Maternal Characteristics	*Mean (SD)*	*n (%)*
Demographics		
Age	29.62 yrs (4.7)	
Migrant Status		
French		1614 (87.6%)
Descendent		196 (9.6%)
Immigrant		77 (2.8%)
Income		
<800€		46 (3.2%)
800 - 1500€		146 (10.2%)
1501 - 2300€		408 (28.5%)
2301 - 3000€		408 (28.5%)
3001 - 3800€		240 (16.8%)
>3800€		182 (12.7%)
Partner Status		
married/legal partnership		791 (55.2%)
cohabitation with father		573 (40.0%)
partner other than the father		1 (0.1%)
single/divorced/widow		68 (4.7%)
Health Status		
BMI	23.17 m^2/kg (4.4)	
Gestational Diabetes Dx		90 (6.3%)
Anemia Dx (before pregnancy)		224 (15.6%)
Hypertension (before pregnancy)		32 (2.2%)
Nausea and Vomiting		1078 (75.5%)
Vitamin supplement 3rd trimester		1045 (73.2%)
Mental Health		
Experienced adverse childhood event		515 (35.9%)
History of mental health problems		323 (22.4%)
EPDS scores	5.29 (4.9)	
STAI scores	10.02 (9.3)	
CESD scores	11.22 (7.6)	

Network Structure

Table 2 presents the components of each of the four final networks. Networks were estimated based on 'macronutrients' and 'micronutrients', before and after adjustment for co-variates. Sample sizes of each network are as follows: *Micronutrients, unadjusted* (n=1429), *Micronutrients, adjusted* (n= 1399), *Macronutrients, unadjusted* (n=1429), *Macronutrients, adjusted* (n= 1399). All models shown are the fully regularized models (LASSO). Figures 1-4 present the network graphs, with green lines signifying positive relationships while red lines signify negative relationships. Grey lines represent undefined positivity or negativity of edges. Edges can be quantified by calling for the exact edge weight in the network model. The color, saturation, and width of an edge become darker and wider in proportion to the absolute weight of the edge.

Table 2: Overview of Network Models

Networks	**Mental Health Variables**	**Nutrient Markers**	**Covariates**
Macronutrients, unadjusted	EPDS/STAI/CESD	Macro	---
Macronutrients, adjusted	EPDS/STAI/CESD	Macro	Yes
Micronutrients, unadjusted	EPDS/STAI/CESD	Micro	----
Micronutrients, adjusted	EPDS/STAI/CESD	Mirco	Yes
Edges			
Red = negative relationship			
Green = positive relationship			
Grey = undefined			

In the *Macronutrient, unadjusted* network (*Figure 1*), the EPDS and Western diet nodes are connected by a positive edge (r=0.037) signifying a positive association between higher Western diet consumption and EPDS score. Additional positive edges connected to the Western diet include 'added sugar' (r=0.404), monounsaturated fatty acids (r=0.235), and total cholesterol (r=0.201). The *Macronutrient, unadjusted* model also shows the Western and Healthy diets are connected by a negative (red line) edge (r= -0.409). 'Calories' is strongly, positively connected to 'animal protein' (r=1.202), 'alcohol' (r=0.862) and 'carbohydrates' (r= 0.845).

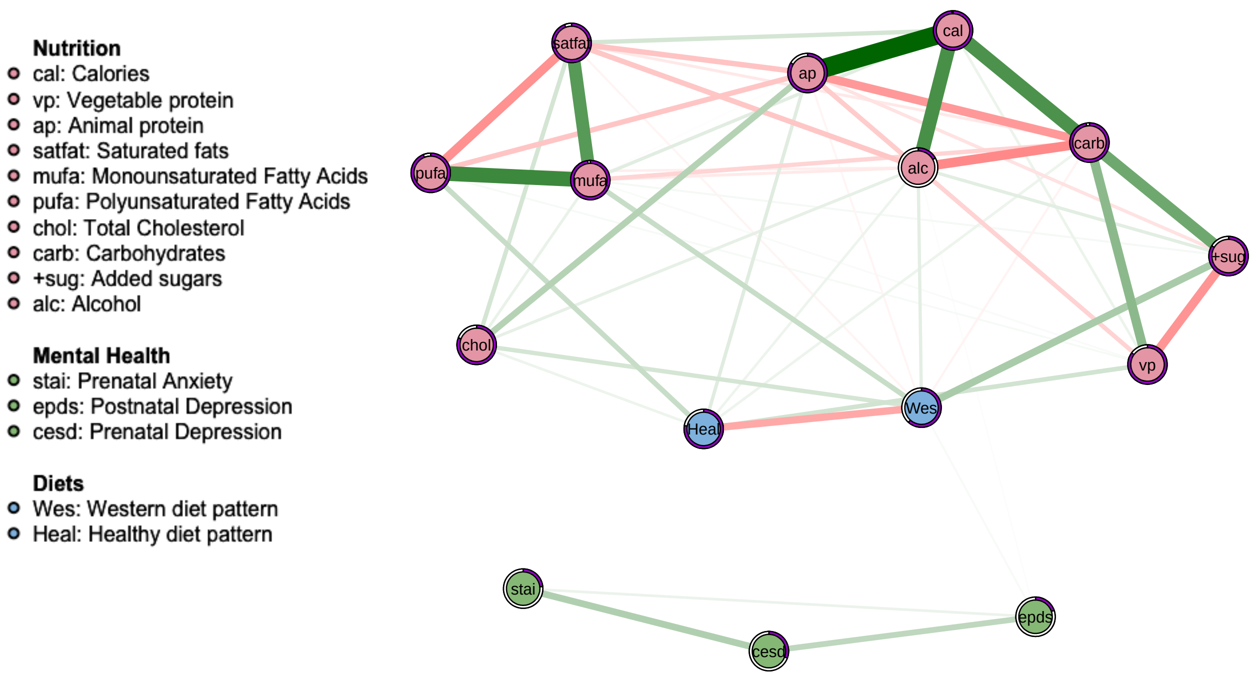

FIGURE 1 MACRONUTRIENT, UNADJUSTED

In the *Macronutrient, adjusted* model (*Figure 2*), the Western and Healthy diets have the same inverse relationship as in the previous model (r= -0.359). The positive edge between the Western diet and EPDS (r=0.0222) remains in the adjusted model. Edges with undefined directionality (grey lines) appear between the covariate 'previous mental health history' and two of the mental health survey nodes (EPDS r=±0.164, CES-D r=±0.132). Red edges connect the education node to the Western diet, BMI, and CESD (r=-0.114, r=-0.077, r=-0.052. The adjusted macronutrients model was the only estimated network in which the Pearson's correlation was below 0.95 (cor=0.88, p-value<0.05) however, all previous edges remained when plotting the graph signifying that the r-value of all edges was different than zero.

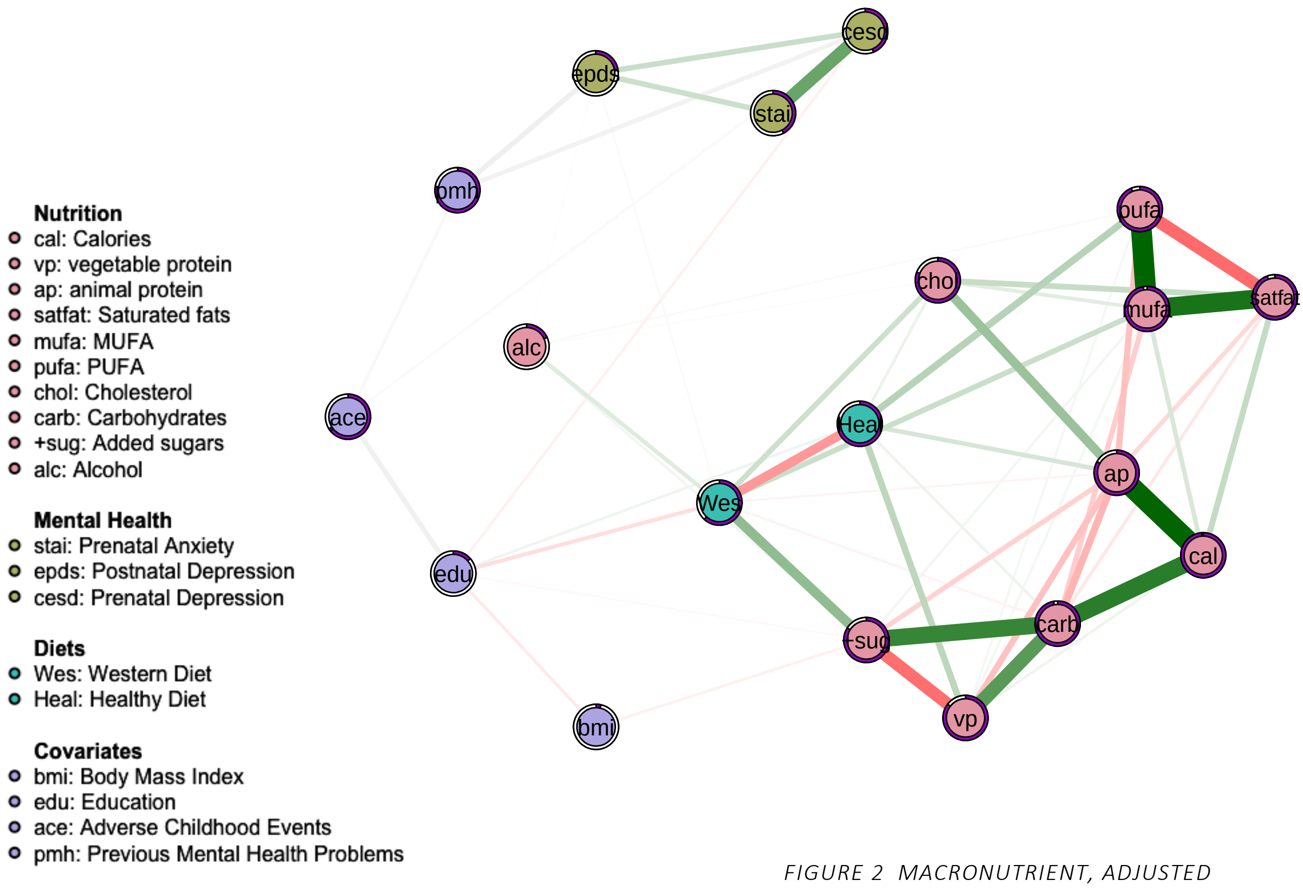

FIGURE 2 MACRONUTRIENT, ADJUSTED

In the *Micronutrient, unadjusted* network (*Figure 3*) a positive edge appears again between EPDS and the Western diet (r=0.072). All three of the mental health markers are connected by positive edges, the strongest being between STAI and CESD (r=0.373), then between EPDS and CESD (r=0.305). A negative edge exists between the Western and Healthy diet (r=

-0.078), and between the Western diet and Vitamin B9 (r= -0.359). Many of the nutritional markers have strong edges between them, particularly omega-3 and Vitamin D (r=0.599), Vitamin A and B12 (r=0.654), omega-6 and Vitamin E (r=0.616).

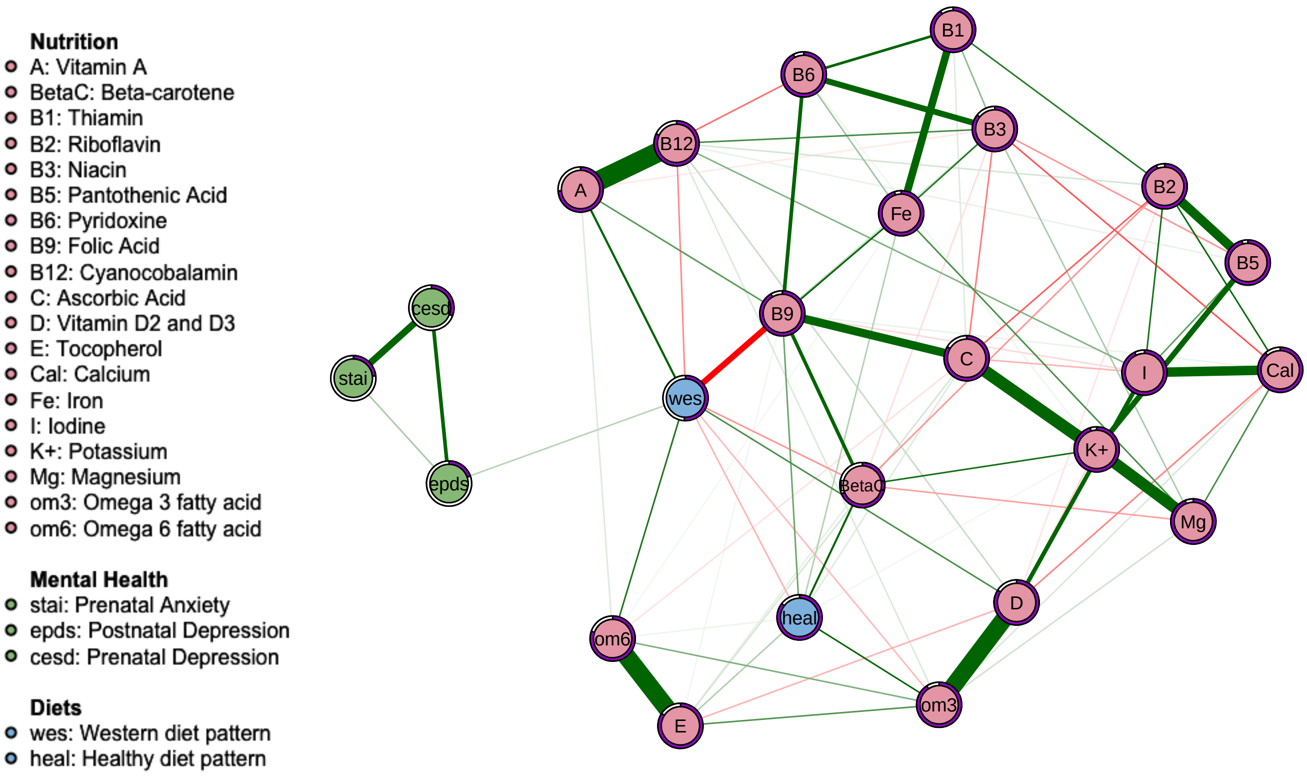

FIGURE 3 MICRONUTRIENT, UNADJUSTED

After adjustment with the covariates in the micronutrient model (Figure 4), the positive edge between the Western diet and EPDS (r=0.025) appears again. This *Micronutrient, adjusted* network exhibits negative edges that connect the following nodes with the covariate ‘education’: Western diet (r= -0.211), CESD (r= -0.066), adverse childhood events (r= -0.180), and BMI (r= -0.080). In all four models, similar patterns between nodes are observed (i.e., Western diet and EPDS scores). The Western diet is central in all four models and is either directly or indirectly connected with the perinatal mental health surveys, covariates, and macro and micronutrients.

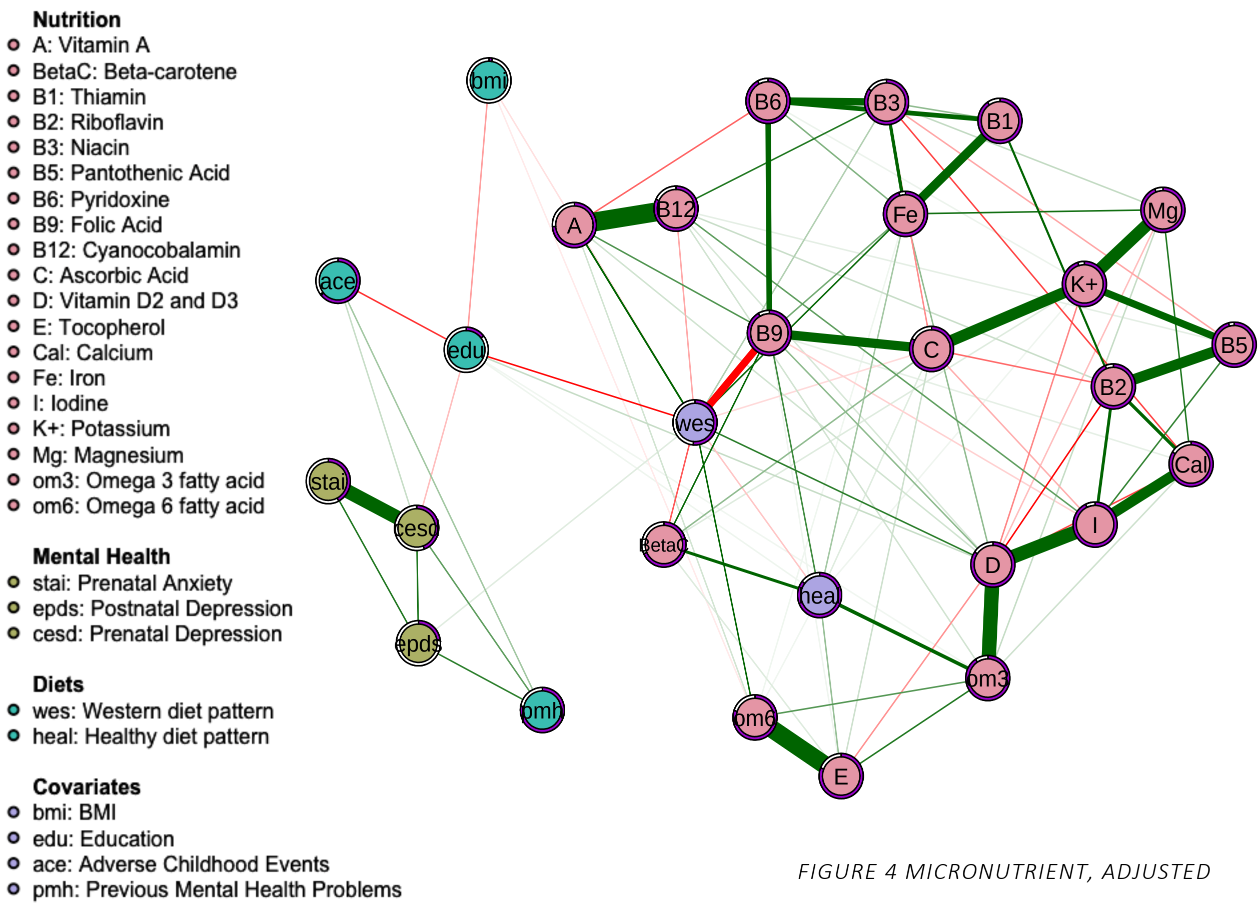

FIGURE 4 MICRONUTRIENT, ADJUSTED

Accuracy of Edges, Node Centrality and Predictability

Table 3 displays the predictability of key nodes within the four networks. Node predictability is the proportion of explained variance The node most explained by other nodes in both the macro and micronutrient adjusted models was the Healthy diet (R^2=0.849, *Micronutrient adjusted*). The Western diet was also well explained in both models, with the highest value in the macronutrient model (R^2=0.612, *Macronutrient adjusted*). The CES-D node was the best explained of the three mental health indicators in *Macronutrient adjusted* (R^2=0.441).

Table 3: Node Predictability

Macro		***Macro (adj)***		***Micro***		***Micro (adj)***	
Node	*R^2*	*Node*	*R^2*	*Node*	*R^2*	*Node*	*R^2*
STAI	0.233	STAI	0.423	STAI	0.233	STAI	0.227
CESD	0.308	CESD	0.441	CESD	0.308	CES-D	0.333
EPDS	0.198	EPDS	0.229	EPDS	0.196	EPDS	0.202
Western	0.617	Western	0.612	Western	0.509	Western	0.514
Healthy	0.777	Healthy	0.767	Healthy	0.854	Healthy	0.849
		Education	0.136			Education	0.165
		BMI	0.034			BMI	0.021
		ACE	0.647*			ACE	0.647*
		PMH	0.778*			PMH	0.778*

**Normalized accuracy, not R^2*

Node centrality measures are presented in *Figures 5 and 6*. In the *Macronutrient adjusted* model carbohydrates, calories and alcohol and the Western diet have high strength (absolute sum of the edges) and are thus very central to the network. Alcohol had the high betweenness (shortest path) and closeness (inverse of the shortest paths) as well. In the *Micronutrient adjusted* model, Vitamin D, B9, and the Western diet and education are important nodes. The Western diet and education are central to the connection between other nodes in the network as they have the high betweenness. Vitamin B9 and the Western diet have high closeness and thus have strong indirect connections to all other nodes in the network.

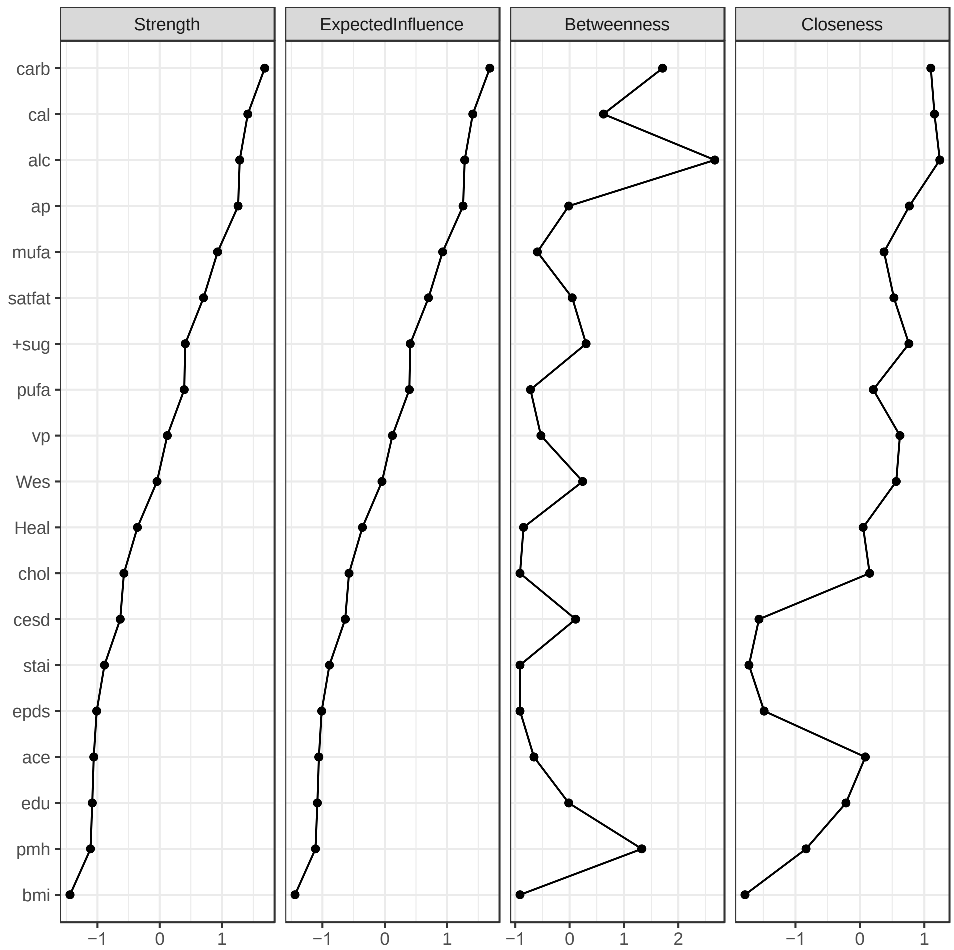

FIGURE 5 NODE CENTRALITY FOR MACRONUTRIENTS, ADJUSTED MODEL

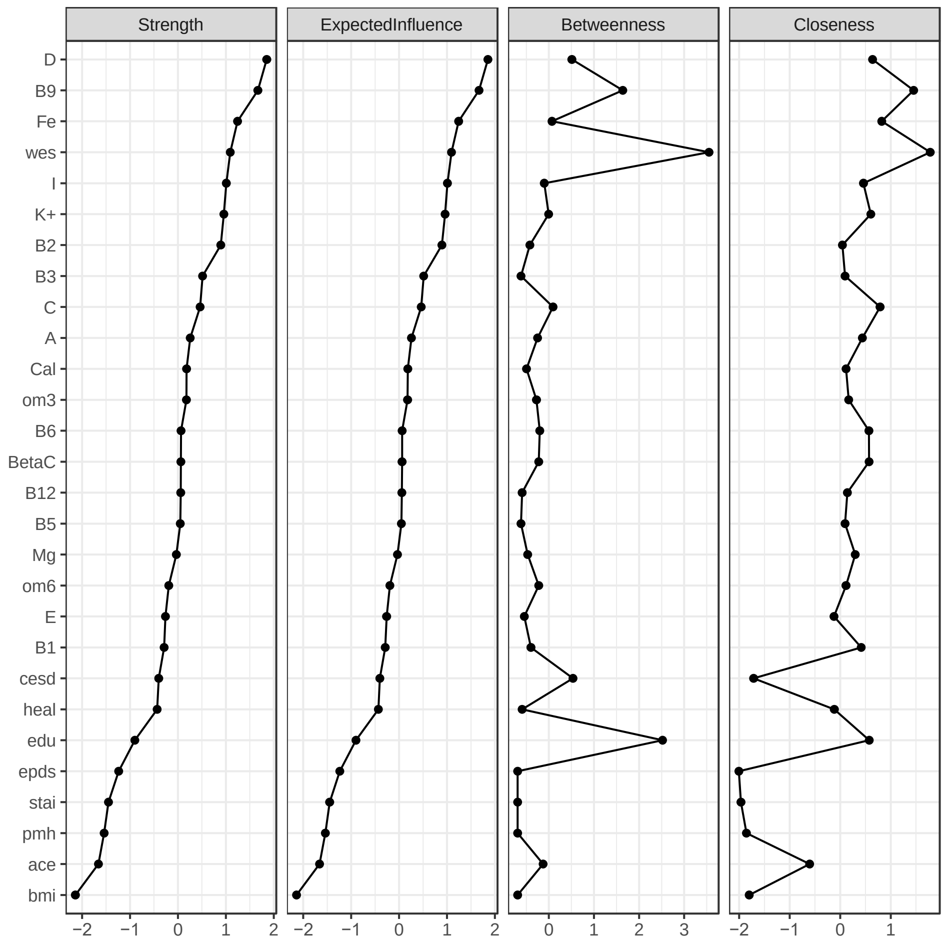

FIGURE 6 NODE CENTRALITY FOR MICRONUTRIENTS, ADJUSTED MODEL

Supplementary Figures 1-4 show the results from the parametric bootstrap for the micronutrient and macronutrient unadjusted and adjusted models. The edges are represented on the y-axis, however, labels have been removed to improve graph interpretability. The point estimate means from the bootstrapped models (represented by the black line) generally follow our sample mean (red line) and our confidence intervals (grey zones) mostly do not overlap with zero. The results of our bootstrap demonstrate that our edges were estimated reliably meaning that our networks were accurate. Additionally, the significance of the difference between edges via the 'edge difference test' in *bootnet* is shown in the Supplementary Figures 5 and 6 (macro and micro adjusted models). Black squares indicate that there is a true difference between two edges (ie. the edge estimate between A and B is truly different than the edge estimated for B and C).

Discussion:

Overview

To our knowledge, this is the first study to examine the relationship between nutrition and symptoms of depression and anxiety in the perinatal period using a network analysis approach. In a cohort of French women, we found a positive association between postnatal depression and prenatal consumption of a Western dietary pattern, in particular increased added sugars, cholesterol, and monounsaturated fatty acids. In the micronutrient model, the Western diet consistently lacked essential micronutrients such as folate and beta-carotene, while the Healthy dietary pattern contained those micronutrients in addition to omega-3 fatty acids and tocopherol. As postnatal depression was negatively connected to folate and omega-3 via the Western diet pattern, our results support findings from prior studies concerning the negative impact of a Western diet and a lack of certain micronutrients on postnatal depression (Madeghe et al., 2021, Chang et al., 2018, Khan et al., 2020). Contrary to previous studies examining diet patterns and perinatal mental health (Silva et al 2019, Baskin et al., 2015), we found no negative or inverse relationship between a Healthy diet and symptoms of prenatal depression and anxiety. Beyond dietary patterns and macro and micronutrients, our study revealed that associations between postnatal mental health and the Western diet vary by educational level.

When looking for nutritional determinants of perinatal mental health outcomes, using network analysis enables a more holistic and comprehensive approach. As the etiology of perinatal depression and anxiety most likely involves many factors (i.e., genetics, psychology, neurochemistry, and physical health) it is unlikely that a single nutrient deficit is the underlying cause. Systematic reviews of studies that aim to isolate specific nutrients and their effects on perinatal mental health identify many limitations related to the heterogeneity of studies and highlight the need for further research (Kahn et al., 2020, Sparling et al., 2017). A more inclusive approach is beneficial when exploring these complex relationships, with network analysis being an innovative and strategic research methodology that could contribute to this endeavor. While our findings support previous findings on the potential link between prenatal nutrition and post-natal depressive symptoms, by using network analysis we have expanded on them by encompassing the complex dynamic between diet pattern, micro and macronutrient function, and external contributing factors (Baskin et al., 2015, Kahn et al., 2020, Oakes et al., 2018).

Western versus Healthy Diets and Perinatal Mental Health

Overall, this study provides additional evidence to support the theory that specific dietary patterns determine nutritional status which could affect mental health during the perinatal period, as has been found in the general population (Arab et al., 2019). The Western and Healthy dietary patterns determined by Yuan et al (2016) are congruent with previously studied maternal dietary patterns in similar epidemiological studies around the globe (Silva et al., 2018 & Chen et al., 2016). We found a connection between postnatal depression and the Western diet in all four models, however, not between prenatal depression or anxiety. The lack of association between prenatal symptoms and the Western diet could be explained by pathophysiological changes that occur throughout the course of pregnancy. Medical guidelines for diet requirements during pregnancy have established that the demand for essential nutrients increases during pregnancy immensely and that the Western diet is inadequate to fulfill many of these nutritional demands (Marangoni et al., 2016). Nutritional imbalances are potentially exacerbated throughout pregnancy and could later be associated with postnatal depression whereas their impact on mental health symptoms may not yet be clearly present at earlier stages of pregnancy.

Second, perinatal physiological changes are often associated with changes in general diet pattern. Although the reasons for these changes are not well studied, women's dietary patterns often change at the start of pregnancy and vary in their adherence to recommended prenatal nutrition (Forbes et al., 2018 Fowles et al., 2012). Certain changes in consumption patterns could lead to altered nutritional status worsened by the heightened nutrient demand of pregnancy. In this study, the diet pattern reflects the last trimester of the pregnancy and diet patterns concerning earlier trimesters or in the year before pregnancy were not included. Therefore, we cannot make any assumptions about changes in dietary pattern from before until the end of pregnancy. It is possible, however, some participants engaged in a higher consumption of Western diet foods at the time of pregnancy. Beyond these potential explanations, it is certain that the nutritional demands of pregnancy and lactation are grossly unmet by the Western diet, and this could play a role in the emergence of postpartum depression symptomatology (Kominiarek & Rajan, 2017). As the trend of the Western diet continues globally, more observational studies need to assess its mental health impact on pregnant populations.

Macronutrients

Our network analysis demonstrated that the Western diet is associated with increased consumption of added sugars, cholesterols, and alcohol. In addition, our macronutrient model showed a link between total cholesterol (e.g., triglycerides) and the Western diet, which linked to postnatal depression scores. Other studies have also demonstrated the connection between increased consumption of certain macronutrients, such as refined sugars, carbohydrates and alcohol, and perinatal depression (Silva et al., 2019).

It is important to discern the type of macronutrient consumption when studying how diet interacts with perinatal depression and anxiety. The type of macronutrient calories consumed ultimately determines the cascades of energy utilization and biological reactions. The association between a diet high in added sugars and increased depression scores could be explained by the biological mechanisms behind how the body reacts to a diet high in sugar when essential nutrients are lacking. For example, unlike glucose, calories coming from fructose (a sweeter form of glucose often used in processed foods like soft drinks) can produce a rise in circulating triglycerides and affect levels of key hormones like insulin, ghrelin and leptin, primary signalers in the central nervous system (Teff et al., 2004).

Most research surrounding macronutrient intake during pregnancy is specific to prevention of gestational disease pathologies such as diabetes or hypertension and very little research exists on macronutrient balance and maternal mental health (Mousa et al., 2019). There have, however, been studies on the associations between polyunsaturated fats and perinatal mental health, indicating that the balance between omega-3 and omega-6 is paramount to understanding the effects of this macronutrient on perinatal mental health (Chong et al., 2015, Hoge et al., 2019). In our macronutrient model, we saw a connection between the healthy diet pattern and polyunsaturated fatty acids, while the Western diet was associated with monounsaturated fatty acids. The breakdown of the specific components for the fatty acids was considered within our micronutrient model.

Micronutrients

Observational studies of the general adult population have proven the importance of specific micronutrients as related to mental health and brain function, yet causal inference and mechanism still require further study (Arab et al., 2019, Adan et al., 2019). An array of studies has attempted to isolate a link between key micronutrients and perinatal depression and anxiety, but evidence remains inconclusive, and these relationships should not be oversimplified (Chong et al. 2014, Trujillo et al. 2018, Kahn et al. 2020). The roles of micronutrients and their vital functions during pregnancy have previously shown to be critical for development of the fetal nervous system and reduce incidence of low birth weight and preterm birth (De-Regil 2015, Middleton 2018). While the priority of micronutrients during pregnancy for the fetus has been well established, the consequences of maternal micronutrient deficits are still unclear. Our micronutrient model supports previous evidence demonstrating that a lack of polyunsaturated fats (Omega-3) is associated with postpartum depression (Urech et al., 2020). In the adult population, increased saturated fat intake and low polyunsaturated fat intake leads to inflammation in the brain and a disruption in the dopaminergic system (Rapaport et al., 2016, Adan et al., 2019). While there is some evidence to support that supplementation of omega-3 fatty acids during pregnancy in a population of women with pregestational nutritional deficits prevents symptoms of postnatal depression, a systematic review by Newberry et al found the overall evidence to be inconclusive (Hsu et al 2018, Newberry et al 2016). Vitamin D was not directly linked to depression or anxiety in our models but has been previously studied in perinatal mental health. Because it aids in the synthesis of neurotransmitters and closely works in tandem with calcium in the nervous system, there are plausible biological mechanisms worth investigating (Trujillo et al., 2018).

Previous Mental Health, Education, BMI

The associations we found between prenatal anxiety and depression and risk of postpartum depression are well reported in the literature (Davey et al. 2011, Beck 2001). In the current study, we attempted to control for several covariates related to mental health and nutrition, while many previous studies have focused on solely BMI and socioeconomic status (Lukose et al., 2014). Research has often identified *prenatal* depression as a predictor of post-partum depression, however, secondary factors such as childcare stress, self-esteem, prenatal anxiety, and life stress also contribute (Beck et al., 2001). The stress and sudden changes surrounding care for a new infant child can be considered a triggering event in those populations with previous history of mental health diagnosis or prenatal symptoms of depression and anxiety. Thus, we considered it paramount to control for mental health history as well as experiences of Adverse Childhood Events as they are known risk factors for perinatal mental health problems (Hutchens & Kearney, 2020).

Controlling for characteristics related to nutritional status should be standard practice when looking at associations of perinatal mental health and nutrition. Physical wellness is generally associated with proper nutrition and general health, while those who are not physically well often follow similar unhealthy life-style habits and eating patterns. For example, obesity is associated with multiple disease pathologies and many of its causes are associated with dietary intake (Centers for Disease Control, 2021). Therefore, to identify the effects of nutrition on mood disorders, research should control for physical characteristics that might be influenced by nutritional status. In our models BMI was positively associated with ‘added sugars’, and the Western diet.

Educational attainment could provide key insight into the dynamic between nutrition and maternal mental health. It has been shown in the general population in HIC that persons with a lower level of education and SES experience a higher prevalence of mental health problems when compared to the general population (Alegría et al. 2000, Wang et al. 2000, Steele et al., 2007). In particular, education appeared as a connector node in our networks in both the micro and macro nutrient models and was negatively associated with consumption of the Western diet, meaning that fewer years of education were related to a higher Western diet score. Previous studies demonstrate a link between maternal education level and nutritional status in offspring, however few studies examine the roll of nutritional status during pregnancy and maternal education. Education often determines a myriad of other factors, such as socioeconomic status, which in turn can dictate access to vital health related resources. Socioeconomic status could also affect access to mental health or primary care services, further increasing the risk for perinatal depression and anxiety (Filc et al., 2014). Although we are unable to address temporality in our study, lower educational achievement could be a risk marker for the consumption of the Western diet and be part of the mechanism of action that leads to perinatal depression and anxiety.

Strengths and limitations

A strength of our study is that it takes a holistic approach in its attempt to disentangle the mechanisms behind perinatal depression and anxiety. We look at both the macro and micronutrients associated with dietary patterns while also accounting for socioeconomic status and previous mental health history. We have applied an innovative analysis to existing data creating a methodology that is easily replicated with other similar cohorts. Our study uses data from a large cohort which is particularly advantageous in the employment of network analysis; network analysis requires a large sample size in order to gain enough power and our cohort sample was sufficient to make sound associations between variables. This is often a challenge in studies that require expensive resources for data collection. Advantageously, preconception FFQ data is available in the EDEN cohort to be investigated for similar findings to support the current study. Finally, our study addresses a modifiable aspect of perinatal mental health that is feasible and affordable and adds to the building realm of research in perinatal nutrition.

However, we should also acknowledge some limitations. First, our study is an observational study and therefore cannot make causal claims. Large and longitudinal studies are needed to clarify the roll of diet pattern, macro and micronutrients, and perinatal mental health to be able to make more robust conclusions about the mechanisms of action. Second, the network analysis approach allows for global insights but is statistically limited in its ability to make causal inferences. In addition, we used a mixed graphical model which treats all variables equally and does not address temporality. Future studies should ideally use the mixed Vector Autoregressive Model to estimate a network using measurements taken across different time points (Haslbeck 2021).

Third, it is important that baseline serum levels of biomarkers and diet patterns be established prior to pregnancy. Serum biomarkers capture a point estimate of bioavailable nutrients, while diet patterns can give a more global measure of food consumption over time.

Future studies should also incorporate both the benefits of FFQ and confirmatory use of biomarkers to more accurately determine the effects of nutrients on mood. The network analysis approach should be repeated on previously collected data in similar cohorts such as ELFE, BiSC, or INMA to replicate the current study findings.

Recommendations for public health and Practice

Perinatal depression and anxiety are far-reaching public health issues that influence the health of mother, baby and the family unit. Symptoms negatively affect the period surrounding pregnancy, childbirth, mother-infant bonding, the mother's health, and can have long-term consequences on children's development. Building evidence suggests that the lasting impact of perinatal depression and anxiety makes it an urgent matter in public health. For the mother, perinatal self-reported symptoms of depression affect health seeking behavior, post-partum physical health, the ability to care for the new infant, and partner relationships (Slomian et al., 2019). For offspring born to mother's experiencing perinatal depression and or anxiety, adverse outcomes include an increased risk of spontaneous preterm birth, lower APGAR scores, low birth weight and higher rates of admittance to the nursery unit (Dowse et al. 2020, Staneva et al. 2015). The Developmental Origins of Health and Disease (DOHaD) theory postulates that the developing fetus is influenced by its environment in a way that can have long term consequences throughout childhood and adulthood, thus repercussions of perinatal depression and anxiety are not only limited to maternal health and birth outcomes. The economic and financial consequences are also well documented. A study in the US estimated that the economic cost to mothers with perinatal depression and anxiety and their children was 14 billion dollars in total for those born in the year of 2017, or $31, 800 for each mother-child dyad (Luca et al., 2020). Beyond the economic costs, the lives of the children of affected mothers are potentially affected into adulthood (Tirumalaraju et. al., 2020). Thus, untreated perinatal depression and anxiety result in deep-rooted, long-term consequences for both mother, child, family unit and society.

The need to identify factors that contribute to maternal mental health, specifically during the vulnerable period of pregnancy, remains a challenge. Ideally, modifiable risk factors should be addressed to prevent or decrease the risk of perinatal depression and anxiety leading to healthier mothers and children who grow into healthy adulthood. Health care providers should assess risk factors and target areas that are appropriate for intervention. The patient should be made aware of available mental health care resources by her healthcare provider. Mental health screening for all pregnant women should be standard of care. While it is important to determine predictive factors of depression and anxiety during pregnancy, practice should also focus on determinants that can be modified during pregnancy, such as diet and lifestyle choices. Improving diet pattern and nutritional status could be a safe, low-risk option to prevent or improve symptoms of depression and anxiety, and inherently has added benefits related to general health and wellness. Improving nutrition is a feasible and relatively acute intervention in the pregnant population. Nutritional status is measurable and deficits are easily recognized during preconception and in early pregnancy. Pending that economic status does not present a barrier to high-quality nutritional intake, mothers could undergo nutritional counseling (Darmon & Drewnowski, 2008). Nutritional counseling should be an addition to current pregnancy dietary recommendations and has the added advantage that it is very low risk. Currently, in the United States nutrition counseling programs are not publicly offered and the responsibility of nutritional education falls on the obstetric healthcare provider (US Institute of Medicine, 1992). The Special Supplemental Nutrition Program for Women, Infants, and Children (WIC) is a program funded by the US Department of Agriculture to help lower SES women afford proper nutrition. However, its materials are limited to short pamphlets and publications for healthcare providers, and it does not serve as a nutritional intervention program. The French Ministry of Health has funded research for a nutritional intervention program to address pregnancy related maternal and childhood obesity (Parat et al., 2019). While very few nutritional counseling programs have been proven effective in the public sector, a recent systematic review assessed dietary intervention programs for pregnant women. It found that while effectiveness of the programs varied, almost half of the programs demonstrated an improvement in dietary behaviors and nutrition status of the women (Beulen et al., 2020). Almost all of the interventions were provided by nutritionists or dieticians and only some were designed for low socioeconomic populations. More research is needed about the effectiveness of nutritional intervention programs and specifically, programs geared towards at-risk populations.

Conclusion:

The current study was the first to use network analysis to explore the associations between perinatal mental health and nutrition. We determined that a Western diet is associated with increased postnatal depression scores and that this relationship may vary by education level. The Western diet does not address maternal nutritional needs during pregnancy on the macro or micronutrient scale. Nutrition plays an important role in biological processes of fetal development during pregnancy and possibly influences mood, as has been found in the general population. It is well known that proper nutrition benefits the mother and her fetus in many different ways; however, its impact on maternal mental health still needs further study to understand the precise associations with certain dietary patterns and the effects of their nutritional components. Because nutritional status is modifiable, affordable, measurable, and feasible intervention, it could be a future factor of perinatal depression and anxiety prevention.

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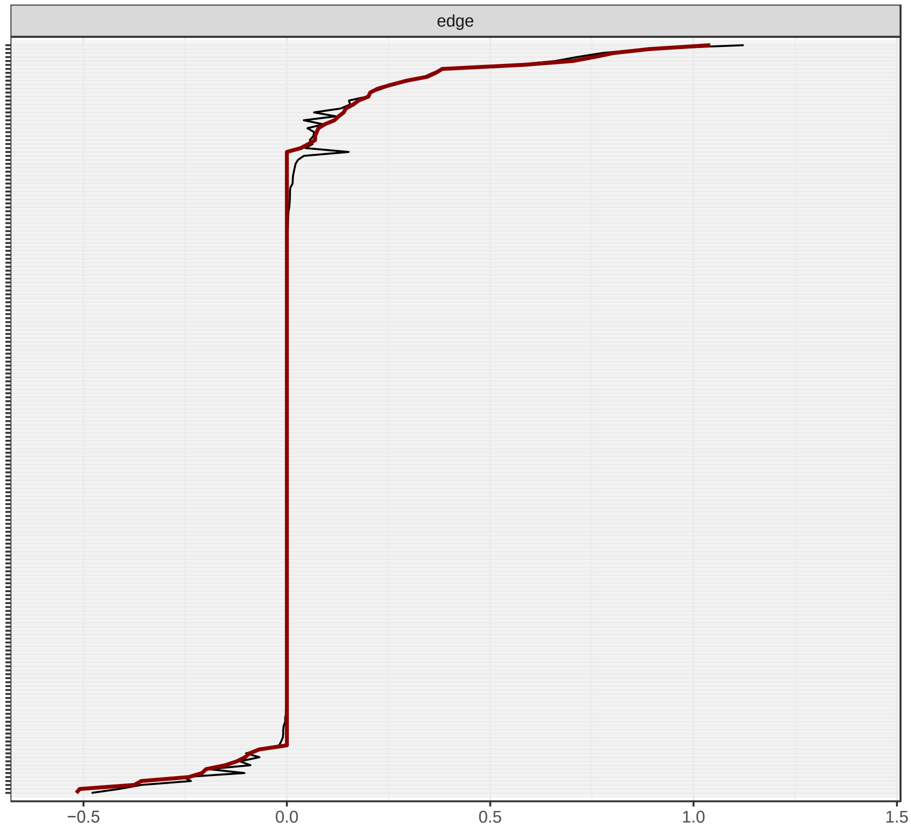
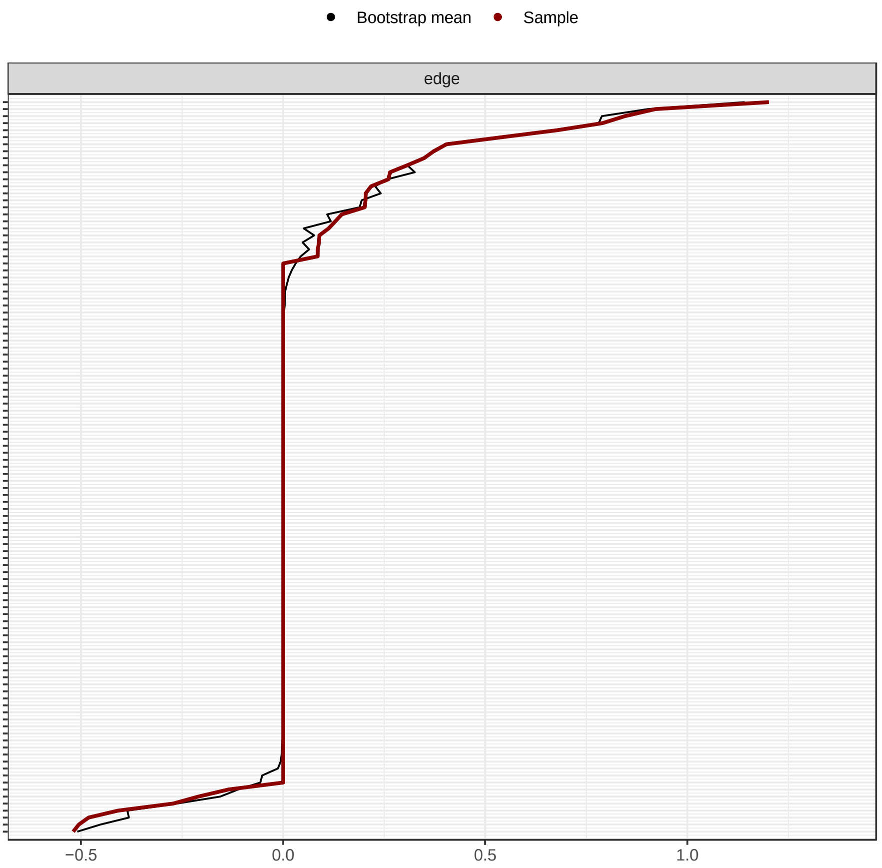
Annex:

Supplementary Table 1: Sample versus Cohort

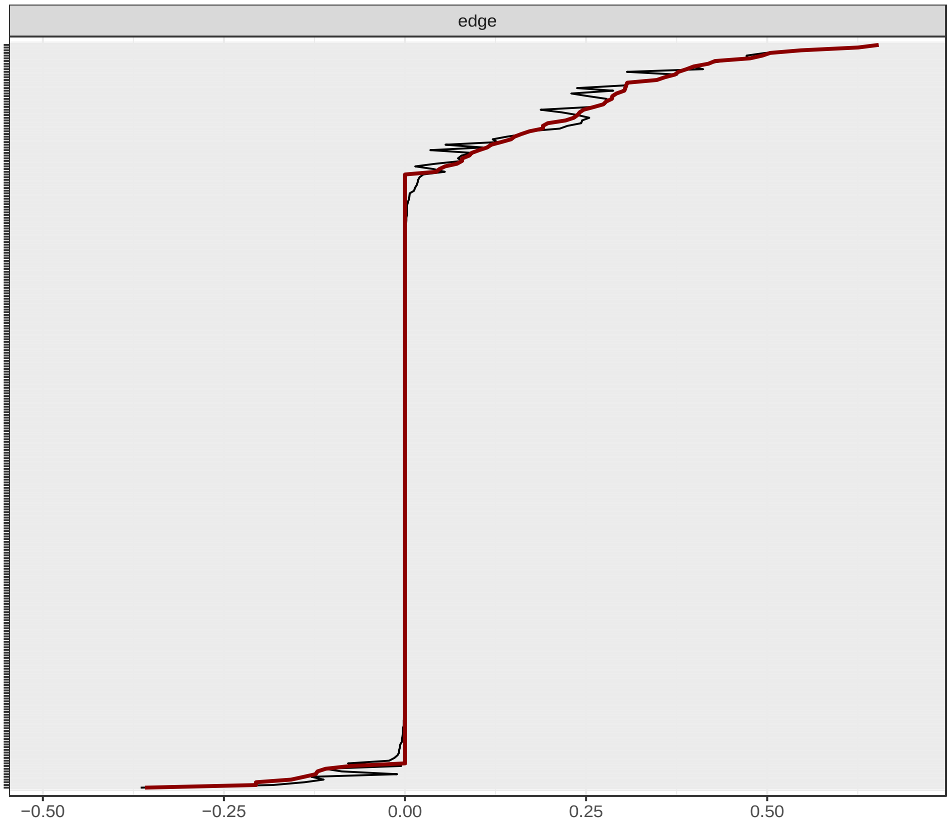
EPDS and FFQ Respondents	No	Yes (sample)	p-value
n	564	1438	
	n (mean or %)	n (mean or %)	
Age	29.05 (5.21)	29.62 (4.78)	0.028
Migrant Status			<0.001
French	377 (79.4%)	1237 (87.6%)	
Descendent	61 (12.8%)	135 (9.6%)	
Immigrant	37 (7.8%)	40 (2.8%)	
Years of Educations	12.64 (2.76)	13.90 (2.58)	<0.001
Income (%)			<0.001
<800€ (1)	2.4%	2.4%	
800 - 1500€ (2)	4.6%	7.6%	
1501 - 2300€ (3)	8.4%	21.3%	
2301 - 3000€ (4)	4.9%	21.3%	
3001 - 3800€ (5)	2.8%	12.5%	
>3801€	2.1%	9.5%	
Partner Status			<0.001
married/legal partnership	216 (44.7%)	791 (55.2%)	
cohab with father	216 (44.7%)	573 (40.0%)	
partner other than the father	0 (0.0%)	1 (0.1%)	
single/divorced/widow	51 (10.6%)	68 (4.7%)	
Life events during pregnancy	0.74 (0.93)	0.66 (0.84)	0.096
Experienced adverse childhood event	216 (44.7%)	515 (35.9%)	0.001
History of mental health problems	117 (24.0%)	323 (22.5%)	0.517
Mental health treatment during pregnancy	69 (14.2%)	207 (14.4%)	0.961
Tobacco (# of cig/day during preg)	2.32 (4.58)	1.24 (2.98)	<0.001
Alcohol (# of drinks per week)	0.39 (1.22)	0.56 (1.52)	0.024
Mental health treatment 4m	17 (7.5%)	97 (6.8%)	0.789
Food Insecurities	33 (6.9%)	31 (2.2%)	<0.001
average gestational weight gain (kg)	11.35 (5.84)	11.16 (4.58)	0.461
bmi	23.49 (5.20)	23.17 (4.42)	0.189
obese			0.105
normal	342 (72.2%)	1046 (74.2%)	
overweight	79 (16.7%)	251 (17.8%)	
obese	53 (11.2%)	113 (8.0%)	
Gestational Diabetes Dx	33 (7.1%)	90 (6.3%)	0.613



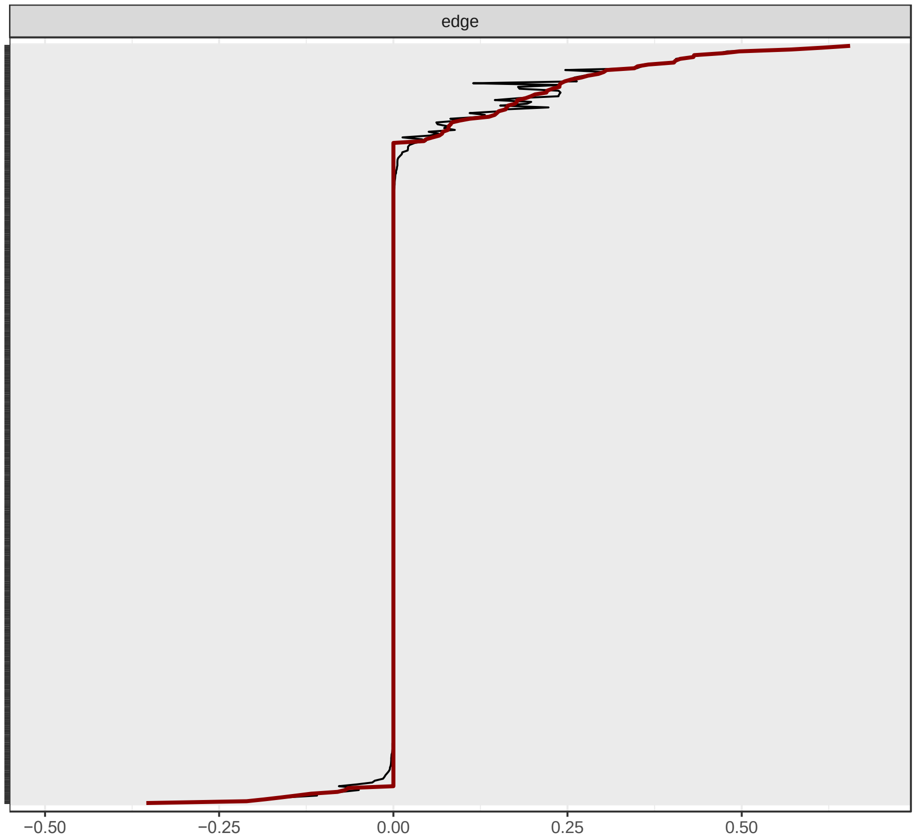
SUPPLEMENTARY FIGURE 1 MACRONUTRIENT, UNADJUSTED SAMPLE VERSUS BOOTSTRAP EDGE ESTIMATES



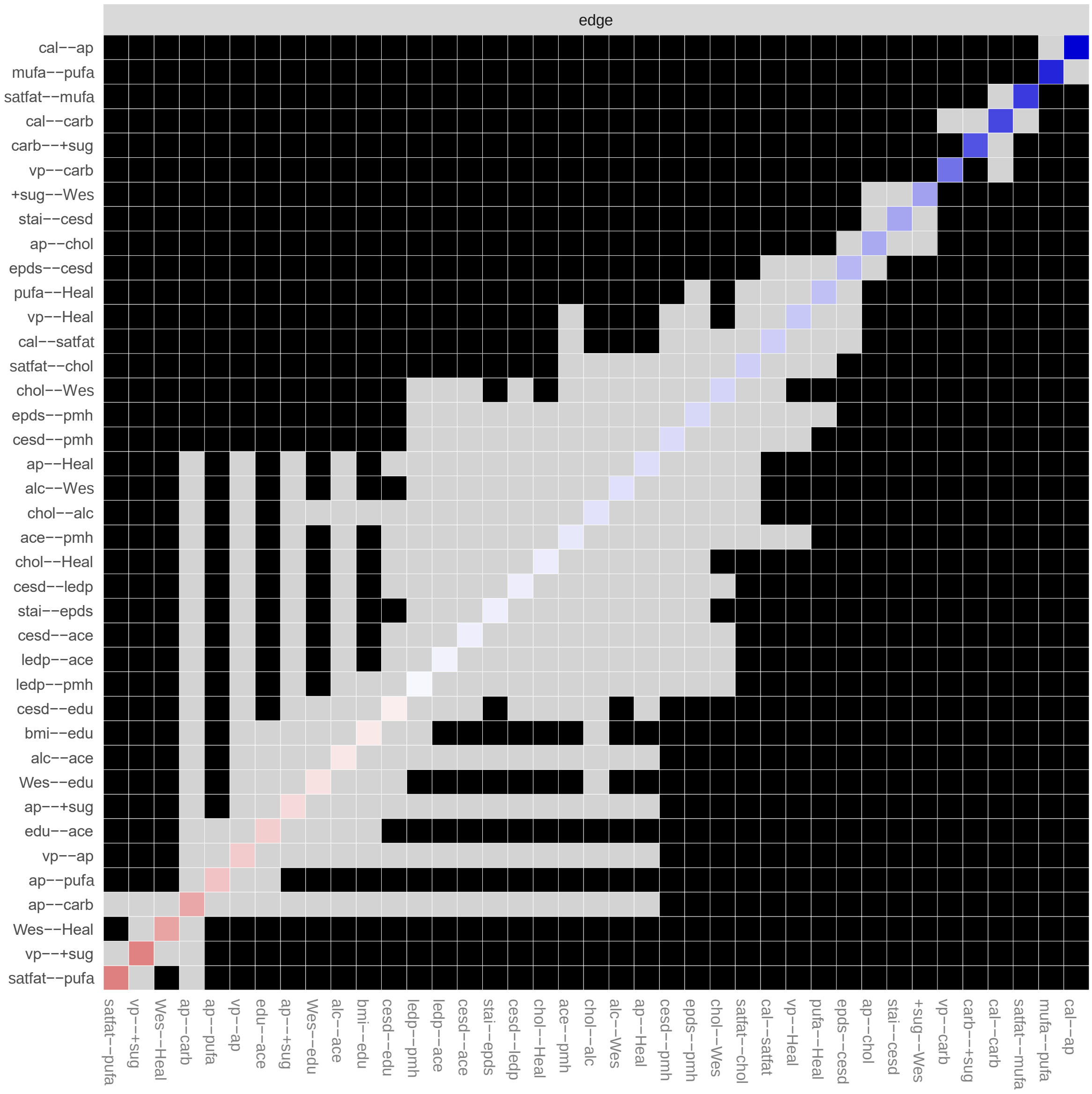
SUPPLEMENTARY FIGURE 2 MACRONUTRIENT, ADJUSTED SAMPLE VERSUS BOOTSTRAP EDGE ESTIMATES



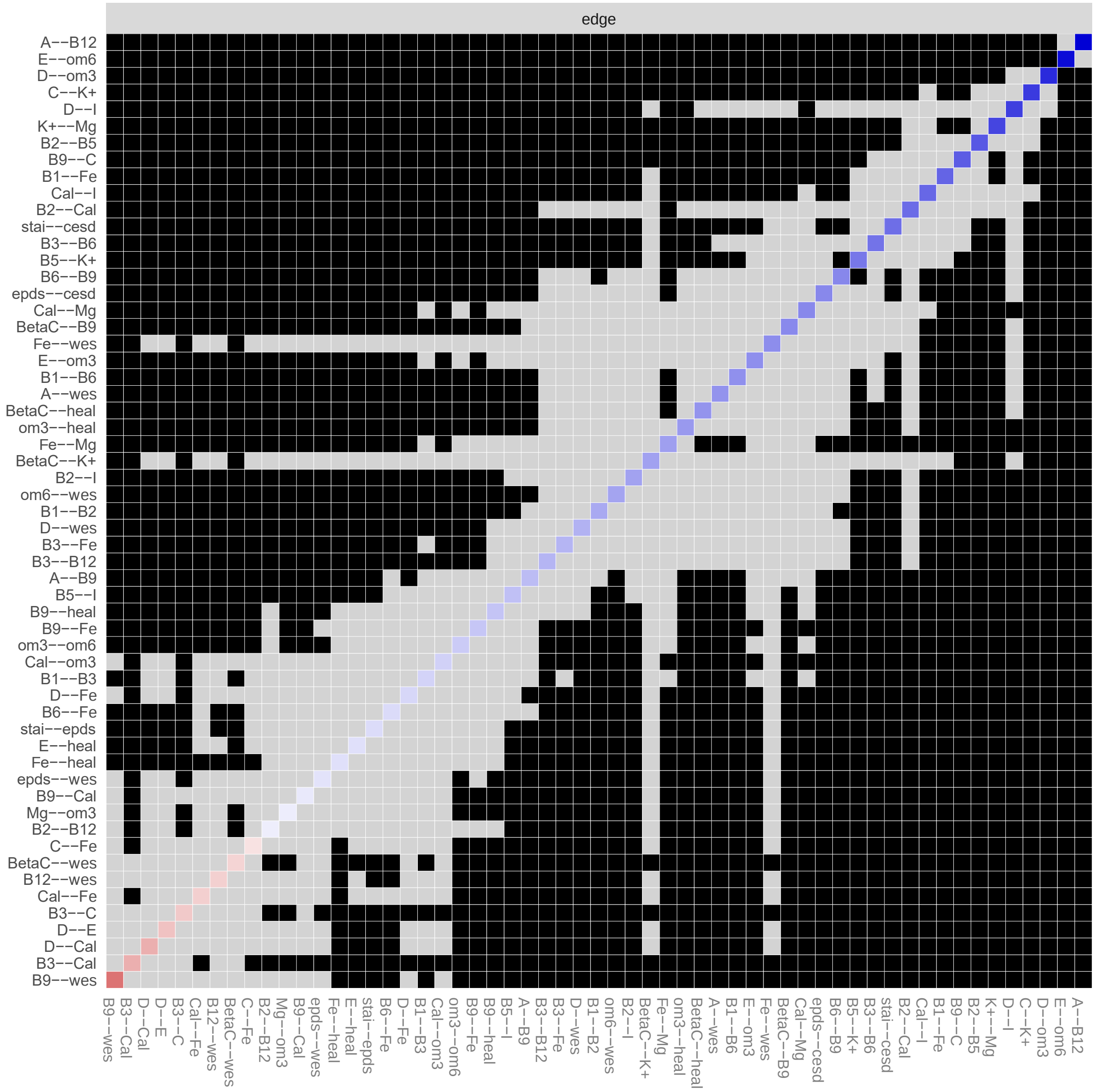
SUPPLEMENTARY FIGURE 3 MICRONUTRIENT, UNADJUSTED SAMPLE VERSUS BOOTSTRAP EDGE ESTIMATES



SUPPLEMENTARY FIGURE 4 MICRONUTRIENT, ADJUSTED SAMPLE VERSUS BOOTSTRAP EDGE ESTIMATES



SUPPLEMENTARY FIGURE 5 MACRONUTRIENT, ADJUSTED EDGE DIFFERENCE TEST



SUPPLEMENTARY FIGURE 6 MICRONUTRIENT, ADJUSTED EDGE DIFFERENCE TEST

Résumé :

Contexte : La dépression et l'anxiété périnatales sont associées à des résultats négatifs pour l'enfant et la mère. L'étiologie de ces troubles de l'humeur est une relation complexe entre des problèmes de santé mentale antérieurs, des changements physiologiques et peut-être des déséquilibres nutritionnels. Cette étude vise à explorer les relations entre la nutrition pendant la grossesse et l'état de santé mentale de la mère, en particulier l'apparition de dépression et d'anxiété périnatales, chez les participants de la cohorte française EDEN.

Méthodes : L'étude EDEN (Etude sur les déterminants pré et post natals précoces du Développement psychomoteur et de la santé de l'ENfant) a été mise en place pour évaluer les déterminants nutritionnels, sociaux et environnementaux pré et post natals du développement et de la santé du nourrisson et de l'enfant. Nous avons utilisé les données d'un échantillon sélectionné sur les résultats de la santé maternelle (n=1438) pour effectuer une analyse de réseau des marqueurs nutritionnels recueillis à partir de questionnaires sur la fréquence des repas et d'enquêtes sur la santé mentale pendant la période péripartum. Quatre réseaux ont été construits et analysés pour la structure, la centralité des nœuds et la prévisibilité.

Résultats : Nous avons trouvé une association entre le régime occidental et l'enquête EPDS dans les réseaux de macronutriments et de micronutriments. L'éducation est apparue comme une covariable centrale associée à la consommation du régime occidental. Les nœuds les plus expliqués par d'autres nœuds dans les modèles de micronutriments et de macronutriments étaient le régime sain ($R2=0,855$, micro) et le régime occidental ($R2=0,617$) après ajustement. L'EPDS et le régime occidental présentaient également l'interrelation la plus élevée dans tous les modèles.

Conclusion : Nous avons déterminé qu'un régime occidental est associé à une augmentation des scores de dépression postnatale et que cette relation peut varier selon le niveau d'éducation. Le régime occidental ne répond pas aux besoins nutritionnels de la mère pendant la grossesse au niveau des macro et micronutriments. Il est bien connu qu'une bonne alimentation est bénéfique à la mère et au fœtus de différentes manières, même si son impact sur la santé mentale de la mère doit encore faire l'objet d'études plus approfondies pour comprendre les associations précises avec certains schémas alimentaires et leurs composants nutritionnels. Étant donné que l'état nutritionnel est une intervention modifiable, abordable, mesurable et réalisable, il pourrait être une composante future de la prévention de la dépression et de l'anxiété périnatales.