



UNIVERSIDADE FEDERAL DO RIO DE JANEIRO
CENTRO DE CIÊNCIAS DA SAÚDE
INSTITUTO DE NUTRIÇÃO JOSUÉ DE CASTRO
PROGRAMA DE PÓS-GRADUAÇÃO EM NUTRIÇÃO
DOUTORADO EM CIÊNCIAS NUTRICIONAIS



**PADRÕES ALIMENTARES E SAÚDE MENTAL MATERNA E
DESENVOLVIMENTO NEUROPSICOLÓGICO INFANTIL:
RESULTADOS DE ESTUDOS DE COORTE DO RIO DE JANEIRO
E BRISTOL/REINO UNIDO**

Ana Amélia Freitas Vilela

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Ana Amélia Freitas Vilela

Tese apresentada à banca examinadora e ao Programa de Pós-Graduação em Nutrição, do Instituto de Nutrição Josué de Castro da Universidade Federal do Rio de Janeiro, como parte dos requisitos necessários à obtenção do título de **Doutor em Ciências Nutricionais**.

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**„O que vale na vida não é o ponto de partida e sim a caminhada.
Caminhando e semeando, no fim terás o que colher. ö**

(Cora Coralina)

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LISTA DE ABREVIATURAS

95% CI	<i>95% Confidence Intervals</i>
ACP	Análise de Componentes Principais
AIC	<i>Akaike Information Criterion</i>
ALSPAC	<i>Avon Longitudinal Study of Parents and Children</i>
ANOVA	Análise de variância
BIC	<i>Bayesian Information Criterion</i>
BMI	<i>Body Mass Index</i>
CAPES	Coordenação de Aperfeiçoamento de Pessoal de Nível Superior
CEP	Comitê de Ética em Pesquisa
CES-D	Escala de Depressão do Centro de Estudos Epidemiológicos
CID-10	Classificação Estatística Internacional de Doenças e Problemas Relacionados à Saúde
CMSHB	Centro Municipal de Saúde Heitor Beltrão
CNPq	Conselho Nacional de Desenvolvimento Científico e Tecnológico
CSPro	<i>Census and Survey Processing System</i>
DCNT	Doenças Crônicas Não Transmissíveis
DHA	<i>Docosahexaenoic acid</i>
DHA/UK	<i>District Health Authority - United Kingdom</i>
DHEG	Doença Hipertensiva Específica da Gravidez
DM	Dieta do Mediterrâneo
DMG	Diabetes Mellitus Gestacional
DPP	Depressão Pós-Parto
DQI	<i>Dietary Quality Index</i>
DUM	Data da Última Menstruação
ECCAGE	Estudo do consumo e do comportamento alimentar na gestação
EDM	Episódio Depressivo Maior
EPA	<i>Eicosapentaenoic acid</i>
EPDS	<i>Edinburg Postnatal Depressive Scale</i>
EPDS	Escala de Depressão Pós-Parto de Edimburgo
FAPERJ	Fundação de Amparo à Pesquisa do Estado do Rio de Janeiro
FFQ	<i>Food Frequency Questionnaire</i>

FMI	<i>Fraction of Missing Information</i>
GIG	Grandes para a Idade Gestacional
HANES	<i>Health and Nutrition Examination Survey</i>
HDI	<i>Healthy Diet Index</i>
HEI	<i>Health Eating Index</i>
IAS	Índice de Alimentação Saudável
IC 95%	Intervalo de Confiança de 95%
IDATE	Inventário de Ansiedade Traço-Estado
IMC	Índice de Massa Corporal
INA	Inquérito Nacional de Alimentação
INJC	Instituto de Nutrição Josué de Castro
IOM	<i>Institute of Medicine</i>
IPUB - UFRJ	Instituto de Psiquiatria da Universidade Federal do Rio de Janeiro
IQ	<i>Intelligence Quotient</i>
IQD	Índice de Qualidade da Dieta
KMO	<i>Kaiser-Meyer-Olkin</i>
MAR	<i>Missing At Random</i>
MDS	<i>Mediterranean Diet Score</i>
MICE	<i>Multiple Imputation by Chained Equations</i>
MINI	<i>Mini International Neuropsychology Interview</i>
LC n-3PUFAs	<i>Long chain omega-3 polyunsaturated fatty acids</i>
LME	<i>Longitudinal Mixed Effects</i>
OMS	Organização Mundial da Saúde
PCA	<i>Principal Component Analysis</i>
PDSE	Programa de Doutorado Sanduíche no Exterior
PIG	Pequeno para a Idade Gestacional
PN	Pré-Natal
POF	Pesquisa de Orçamento Familiar
PPD	<i>Postpartum Depression</i>
PRIME-MD	<i>The Primary Care Evaluation of Mental Disorders</i>
PUFA	<i>Polyunsaturated Fatty Acids</i>
QFA	Questionário de Frequência Alimentar
QI	Coeficiente (quociente) de Inteligência

QIE	Quocientes de Inteligência Execução
QIG	Quocientes de Inteligência Global
QIV	Quocientes de Inteligência Verbal
RRR	<i>Reduced Rank Regression</i>
RU	Reino Unido
SD	<i>Standard Deviations</i>
SE	<i>Standard Error</i>
SMS	Secretaria Municipal de Saúde
STAI	<i>State-Trait Anxiety Inventory</i>
STATA	<i>Stata Data Analysis and Statistical Software</i>
TACO	Tabela Brasileira de Composição de Alimentos
TCLE	Termo de Consentimento Livre e Esclarecido
UERJ	Universidade do Estado do Rio de Janeiro
UFRJ	Universidade Federal do Rio de Janeiro
UK	<i>United Kingdom</i>
USDA	<i>United States Department of Agriculture</i>
USG	Ultrassonografia
WISC	<i>Wechsler Intelligence Scale for Children</i>

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APRESENTAÇÃO

A presente tese de doutorado apresenta resultados de dois estudos de coortes, que foram conduzidos e avaliados de forma independente. O primeiro é uma coorte de gestantes atendidas em uma unidade de saúde no Rio de Janeiro e o segundo refere-se a uma coorte de nascimentos do antigo condado de Avon em Bristol/Reino Unido.

Os resultados obtidos da coorte brasileira foram um recorte do estudo intitulado *Saúde mental e estado nutricional na gestação e no pós-parto: estudo prospectivo com ensaio clínico randomizado aninhado*, que foi realizado no Centro Municipal de Saúde Heitor Beltrão (CMSHB), da Secretaria Municipal de Saúde (SMS) do Rio de Janeiro. O recrutamento das mulheres ocorreu entre novembro de 2009 e outubro de 2011, e a coleta de dados terminou em junho de 2012.

Este estudo foi realizado por pesquisadores do Observatório de Epidemiologia Nutricional do Instituto de Nutrição Josué de Castro (INJC) e contou com a parceria do Instituto de Psiquiatria da Universidade Federal do Rio de Janeiro (IPUB - UFRJ). A pesquisa foi financiada pela Fundação de Amparo à Pesquisa do Estado do Rio de Janeiro (FAPERJ) e do Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq).

Os resultados dos estudos da coorte britânica foram obtidos durante o Programa de Doutorado Sanduíche no Exterior (PDSE), financiado pela Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES). O PDSE foi realizado na *University of Bristol*, Bristol/Reino Unido, entre abril e agosto de 2015 e Pauline M. Emmett foi a coorientadora no exterior.

Os dados utilizados na coorte britânica foram provenientes do estudo longitudinal de pais e filhos de Avon - *The Avon Longitudinal Study of Parents and Children* (ALSPAC), uma coorte de nascimentos que teve o objetivo de investigar os determinantes de saúde e doença de mulheres durante a gestação e seus filhos ao longo dos anos. As gestantes que residiam no condado de Avon e tinham data prevista do parto entre abril de 1991 e dezembro 1992 foram elegíveis para participar do estudo. Até os dias atuais são coletados dados das mães, filhos e pais.

Este documento está estruturado nas seguintes seções: (i) resumo/*abstract*, (ii) introdução, (iii) revisão de literatura, (iv) justificativa e hipóteses, (v) objetivos, (vi) métodos, (vii) resultados, (viii) conclusões, (ix) considerações finais, (x) referências bibliográficas e (xi) anexos. Os anexos online se referem aos questionários utilizados das duas coortes avaliadas nessa tese de doutorado, porém devido ao elevado número de páginas (249 p.)

optamos por não incluir todos os esses arquivos impressos, mas podemos disponibilizá-los via e-mail (anaameliafv@gmail.com).

A seção de resultados/discussão foi composta por quatro manuscritos científicos. Os dois artigos referentes à coorte brasileira já foram publicados e as versões finais aprovadas pelas revistas constam no corpo da tese. Devido aos direitos autorais das revistas, apenas a primeira página das versões editadas foi incluída em anexo. O primeiro artigo foi publicado na revista *The Journal of Nutrition* e intitulou-se ‘*Prepregnancy healthy dietary pattern is inversely associated with depressive symptoms among pregnant Brazilian women*’. O segundo foi publicado na revista *Journal of the Academy of Nutrition and Dietetics* e intitulou-se ‘*Association of prepregnancy dietary patterns and anxiety symptoms from midpregnancy to early postpartum in a prospective cohort of Brazilian women*’.

O terceiro manuscrito e quarto artigos foram baseados nos dados do ALSPAC e foram submetidos para publicação. Os mesmos foram intitulados ‘*Dietary patterns by clusters analysis in pregnant women: relationship with nutrient intakes and dietary patterns in 7 years old offspring*’, e ‘*Maternal dietary patterns during pregnancy and intelligence quotient in the offspring at 8 years of age: findings from the ALSPAC cohort*’, respectivamente.

Na seção conclusões foram apresentados os principais resultados baseados nos quatro manuscritos realizados baseados nas duas coortes. As referências da tese obedecem ao estilo Vancouver, assim como os artigos que ainda não foram submetidos para publicação. As referências dos artigos publicados obedecem ao formato exigido pela revista.

RESUMO

Introdução: A adesão a padrões alimentares pode influenciar a saúde mental materna na gestação e pós-parto e o desenvolvimento infantil. **Objetivo:** 1. Identificar padrões alimentares no período pré-gestacional e associá-los com sintomas de depressão durante a gestação. 2. Verificar a associação entre os padrões alimentares e sintomas de ansiedade durante a gestação e pós-parto. 3. Obter padrões alimentares no período gestacional, avaliar o consumo de nutrientes dos mesmos e comparar os padrões alimentares das mães e seus filhos. 4. Associar os padrões alimentares maternos e o coeficiente de inteligência (QI) de seus filhos aos 8 anos. **Métodos:** Para consecução dos objetivos 1 e 2 utilizou-se dados uma coorte prospectiva de gestantes avaliadas nos seguintes períodos: 5-13, 20-26 e 30-36 semanas gestacionais e 30-45 dias pós-parto. O consumo alimentar foi obtido por meio de um questionário de frequência alimentar (QFA), referente aos 6 meses anteriores a gestação. Os padrões alimentares foram obtidos por análise de componente principal. Os sintomas de depressão foram mensurados pela Escala de Depressão Pós-Parto de Edimburgo nos três trimestres gestacionais, e os sintomas de ansiedade foram avaliados pelo Inventário de Ansiedade Traço-Estado, no segundo e terceiro trimestres gestacionais e no pós-parto. Modelos de regressão de efeitos mistos foram empregados e foram ajustados por fatores obstétricos, socioeconômicos, demográfico e consumo energético total. Para os objetivos 3 e 4 foi utilizado a base de dados do *Avon Longitudinal Study of Parents And Children* (ALSPAC), uma coorte de nascimentos realizada no antigo condado de Avon/Reino Unido. O consumo alimentar foi avaliado por um QFA na 32^a semana gestacional. Foi utilizada a análise de cluster para obter os padrões alimentares. A ingestão de nutrientes absoluta e ajustada por energia foram descritas para cada padrão alimentar obtido. A tabulação cruzada e a regressão multinomial foram utilizadas para comparar e verificar a associação entre os padrões alimentares maternos e de seus filhos. O QI foi avaliado aos 8 anos pela *Wechsler Intelligence Scale for Children-III*. Foram elaborados modelos de imputação para os dados faltantes e posteriormente modelos de regressão linear simples e ajustados. **Resultados:** 1. Três padrões alimentares pré-gestacionais foram identificados em 248 mulheres: ‘comum-brasileiro’, ‘saudável’ e ‘processado’. O padrão ‘saudável’ associou-se negativamente com sintomas de depressão durante a gestação. 2. Foram avaliadas 196 mulheres nesse estudo. Os padrões ‘comum-brasileiro’ e o ‘saudável’ associaram-se negativamente com os sintomas de ansiedade durante a gestação e pós-parto. 3. Três padrões alimentares foram obtidos de 12.195 gestantes avaliadas pelo ALSPAC, os quais foram intitulados ‘frutas e vegetais’,

‘carnes e batatas’ e ‘pão branco e café’. O padrão ‘frutas e vegetais’ apresentou o melhor perfil nutricional após o ajuste por energia. Os filhos na infância aderiram padrões alimentares similares ao que a mãe aderiu durante a gestação, principalmente os padrões alimentares compostos por alimentos saudáveis. **4.** As mulheres que aderiram aos padrões ‘carnes e batatas’ e ‘pão branco e café’ tiveram maior risco de ter filhos com menor QI aos 8 anos quando comparadas as mulheres que aderiram o padrão ‘frutas e vegetais’ durante a gestação. **Conclusões:** A maior aderência aos padrões alimentares caracterizados por alimentos saudáveis, como ‘comum-brasileiro’, ‘saudável’ e ‘frutas e vegetais’ reduzem o risco de sintomas de depressão e ansiedade durante a gestação e pós-parto e baixos escores de QI na infância.

Palavras chaves: Depressão; Ansiedade; Coeficiente de inteligência, Padrão alimentar; Gestantes; Crianças; Estudos de coorte.

Abstract

Background: The adherence to dietary patterns may influence the maternal mental health during pregnancy and postpartum, and the infant development. **Objective:** **1.** To identify dietary patterns in pre-pregnancy and to associate them with the depressive symptoms during pregnancy. **2.** To verify the association between dietary patterns and the anxiety symptoms from mid-pregnancy to postpartum. **3.** To obtain dietary patterns during pregnancy, to examine the nutrients intake of them, and to compare the dietary patterns of mothers and their children. **4.** To associate the maternal dietary patterns and intelligence quotient (IQ) children at childhood. **Methods:** To achieve the objectives **1 and 2** we used data from a prospective cohort of pregnant assessed at 5-13, 20-26, and 30-36 gestational weeks, and 30-45 days postpartum. The dietary intake was obtained using a food frequency questionnaire (FFQ), it had the six months before pregnancy as the time frame. The dietary patterns were obtained by principal component analysis. The depressive symptoms were measured by Edinburg Postnatal Depressive Scale during three gestational trimesters, and the anxiety symptoms were assessed by State-Trait Anxiety Inventory, and it was applied to mid-pregnancy to early postpartum. Longitudinal mixed effects models were employed, and were adjusted for obstetric, socioeconomic, demographic factors, and energy intake. The objectives **3 and 4** were achieved using the dataset of Avon Longitudinal Study of Parents And Children (ALSPAC), a longitudinal birth cohort conducted in the former county of Avon/UK. The dietary intake was assessed by a FFQ at 32 weeks' gestation. The cluster analysis was applied to obtain the dietary patterns. The absolute and energy-adjusted nutrient intakes were described according to each clusters obtained. The cross-tabulating and multinomial regression were used to compare and to verify the association between the maternal and children dietary patterns. The IQ was assessed at 8 years of age by *Wechsler Intelligence Scale for Children-III*. Models of imputation were performed to the missing data. Unadjusted and adjusted linear regression models were applied. **Results:** **1.** Three pre-pregnancy dietary patterns were identified from 248 women: '*common-Brazilian*', '*healthy*', and '*processed*'. The '*healthy*' dietary pattern was negatively associated with depression symptoms during pregnancy. **2.** A total of 196 women were evaluated in this study. The '*common-Brazilian*' and the '*healthy*' patterns were negatively associated with anxiety symptoms during pregnancy and postpartum. **3.** Three clusters dietary patterns were obtained of 12,195 pregnant women, which were labeled '*fruit and vegetable*', '*meat and potatoes*' and '*white bread and coffee*'. The '*fruit and vegetable*' cluster showed the better profile of almost all

nutrients after energy adjustment. The children at childhood adhered similar dietary patterns that the mothers adhered during pregnancy, it was verified mainly between the dietary patterns composed by healthy foods. **4.** The pregnant women who adhered the '*meat and potatoes*' and '*white bread and coffee*' clusters had children with lower IQ at 8 years of age, when compared with mothers who adhered the '*fruit and vegetables*' clusters. **Conclusions:** The higher adherence to dietary patterns characterized by healthy foods, as '*common-Brazilian*', '*healthy*' and '*fruit and vegetables*' patterns reduce the risk of depressive and anxiety symptoms during pregnancy and postpartum, and lower IQ scores at childhood.

Keywords: Depression; Anxiety; Intelligence Quotient; Dietary patterns; Pregnancy; Children; Cohort study.

1. INTRODUÇÃO

O período gestacional é marcado por mudanças psíquicas, comportamentais e metabólicas, além do aumento nas demandas nutricionais. Estes fatores podem influenciar no curso da gestação e desenvolvimento fetal, e também em desfechos maternos e infantis a longo prazo. Dessa forma, o acompanhamento pré-natal das gestantes pode prevenir ou amenizar alguns fatores de risco que a mulher está exposta durante a gestação (Marcus, 2009; Fazio et al., 2011; Rodrigues et al., 2011; Koutra et al., 2013).

O estado nutricional materno antes e durante a gravidez apresenta elevado impacto sobre o crescimento e desenvolvimento fetal e do recém-nascido. Mulheres que engravidam com baixo peso pré-gestacional apresentam maior risco de ter parto prematuro, filhos pequenos para a idade gestacional (PIG) e baixo peso, enquanto mulheres com sobrepeso ou obesidade apresentam maior risco para doença hipertensiva específica da gravidez (DHEG), pré-eclâmpsia, diabetes mellitus gestacional (DMG), parto prematuro, filhos grandes para a idade gestacional (GIG) e macrossomia (Dean et al., 2014). O ganho de peso gestacional influencia no pós-parto e aumenta os fatores de risco metabólicos com a adiposidade central, dislipidemia, obesidade, diabetes tipo 2 e síndrome metabólica, além de maior adiposidade infantil no nascimento (Gilmore et al., 2015).

O consumo alimentar é considerado um fator importante para o melhor desenvolvimento gestacional. A dieta inadequada durante a gestação está associada com desfechos indesejáveis como a obesidade, doenças cardiovasculares, diabetes mellitus e diversos tipos de câncer (Sullivan et al., 2011; Garmendia et al., 2014). Porém, não é apenas durante a gestação que a dieta tem um papel importante. A formação fetal inicia nas primeiras semanas de gestação, assim o consumo alimentar pré-gestacional é essencial para o desenvolvimento fetal, uma vez que a disponibilidade e fornecimento de nutrientes para o feto em desenvolvimento depende do estado nutricional materno, consequentemente depende de suas reservas e necessidades nutricionais e a ingestão alimentar pré-gestacional. Estudos avaliaram consumo alimentar pré-gestacional por meio de nutrientes, alimentos e padrões alimentares, está relacionado a desfechos da saúde materna e infantil (Ramakrishnan et al., 2012; Bao et al., 2014; Nohr et al., 2014; Schoenaker et al., 2015).

O aumento das necessidades nutricionais durante a gestação e a preocupação das mulheres em terem uma gestação saudável, contribuem para mudanças nos hábitos alimentares nesse período. Assim, os hábitos alimentares durante o período gestacional podem ser influenciados por diversos fatores, ressaltando aqueles de natureza socioeconômica e

demográfica. Ademais, o consumo elevado de alimentos não saudáveis pode aumentar o risco de transtornos da saúde mental durante a gestação e no pós-parto (Northstone et al., 2008b; Rocha & Kac, 2012; Miyake et al., 2013; Castro et al., 2014).

Segundo Greenwood & Craig (1987) há ao menos três importantes mecanismos relacionados a dieta que podem afetar o desenvolvimento neuropsicológico: (i) a ingestão de alimentos aumenta a disponibilidade de precursores necessários para a síntese de neurotransmissores; (ii) as vitaminas e minerais, que são obtidas pelos alimentos, servem como cofatores essenciais para as enzimas que sintetizam os neurotransmissores; e (iii) as dietas ricas em gordura alteram a composição da membrana celular nervosa e da bainha de mielina, e que, por sua vez, influencia na função neural.

Estudos recentes verificaram associação entre consumo alimentar durante a gestação e transtornos mentais, como a depressão e a ansiedade durante a gestação e no pós-parto (Chatzi et al., 2011; Okubo et al., 2011; Vaz et al., 2013, Baskin et al., 2015). Além desses desfechos, alguns estudos observaram que a qualidade da dieta materna durante a gestação pode influenciar no desenvolvimento neurocognitivo infantil, destacando o coeficiente de inteligência infantil (Hibbeln et al., 2007; Julvez et al., 2009; Zhang et al., 2009; Chatzi et al., 2012; Anjos et al., 2013; Bath et al., 2013; Bernard et al., 2013).

Considerando que durante a gestação as mulheres estão mais vulneráveis a desenvolver transtornos mentais que podem afetar a saúde e o bem-estar materno e infantil, o que também inclui o desenvolvimento infantil, faz-se necessário explorar os fatores de exposição antes e durante a gestação, como a dieta, devido à escassez de estudos que exploraram esse tema.

2 REVISÃO DE LITERATURA

2.1 SAÚDE MENTAL DURANTE A GESTAÇÃO

Os transtornos mentais são considerados atualmente um problema de saúde pública e, segundo a Organização Mundial de Saúde (OMS), aproximadamente 450 milhões de pessoas sofrem de algum transtorno mental e uma em quatro pessoas irá desenvolver um ou mais transtornos comportamentais ou mentais durante a vida (WHO, 2002; WHO, 2004). Os transtornos do humor ou afeto estão entre os mais prevalentes transtornos da saúde mental, e são aproximadamente duas vezes mais comuns nas mulheres do que nos homens (WHO, 2009). A depressão é o transtorno de humor mais comum e estima-se que aproximadamente 350 milhões de pessoas no mundo sofrem de depressão, e foi classificada como a quarta principal causa de doenças da saúde mental (WHO, 2002; WHO, 2004; Ministério da Saúde, 2008; Kessler & Bromet, 2013; WHO, 2015).

Durante a gestação, a mulher está vulnerável a desenvolver alguns transtornos mentais, os quais podem ocorrer tanto no período gestacional, como no pós-parto. Os transtornos mentais mais estudados nestes períodos são a depressão, a ansiedade, o risco de suicídio, o episódio depressivo maior (EDM), o transtorno bipolar e a agorafobia (Marcus et al., 2009; Figueiredo & Conde, 2011; Giardinelli et al., 2012; Farias et al., 2013; Koutra et al., 2013; Siegel & Brandon, 2014; Vaz et al., 2014).

A depressão durante a gestação e no pós-parto é um importante problema de saúde pública que afeta mulheres em todo o mundo, sendo mais prevalente em países em desenvolvimento. Os sintomas depressivos nesse período podem prejudicar a relação entre mãe e filho, o que compromete os cuidados nutricionais com as crianças, assim como o desenvolvimento físico e mental (Brummelte & Galea, 2015; Rwakarema et al., 2015). A ansiedade está associada à depressão, consequentemente é comum a gestante apresentar desfechos indesejáveis semelhantes aos da depressão (Heron et al., 2004; Micali et al., 2011).

Considerando as elevadas prevalências de depressão e ansiedade durante a gestação e pós-parto, é importante explorar os fatores que estão associados à depressão e ansiedade durante esse período, e assim tentar relacionar as causas desses sintomas e reduzir as prevalências de depressão e ansiedade em gestantes e puérperas, e consequentemente melhorar a saúde materna e infantil (Heron et al., 2004; Figueiredo & Conde, 2011; Farias et al., 2013; Micali et al., 2011; Rwakarema et al., 2015).

2.1.1 DEPRESSÃO E ANSIEDADE

A depressão é um transtorno mental que pode causar mudanças de humor ou irritação, redução da energia e diminuição da atividade. É comum ocorrerem mudanças de comportamento em indivíduos depressivos tais como ansiedade, desânimo, cansaço, dificuldade de concentração, pensamentos negativos, perda de interesse, incapacidade parcial ou total de sentir alegria ou prazer pelas coisas que fazia habitualmente, perda de interesse, dificuldade de planejar o futuro, problemas do sono, diminuição do apetite, perda da libido, além da diminuição da autoestima, da autoconfiança e ideias frequentes de culpa ou de indignidade, mesmo nas formas leves. Em casos mais graves e frequentes, pode ocorrer lentidão física e mental, ou ainda, intensa agitação psicomotora, alucinações e delírios. Esses três últimos sintomas são comuns em caso de depressão psicótica (Cox et al., 1987; Nemeroff & Kelsey 1998; WHO, 2002; Santos et al., 2007; Ministério da Saúde, 2008; Marcus, 2009; Schmied et al., 2013).

Segundo a Classificação Estatística Internacional de Doenças e Problemas Relacionados à Saúde (CID-10), os episódios depressivos podem ser classificados em três graus: leve, moderado ou grave. No episódio depressivo leve (F32.0), o indivíduo apresenta ao menos dois ou três sintomas citados anteriormente, porém ele pode desempenhar a maioria das atividades de rotina. O episódio depressivo moderado (F32.1) é caracterizado pela presença de quatro ou mais dos sintomas apresentados, porém os mesmos afetam as rotinas diárias. O episódio depressivo grave é dividido em dois grupos: sem (F32.2) e com (F32.3) sintomas psicóticos. No episódio depressivo grave sem sintomas psicóticos é comum apresentar diversos sintomas da depressão, principalmente aqueles relacionados à autoestima e ideias desviadas ou culpa, e ainda pode ocorrer ideias e atos suicidas. O episódio depressivo grave com sintomas psicóticos é equivalente ao sem sintomas psicóticos, porém é acompanhado de alucinações, delírios, lentidão psicomotora ou estupor de uma gravidade que impossibilita qualquer atividade social. Nesse tipo de depressão existe o risco de suicídio, de desidratação ou de desnutrição (Ministério da Saúde, 2008).

A ansiedade está relacionada com as emoções do ser humano, que está presente na maioria dos eventos ou atividades, e em quase todo tempo. A inquietação, fadiga, dificuldade de concentração, irritabilidade, tensão muscular e distúrbios no sono são sintomas comuns em indivíduos com ansiedade (DSM, 1994). A ansiedade não é desencadeada apenas durante exposição a uma determinada situação, ela também pode vir acompanhada de sintomas depressivos ou obsessivos e de manifestações que traduzem uma ansiedade fóbica, desde que sejam manifestações secundárias ou pouco graves (Ministério da Saúde, 2008).

A ansiedade pode ser dividida em ansiedade-estado e traço. A ansiedade-estado é uma condição emocional transitória, e podem ser verificadas mudanças dos escores no tempo avaliado de acordo com a intensidade das situações vividas. A ansiedade-traço é uma condição mais estável e ocorre em situações percebidas como não ameaçadoras, pois quando o indivíduo se sente ameaçado, aumenta a ansiedade-estado (Spielberger et al., 1970). O aumento da ansiedade durante a gestação está relacionado com a preocupação com a saúde e o bem estar do feto e da própria gestante. A apreensão com o parto e suas possíveis consequências e a preocupação em cuidar da criança após o nascimento podem provocar o aumento dos sintomas de ansiedade durante esse período (Schetter & Tanner, 2012).

2.1.2 FATORES DE RISCO DE TRANSTORNOS MENTAIS NA GESTAÇÃO E NO PÓS-PARTO

A gestação pode ser um momento de alegria, quando a gestação é planejada, porém em gestações indesejadas alguns fatores podem contribuir para o desencadeamento de transtornos da saúde mental na gestante. Há relatos na literatura de que alguns fatores podem aumentar o risco de transtornos mentais durante a gestação e no pós-parto. Entre esses, os mais relevantes são história pregressa de depressão, gravidez indesejada, baixa renda, dependência financeira, baixa escolaridade, multiparidade, desemprego, estado marital, falta de apoio social, problemas no relacionamento, alcoolismo, hábito de fumar e/ou consumo de drogas, história de violência e adesão a uma alimentação inadequada (Pereira et al., 2010; Chatzi et al., 2011; Rodrigues & Schiavo, 2011; Almeida et al., 2012; Woolhouse et al., 2012; Vaz et al., 2013; Vaz et al., 2014).

2.1.3 ESTUDOS SOBRE SAÚDE MENTAL NA GESTAÇÃO E PÓS-PARTO

No estudo de Almeida et al. (2012), realizado em Porto Alegre e Bento Gonçalves-RS com gestantes entre 16 e 36 semanas de gestação foi utilizado o instrumento Avaliação de Transtornos Mentais para Atenção Primária (*The Primary Care Evaluation of Mental Disorders: PRIME-MD*) para avaliar a presença de sintomas psiquiátricos. Os autores verificaram que 21,6% dessas mulheres apresentaram sintomas de depressão e 19,8% sintomas de ansiedade.

Giardinelli et al. (2012) avaliaram mulheres italianas durante a gestação, entre 28 e 32 semanas e 3 meses após o parto, com o objetivo de avaliar a prevalência de depressão e ansiedade nessas mulheres. A Escala de Depressão Pós-Parto de Edimburgo (EPDS) e Inventário de Ansiedade Traço-Estado (IDATE) foram os instrumentos utilizados. O ponto de corte utilizado para avaliar os sintomas de depressão foi ≥ 10 pontos. Dessa forma, os autores

verificaram a prevalência de depressão de 21,9% e 13,2% durante a gestação e no pós-parto, respectivamente. A ansiedade foi avaliada somente durante a gestação e foi utilizado o ponto de corte ≥ 40 pontos. Os autores observaram uma prevalência de 20,5% para ansiedade-estado e 25,3% para ansiedade-traço nessas gestantes.

Ibanez et al. (2012) avaliaram mulheres francesas que participaram do estudo “*EDEN mother-child*” entre a 24^a e 28^a semana gestacional e observaram que a prevalência de ansiedade nessas gestantes foi de 7,9%. Nesse último estudo, o instrumento utilizado para avaliar os sintomas de ansiedade foi o IDATE. O ponto de corte ≥ 37 foi empregado e correspondeu ao percentil 80 do estudo. Essa estratégia foi estabelecida, uma vez que não há consenso na literatura sobre o ponto de corte ideal.

Os sintomas de depressão e ansiedade ao longo da gestação e no pós-parto tendem a reduzir, porém entre o último trimestre gestacional e o parto é comum ocorrer um aumento dos sintomas de ansiedade e após o parto ocorrer uma queda. Estudos que avaliaram mulheres desde o início da gestação até o pós-parto observaram a redução de sintomas de depressão ao longo do tempo e o aumento da ansiedade no último trimestre gestacional seguindo de uma acentuada queda no pós-parto (Heron et al., 2004; Figueiredo & Conde, 2011; Micali et al., 2011; Liou et al., 2014).

Os estudos longitudinais são mais adequados quando o objetivo é verificar a evolução dos sintomas de saúde mental a longo prazo. No estudo realizado em Porto, Portugal, as mulheres foram acompanhadas três vezes durante a gestação (T1 = 8 à 14 semanas, T2 = 20 à 24 semanas, T3 = 30 à 34 semanas) e duas no pós-parto (T4 = 1 à 3 dias, T5 = 3 meses). Os autores utilizaram a EPDS ≥ 10 como ponto de corte para suspeição de depressão. A escala utilizada para avaliar os sintomas de ansiedade foi o IDATE e o ponto de corte foi ≥ 45 . Foi observado que a prevalência de depressão nos cinco pontos avaliados foi de 20,0%, 19,6%, 17,4%, 17,6% e 11,1%, respectivamente. Considerando os sintomas de ansiedade nos cinco pontos avaliados, as prevalências foram, respectivamente, 13,1%, 12,2%, 18,2%, 18,6% e 4,7% (Figueiredo & Conde, 2011).

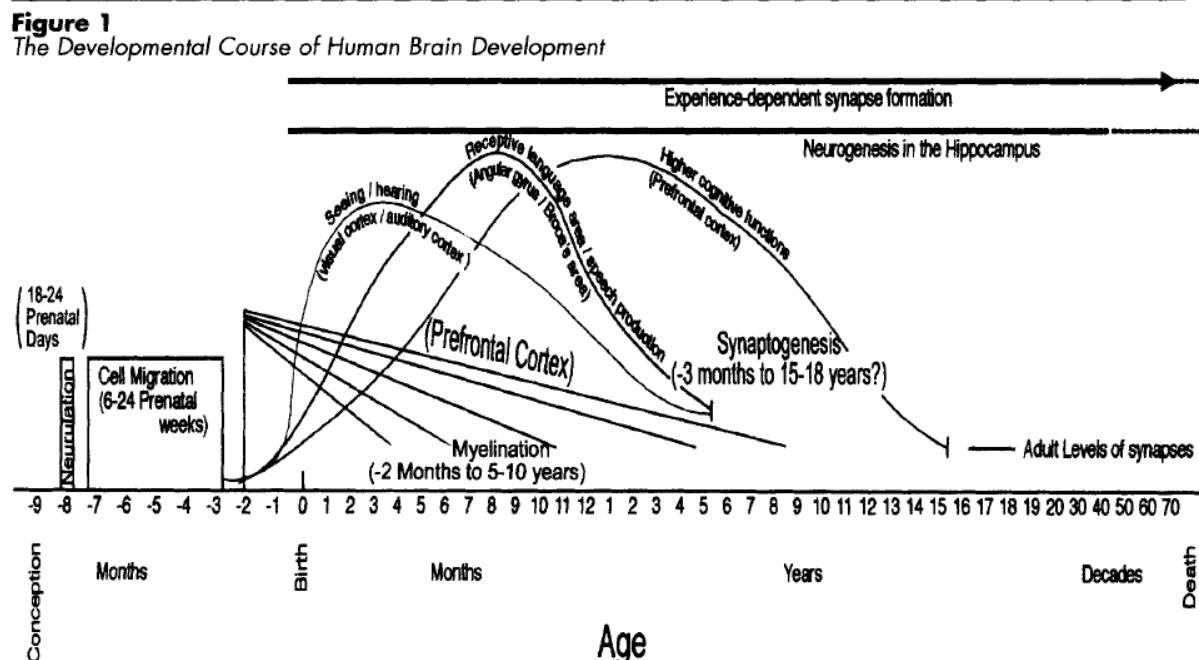
Os sintomas de depressão também podem ser avaliados de forma contínua, como apresentado no estudo de Liou et al. (2014). Os autores utilizaram a Escala de Depressão do Centro de Estudos Epidemiológicos (CES-D) e avaliaram quatro pontos durante a gestação e um no pós-parto (T1 = 25 à 29 semanas gestacionais, T2 = 30 à 34 semanas gestacionais, T3 = 34 semanas até o parto e T4 = 4 à 6 semanas pós-parto) e verificaram as seguintes médias (desvio padrão) de escore de sintomas de depressão: T1= 11,16 (8,32), T2= 11,53 (8,04), T3= 11,16 (7,89) e T4= 10,74 (11,01).

2.2 DESENVOLVIMENTO NEUROPSICOLÓGICO INFANTIL

O desenvolvimento do sistema nervoso central da criança inicia na trigésima semana de gestação e vai até os dois primeiros anos de vida, período no qual ocorre a maior maturação cerebral. Consequentemente, se não houver um desenvolvimento adequado, o risco de dano nas funções neurológicas permanentes é elevado (Brasil, 2002; Georgieff, 2007; Greenberg et al., 2008). O desenvolvimento neuropsicológico infantil pode ser afetado pelas condições maternas durante a gestação e após o parto, tais como saúde mental, estado nutricional, incluindo a dieta, tabagismo, fatores socioeconômicos e demográficos, relações ou estímulos realizados com a criança por outros indivíduos que convivem com ela desde os primeiros meses de vida, entre outros fatores (Brasil, 2002; Innis, 2008; Leung et al., 2011; Wehby et al., 2011; Hinkle et al., 2012; Koutra et al., 2012; Koutra et al., 2013).

A detecção precoce de atrasos no desenvolvimento neuropsicológico infantil contribui para prevenir potenciais riscos de atrasos e deficiências emocionais, de desenvolvimento e de comportamento, uma vez que atualmente alguns estudos verificaram que os principais comprometimentos no desenvolvimento neuropsicológicos das crianças são: déficit sensorial (audição evisão), atraso no desenvolvimento motor (fino e grosso), déficit cognitivo, como a dificuldade de aprendizagem, as desordens de linguagem e comunicação, entre outras. Dessa forma, as escalas/inquéritos/questionários são os instrumentos mais adequados para avaliar o desenvolvimento infantil, pois os mesmos são validados para uma população específica, segundo faixas etárias e desfecho de interesse (Briggs-Gowan & Carter, 2008; Dunstan, et al., 2008; Bakker et al., 2009; Guedes et al., 2011; Guadarrama-Celaya et al., 2012; Bernard et al.; 2013; Wendland et al., 2014).

A **Figura (Figure)** 1 foi retirada do estudo de Thompson & Nelson (2001). Os autores apresentam o desenvolvimento do cérebro humano ao longo do tempo, desde a concepção até velhice. A gestação é um período importante para a formação do cérebro, pois funções neurológicas essenciais começam a se desenvolver durante esse período.



Note. This graph illustrates the importance of prenatal events, such as the formation of the neural tube (neurulation) and cell migration; critical aspects of synapse formation and myelination beyond age three; and the formation of synapses based on experience, as well as neurogenesis in a key region of the hippocampus [the dentate gyrus], throughout much of life.

2.2.1 AVALIAÇÃO DO DESEMPENHO INTELECTUAL - COEFICIENTE DE INTELIGÊNCIA

A avaliação do desempenho intelectual é definida pelo coeficiente de inteligência (quociente de inteligência - QI) e refere-se à capacidade mental geral, como a aprendizagem, habilidades, raciocínio, resolução de problemas, e assim por diante (DSM-IV, 1994). A deficiência intelectual é definida como Transtornos do desenvolvimento psicológico, segundo o CID-10. Esses transtornos são classificados em: Transtornos específicos do desenvolvimento da fala e da linguagem (F80), Transtornos específicos do desenvolvimento das habilidades escolares (F81), Transtorno específico do desenvolvimento motor (F82), Transtornos específicos misto do desenvolvimento (F83), Transtornos globais do desenvolvimento (F84), Outros transtornos do desenvolvimento psicológico (F88) e Transtorno do desenvolvimento psicológico não especificado (F89) (Ministério da Saúde, 2008).

Os transtornos mencionados anteriormente são assim caracterizados: F80: desde os primeiros estágios do desenvolvimento infantil há um comprometimento das modalidades normais de aquisição da linguagem como dificuldades da leitura e da soletração, perturbação nas relações interpessoais, transtornos emocionais e transtornos comportamentais; F81: as modalidades de aprendizado estão alteradas desde as etapas iniciais do desenvolvimento; F82:

grave comprometimento da coordenação motora, a qual pode não estar relacionada a um retardo mental global ou a uma doença neurológica; F83: há sinais de transtorno específico do desenvolvimento da fala e da linguagem, das habilidades escolares, e das funções motoras ao mesmo tempo; F84: indivíduos com transtornos globais apresentam alteração em interações sociais, comunicação, interesses, além de realizarem atividades restritas, serem estereotipados e repetitivos. Nenhum dos sintomas presente em F83 não são predominantes nos transtornos globais; F88: agnosia de desenvolvimento (perda da capacidade de reconhecer ou identificar pessoas ou objetos); F89: transtorno do desenvolvimento sem outra especificação (Ministério da Saúde, 2008).

O desempenho intelectual é obtido por meio de testes de inteligência avaliado exclusivamente pelo psicólogo. *Wechsler Intelligence Scales for Children - WISC*, *Stanford-Binet* e *Kaufman Assessment Battery for Children* são exemplos de instrumentos utilizados para avaliar o QI. Normalmente, escores abaixo de 70 indicam desempenho intelectual abaixo da média (DSM-IV, 1994).

2.2.2 DIETA E DESENVOLVIMENTO NEUROPSICOLÓGICO INFANTIL

A nutrição exerce um papel importante para o melhor crescimento e desenvolvimento infantil. Hábitos alimentares saudáveis e ganho de peso adequado durante a gestação, o aleitamento materno exclusivo até os seis primeiros meses de vida, a alimentação complementar e o desenvolvimento nutricional são alguns dos fatores que influenciam o desenvolvimento neuropsicológico infantil (Georgieff, 2007; Nunes et al., 2010; Borja 2013; Ryan et al., 2013). O consumo de ácidos graxos poliinsaturados (AGPI) durante a gestação, seja por meio de alimentos que são fontes de AGPI ou por suplementação, tem apresentado resultados positivos para o desenvolvimento neuropsicológico fetal e infantil, como o desenvolvimento cognitivo, comportamental e motor, e também o desempenho intelectual (Hibbeln et al., 2007; Dunstan, et al., 2008; Innis, 2008; Oken & Bellinger, 2008; Bernard et al., 2013). O consumo adequado de nutrientes durante a gestação, destacando a ingestão de vitaminas A, D, e E e ácido fólico, também está associado a desfechos similares (Chen et al., 2009; Zhang, et al., 2009; Morales et al., 2012; Valera-Gran, et al., 2014).

Os dois primeiros anos de vida são de extrema importância para o desenvolvimento neuropsicológico. Dessa forma, a dieta que a criança adere na primeira infância influencia no desempenho intelectual. Estudos que verificaram a associação entre padrões alimentares e QI na infância foram realizados com crianças da coorte de nascimentos britânica *Avon Longitudinal Study of Parents and Children* (ALSPAC). Northstone et al. (2012) observaram

uma associação negativa entre as crianças que aderiram a um padrão caracterizado por alimentos processado aos 3 anos ('*processed dietary pattern*') e QI aos 8 anos, e também uma associação positiva entre um padrão saudável ('*health-conscious dietary pattern*') e QI, ambos aos 8 anos. Resultados similares foram encontrados por Smithers et al. (2012). Esses autores verificaram uma associação positiva entre padrões com alimentos saudáveis ('*Breastfeeding*' e '*Contemporary*' dietary patterns) e negativa com alimentos não saudáveis ('*Discretionary*' dietary pattern) obtidos em diferentes momentos, aos 6, 15 e 24 meses, com QI aos 8 anos. Até o momento, não foram realizados estudos com padrão alimentar materno e QI dos filhos na infância.

2.3 CONSUMO ALIMENTAR ANTES E DURANTE A GESTAÇÃO

O equilíbrio da dieta, em quantidade e qualidade, é importante em qualquer fase do ciclo vital, uma vez que os nutrientes e energia consumidos são essenciais para o melhor funcionamento e manutenção do organismo. Em estudo com gestantes é comum avaliar a dieta durante a gestação, devido ao aumento da demanda nutricional nesse período. No entanto o período pré-gestacional é tão importante quanto o gestacional, uma vez que os hábitos alimentares antes da concepção estão associados a diferentes desfechos durante a gestação (Cucó et al., 2006; Ramakrishnan et al., 2012; Grieger et al., 2014; Schoenaker et al., 2015).

Ramakrishnan et al. (2012) realizaram uma revisão sistemática sobre o consumo de diferentes nutrientes no período pré-gestacional e no início da gestação e diferentes desfechos gestacionais e neonatais como baixo peso e comprimento ao nascer, restrição de comprimento intra-uterino, parto pré-termo, morbimortalidade, estado nutricional materno e neonatal, aborto, defeitos congênitos e desenvolvimento infantil, e verificaram que a adequação de consumo de nutrientes antes da gestação pode prevenir diversos desfechos indesejáveis, ressaltando o baixo peso ao nascer, parto pré-termo e defeitos no tubo neural. A adesão a padrões alimentares mais saudáveis antes da gestação reduz o risco de parto pré-termo e o desenvolvimento de DHEG's, enquanto a adesão a um padrão alimentar não saudável pode aumentar o risco de diabetes mellitus gestacional (Cucó, et al., 2006; Bao et al., 2014; Grieger et al., 2014; Schoenaker et al., 2015).

A ingestão de uma dieta balanceada e adequada, com alimentos e quantidades variados, pode garantir as recomendações nutricionais e levar ao ganho de peso adequado (Fazio et al., 2011; McGowan et al., 2013b). A dieta inadequada durante a gestação pode trazer graves consequências para o feto, tais como peso, comprimento e medidas

antropométricas no nascimento e desenvolvimento infantil inadequado, além de complicações gestacionais para a mulher, como o desenvolvimento do diabetes gestacional e/ou síndrome hipertensiva da gravidez, e também o ganho de peso excessivo, aumentando o risco de retenção de peso pós-parto (Brantsæter et al., 2009; Okubo et al., 2012; McGowan et al., 2013b; De Giuseppe et al., 2014; von Ruesten et al., 2014).

É comum observar o consumo inadequado de micronutrientes (folato, ferro, zinco, vitaminas A, B6, B12 e C) durante a gestação, uma vez que suas necessidades nutricionais estão mais elevadas (Black et al., 2008). Isso ocorre, em grande parte, devido ao reduzido consumo de dieta balanceada e saudável com variedade de frutas, legumes, grãos integrais, vegetais, entre outros alimentos (Liu, 2013).

A avaliação da dieta somente por nutrientes específicos ou alimentos isolados é considerada limitada, pois a dieta humana é composta por uma combinação de vários alimentos e não apenas de um alimento ou nutriente específico, logo avaliar os efeitos dos nutrientes ou alimentos isoladamente é mais complexo (Hu, 2002; Newby & Tucker, 2004; Wärffelt et al., 2013). Dessa forma, a OMS, propôs avaliar os padrões de consumo alimentar da população, com o objetivo de melhorar as políticas públicas de saúde (WHO, 2003).

2.3.1 PADRÕES DE CONSUMO ALIMENTAR

Os padrões alimentares vêm sendo considerados modelos promissores de análise para avaliar a dieta, e são definidos como combinações de alimentos segundo fatores genéticos, culturais, sociais, de saúde, ambientais, estilo de vida e determinantes econômicos refletem as preferências alimentares individuais e permite avaliar o consumo alimentar em sua totalidade, ao invés de nutrientes específicos ou alimentos/grupos de alimentos (WHO, 2003; Kant, 2004). Os padrões alimentares, juntamente com a atividade física, podem influenciar nos níveis de saúde, e ainda determinar se um indivíduo irá desenvolver alguma doença crônica como câncer, doenças cardiovasculares e diabetes (WHO, 2003).

O padrão de consumo alimentar não pode ser avaliado diretamente, é preciso realizar análises estatísticas que tem como objetivo agregar alimentos consumidos usualmente por determinada população. Esses padrões alimentares são avaliados por meio de inquéritos alimentares ou métodos que forneçam a disponibilidade de alimentos (Olinto, 2007; Wärffelt et al., 2013). Essa abordagem reflete de forma mais realista a prática alimentar do grupo estudado, pois revela a dieta total no lugar de apresentá-la apenas como o consumo de energia e nutrientes ou mesmo alimentos isolados (Hu, 2002; Slattery, 2010).

Estudos que avaliaram padrões de consumo alimentar vêm sendo considerados modelos promissores de análise para avaliar a dieta, uma vez que esse método permite avaliar a associação entre os alimentos e algum desfecho de saúde, sejam doenças crônicas não transmissíveis (DCNT) ou transtornos mentais, e ainda algum outro desfecho relacionado a fatores socioeconômicos e demográficos (Cucó et al., 2006; Olinto et al., 2011; Chatzi et al., 2011; Okubo et al., 2011a; Vaz et al., 2013; Castro et al., 2014; Grieger et al., 2014).

As análises para obter os padrões de consumo alimentar podem ser definidas por dois métodos: orientados por hipóteses e métodos exploratórios, os quais eram conhecidos como *modelosa priori* e *a posteriori*, respectivamente (Hu, 2002; Hoffmann et al., 2004; Schulze & Hoffmann, 2006). A **Figura 2**, traduzida do estudo de Schulze & Hoffmann (2006), apresenta os métodos utilizados para identificar padrões alimentares.

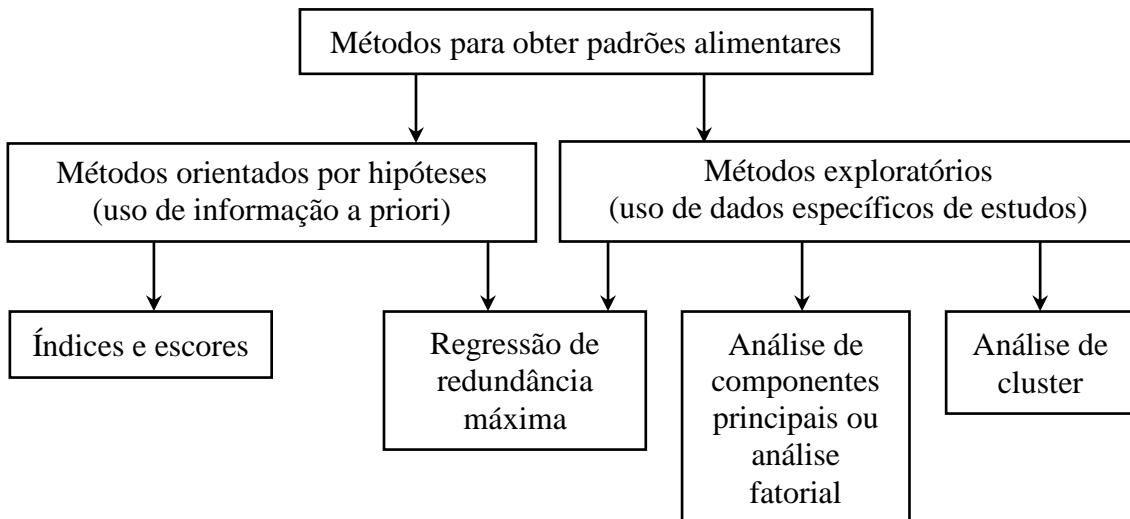


Figura 2. Métodos para obter padrões alimentares em estudos observacionais, traduzido de Schulze & Hoffmann (2006).

Nos métodos orientados por hipóteses, também conhecido como método teórico, (Newby & Tucker, 2004) os padrões alimentares são identificados por meio da qualidade da dieta obtida das diretrizes, recomendações nutricionais e guias alimentares. Esse método obtém padrões alimentares baseado em evidências científicas disponíveis para doenças específicas. Os índices dietéticos ou escores foram os primeiros métodos utilizados para avaliar a combinação de alimentos ou nutrientes com base em critérios pré-definidos relacionada com desfechos da saúde (Schulze et al., 2003; Schulze & Hoffmann, 2006; Wirth et al., 2013). Os índices e escores a seguir são exemplos de métodos orientados por hipóteses: índice de qualidade da dieta (IQD)/ *dietary quality index* (DQI), índice de alimentação

saudável (IAS)/ *health eating index* (HEI)/ *healthy diet index* (HDI), e a dieta do Mediterrâneo (DM)/ *Mediterranean diet score* (MDS) (Olinto, 2007; Wifält et al., 2013).

Os métodos exploratórios ou modelo *a posteriori* consistem em uma abordagem empírica, na qual dados dietéticos serão utilizados para obter os padrões alimentares. Esse é o método mais utilizado para identificar os padrões de consumo alimentar, uma vez que esse modelo permite avaliar o real comportamento alimentar de uma população. O Questionário de Frequência Alimentar (QFA) e o registro dietético são os métodos que melhor avaliam o consumo alimentar, pois possibilitam mensurar um maior número de itens alimentares e a quantidade detalhada de cada alimento consumido. Os métodos estatísticos mais utilizados para identificar os padrões de consumo alimentar *a posteriori* são a análise por componente principal (ACP), de agrupamento (*cluster*) e de regressão de redundância máxima (*Reduced Rank Regression - RRR*) (Olinto, 2007; Tucker, 2010; Schulze & Hoffmann, 2006; Wifält et al., 2013). A análise de classe latente também é utilizada para identificar padrões alimentares. Apesar de ser um método pouco utilizado, é possível avaliar as mudanças entre os padrões alimentares ao longo do tempo (Sotres-Alvarez et al., 2013a; Sotres-Alvarez et al., 2013b; Batis et al., 2014).

A ACP é o método estatístico mais empregado para identificar padrões alimentares. Esse procedimento permite que os itens alimentares contidos nos instrumentos que avaliaram o consumo alimentar sejam agrupados de acordo com o grau de correlação entre eles. Os alimentos são agrupados segundo similaridade nutricional, frequência de consumo e hábitos alimentares regionais. Após a rotação ortogonal e a fixação do número de fatores extraídos, os padrões alimentares não são correlacionados e podem ser avaliados no mesmo modelo de regressão. Na ACP cada indivíduo recebe um escore para cada padrão alimentar identificado e a intensidade de adesão aos padrões varia de indivíduo para indivíduo (Olinto, 2007; Wifält et al., 2013).

A análise de *cluster* é baseada no agrupamento de indivíduos segundo sua frequência de consumo alimentar. O objetivo do método consiste em agrregar indivíduos em subgrupos no qual o consumo alimentar é relativamente homogêneo, maximizando assim a heterogeneidade entre os grupos (Olinto, 2007; Cunha, et al., 2010). Este método é recomendado nas seguintes situações: (1) explorar padrões alimentares quando se suspeita que a análise não seja homogênea; (2) quando inexistem as propriedades estatísticas necessárias para empregar a análise fatorial e (3) quando o investigado não tem como objetivo excluir nenhum item alimentar proposto pelo instrumento (Olinto, 2007).

A análise de redundância máxima, o RRR, é o método mais utilizado em estudos que tem como objetivo verificar a associação entre a dieta e a doença. Nesse procedimento existem as variáveis preditoras, que podem ser alimentos ou os grupos alimentares, e a variável resposta, que são biomarcadores, nutrientes ou alguma doença de interesse. As variáveis preditoras têm como objetivo explicar a variação da variável resposta, possibilitando assim verificar quais os padrões alimentares que melhor explicam a variação na concentração dos biomarcadores, nutrientes e a doença avaliada (Hoffmann et al., 2004; Schulze & Hoffmann, 2006).

A análise de classe latente tem os objetivos similares à análise de cluster: classificar indivíduos que apresentam similaridade na dieta nas mesmas classes, as classes são diferentes entre si e, ainda, cada indivíduo pertence a uma única classe latente. Diferente dos outros métodos, a análise de classe latente permite ajustar por co-variáveis, quantificar a incerteza das associações das classes e avaliar o melhor ajuste de modelo (Sotres-Alvarez et al., 2013b).

As análises para obter padrões de consumo alimentar são importantes, uma vez que é possível avaliar os hábitos alimentares de uma população e assim associar a diversos desfechos.

2.3.2 ESTUDOS SOBRE PADRÕES ALIMENTARES

Alguns dos primeiros estudos sobre padrões de consumo alimentar foram publicados na década de 80. Em 1969, uma Conferência na Casa Branca sobre Alimentos, Nutrição e Saúde recomendou a programas federais examinar a relação entre o consumo de alimentos e padrões de alimentação com a saúde da população americana. Dessa forma, a *Ten-State Nutrition Survey* (1968 a 1970) e *Health and Nutrition Examination Survey (HANES)* I (1971 a 1974) foram os estudos responsáveis para realizar essa proposta (Schwerin et al., 1981; Schwerin et al., 1982).

A saúde da população foi o principal objetivo de estudo com os padrões alimentares, dessa forma muitos estudos relacionando padrões alimentares e o risco doenças crônicas em adultos foram realizados (Hu, 2002; Schulze & Hoffmann, 2006; Wirkfält et al., 2013), porém atualmente diferentes desfechos são avaliados com padrões alimentares e também em diferentes faixas etárias (Newby et al., 2006; Oddy et al., 2009; Cunha et al., 2011; Olinto et al., 2011; Smith et al., 2011; Jacka et al., 2013b; Northstone et al., 2013; Quirk et al., 2013; Vilela et al., 2014a; Schoenaker et al., 2015).

O primeiro estudo sobre padrões alimentares no Brasil foi realizado com adultos residentes no Rio de Janeiro. A autora identificou três padrões alimentares por análise fatorial,

os quais foram intitulados ‘misto’, ‘dieta tradicional’ e ‘dieta Ocidental’, e verificou que o padrão ‘dieta tradicional’ estava associado ao menor risco de sobre peso/obesidade (Sichieri, 2002). Nascimento et al. (2011) identificaram padrões alimentares das cinco regiões brasileiras com dados da Pesquisa de Orçamento Familiar (POF) - 2002/2003, utilizando a ACP. O padrão ‘arroz e feijão’ foi obtido em todos as regiões brasileiras e também foi o padrão com o maior percentual de variância explicada, exceto na região Norte. Nas regiões Norte e Nordeste foram obtidos três padrões em cada região: ‘regional’, ‘arroz e feijão’ e ‘frutas, verdes e doces’; e ‘arroz e feijão’, ‘energia elevada’ e ‘proteína elevada’, respectivamente. Nas demais regiões, Centro-Oeste, Sudeste e Sul foram obtidos apenas dois padrões alimentares, nessas regiões os padrões alimentares receberam a mesma nomeação: ‘arroz e feijão’ e ‘misto’.

Padrões alimentares com dados da POF também foram obtidos por Marchioni et al. (2011). Diferentemente do estudo anterior, os autores obtiveram padrões alimentares da população brasileira e não estratificaram pelas regiões brasileiras. Dois padrões alimentares foram identificados: duplo (*'dual'*) e tradicional (*'traditional'*). O primeiro padrão foi constituído por produtos lácteos, frutas, suco de frutas, vegetais, carnes processadas, refrigerante, doces, pão e margarina, e inversamente com alimentos típicos da alimentação brasileira (arroz, feijão, milho e farinha de mandioca). O segundo padrão foi composto de alimentos utilizados nas preparações domésticas, como arroz, feijão, carne de porco, ovos, mandioca, batata, milho, vegetais folhosos, óleo vegetal, açúcar, carne, frango legumes e raízes e tubérculos.

Massarani et al. (2015) identificaram os padrões alimentares da população brasileira com dados da POF 2008/2009. O consumo alimentar foi obtido pelo Inquérito Nacional de Alimentação (INA). Três padrões alimentares foram identificados e foram intitulados ‘Lanche tradicional’, ‘Grande refeição tradicional’, ‘Lanches tipo *fast food*’. O primeiro padrão alimentar foi caracterizado pelo consumo de pães, queijos, óleos e gorduras e café; o segundo foi constituído de alimentos característico da dieta da população brasileira como arroz, feijão e carnes. O último padrão foi caracterizado pelo consumo de sanduíches, carnes processadas, salgados e pizzas e refrigerantes.

Estudos sobre padrões alimentares com gestantes são escassos no Brasil. O primeiro estudo avaliou gestantes de unidade de saúde de Porto Alegre e Bento Gonçalves/RS, as quais estavam incluídas no *Estudo do consumo e do comportamento alimentar na gestação* (ECCAGe). Os autores identificaram três padrões alimentares: ‘restrito’, ‘variado’ e ‘comum brasileiro’, os quais eram caracterizados pelo consumo de alimentos não saudáveis, saudáveis

e alimentos tradicionais da dieta dos brasileiros, respectivamente (Hoffmann et al., 2013). Castro et al., (2014) avaliaram puérperas do Rio de Janeiro e foram obtidos dois padrões alimentares referentes ao período gestacional: ‘saudável’ e ‘misto’. Em outra coorte de gestantes no Rio de Janeiro, foram identificados padrões alimentares de gestantes referente ao segundo e terceiro trimestre gestacional. Os padrões foram intitulados: ‘saudável’, ‘comum brasileiro’ e ‘processado’ (Eshriqui et al., 2014).

A maior parte dos estudos utilizam a ACP para obter os padrões alimentares da população de estudo (Newby & Tucker, 2004; Cucó et al., 2006; Northstone et al., 2008b; Brantsæter et al., 2009; Crozier et al., 2009; Wirkfält et al., 2013, Castro et al., 2014; Eshriqui et al., 2014). Há estudos que identificaram padrões alimentares utilizando diferentes análises como ACP e análise de cluster (Newby et al., 2004; Crozier et al., 2006; Cunha et al., 2010). A análise de cluster também é explorada, porém não tanto quanto a ACP. Há na literatura apenas quatro estudos que obtiveram padrões alimentares por cluster (Okubo et al., 2011b; Okubo et al., 2012; Hoffmann et al., 2013; McGowan et al., 2013a), incluindo um estudo brasileiro de Hoffmann et al. (2013), que foi apresentado anteriormente. Okubo et al. (2011b e 2012) obtiveram padrões alimentares de gestantes japonesas. Os autores identificaram três clusters que foram intitulados ‘meat and eggs’, ‘wheat products’ e ‘rice, fish and vegetables’. O último estudo foi realizado com gestantes irlandesas e os autores identificaram dois padrões alimentares que foram intitulados ‘Unhealthy’ e ‘Health Conscious’ (McGowan et al., 2013a).

2.3.3 PADRÕES ALIMENTARES E TRANSTORNOS MENTAIS

Estudos com padrões de consumo alimentar e desfechos diversos em mulheres antes e durante a gestação são comuns (Cucó et al., 2006; Northstone et al., 2008b; Crozier et al., 2009; Castro et al., 2014; Grieger et al., 2014; Schoenaker et al., 2015). No entanto, são escassos os estudos que avaliaram padrões de consumo alimentar e a depressão e a ansiedade na gestação e pós-parto (Chatzi et al., 2011; Okubo et al., 2011; Vaz et al., 2013; USDA/HHS, 2015).

Chatzi et al. (2011) avaliaram 529 mulheres na Grécia que participaram do estudo de coorte “Rhea” para verificar a associação entre os padrões alimentares identificados durante a gestação e a depressão pós-parto (DPP). Os padrões foram obtidos pela análise de componentes principais e os alimentos foram provenientes de um QFA. A DPP foi avaliada por meio da EPDS entre 8 a 10 semanas após o parto. Observou-se que a adesão ao padrão “health-conscious”, caracterizado pelo consumo de vegetais, frutas, leguminosas, nozes, laticínios, peixe e azeite de oliva foi associado a menores escores de EPDS.

No Japão, Okubo et al. (2011) avaliaram 865 mulheres com o mesmo objetivo de Chatzi et al. (2011). A DPP foi avaliada entre 2 e 9 semanas após o nascimento da criança. Após ajustados por potenciais fatores de confusão não foi observada associação entre os padrões alimentares identificados e a DPP, nem mesmo para os padrões “*healthy*” e “*Japanese*”. Esses padrões eram compostos por (1) vegetais verdes e amarelos, algas, vegetais brancos, batatas, peixes, frutas, crustáceos e mariscos; e (2) arroz, sopa de missô, frutos do mar, peixes e legumes em conserva, respectivamente.

Vaz et al. (2013) avaliaram mulheres britânicas participantes do ALSPAC com o objetivo de verificar a associação entre os padrões alimentares e o risco de ansiedade durante a gestação. Os autores observaram que a maior adesão ao padrão “*health-conscious*”, caracterizado pelo consumo de salada, frutas, suco de frutas, arroz, massas, aveia/ cereal matinal, peixes, legumes, queijo e pão não-branco, e ao padrão “*traditional*”, composto por legumes, carne vermelha e aves, apresentou associação inversa com maiores escores de ansiedade.

3 JUSTIFICATIVA E HIPÓTESES

Estudos epidemiológicos mostram a relação entre a exposição a determinados fatores socioeconômicos (renda familiar e escolaridade), ambientais (moradia, saneamento e aglomeração), sociais (estado marital, tabagismo e etilismo durante a gestação) e psicológicos (problemas psicológicos prévios e apoio familiar) durante a gestação e o desenvolvimento fetal com saúde e doença ao longo da vida (Halpern et al., 2008; Silveira et al., 2007; Hanson et al., 2012; Heindel et al., 2015). Dessa forma, a gestação e os primeiros anos de vida são considerados os períodos mais importantes do ciclo vital.

O consumo alimentar antes e durante a gestação estão associados a diversos desfechos maternos e infantis, como a saúde mental materna e o desenvolvimento neuropsicológico infantil. A maioria dos estudos que avaliaram o consumo alimentar antes e durante a gestação se referem à deficiência de determinados nutrientes, incluindo as vitaminas, necessários para formação do feto. São poucos os estudos que avaliaram o padrão de consumo alimentar da mulher antes da gestação, relacionando-o com algum desfecho, e são escassos os estudos que associaram o padrão de consumo alimentar e a saúde mental materna e o desenvolvimento neuropsicológico infantil.

Dessa forma, os resultados obtidos nessa tese de doutorado podem contribuir para o desenvolvimento de políticas públicas, promovendo programas de intervenção com mulheres em idade reprodutiva sobre a importância de uma dieta saudável não apenas durante a gestação, uma vez que é cada vez maior a prevalência de doenças da saúde mental em gestantes e crianças como o atraso no desenvolvimento neuropsicológico.

Nesse contexto, as hipóteses levantadas para os estudos dessa tese de doutorado são:

Hipótese 1. A maior adesão a um padrão alimentar no período pré-gestacional caracterizada por alimentos saudáveis reduz o risco de sintomas de depressão e ansiedade ao longo da gestação e início do pós-parto.

Hipótese 2. Mães, durante a gestação, e filhos aderem a padrões alimentares semelhantes ao longo do tempo, principalmente aqueles caracterizados por alimentos saudáveis.

Hipótese 3. Mulheres que aderem a um padrão alimentar composto por alimentos não saudáveis durante a gestação aumentam o risco de ter filhos com menores escores de coeficiente de inteligência aos 8 anos.

4 OBJETIVOS

4.1 OBJETIVO GERAL

Identificar padrões de consumo alimentar em mulheres e verificar a associação dos padrões alimentares com os sintomas de depressão e de ansiedade durante a gestação e pós-parto e com o coeficiente de inteligência na infância.

4.2 OBJETIVOS ESPECÍFICOS

4.2.1 ARTIGO 1

- i) Identificar padrões de consumo alimentar referente ao período pré-gestacional e verificar a associação entre os padrões alimentares identificados e as variações dos sintomas de depressão durante a gestação.

4.2.2 ARTIGO 2

- ii) Examinar a associação entre os padrões alimentares pré-gestacionais e as variações dos sintomas de ansiedade durante a gestação e pós-parto.

4.2.3 ARTIGO 3

- iii) Obter padrões alimentares em mulheres durante a gestação, avaliar o consumo de nutrientes de acordo com os padrões alimentares identificados e comparar padrões alimentares das mães e seus filhos aos 7 anos de idade.

4.2.4 ARTIGO 4

- iv) Verificar a associação entre os padrões alimentares maternos e o coeficiente de inteligência de seus filhos aos 8 anos de idade.

5 MÉTODOS

COORTE BRASILEIRA: “SAÚDE MENTAL E ESTADO NUTRICIONAL NA GESTAÇÃO E NO PÓS-PARTO: ESTUDO PROSPECTIVO COM ENSAIO CLÍNICO RANDOMIZADO ANINHADO”

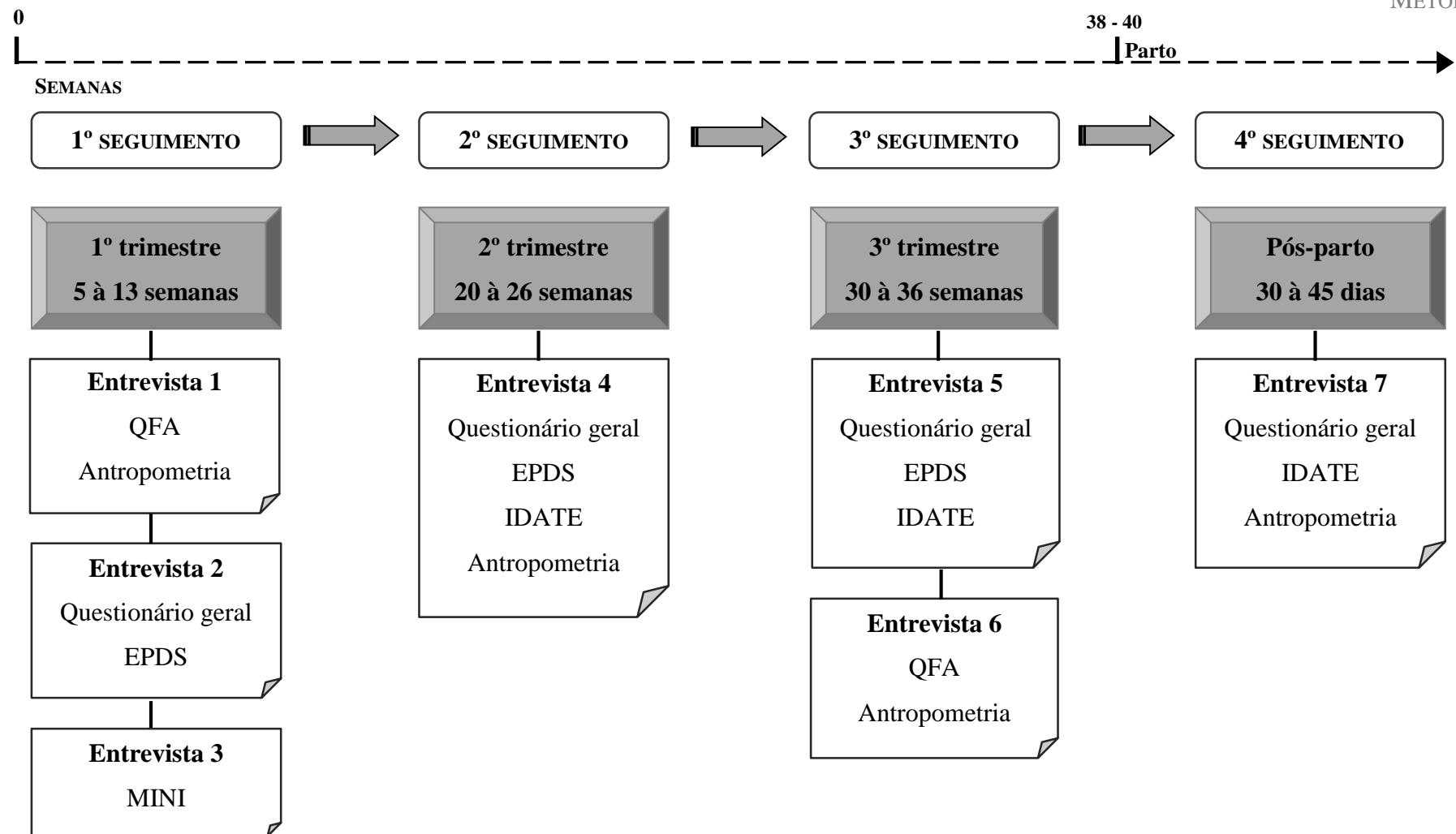
5.1 DESENHO DO ESTUDO

O presente estudo consiste em uma coorte prospectiva com gestantes, que foi desenvolvido no Centro Municipal de Saúde Heitor Beltrão (CMSHB), na cidade do Rio de Janeiro. As mulheres que compuseram a amostra foram entrevistadas em quatro períodos do seguimento: três seguimentos na gestação e um no pós-parto. Durante a gestação, elas foram avaliadas no primeiro trimestre entre a 5^a a 13^a semana (linha de base), no segundo trimestre entre a 20^a a 26^a semana e no terceiro trimestre gestacional entre a 30^a a 36^a semana. Já a última entrevista ocorreu com 30 a 45 dias após o parto (**Figura 3**).

As avaliações foram realizadas presencialmente em uma sala exclusiva destinada ao projeto, quando foram obtidas informações sobre transtornos mentais comuns, dados socioeconômicos, do estilo de vida, dietéticos, medidas antropométricas, informações reprodutivas pregressas e do curso da gestação. As entrevistas e a antropometria foram realizadas em dias previamente agendados e por entrevistadores devidamente treinados (alunos de iniciação científica, mestrado e doutorado da Nutrição, Psiquiatria e Psicologia da UFRJ e da UERJ).

5.2 CAPTAÇÃO DAS GESTANTES

As gestantes que procuraram o CMSHB para o serviço de atendimento ao pré-natal ou que obtiveram resultado positivo para o teste imunológico de gravidez foram abordadas e informadas sobre o estudo. Em seguida, as mulheres contatadas responderam um questionário com alguns itens (data da última menstruação, idade, escolaridade, peso pré-gestacional, número de filhos prévios, informações sobre DCNT e doenças infecciosas, local da residência e local no qual seria realizado o pré-natal), objetivando identificar as mulheres que atendiam os critérios de elegibilidade do estudo. As gestantes que atenderam aos critérios de inclusão foram convidadas a participar do estudo e aquelas que aceitaram, assinaram o Termo de Consentimento Livre e Esclarecido (TCLE) e agendaram a primeira entrevista. A captação de gestantes ocorreu entre os períodos de novembro de 2009 a outubro de 2011.



Nota: QFA = Questionário de Frequência Alimentar; EPDS = Escala de Depressão Pós-Parto de Edimburgo; IDATE = Inventário de Ansiedade Traço-Estado; MINI = *Mini International Neuropsychiatry Interview*.

Figura 3. Ondas de seguimento e avaliações realizadas durante a gestação e no pós-parto.

5.3 CRITÉRIOS DE ELEGIBILIDADE

As mulheres que atenderam aos seguintes critérios de elegibilidade foram convidadas a participar do estudo:

- i) Terem no máximo 13 semanas de gestação;
- ii) Terem entre 20 e 40 anos;
- iii) Estarem livres de DCNT, exceto obesidade;
- iv) Estarem livres de doenças infecciosas;
- v) Não apresentarem gestação gemelar e;
- vi) Realizarem o acompanhamento pré-natal no local de estudo.

5.4 CONTROLE DE QUALIDADE

O controle de qualidade foi realizado com o objetivo de evitar possíveis vieses no estudo. Foram elaborados protocolos para a aplicação do questionário geral e o QFA. Os dados antropométricos foram padronizados seguindo o protocolo de Gordon et al. (1988). Os entrevistadores receberam treinamento teórico e prático para a coleta dos dados e seguiram padronizações previamente estabelecidas.

Foi realizado um estudo piloto no CMSHB, com o objetivo de testar os instrumentos de coleta de dados, no período de setembro a outubro de 2009. Assim, foram propostas e executadas modificações nos questionários, técnicas de aferição e a logística do estudo. Em novembro de 2009 iniciou-se a coleta de dados com as gestantes.

Após cada entrevista, os questionários foram revisados pelo entrevistador e posteriormente, por um revisor, visando minimizar erros de preenchimento.

5.5 LOGÍSTICA DO ESTUDO

No primeiro trimestre gestacional foram realizados três encontros. No primeiro encontro foram coletadas informações sobre consumo alimentar por meio de um QFA referente ao período pré-gestacional (**Anexo online 1**) e realizada as medidas de peso e de altura. No segundo encontro foi aplicado o Questionário Geral-1 (**Anexo online 2**). No último encontro neste trimestre foi aplicado o *Mini International Neuropsychiatric Interview* (MINI), um questionário com perguntas sobre aspectos de saúde mental, porém os dados obtidos nesse instrumento não foram incluídos nesse estudo.

O quarto encontro ocorreu no segundo trimestre gestacional e foi aplicado o Questionário Geral-2 (**Anexo online 3**) e aferido o peso das mulheres. No último trimestre de gestação foram realizados dois encontros. No primeiro foi aplicado o Questionário Geral-3

(**Anexo online 4**) e novamente aferido o peso das gestantes. No segundo encontro foi aplicado o QFA referente ao período gestacional (**Anexo online 5**) e novamente coletado o peso. Neste último encontro, as mulheres foram instruídas a comparecer a sala do projeto todas as vezes que estivesse no CMSHB para atendimento ambulatorial, para que fossem pesadas e assim continuarmos a fazer o registro/acompanhamento do ganho de peso gestacional.

A última onda de seguimento ocorreu aproximadamente de quatro a seis semanas após o parto. Neste momento foi aplicado o Questionário Geral de pós-parto (**Anexo online 6**) e aferido o peso da mulher.

Para evitar as perdas de seguimento, no dia anterior às entrevistas, as mulheres eram contatadas por telefone para confirmar o agendamento. A remarcação da entrevista também foi realizada por telefone para as gestantes que não puderam comparecer no dia que estava agendada a entrevista, porém quando não foi possível o contato telefônico, foram enviadas cartas para o endereço fornecido pela gestante para que ela entrasse em contato com a equipe do projeto para agendar a entrevista. A equipe da coletada de dados do projeto tinha acesso a agenda de atendimentos ao pré-natal do CMSHB. Assim, era possível saber quando as gestantes envolvidas na coorte teriam consultas e estariam no posto de saúde. Dessa forma, a equipe do projeto entrou em contato com as gestantes que se ausentaram do atendimento ao pré-natal no posto de saúde e que estavam próximas a data provável do parto, para certificar se já tinha se o bebê tinha nascido e assim agendar a última entrevista do seguimento no pós-parto.

A **Figura 4** apresenta o fluxograma da coorte prospectiva das mulheres que foram acompanhadas desde a gestação até o pós-parto.

Foram elegíveis para participar do estudo 299 mulheres, porém nas primeiras entrevistas foram identificadas mulheres que não atendiam os critérios de elegibilidade, como DCNT e infecciosas ($n = 13$), semana gestacional > 13 semanas ($n = 16$), gestação gemelar ($n = 4$) e transferiu a unidade do pré-natal ($n = 1$). Foram excluídas, para os estudos dessa tese, mulheres que não compareceram a entrevista ($n = 6$), sem informações sobre idade gestacional ($n = 3$) e dados de EPDS ($n = 5$); e ainda 3 mulheres tiveram aborto. Dessa forma, 248 mulheres foram consideradas elegíveis na linha de base do estudo.

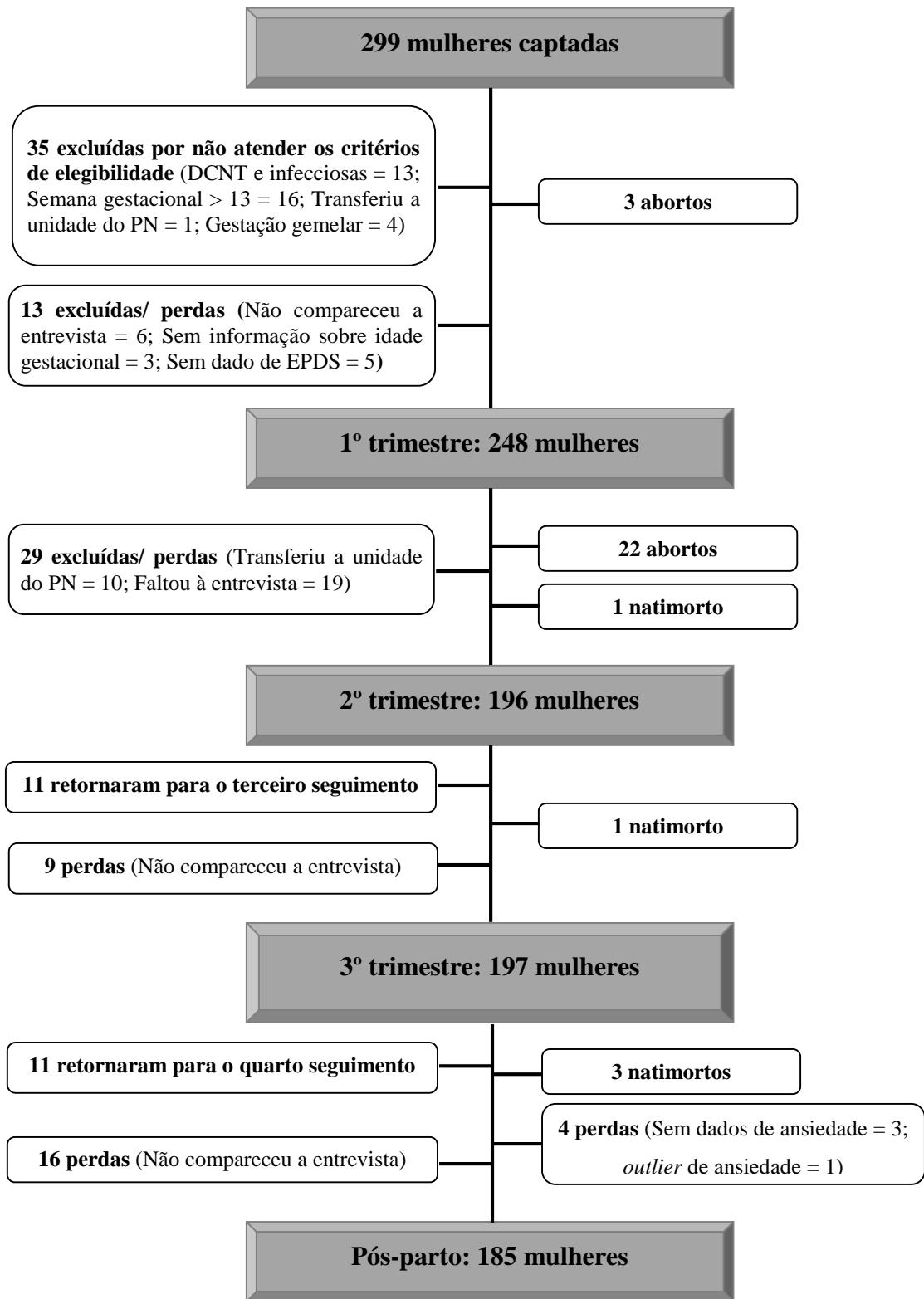


Figura 4. Fluxograma do estudo de coorte prospectiva de mulheres atendidas em uma unidade de saúde pública do município do Rio de Janeiro.

No segundo trimestre gestacional foram avaliadas 196 mulheres, pois das 248 gestantes ativas no trimestre anterior, 10 transferiram a unidade de pré-natal e 19 faltaram a entrevista, e ainda ocorreram 22 abortos e 1 conceito natimorto. Do segundo para o terceiro trimestre, 11 mulheres que faltaram a entrevista no trimestre anterior retornaram para a coorte, porém ocorreu 1 conceito natimorto e 9 mulheres faltaram a entrevista. Dessa forma, foram avaliadas 197 mulheres no terceiro trimestre gestacional. No último seguimento do estudo, o pós-parto, 10 mulheres que se ausentaram na entrevista anterior retornaram para esse seguimento, mas ocorreram 3 conceitos natimortos, 16 mulheres faltaram a entrevista, 3 tinham dados faltantes de ansiedade e 1 mulher tinha valor *outlier* de ansiedade em relação as demais mulheres, assim foram avaliadas 185 mulheres no ultimo seguimento do estudo.

Devido à natureza do estudo, é comum ocorrer perdas de seguimento ao longo período. Em relação ao número de mulheres que foram recrutadas para o estudo, porém não atendiam os critérios de elegibilidade, os quais os foram certificados após o início do protocolo do estudo, houve perda de 17,1% (248/299). Em relação as mulheres que foram elegíveis para o estudo, a perda de seguimento foi de 21,0% (196/248), 20,6% (197/248) e 25,4% (185/248) no segundo, terceiro trimestres gestacionais e pós-parto, respectivamente.

5.6 ENSAIO CLÍNICO ANINHADO

Na linha de base foi realizada uma triagem para identificar mulheres com possível risco de DPP. As gestantes que relataram história pregressa de depressão ou apresentaram escores ≥ 9 , baseada na EPDS, foram selecionadas para o ensaio clínico, que tinha como objetivo verificar o efeito da suplementação de ômega-3 na DPP.

Durante o atendimento do segundo trimestre (entrevista 4), uma sub-amostra de 61 mulheres foi convidada para participar do ensaio clínico aninhado a coorte. As gestantes randomizadas receberam cápsulas contendo ômega-3 ou placebo. As cápsulas do grupo que recebeu o tratamento continham uma dose total diária de 1,8 gramas de ômega-3 (1,08 g de EPA - *eicosapentaenoic*, e 0,72 g de DHA - *docosahexaenoic*). O grupo controle recebeu cápsulas com óleo de soja, uma vez que é o óleo mais utilizado pela população brasileira para preparar as refeições. Apenas 41 mulheres finalizaram o protocolo do ensaio clínico, das quais 20 receberam a suplementação com ômega-3.

Considerando o objetivo do ensaio clínico e que as mulheres que foram incluídas nesse estudo aninhado foram aquelas que apresentaram os maiores sintomas de depressão na linha de base, o desfecho do primeiro artigo incluído nessa tese, tornou-se importante avaliar se a suplementação de ômega-3 influenciou nos sintomas de depressão no terceiro trimestre

gestacional, dessa forma diferentes modelos estatísticos foram realizados. Mais informações no tópico sobre análises estáticas do artigo 1.

5.7 CÁLCULO DO TAMANHO DA AMOSTRA

O cálculo amostral para o estudo maior foi obtido por meio do desfecho de menor frequência de ocorrência, que no caso foi o baixo peso ao nascer (10%). Porém, para os estudos realizados nessa tese de doutorado, a amostra foi estimada considerando o número de indivíduos necessários para a identificação de padrões de consumo alimentar por meio da análise fatorial por componentes principais.

Segundo Olinto (2007), são necessários dez indivíduos para cada agrupamento alimentar quando os alimentos são agrupados em até 15 itens alimentares ($10 *$ número de grupos de alimentos). Porém, se forem agrupados mais de 15 itens, a amostra deve ser cinco vezes maior ($5 *$ número de grupos) que o número de grupos alimentares.

Para estimar o número de mulheres que seriam necessárias para a identificação dos padrões de consumo alimentar, foram considerados agrupamentos realizados em alguns estudos brasileiros (Cunha et al., 2010; Olinto et al., 2011; Vilela et al., 2014a) que fizeram o mesmo tipo de análise e possuíam o número de itens alimentares do QFA semelhantes a este estudo. Assim, para o presente estudo foi estimado que seriam agrupados aproximadamente 25 itens alimentares ($5 * 25$), sendo necessário no mínimo 125 gestantes em cada ponto que foi avaliado o QFA.

5.8 VARIÁVEIS DO ESTUDO

5.8.1 VARIÁVEIS DEPENDENTES

5.8.1.1 SINTOMAS DEPRESSIVOS (ARTIGO 1)

A EPDS foi o instrumento utilizado para avaliar a depressão materna durante a gestação. O instrumento foi aplicado no primeiro, segundo e terceiro trimestres gestacionais. A escala contém 10 enunciados com quatro opções de respostas, que pontuam de 0 a 3 de acordo com a presença e a intensidade do sintoma depressivo nos sete dias anteriores a entrevista. A pontuação total varia de 0 a 30. O tempo gasto em média para aplicação da escala é de aproximadamente 5 minutos. O instrumento foi desenvolvido por Cox et al. (1987) para avaliar a DPP, porém foi validada para avaliar a suspeição de depressão durante a gestação (Murray & Cox, 1990).

O instrumento utilizado no presente estudo foi traduzido e validado por Santos et al. (2007) em uma amostra de mães da coorte de nascimentos de Pelotas – Rio Grande do Sul. O ponto de corte utilizado pelos autores para avaliação da suspeição de depressão neste estudo foi de 11, uma vez que apresentou melhores valores para sensibilidade e especificidade, 83,8% e 74,7%, respectivamente. Para o ponto de corte 10 a sensibilidade foi 82,6% e a sensibilidade 65,4%. No presente estudo, utilizamos os escores de EPDS contínuos de cada trimestre de gestação.

5.8.1.2 SINTOMAS DE ANSIEDADE (ARTIGO 2)

Os sintomas de ansiedade foram avaliados por meio da aplicação do IDATE no segundo e terceiro trimestres gestacionais e no pós-parto. Esse instrumento foi elaborado por Spielberger et al. (1970) para a população em geral. Recentemente essa escala foi validada em mulheres portuguesas durante a gestação e no pós-parto (Tendais et al., 2014). No presente estudo empregou-se uma versão traduzida, adaptada e validada para o Brasil (Biaggio & Natalício, 1979). Os estudos brasileiros que validaram este instrumento, não incluem gestantes ou mulheres no pós-parto (Biaggio & Natalício, 1979; Gorenstein & Andrade, 1996; Fioravanti-Bastos et al., 2011).

Dois tipos de ansiedade podem ser avaliados utilizando esse instrumento: traço e estado. A ansiedade-traço é caracterizada pelo aspecto mais estável de ansiedade ao longo de sua vida, e a ansiedade-estado refere-se a um estado emocional transitório que pode ser refletida pela situação de adversidade em um momento específico (Cattell & Scheier, 1961). No estudo maior, foi avaliada a ansiedade-traço na linha de base e a ansiedade-estado nos demais pontos de seguimento (segundo e terceiro trimestres gestacionais e pós-parto). Na presente tese foi avaliado somente a ansiedade-estado nas mulheres.

O instrumento IDATE contém 20 itens com quatro opções de resposta: absolutamente não, um pouco, bastante e muitíssimo. As respostas variam de 1 (pouco ansioso) a 4 (muito ansioso), de acordo com a intensidade de ansiedade da mulher. O escore de pontuação do instrumento varia de 20 a 80. Quanto maior a pontuação, maior a presença de sintomas de ansiedade (Biaggio et al., 1977). Utilizamos os escores de IDATE contínuos obtidos nos períodos avaliados.

5.8.2 VARIÁVEL INDEPENDENTE

5.8.2.1 PADRÃO DE CONSUMO ALIMENTAR

O padrão de consumo alimentar das mulheres foi obtido por meio de um QFA com 82 itens alimentares adaptado para essa coorte. O QFA adaptado para o nosso estudo foi validado para funcionários da UERJ. Os autores utilizaram o recordatório de 24 horas como padrão-ouro e verificaram que o coeficiente de correlação entre os dois instrumentos variou entre 0,18 (vitamina A) a 0,55 (cálcio) para os nutrientes. Os coeficientes de correlação para energia, carboidrato, proteína, e gordura foram 0,44, 0,34, 0,44, e 0,41 respectivamente (Sichieri & Everhart, 1998).

O QFA foi aplicado no primeiro e no terceiro trimestre gestacional. A primeira avaliação referiu-se ao consumo alimentar da mulher nos seis meses anteriores a concepção e a segunda correspondeu aos últimos seis meses anteriores à última entrevista. Para os estudos incluídos nessa tese, foram utilizados os dados do consumo alimentar referente ao período pré-gestacional.

O QFA possui oito opções de frequência: (i) mais de três vezes ao dia, (ii) duas a três vezes ao dia, (iii) uma vez ao dia, (iv) cinco a seis vezes por semana, (v) duas a quatro vezes por semana, (vi) uma vez por semana, (vii) uma a três vezes por mês e (viii) nunca ou quase nunca. A frequência de consumo do QFA foi transformada em frequência diária, sendo atribuído 1,0 ao consumo de uma vez por dia. As demais opções foram proporcionais à frequência: (i) 4, (ii) 2,5, (iii) 1, (iv) 0,79, (v) 0,43, (vi) 0,14, (vii) 0,07 e (viii) 0 vezes ao dia. As medidas caseiras dos alimentos da lista do QFA foram convertidas em gramas (g) e mililitros (ml) utilizando a tabela de medidas caseiras da Pinheiro et al. (2005). A quantidade diária foi obtida pela multiplicação da frequência diária e a medida caseira. O software DietSys versão 4.02 (HHHQ, 1999) foi utilizado para estimar o consumo energético total e os nutrientes dos alimentos. Uma vez que o software utilizado para conversão dos alimentos continha dados americanos para estimar os nutrientes, optamos por modificar essas informações e incluir uma base de dados que foi constituída pelos alimentos da Tabela Brasileira de Composição de Alimentos (TACO, 2011) e na ausência de algum alimento, a tabela americana *United States Department of Agriculture* (USDA, 2011).

Para identificar os padrões alimentares foi utilizado a frequência alimentar diária. Alguns alimentos foram excluídos da análise por apresentarem consumo menor que 20% {banha de porco (1,2%) e bebidas alcoólicas [vinho (11,2%), cerveja (41,8%) e outras bebidas alcoólicas (7,2%)]} e por constituir o mesmo item alimentar na lista do QFA, porém com a composição nutricional diferente (carne seca ou bacalhau - 46,2%). O consumo de cerveja foi

maior que 20%, mas mesmo assim optamos por retirar, pois nas análises preliminares o consumo de bebidas alcóolicas apresentou baixas cargas fatorais nos diferentes modelos que foram testados para identificar os padrões alimentares, assim esse grupo de alimentos/bebidas não representava um consumo habitual das mulheres avaliadas nesse estudo. Os alimentos que apresentaram frequência menor que 20% foram excluídos, pois esses alimentos não caracterizam uma dieta habitual dos indivíduos e ainda apresentavam baixa correlação com os demais grupos definidos (Hu, 2002; Wärffel et al., 2013). Dessa forma, os 77 itens alimentares resultaram em 19 grupos alimentares. Os alimentos foram agrupados de acordo com sua à similaridade nutricional, frequência de consumo e segundo os hábitos alimentares regionais. Alguns alimentos foram mantidos separados, pois apresentaram frequência de consumo maior que 80% (Olinto et al., 2011) ou não tinha semelhança a nenhum outro alimento ou grupo de alimento (arroz, feijão, pães, açúcar, peixes, café e chá). O **Quadro 2** apresenta os 19 grupos alimentares, seus respectivos alimentos do QFA e percentual de frequência de consumo.

5.8.3 VARIÁVEIS SOCIOECONÔMICAS, DEMOGRÁFICAS, OBSTÉTRICAS E DE ESTILO DE VIDA

As variáveis socioeconômicas, demográficas, obstétricas e de estilo de vida foram obtidas por meio de questionários estruturados mencionados anteriormente (**Anexos online 1 a 6**).

As informações foram coletadas em todas as ondas de seguimento. As variáveis avaliadas no presente estudo foram: idade (anos), escolaridade (anos), estado marital (casada/em uma relação estável ou solteira), paridade (número de filhos), desejo de engravidar [sim (estava querendo engravidar) ou não (queria esperar mais ou não queria engravidar)], tabagismo durante a gestação (nunca fumou, fumante atual ou ex-fumante) e consumo de álcool durante a gestação (sim ou não).

5.8.4 VARIÁVEIS ANTROPOMÉTRICAS

As variáveis antropométricas avaliadas no presente estudo foram o peso e a altura, as quais foram utilizadas para calcular o Índice de Massa Corporal (IMC) gestacional. As medidas antropométricas foram aferidas de acordo com protocolos padronizados (Gordon et al., 1998) e entrevistadores treinados e capacitados para realizar as medidas.

Quadro 2. Agrupamentos dos alimentos do questionário de frequência alimentar e frequência¹ de consumo dos grupos de alimentos para a identificação dos padrões alimentares.

GRUPO DE ALIMENTOS	ALIMENTOS DO QFA	%
Arroz	Arroz	100,0
Feijão	Feijão	96,8
Pães	Pão/ pão francês/ pão de forma	98,4
Massas, raízes e tubérculos	Mijo/macarrão; lasanha/nhoque/ravioli; batata cozida/purê; mandioca/aipim/inhame; polenta/angu; farinha de mandioca/farofa	99,2
Bolos e biscoitos	Bolo; biscoito recheado; biscoito doce/maizena®/Maria®; biscoito salgado/cream cracker.	98,0
<i>Fast food e Snacks</i>	Pizza; batata frita, chips/palha; salgados (risoli, coxinha, pastel, kibe); maionese; alimentos enlatados (ervilha, azeitona, palmito, picles, pepino); carne de hambúrguer; salgadinhos tipo Cheetos®, Fofura®, Torcida®; pipoca (doce/salgada, arroz, milho); amendoim	97,6
Gorduras	Manteiga; margarina	91,6
Leite e derivados	Leite; queijo; iogurte; requeijão	96,0
Vegetais e legumes	Lentilha/ervilha/grão de bico; alface; couve; repolho; couve-flor/brócolis; tomate; pepino cru; chuchu; abobrinha verde; abóbora; cenoura; beterraba; quiabo; vagem	98,4
Frutas e suco	Laranja/tangerina; banana; mamão; maçã; melancia/melão; abacaxi; manga; uva; suco da fruta/polpa	98,8
Carnes e ovos	Ovos; carne de porco/carré; frango; carne vermelha/bife/carne ensopada/moída; bucho/fígado/moela/coração; churrasco de carne vermelha	100,0
Peixes	Peixe; sardinha/atum enlatado	73,7
Embutidos	Salsicha/salsichão; frios (mortadela, presunto, apresuntado, salame); bacon/toucinho/torresmo; linguiça	92,4
Temperos	Alho; cebola; pimentão	98,4
Doces	Sorvete; balas; Chocolate em pó/Nescau®; chocolate barra/bombom; doce à base de leite (pudim, doce leite); doce à base de fruta (goiabada, bananada)	93,6
Açúcar	Açúcar	91,6
Refrigerantes	Refrigerantes à base de cola (coca-cola, pepsi) e outros refrigerantes (guaraná, fanta, Guaravita®)	89,6
Café	Café	75,7
Chá	Chá/mate	35,9

¹ Para o cálculo da frequência diária foram incluídos todos os indivíduos que relataram pelo menos uma das frequências de consumo, exceto “nunca ou quase nunca”.

5.8.4.1 PESO

O peso (kg) foi aferido em todas as ondas de seguimento utilizando uma balança digital (Filizzola PL 150, Filizzola Ltda., Brasil) com capacidade para 150 kg e variação de 0,1 kg. Devido a precisão da balança digital foi aferido apenas uma única medida em cada visita. Na última entrevista durante a gestação, a mulher foi orientada a procurar a sala do projeto, quando comparecesse ao CMSHB para o pré-natal, para acompanhamos o ganho de peso nas últimas semanas gestacionais.

5.8.4.2 ALTURA

A altura (cm) foi aferida em duplicata com o uso de um estadiômetro portátil (Seca Ltda., Hamburgo, Alemanha) fixado à parede, tipo trena e com escala de 220 cm. Quando a diferença entre as medidas era maior que 0,5 cm, uma terceira medida era aferida e a média das duas medidas mais próximas foi utilizada. Esta medida foi aferida apenas no primeiro trimestre gestacional.

5.8.4.3 IMC GESTACIONAL

O IMC gestacional foi obtido pela razão do peso e o quadrado da altura [peso (kg)/estatura (m^2)]. A variável foi calculada em cada onda de seguimento, considerando o peso aferido naquele momento, porém classificado segundo a proposta do *Institute of Medicine* (IOM, 2009) que considera o peso pré-gestacional. O IMC obtido em cada seguimento foi incluído na análise como contínuo e no segundo artigo foi categorizado em mulheres com ($\geq 25 \text{ kg/m}^2$) e sem excesso de peso ($< 25 \text{ kg/m}^2$), seguindo a proposta do IOM (2009) (**Quadro 3**).

Quadro 3. Classificação do IMC pré-gestacional e respectivos pontos de corte.

IMC PRÉ-GESTACIONAL	IMC (kg/m^2)
Baixo peso	18,5
Eutrofia	18,5 - 24,9
Sobrepeso	25,0 - 29,9
Obesidade	$\geq 30,0$

5.8.5 IDADE GESTACIONAL

A idade gestacional, avaliada em semanas, foi calculada a partir dos dados obtidos na primeira ultrassonografia (USG) realizada antes de 26 semanas de gestação. Na ausência de

informação sobre a semana gestacional pela USG, foi utilizada a data da última menstruação (DUM) para estimar a semana gestacional.

5.9 ANÁLISES ESTATÍSTICAS

5.9.1 ANÁLISE DESCRIPTIVA

Foram realizadas análises descritivas com o objetivo de verificar as características da população de estudo. Procedimentos clássicos como médias e intervalo de confiança de 95% (IC 95%) ou frequência e proporção foram realizados para variáveis contínuas e categóricas, respectivamente.

5.9.2 IDENTIFICAÇÃO DOS PADRÕES ALIMENTARES POR ANÁLISE DE COMPONENTES PRINCIPAIS

Os padrões alimentares das mulheres avaliadas foram definidos *a posteriori* e o método estatístico empregado para a identificação dos padrões alimentares foi a análise fatorial por componente principal (ACP). A análise fatorial reduz os dados em padrões baseado na correlação dos grupos alimentares. A ACP consiste (1) na preparação da matriz de correlação, (2) extração de fatores da matriz de correlação, (3) rotação dos fatores para melhorar sua interpretação, (4) interpretação e (5) denominação dos fatores (Hu, 2002; Newby et al., 2004; Olinto, 2007; Cunha et al., 2010; Slattery et al., 2010).

O teste estatístico de Kaiser-Meyer-Olkin (KMO) é o mais utilizado em estudos epidemiológicos com o objetivo de identificar padrões alimentares, pois avalia a correlação entre os grupos alimentares. Coeficientes de correlação mais próximos a 1 são mais adequados, porém para a obtenção de padrões alimentares, o ideal é que seja maior que 0,6. O teste de esfericidade de Bartlett testa a qualidade das correlações entre as variáveis e requer p-valor < 0,05 (Newby et al., 2004; Olinto, 2007; Wurfält et al., 2013).

A etapa seguinte consiste na aplicação da rotação ortogonal Varimax que permite uma melhor interpretabilidade dos fatores (Olinto, 2007). O número de fatores extraídos pode ser baseado em autovalores maiores que 1,5 e o teste gráfico de Cattel (*scree plot*), no qual os pontos de maior declive indicam o número apropriado de fatores que devem ser retidos. No nosso estudo, optamos por utilizar autovalores maiores que 1,5, pois obtivemos melhor interpretação dos dados. As communalidades e cargas fatorais $> 0,20$ foram consideradas fortemente associadas com o padrão. Outros estudos também utilizaram carga fatorial $> 0,20$ (Cucó et al., 2006; Newby et al., 2006). Cargas fatoriais positivas indicam que o grupo alimentar apresentou uma associação positiva com este fator, enquanto cargas negativas indicam uma

associação inversa (Cucó et al., 2006; Newby et al., 2006). Os padrões alimentares foram nomeados segundo (i) os principais grupos alimentares que constituíram cada fator, (ii) maiores cargas fatoriais de cada padrão identificado, e (iii) interpretação dos padrões alimentares. Ao final da análise, foram gerados escores de cada padrão alimentar, e cada gestante recebeu um escore para cada fator de padrão alimentar identificado (Hu, 2002).

Os gráficos de *scree plot* utilizados para auxiliar no número de fatores fixados para a identificação dos padrões alimentares não foram incluídos nos artigos, mas são apresentados em anexo (**Anexo 1**).

5.9.3 ANÁLISES LONGITUDINAIS

Modelos de regressão longitudinal de efeitos mistos (*LME – longitudinal mixed effects*) foram empregados para avaliar as associações longitudinais entre padrões alimentares e saúde mental durante a gestação e no pós-parto. O modelo LME acomoda co-variáveis tempo-dependentes e tempo-independentes e possibilita analisar dados com medidas repetidas não equidistantes. Além disso, este modelo é adequado quando os dados do estudo apresentam valores faltantes (Pinheiro, 2000; Singer, 2003; Twisk, 2003).

Foram consideradas variáveis referentes ao tempo no **Artigo 1** a idade gestacional e no **Artigo 2** a idade gestacional e a idade gestacional quadrática, pois o padrão de evolução da ansiedade se assemelha a uma parábola. A idade gestacional foi incluída como um efeito aleatório no modelo, para assim verificar as variações individuais dos sintomas de depressão e ansiedade ao longo do tempo, enquanto que os escores de padrão alimentar e as demais variáveis foram considerados como efeitos fixos, permitindo assim verificar o efeito da variação comum entre as mulheres avaliadas.

Os modelos mais adequados foram selecionados considerando os seguintes critérios: razão de verossimilhança restrita, critério de informação de Akaike (*Akaike Information Criterion - AIC*) e o critério de informação de Bayes (*Bayesian Information Criterion - BIC*). Ainda no processo de modelagem, 3 tipos de gráficos foram produzidos: gráficos para avaliar a estrutura de auto-correlação e também gráficos do tipo *scatter plots* e *quantile-quantile plots* para avaliar padrões específicos e para checar a normalidade dos resíduos, respectivamente (Fitzmaurice et al., 2004).

Para todos os modelos foram testados a interação entre os padrões alimentares e a variável referente ao tempo. No modelo final, foi considerada a interação somente se a mesma apresentasse associação significativa. A seleção das variáveis para o modelo final se deu a partir

da análise bivariada que apresentaram p-valor < 0,20 e por plausibilidade biológica. Nas análises multivariadas, considerou-se uma associação significativa valores de p-valor < 0,05.

5.9.3.1 ARTIGO 1

O primeiro artigo refere-se as análises sobre padrões alimentares pré-gestacionais e depressão gestacional. Foram realizadas análises exploratórias de acordo com a maior aderência a um único padrão alimentar. Para classificar as mulheres exclusivamente a um padrão alimentar, os escores foram divididos em quintis e a mulher que estava no maior quintil de um dos padrões alimentares era classificada como tendo maior aderência àquele padrão, porém se a mulher fosse classificada em mais de um padrão, a mesma era classificada naquele padrão alimentar com menor intervalo do escore. Para verificar a diferença entre as médias das variáveis contínuas de acordo com a maior aderência a um único padrão alimentar, empregou-se a análise de variância (ANOVA) e para testar a diferença das proporções das variáveis categóricas foi realizado o teste de qui-quadrado.

As mulheres que participaram do ensaio clínico aninhado ao estudo de coorte apresentaram maiores escores de depressão. Dessa forma, foram realizadas análises estatísticas para avaliar se a amostra de mulheres que deram seguimento ao estudo, totalizando 41 mulheres, poderiam ser incluídas no processo de modelagem. O objetivo foi evitar viés de seleção devido à exclusão das mulheres com maior risco de desenvolver depressão e também para aumentar o tamanho da amostra do estudo. Três modelos de LME foram propostos: (i) **Modelo 1** foram excluídas as informações das gestantes que participaram do ensaio clínico apenas a partir do terceiro trimestre (período em que a suplementação estava vigente). Nesse caso, foram incluídas as informações destas mulheres no primeiro e segundo trimestres gestacionais. (ii) **Modelo 2** incluiu todas as mulheres (da coorte observacional e do ensaio clínico) em todos os trimestres da gravidez na análise longitudinal. (iii) **Modelo 3** incluiu todas as mulheres (da coorte observacional e do ensaio clínico) em todos os trimestres gestacionais, mas a análise foi ajustada por uma variável que classificava as gestantes de acordo com tipo de estudo em que foram inseridas (de coorte observacional, grupo de tratamento ou placebo). Esse ajuste foi utilizado para eliminar o efeito da suplementação da análise. Após comparar o resultado dos modelos citados acima, verificamos pequenas diferenças no coeficiente e no p-valor entre os modelos. Dessa forma o modelo 3 foi selecionado como final, pois foi considerado o mais adequado.

Devido à perda de seguimento durante o estudo, foram realizadas análises para comparar as mulheres que finalizaram e aquelas que não finalizaram o estudo no terceiro trimestre

gestacional segundo variáveis selecionadas: EPDS (<11 ou \geq 11), idade (20-29 ou \geq 30 anos), estado marital (casada/em uma relação estável ou solteira), paridade (0-1 ou \geq 2 partos) e peso pré-gestacional (< 25 ou \geq 25 kg/m²).

5.9.3.2 ARTIGO 2

O segundo artigo refere-se à associação entre os padrões alimentares pré-gestacionais e sintomas de ansiedade durante a gestação e pós-parto. Nas análises descritivas desse artigo, além da análise que caracterizou a amostra de acordo com as variáveis selecionadas para o estudo, verificou-se a média de escores de sintomas de ansiedade em cada trimestre de seguimento que continha esses dados (segundo e terceiro trimestres gestacionais e pós-parto) por categorias das principais variáveis que foram para o modelo final do LME. As variáveis contínuas foram categorizadas da seguinte forma: (1º tercil/ 2º ou 3º tercis), idade (< 30/ \geq 30 anos), anos de escolaridade (\leq 8/> 8 anos), estado marital (casada ou união estável/solteira), número de partos (0 ou 1/ \geq 2 partos), IMC do início da gestação (< 25/ \geq 25 kg/m²), tabagismo (nunca fumou/fumante atual/ex-fumante), consumo de álcool gestacional (sim/não) e consumo energético total (1º ou 2º tercis/3º tercil). O LME foi empregado para avaliar as análises longitudinais bivariada e multivariada do estudo.

Os gráficos construídos para seleção dos modelos mais adequados não foram incluídos nos artigos, mas são apresentados em anexo (**Anexo 2**).

5.9.4 BANCO DE DADOS E SOFTWARE UTILIZADO PARA AS ANÁLISES ESTATÍSTICAS

Os dados coletados foram digitados em duplicata, seguido da análise de consistência. Os procedimentos anteriores foram realizados no *Census and Survey Processing System* (CSPro) versão 4.1. As análises estatísticas foram realizadas no *Stata Data Analysis and Statistical Software* (STATA) versão 12.0.

5.10 ASPECTOS ÉTICOS

O estudo que deu origem a este projeto de tese foi aprovado (**Anexo 3**) pelos Comitês de Ética em Pesquisa (CEP) da Maternidade Escola (Processo nº 0023.0.361.000-08) e do Instituto de Psiquiatria (Processo nº 0012.0.249.000-09), ambos da UFRJ, e pelo CEP da Secretaria Municipal de Saúde e Defesa Civil do Rio de Janeiro. A proposta está de acordo com os princípios éticos de não maleficência, beneficência, justiça e autonomia, contidos nas resoluções nº 196/96 e 466/12 do Conselho Nacional de Saúde (CNS, 1999 - Resolução nº 196/96; CNS, 2012 - Resolução nº 466/12) e assim como de acordo com o Código de Ética

Médica de 1988, no que diz respeito aos artigos 122 a 130 (CFM, 2001 - Resolução CFM nº 1.246/88).

As mulheres que aceiram participar do estudo, após esclarecimentos sobre o mesmo, assinaram duas vias do TCLE (**Anexo 4**), que foi obtido de forma livre e espontânea.

COORTE BRITÂNICA: THE AVON LONGITUDINAL STUDY OF PARENTS AND CHILDREN – ALSPAC

5.11 DESENHO DO ESTUDO

O ALSPAC também conhecido como ‘As Crianças dos anos Noventa’ - ‘*Chidren of the Nineties*’ é uma coorte de nascimentos de base geográfica com o objetivo de investigar fatores que influenciam a saúde, os comportamentos e o desenvolvimento ao longo da gestação, da infância e até a vida adulta. A **Figura 5** apresenta um diagrama estruturado, proposto por Golding & ALSPAC Study Team (2004) com os principais objetivos, incluindo possíveis exposições e desfechos, para o desenvolvimento dessa coorte de nascimento.

O estudo foi realizado no antigo condado de Avon, situado na região sudoeste da Inglaterra. A área de captação das gestantes ocorreu em três distritos de saúde (*District Health Authority - United Kingdom* - DHA/UK), o Southmead DHA, Frenchay DHA e Bristol & Weston DHA, os quais eram compostos pela cidade de Bristol e áreas urbanas e rurais em torno de Bristol, incluindo vilas, aldeias e comunidades agrícolas. A área de Avon em torno de Bath foi excluída.

A coleta de dados foi realizada por meio de questionários autopreenchidos, os quais foram enviados às gestantes. Após o preenchimento as mulheres devolviam os questionários por correios para o ‘*Institute of Child Health*’ em Bristol. Após o nascimento, 10% dos nascidos vivos foram selecionados aleatoriamente para participarem do estudo clínico do ALSPAC. Essas crianças foram acompanhadas aos 4, 8 e 12 meses e após esse período foram avaliadas de 6 em 6 meses até os 61 meses de idade (~ 5 anos).

O ALSPAC, até o momento, está dividido em três grandes fases: (i) período gestacional até primeira infância (< 7 anos), (ii) infância (7 anos) e (iii) infância tardia (> 7 até 13 anos), adolescência (≥ 13 e ≤ 16 anos) e transição para vida adulta (> 16 e ≤ 18 anos). A segunda fase ficou conhecida como “*Focus@7*”. Todas as crianças que estavam envolvidas no estudo nessa fase eram elegíveis, assim como os filhos das gestantes que foram recrutadas em 1991-92, mas não responderam aos questionários no período gestacional.

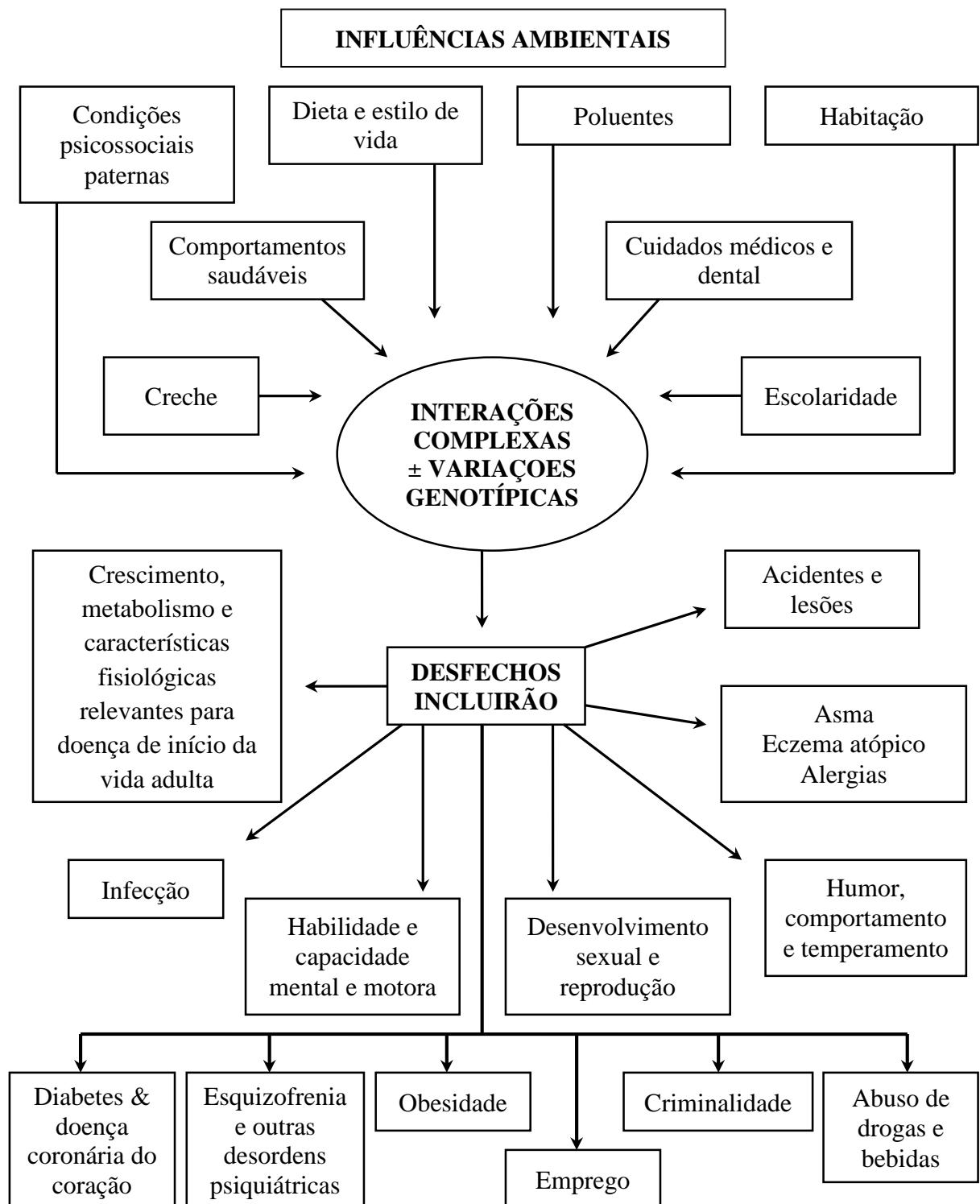


Figura 5. Diagrama estruturado dos objetivos planejados para o estudo, traduzido de Golding & ALSPAC Study Team (2004).

Os primeiros ensaios clínicos dessa coorte com toda a amostra ocorreram quando as crianças completaram 7 anos (fase II) e 8 anos (fase III). Aos 7 anos foram coletados dados antropométricos; exames na pele para verificar a ocorrência de eczema; pressão arterial e batimentos cardíacos; teste cutâneo de alergia; teste visual; timpanometria e audiometria; coordenação motora; testes de leitura, escrita e fonêmica; além de amostras sanguíneas e diários dietéticos. Aos 8 anos, essas crianças foram submetidas a testes de função pulmonar e brônquica; de habilidade cognitiva (coeficiente de inteligência); de fala e linguagem; de concentração; de acurácia não-verbal; e de memória em curto prazo. A partir da fase II as crianças começaram a responder alguns questionários, mas as principais informações, sobre dados socioeconômicos e demográficos, estilo de vida, hábitos alimentares e as demais informações coletadas da criança eram informados pelas mães em questionários específicos sobre a criança, ressaltando que a mãe também respondia um questionário com informações sobre ela.

Estudos metodológicos sobre a coorte de ALSPAC (Golding et al., 2001; Golding & ALSPAC Study Team, 2004; Boyd et al., 2013; Fraser et al., 2013) e uma página na internet (<http://www.bristol.ac.uk/alspac/>) estão disponíveis com as principais informações sobre o estudo. Atualmente as crianças que ingressaram na coorte estão no ‘Focus@24+’ e também está em andamento uma coorte com a segunda geração do ALSPAC com os filhos das crianças de 1991-92, ALSPAC - Generation 2 (ALSPAC - G2), *Children of the Children of the 90s study* (COCO90s).

5.12 CAPTAÇÃO DAS GESTANTES

Diferentes abordagens foram realizadas para captar as mulheres para participarem dessa coorte:

- i) Cartazes com o logo do estudo “*Children of the Nineties*” foram fixados em lojas, bibliotecas, farmácias, grupos maternos e infantis, clínicas de pré-natal, e qualquer outro local que uma gestante poderia visitar. Essas mulheres foram encorajadas a entrar em contato com a equipe do estudo para saber as informações e iniciar o protocolo do estudo, desde que atendesse os critérios de elegibilidade.
- ii) A equipe do ALSPAC abordou mulheres elegíveis para o estudo em rotinas de USG.
- iii) As parteiras comunicavam as gestantes sobre o estudo e as instruíam a entrar em contato com a equipe responsável pelo projeto.
- iv) Cobertura da mídia local e nacional em jornais, rádio e televisão convidando as gestantes para participarem do estudo.

5.13 CRITÉRIOS DE ELEGIBILIDADE

Os critérios de elegibilidade para participar desse estudo foram:

- i) Residir no condado de Avon;
- ii) Ter data prevista para o parto entre 1º de abril de 1991 e 31 de dezembro de 1992.

As mulheres que iniciaram o estudo, mas que mudaram da área programática foram excluídas da coorte de seguimento. No entanto, aquelas mulheres que finalizaram o protocolo do estudo durante a gestação (responderam todos os questionários do estudo referente ao período gestacional) e mudaram da região onde foi desenvolvido o estudo, não foram excluídas, mesmo se ainda estivessem grávidas no momento da mudança.

A **Figura 6**, proposta por Boyd et al. (2013), apresenta o processo de recrutamento de gestantes para o ALSPAC e mulheres que entraram para a coorte na fase II e III.

5.14 LOGÍSTICA DO ESTUDO

O ALSPAC coletou dados das mães, dos pais e das crianças e até os dias atuais coletam dados dessas crianças. Todos os questionários que foram enviados ou aplicados aos participantes estão disponíveis na página da internet do estudo. Os manuscritos incluídos nessa tese de doutorado utilizaram dados maternos durante a gestação e dos filhos aos 7 e 8 anos de idade. Dessa forma serão apresentados apenas a logística do estudo considerando os períodos mencionados anteriormente.

Durante a gestação quatro questionários foram enviados às mulheres: **A** ‘*Your Environment*’ (**Anexo online 7**), **B** ‘*Having a Baby*’ (**Anexo online 8**), **C** ‘*Your Pregnancy*’ (**Anexo online 9**), **D** ‘*About Yourself*’ (**Anexo online 10**). Apenas o segundo **B** e terceiro **C** questionários necessitavam ser enviados para a equipe do estudo em período fixo durante a gestação, na 18^a e 32^a semanas gestacionais, respectivamente. Esses questionários relatavam informações maternas sobre o período gestacional. Os dados de consumo alimentar gestacional foram obtidos no questionário **C**. O primeiro questionário **A** tinha o objetivo de investigar as possíveis causas de desfechos fetais indesejáveis e o mesmo era administrado após a inclusão da mulher no estudo, antes da 14^a semana gestacional.

O último questionário também não tinha um período fixo para ser enviado para a equipe do ALSPAC, e podia ser enviado após o nascimento da criança, porque nesse questionário eram coletados dados clínicos, sociais e ambientais anteriores a gestação. As gestantes que foram recrutadas após a 18^a semana, receberam um único questionário, ‘*Your Home & Lifestyle*’ (não disponível na página do ALSPAC), com a combinação de informações contidas nos questionários **A** e **B**.

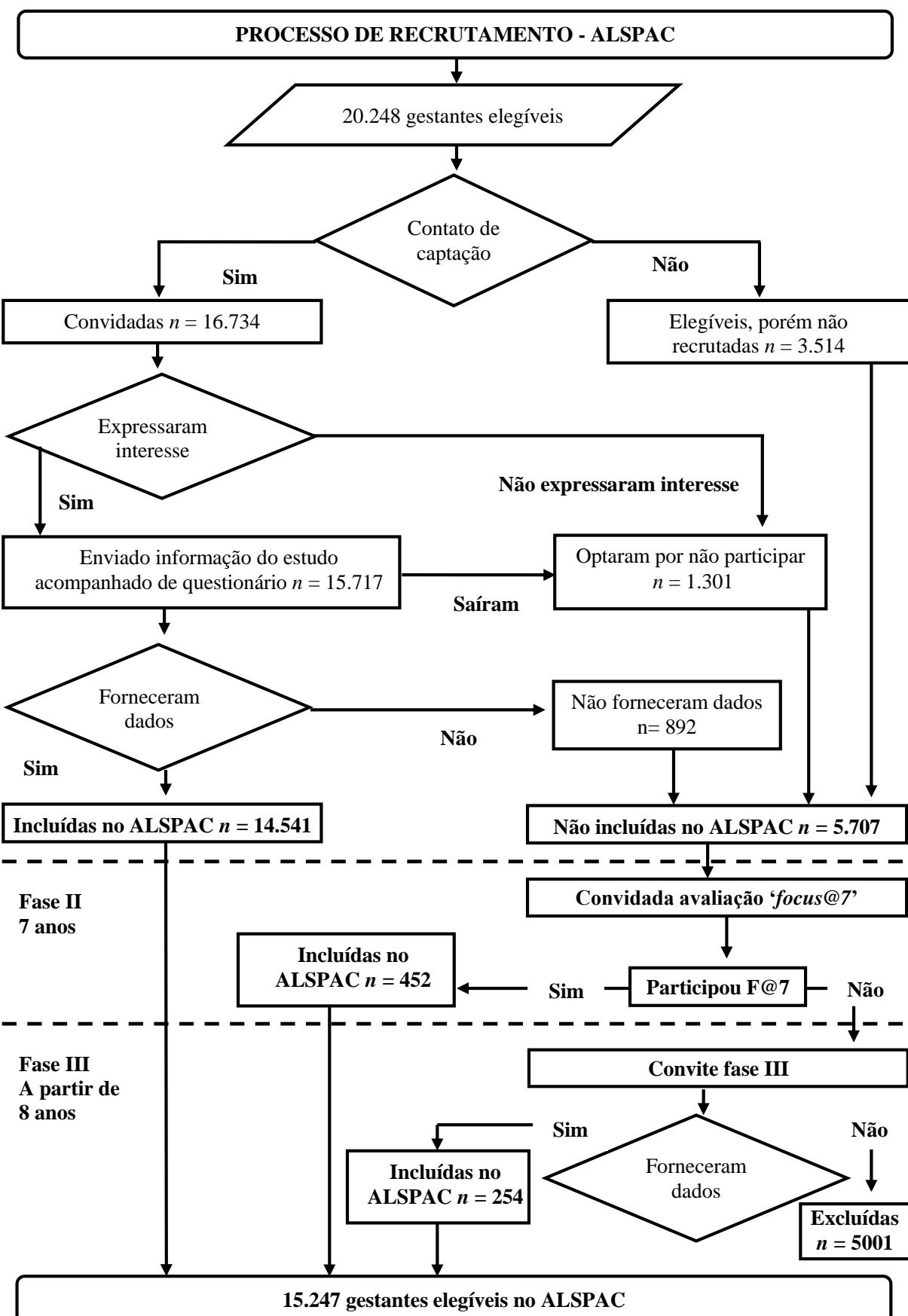


Figura 6. Fluxograma de recrutamento ALSPAC, traduzido de Boyd et al., 2013.

Aos 7 anos (81 meses) as mães responderam um questionário **KQ** ‘*My Daughter/Son at School*’ (**Anexo online 11**) com vários dados sobre as crianças, inclusive consumo alimentar. Dados sobre desenvolvimento neurológico infantil foram coletados por meio de instrumentos validados aplicados diretamente com a criança.

5.15 VARIÁVEIS DO ESTUDO

5.15.1 AVALIAÇÃO DO CONSUMO ALIMENTAR DURANTE A GESTAÇÃO

As mulheres autopreencheram um QFA não quantitativo composto dos principais alimentos consumidos no Reino Unido quando tinham aproximadamente 32 semanas gestacionais. O QFA era composto por 43 alimentos com cinco opções de frequência: (i) nunca ou quase nunca, (ii) uma vez em duas semanas, (iii) uma a três vezes por semana, (iv) quatro a sete vezes por semana e (v) mais de uma vez ao dia. As opções de frequência foram convertidas em frequências semanais, as quais foram (i) 0 vezes/semana, (ii) 0,5 vezes/semana, (iii) 2 vezes/semana, (iv) 5,5 vezes/semana e (v) 10 vezes/semana (Rogers & Emmett, 1998).

Foram coletados dados sobre a frequência diária para alguns alimentos com alta frequência de consumo, como números de copos de chá e café e números de fatias de pães. Havia cinco opções de frequências de consumo diário, as quais foram convertidas em frequências semanais: (i) menos que uma vez ao dia = 0 vezes/semana, (ii) uma a duas vezes ao dia = 10,5 vezes/semana, (iii) três a quatro vezes ao dia = 24,5 vezes/semana e (iv) cinco ou mais vezes ao dia = 42 vezes/semana. O tipo de pão (branco e outros) e o tipo de leite (integral e outros) também foram referidos. A quantidade de leite consumido foi obtida pela soma do total consumido em chá, café, cereal matinal, sobremesas a base de leite, leite puro e em bebidas lácteas (Rogers & Emmett, 1998). As gestantes com mais de 10 itens alimentares faltantes foram excluídas das análises de consumo alimentar, porém quando o número de dados faltantes era menor que 10 foi atribuída a menor frequência semanal ou diária para esses itens alimentares (Northstone et al., 2008b; Smith et al., 2011).

5.15.2 VARIÁVEIS INCLUÍDAS NO ARTIGO 3

5.15.2.1 NUTRIENTES MATERNOS

O consumo diário de nutrientes foi estimado por meio do QFA e a base de dados da composição dos alimentos foi obtida das seguintes tabelas de composição nutricional: *5th edition of McCance and Widdowson’s, ‘The Composition of Foods’* e suplementos (The Royal Society of Chemistry 1988 - 1993). O QFA não era quantitativo, assim foram estimadas porções

médias e padronizadas para estimar a porção consumida (Ministry of Agriculture, 1993). Os dados obtidos do QFA foram convertidos em frequências de consumo semanais, porém os nutrientes foram estimados em consumo de nutrientes diários. Assim, os valores dos nutrientes obtidos foram divididos por sete (Rogers & Emmett, 1998).

5.15.2.2 PADRÕES ALIMENTARES DOS FILHOS AOS 7 ANOS

O questionário **KQ** enviado às mães quando os filhos estavam com 81 meses (~7 anos) incluíam um QFA composto por 94 itens alimentares e bebidas. Esse questionário tinha como objetivo avaliar as refeições, alimentos e bebidas oferecidas as crianças pelas mães. Assim, os itens alimentares consumidos fora de casa (como em escolas, festas e outros) não foram incluídos. Os dados obtidos no QFA foram agrupados em 57 grupos alimentares, os quais foram utilizados para identificar os padrões alimentares por análise de cluster (Smith et al., 2011).

Três padrões alimentares por cluster foram identificados. O maior cluster (4.177 crianças) foi denominado de alimentos processados, ‘*Processed food cluster*’, e foi caracterizado por maior consumo de pão branco, carne processada, bebidas gaseificadas, suco industrializados, salgadinhos chips, batata frita, biscoitos, doces e sorvete e menor consumo de frutas, vegetais, batatas (não fritas), cereais integrais e água, em relação aos demais padrões alimentares.

O segundo cluster (2.065 crianças) foi composto por crianças que tinha o maior consumo de pães não branco, frutas, vegetais, proteína vegetal para substituir a carne, alimentos vegetarianos, peixe, massas, arroz, cereais integrais e água e tinham menor consumo de carnes, bebidas gaseificadas, suco industrializados, chá, café e salgadinhos chips, quando comparado aos demais padrões alimentares, e por isso foi denominado a base de planta, ‘*Plant-based cluster*’.

O terceiro padrão alimentar (2.037 crianças) foi denominado tradicional britânico, ‘*Traditional British cluster*’, pois foi caracterizado por crianças com elevado consumo de carnes e batatas e menos de proteína vegetal para substituir a carne, mas ainda tinha frequente consumo de leite e produtos lácteos e sobremesas a base de leite.

5.15.3 VARIÁVEL INCLUÍDA NO ARTIGO 4

5.15.3.1 COEFICIENTE DE INTELIGÊNCIA - QI (VARIÁVEL DEPENDENTE)

Aos 8 anos todas as crianças que estavam incluídas no ALSPAC e filhos das mulheres que foram recrutadas durante a gestação, porém não participaram do estudo, foram convidadas

a participar dessa nova fase da coorte (fase III), quando foram avaliadas as habilidades cognitivas das crianças por psicólogos treinados e com procedimentos neuropsicológicos padronizados.

O coeficiente de inteligência, também conhecido como QI, foi avaliado por uma versão adaptada e reduzida da *Wechsler Intelligence Scale for Children* (WISC) - III (Wechsler et al., 1992). A WISC III é dividida em 13 subtestes e com os escores obtidos dos subtestes é possível ponderar os Quocientes de Inteligência verbal (QIV) e de execução (QIE) e do Quociente global (QIG). Os subtestes são divididos em (i) escala verbal: informação, semelhanças, aritmética, vocabulário, compreensão e dígitos; e (ii) escala de execução ou não-verbal (performance): completar figuras, arranjo de figuras, código, organizar blocos (cubos), armar objetos, procurar símbolos e labirintos. Além dos dados de QI, a WISC III permite avaliar compreensão verbal (abrangendo os subtestes informação, semelhanças, vocabulário e compreensão), organização perceptual (completar figuras, arranjo de figuras, e armar objetos), resistência a distração (aritmética e dígitos) e velocidade de processamento da informação (códigos e procurar símbolos) (Wechsler, 1992; Wechsler, 2002; Mello et al., 2011).

Foram aplicados itens selecionados de cada subteste da WISC - III (5 itens do subteste verbal e 5 do subteste de execução), exceto para o subteste de codificação, o qual foi aplicado completo. Foram calculados escores brutos pela soma dos itens individuais de cada subteste e multiplicado por 2 para completar figuras, informação, aritmética, vocabulário, compreensão e arranjo de figuras; multiplicado por cinco terços (~ 1,67) para semelhanças; e multiplicado por 3 meios (~ 1,5) para a armar objetos e organizar blocos. Esse procedimento foi realizado para tornar comparável os escores obtidos da escala resumida com a escala completa. Os escores brutos obtidos foram convertidos em escores padronizados por idade utilizando tabelas fornecidas no manual da WISC - III. Dessa forma, foram determinados os escores da escala completa do QI e das subescalas QI verbal e QI de execução (Joinson et al., 2007).

5.15.4 VARIÁVEIS SOCIOECONÔMICAS, DEMOGRÁFICAS, OBSTÉTRICAS E DE ESTILO DE VIDA

As variáveis socioeconômicas, demográficas, obstétricas e de estilo de vida foram obtidas por meio dos questionários autopreenchidos durante a gestação (**Anexos online 7 a 11**). As variáveis incluídas nos estudos realizados com dados da coorte do ALSPAC foram: escolaridade materna [baixa (sem exames acadêmicos ou formação de nível profissional), média (Nível O - exame acadêmico normalmente realizado aos 16 anos) e alta (Nível A - exame acadêmico normalmente realizado aos 18 anos ou graduado)], habitação (hipotecada/própria,

casas públicas e outro), número de indivíduos por cômodos (< 1 e > 1 pessoa/cômodo), eventos estressantes da vida (0-7 e 8-18), idade materna (< 20 anos, 20 a 30 anos e > 30 anos), dificuldade financeira (sem, alguma e muitas), estado marital (sim e não), tabagismo durante a gestação (nunca fumou, ex-fumante e fumante atual), consumo de álcool durante a gestação (nunca bebeu, parou de beber e continua bebendo), paridade (0, 1 e ≥ 2) e origem étnica (branco, negro e asiático). A dificuldade financeira foi obtida baseada em uma lista com cinco itens [alimentação, vestuário, aquecimento, aluguel/hipoteca e itens (não especificados) para as crianças] com quatro opções de dificuldade (muita, razoável, alguma e não). A pontuação máxima obtida nessa lista era 20 pontos, os quais foram categorizados em sem dificuldade financeira (escore = 0), alguma (escore ≥ 1 a ≤ 5) ou muita (escore ≥ 6).

Ainda foram coletadas informações sobre o sexo da criança (masculino e feminino), idade da criança (anos) e amamentação [sim (duração da amamentação foi de < 1 mês a > 6 meses) e não (nunca amamentou)]. Essas informações foram utilizadas exclusivamente no artigo 4.

5.15.5 VARIÁVEIS ANTROPOMÉTRICAS

As variáveis antropométricas obtidas nessa coorte foram o peso pré-gestacional e a altura, ambos auto-referidos na 12^a semana gestacional. Com essas medidas foi possível calcular o IMC pré-gestacional [peso (kg)/ altura² (m)] e classificar segundo os pontos de corte propostos pela IOM (2009): baixo peso ($< 18,5$ kg/m²), eutrofia (18,5 - 24,9 kg/m²), sobrepeso (25,0 - 29,9 kg/m²) e obesidade ($\geq 30,0$ kg/m²). O IMC pré-gestacional foi utilizado como categórico no terceiro artigo e contínuo no quarto artigo.

5.16 ANÁLISES ESTATÍSTICAS

5.16.1 IDENTIFICAÇÃO DOS PADRÕES ALIMENTARES POR ANÁLISE DE CLUSTER

Os padrões alimentares das gestantes do ALSPAC foram obtidos por análise de cluster. A análise de cluster agrupa os indivíduos em subgrupos/clusters não sobrepostos, isto é, exclusivamente em um único cluster (padrão alimentar) que apresenta um consumo alimentar relativamente homogêneo. O método mais utilizado para identificar padrões alimentares é o k-médias (*k-means*). Esse método minimiza a soma dos quadrados das distâncias entre a ingestão alimentar de cada mulher e da média do cluster (Newby & Tucker, 2004).

Os clusters foram obtidos por meio de 47 itens alimentares do QFA. Para esse estudo foram utilizando os 44 grupos de alimentos definidos por Northstone et al. (2008b) em seu estudo que identificaram padrões alimentares por ACP nessas gestantes. Além desses grupos

de alimentos, foram incluídos 3 novos grupos: leite integral, outros leites e álcool. Alguns alimentos incluídos no QFA foram mensurados por escalas diferentes, como o chá, café, refrigerante a base de cola, pães e leite. Assim, todos os itens alimentares do QFA foram padronizados pela subtração da média e divisão pela variação (menor e maior valor) de cada variável. A padronização das variáveis normalmente é feita pela subtração da média e dividida pelo desvio padrão de cada variável (Northstone et al., 2008b; Northstone et al., 2008c; Smith et al., 2011), entretanto, o método de padronização apresentado anteriormente é considerado o mais adequado para análise de clusters (Gnanadesikan et al., 1995). O algoritmo k-média padronizado pode não encontrar a melhor solução que minimiza essa soma dos quadrados das médias (Everitt et al., 2001), por isso, o algoritmo foi executado 100 vezes, com diferentes posições iniciais, com o objetivo de encontrar o padrão com a menor soma dos quadrados.

Para obter os padrões alimentares por clusters foram realizadas análises fixando de 2 a 7 clusters. O algoritmo foi aplicado em todas as análises com os diferentes números de soluções fixadas. O melhor modelo foi escolhido considerando a variância total explicada, o número de indivíduos em cada cluster e a interpretação de cada solução obtida. A análise discriminante linear também foi utilizada para selecionar o melhor modelo. Essa análise avalia o número de mulheres que mudariam de cluster se essas fossem separadas em grupos e as análises fossem realizadas separadamente. A análise de variância (ANOVA) e o método de Tukey-Kramer foram aplicados para verificar a diferença entre as médias de cada item alimentar segundo os clusters.

5.16.2 ARTIGO 3

Foram realizadas análises descritivas com as variáveis selecionadas para esse estudo com o objetivo de caracterizar a amostra com e sem informação de dados dietéticos e segundo os padrões alimentares identificados. Para isso foi utilizada o teste qui-quadrado, uma vez que todas as variáveis eram categóricas. A ingestão de nutrientes absoluta e ajustada por energia (Willett et al., 1997) foi descrita para cada padrão alimentar obtido e para testar a diferença entre as médias dos nutrientes em cada cluster foi utilizado a análise de variância ANOVA e o método de Tukey-Kramer.

Os padrões alimentares maternos e de seus filhos foram comparados por meio de tabulação cruzada (*cross-tabulation*) e foi calculada a proporção de crianças que permaneceram em padrões alimentares similares aos que foram aderidos pelas mães durante a gestação. Foi realizada regressão logística multinomial para verificar a associação entre o cluster materno e o cluster dos filhos. Foram realizados modelos de regressão logística multinomial para a

análise bivariada. Nesses modelos cada cluster materno e infantil foi a categoria de referência. Na análise ajustada, foram selecionados os modelos que apresentaram os maiores valores de razão de risco relativos, pois foram os padrões alimentares que tiveram maior associação.

5.16.3 ARTIGO 4

Para as análises realizadas nesse artigo foram mantidas as crianças de gestação única e a primeira criança da gestação de gêmeos (Hibbeln et al., 2007). As variáveis de confusão incluídas nesse estudo estavam associadas ($p < 0,20$) à exposição (padrões alimentares maternos) e desfecho (QI aos 8 anos). O teste T de *Student* e o teste qui-quadrado foram utilizados para verificar a diferenças das variáveis de confusão, contínuas e categóricas, respectivamente, entre crianças com e sem informação sobre QI. Para verificar a diferença entre as variáveis de confusão e os padrões alimentares foi utilizado ANOVA, método de Tukey-Kramer e teste qui-quadrado.

A imputação múltipla é uma alternativa para amenizar perdas de seguimento, que é um problema comum em estudos longitudinais. Os dados faltantes tendem a reduzir o poder amostral do estudo. No ALSPAC, há informações substanciais para imputar os dados faltantes. As múltiplas imputações por equações em cadeia (*Multiple Imputation by Chained Equations - MICE*) é o método mais utilizado para a imputação de dados (White et al., 2011). Este método baseia-se na perda de dados ao acaso ('*missing at random*' - MAR), o qual supõe que os dados faltantes podem ser previsíveis por outros dados observados no estudo. Dessa forma, a primeira etapa da imputação para esse estudo consistiu em verificar as variáveis que apresentavam boa correlação entre os dados de QI. As variáveis preditoras para a imputação foram os diferentes desfechos de neurodesenvolvimento infantil avaliados anteriormente ao QI aos 8 anos. Correlações com p-valor maior que 0,2 foram incluídas nos modelos de MICE. As seguintes variáveis apresentaram elevada correlação com os dados de QI: escores de vocabulário e gramática aos 24 meses, QI verbal e de performance aos 49 meses, motor fino aos 42 meses e escores de hiperatividade aos 81 meses. Essas variáveis foram incluídas como variáveis preditoras em todos os modelos de imputação.

Dois modelos de imputações foram realizados nesse estudo e foram imputados dados para aqueles indivíduos que tinham informações sobre consumo alimentar durante a gestação ($n = 12.039$ gestantes). Em ambos os modelos foram imputados dados de QI e todos as variáveis de confusão. Entretanto, no primeiro modelo foram mantidos apenas os indivíduos que tinham pelo menos um dado de QI aos 8 anos e algum dado das variáveis de neurodesenvolvimento infantil que tiveram boa correlação com QI ($n = 6.817$ indivíduos). No segundo modelo de

imputação foram incluídos todos os indivíduos que tinha dados de consumo alimentar durante a gestação e foram imputados dados para QI e demais variáveis ($n = 12.039$ indivíduos). Foram gerados 100 padrões de dados incompletos e todas as variáveis foram imputadas ao mesmo tempo, utilizando métodos adequados de imputações multivariadas, isso é diferentes modelos de regressão (linear, logística e multinomial). A fração de dados faltantes (*fraction of missing information - FMI*) foi utilizada para verificar se o número de imputações era suficiente para a análise. A regra de *thumb* sugere que o número de imputações (m) deve ser pelo menos igual ao percentual de dados faltantes do banco de dados, o qual pode ser avaliado pela equação: $m \geq 100 * \text{FMI}$ (White et al., 2011).

Modelos de regressão linear não ajustados e ajustados foram realizados para verificar a associação entre os padrões alimentares maternos e o QI aos 8 anos. As variáveis de exposição QI verbal, QI de performance e escala completa de QI foram analisadas separadamente. O padrão alimentar materno caracterizado por alimentos saudáveis foi considerado a categoria de referência entre os padrões alimentares. A análise multivariada foi ajustada por todos as variáveis que foram associadas com os padrões alimentares maternos e o QI aos 8 anos.

As regressões lineares foram analisadas em três modelos diferentes: (i) todos os dados disponíveis sem imputação ($n = 5.413$ a 6.582 indivíduos avaliados, devido o número de dados faltantes), (ii) dados faltantes imputados, considerando apenas os indivíduos que tinham pelo menos um dado de QI aos 8 anos e algum dado das variáveis de neurodesenvolvimento infantil que tiveram boa correlação com QI aos 8 anos ($n = 6.817$ indivíduos), (iii) todos os dados faltantes de QI aos 8 anos e variáveis de confusão dos indivíduos que tinham dados de consumo alimentar durante a gestação ($n = 12.039$ indivíduos).

5.16.4 BANCO DE DADOS E SOFTWARE UTILIZADO PARA AS ANÁLISES ESTATÍSTICAS

Para acessar o banco de dados do ALSPAC inicialmente foi necessário fazer uma proposta de um projeto o qual foi submetido e avaliado pelos coordenadores do estudo. O projeto proposto para os estudos com os dados do ALSPAC incluídos nessa tese de doutorado foi aprovado e o número do projeto é B2354 (**Anexo 5**). A proposta pode ser acessada pela seguinte página de internet: <https://alspac.cse.bris.ac.uk/researchproposals/rps/>. A etapa posterior consistiu na seleção das variáveis que foram incluídas e necessárias para desenvolver o projeto. Na seguinte página da internet <http://www.bristol.ac.uk/alspac/researchers/data-access/data-dictionary/> é possível verificar o dicionário de dados e o catálogo das variáveis. O banco de dados foi liberado após o pagamento e o acesso devia ser exclusivo em um único

computador, de preferência na *University of Bristol*, para evitar o compartilhamento das informações desse estudo.

As análises foram realizadas no STATA versão 13.1.

5.17 ASPECTOS ÉTICOS

O estudo teve aprovação do comitê de ética do ALSPAC, e todos os comitês de ética das unidades de saúde de Bristol, Southmead e Frenchay onde foi realizado (**Anexo 6**) <http://www.bristol.ac.uk/alspac/researchers/data-access/ethics/lrec-approvals/>.

6 RESULTADOS

A seção de resultados foi dividida em quatro artigos elaborados para a tese de doutorado, sendo os dois primeiros publicados e os dois últimos prontos para sumissão.

6.1 ARTIGO 1: *Prepregnancy healthy dietary pattern is inversely associated with depressive symptoms among pregnancy Brazilian women.*

6.2 ARTIGO 2: *Association of prepregnancy dietary patterns and anxiety symptoms from midpregnancy to early postpartum in a prospective cohort of Brazilian women.*

6.3 ARTIGO 3: *Dietary patterns by clusters analysis in pregnant women: relationship with nutrient intakes and dietary patterns in 7 years old offspring.*

6.4 ARTIGO 4: *Maternal dietary patterns during pregnancy and intelligence quotient in the offspring at 8 years of age: findings from the ALSPAC cohort.*

6.1 ARTIGO 1. PRE-PREGNANCY HEALTHY DIETARY PATTERN IS INVERSELY ASSOCIATED WITH DEPRESSIVE SYMPTOMS AMONG PREGNANT BRAZILIAN WOMEN (Anexo 7)**Abstract**

Dietary patterns before pregnancy may be associated to depressive symptomatology during pregnancy. The aim of this study was to identify dietary patterns before pregnancy, and to examine the association between these dietary patterns and depressive symptoms during pregnancy. A prospective cohort of 248 healthy pregnant women was followed at 5–13, 20–26, and 30–36 gestational weeks. Dietary intake was obtained using a food frequency questionnaire administered between 5–13 gestational weeks, referring to the 6 months preceding gestation, and factor analysis (principal components) was applied to identify dietary patterns. The Edinburgh Postnatal Depressive Scale (EPDS) was used to evaluate depressive symptoms during three follow-up pregnancy points. A multiple linear mixed-effect model was applied to verify the association between dietary patterns and depressive symptoms adjusted for obstetric factors, socioeconomic status, and energy intake. Three pre-pregnancy dietary patterns were identified: *common-Brazilian*, *healthy*, and *processed*. Together, these patterns explained 36.1% of the total percentage of variance, and the eigenvalues were 2.88, 2.12, and 1.86, respectively. The mean depressive symptoms scores were 9.0 (95%CI: 8.4, 9.6), 7.2 (95%CI: 6.5, 7.8), and 7.0 (95%CI: 6.4, 7.7) for the 1st, 2nd and 3rd trimester, respectively. The rate of decrease in depressive symptoms was -0.088/week (95%CI: -0.115, -0.061; $P < 0.001$). In the multiple longitudinal linear regression model, the *healthy* dietary pattern before pregnancy was inversely associated with depressive symptoms (β : -0.723; 95%CI: -1.277, -0.169; $P = 0.011$). High adherence to the *healthy* pattern before pregnancy was associated with lower EPDS scores during pregnancy in women from Rio de Janeiro, Brazil.

Keywords: Depression, Food consumption, Pregnancy, Cohort study.

Introduction

During pregnancy, women undergo environmental, psychological and metabolic changes, increasing the likelihood of mental health disorders (1). The prevalence of depressive symptoms during pregnancy varies from 10% to 20% in developed and developing countries (2). Depressive symptoms increase the risk of maternal and fetal adverse outcomes, such as inadequate prenatal care, insufficient gestational weight gain, low birth weight and postpartum depression (3-5).

Socio-demographic factors such as poverty and lack of a partner have been shown to be risk factors for depressive symptoms during pregnancy (1,6,7). In addition, nutrient and energy requirements often increase during pregnancy and many nutrients are critically important during this period (8,9), with deficiencies associated with depressive symptoms (10-13).

Different from the single nutrient-based approach, the evaluation of dietary patterns identifies dietary habits based on an assessment of food group intake. This method enables a broader analysis of the diet, including the associations and interactions between nutrients (13,14). In this way, this type of dietary analysis may be a useful tool to evaluate the association between nutritional status and depression during pregnancy.

Based on this context, some studies have recently investigated the association between dietary intake during pregnancy and depressive symptoms during pregnancy and postpartum (10,11,15,16). Chatzi et al. (15) evaluated 529 pregnant women and observed that the women's adherence to a 'health conscious' dietary pattern during pregnancy was associated with lower postpartum depressive symptom scores. Similarly, a study that evaluated 1,745 pregnant women found that a higher intake of fish and polyunsaturated n-3 fatty acids (eicosapentaenoic (EPA) and docosahexaenoic (DHA) acids) were independently associated with a lower prevalence of depressive symptoms during pregnancy (11). Studies investigating dietary patterns among non-pregnant population have shown a lower likelihood of depression among women with higher adherence to dietary patterns considered as 'healthy' or 'traditional' (12,17,18). Le Port et al. (17) assessed the dietary patterns of 3,132 French women aged 35-59 years and found a protective association of higher adherence to the 'healthy' and 'traditional' dietary patterns and less likelihood to report depressive symptoms at both study baseline and 9 years of follow-up, while higher adherence to the 'snacking' pattern was directly associated with depressive symptoms. Jacka et al. (18) evaluated 1,046 women aged 20-93 years and found that a 'traditional' pattern, which was characterized by healthy food, was inversely associated with major depression, while the 'Western' pattern was directly associated with major depression.

Considering the prevalence of depressive symptoms during pregnancy and the relations previously shown between dietary patterns and depressive symptoms among non-pregnant populations, the aim of this study was to identify dietary patterns before pregnancy and to examine their longitudinal association with depressive symptoms. We hypothesized that a higher adherence to a dietary pattern before pregnancy composed of healthy foods is associated with lower depressive symptoms during pregnancy.

Methods

This study comprised a prospective observational cohort of pregnant women that received prenatal care at a public health center in Rio de Janeiro, Brazil. Pregnant women seeking prenatal services were invited to participate and were recruited for enrollment if they met the following eligibility criteria: (i) between 5 and 13 weeks of pregnancy during the enrollment period; (ii) aged between 20 and 40 years; (iii) free from any chronic diseases (except obesity measured as pre-pregnancy Body Mass Index - $BMI \geq 30 \text{ kg/m}^2$); (iv) free from infectious diseases; (v) singleton pregnancy; (vi) residence next to the study catchment area; and (vii) maintained prenatal care where the study was performed. Recruitment occurred between November 2009 and October 2011 in Heitor Beltrão public health center. The pregnant women were followed three times during pregnancy, at 5-13, 20-26 and 30-36 gestational weeks.

A total of 299 pregnant women were recruited for this study. After entering the study, we excluded women who changed their prenatal care health unit ($n = 1$), had twin pregnancies ($n = 4$), were diagnosed with an infectious or non-communicable disease ($n = 12$), presented missing data at baseline ($n = 15$), were at > 13 gestational weeks ($n = 16$), and reported miscarriage ($n = 3$). After exclusions, the total sample comprised 248 pregnant women.

After the second trimester visit (week 20-26 of gestation), a sub-sample of 61 women were invited to participate in a clinical trial that aimed to investigate the effect of omega-3 supplementation on postpartum depression (PPD) and was nested within the cohort. Thirty-four of these women received the omega-3 supplementation. These women were identified as being at risk for PPD based on a past history of depression or a depressive symptom score ≥ 9 based on the Edinburgh Postnatal Depression Scale (EPDS). These data were obtained at baseline using specific questionnaires. The women were randomized to receive gelatin capsules containing omega-3 (fish oil) or placebo composed by soybean oil, the most used cooking oil for the Brazilian population. The treatment group capsules contained a total dose of 1.8 grams

of omega-3 per day (1.08 g of EPA and 0.72 g of DHA). Only 41 women completed the supplemental trial, and 20 of them were supplemented.

Dietary patterns

Dietary intake was obtained through a semi-quantitative food frequency questionnaire (FFQ) that included 82 food items, nonalcoholic and alcoholic beverages, and was based on a FFQ validated for the adult population of Rio de Janeiro (19). This FFQ was administered between 5 and 13 weeks of gestation and referred to the six months preceding the gestational period.

The FFQ had eight frequency options: (i) more than three times a day; (ii) two to three times a day; (iii) once a day; (iv) five to six times a week; (v) two to four times a week; (vi) once a week; (vii) one to three times a month; and (viii) never or hardly ever. The frequency options were transformed into daily frequencies as follows: (i) 4; (ii) 2.5; (iii) 1; (iv) 0.79; (v) 0.43; (vi) 0.14; (vii) 0.07; and (viii) 0 times per day. The daily energy intake in kilocalories and nutrient intake were obtained using the DietSys software, version 4.02 (20). We used the Brazilian Food Composition Table (21) and added food items from the United States Department of Agriculture, National Nutrient Database for Standard Reference (22).

Foods that were not regularly consumed by the subject (e.g. consumed by fewer than 20% of the women) were excluded. They included lard and alcoholic beverages (wine, beer and vodka) and dried meat/codfish. These foods did not compose a regular diet of the subjects and had lower correlations with other defined food groups (13,23). The remaining 77 food items were combined into 19 food groups based on similarities in nutrient composition, frequency of consumption, and the particular dietary habits of this population. Items that were consumed by 80% or more of the subjects (24) or presented differences in nutritional composition were kept separately (rice, beans, bread, sugar, fish, coffee, and tea). The same food groups were used to identify the dietary patterns before pregnancy and during pregnancy.

The 19 food groups were as follows: (i) rice; (ii) beans; (iii) breads; (iv) cakes and cookies-crackers; (v) pasta, roots and tubers - pasta; gnocchi/lasagna/ravioli; baked/mashed potato; cassava/yam; cassava flour; and polenta; (vi) meats and eggs - pork; beef; chicken; barbecue; giblets (gizzard, heart, liver, stomach/tripe, kidneys); and eggs; (vii) vegetable spices - onion; garlic; and red/green/yellow pepper; (viii) dairy products - cheese; milk; cottage cheese; and yogurt; (ix) green vegetables and legumes - lentils/peas/chickpeas; lettuce; cabbage; kale; cauliflower/broccoli; tomato; cucumber; chayote; squash; zucchini; carrots; beets; okra; and pea pods; (x) fruit and fruit juice - orange/tangerine; banana; papaya; apple;

watermelon/melon; pineapple; grape; mango; and fruit juices/pulp; (xi) fish; (xii) sausages and deli meats - sausage/frankfurter; cold cuts (bologna, ham, fatty ham, and salami); and bacon; (xiii) fat - butter and margarine; (xiv) fast food and snacks - pizza; hamburgers; French fries/chips,straw potatoes; mayonnaise; snacks; popcorn; fried/baked salted pastries; canned vegetables; and peanuts; (xv) coffee; (xvi) tea; (xvii) sodas; (xviii) candies - ice cream; candies/caramels; chocolate powder; chocolate bars/bonbon; fruit jam/jelly; and sweet dairy; and (xix) sugar.

The sample size of the present study was sufficient to identify dietary patterns by applying principal component analysis (PCA). This dietary analysis requires at least 5 subjects for each food group when the FFQ has more than 15 foods items (23,25). We aggregated the 19 food groups to identify the dietary patterns before pregnancy. Therefore, the analysis required at least 95 women. The number of subjects analyzed in this study was consistent with the method requirements.

Depressive symptoms

The EPDS was administered to measure depressive symptoms at all three gestational follow-up visits. This instrument consists of a 10-item screening scale that inquires about the mother's mood in the past seven days. Each item has four answer options that are assigned a score from 0 to 3 (total scores range from 0 to 30). The EPDS was developed for use in the postpartum period (26) and has also been validated for use in pregnancy (27).

Santos et al. (28) translated the EPDS scale into Portuguese and validated it in a sample of mothers from Pelotas, southern Brazil. In the current study, depressive symptoms were measured using the Portuguese version of the EPDS administered by trained interviewers. The internal consistency reliability of the EPDS for our study sample revealed a Chronbach's alpha of 0.74, 0.79, and 0.78 for the first, second and third trimester of pregnancy, respectively.

Covariates assessment

The following variables were included in the analysis: age (years), education (years of education), marital status (married/stable partnership or single), parity (number of deliveries), and unplanned pregnancy (no/yes). These data were obtained using a structured questionnaire administered at baseline.

The gestational age (weeks) was measured using the first obstetric ultrasonography if the age was assessed before 26 weeks of gestation ($n = 210$, 84.7%). When the pregnant women

did not have the ultrasonography available ($n = 38$, 15.3%), we used the reported date of the last menstrual period to calculate the gestational age.

Weight and height were measured using standard methods by trained interviewers (29). Height was measured in duplicate using a portable stadiometer (Seca Ltd., Hamburg, Germany). When the measurements differed by more than 0.5 cm, a third measurement was performed, and the mean of the two similar measurements was used. Height was measured only at the first follow-up visit. Weight was assessed in each gestational trimester with an electronic scale (Filizzola PL 150, Filizzola Ltda, Brazil) with a 150-kg capacity and 0.1-kg variation. BMI [weight (kg)/height (m)²] was calculated at all three follow-up visits.

The total energy intake obtained by the FFQ before pregnancy was used as a co-variable to adjust the longitudinal models.

Statistical analyses

Dietary patterns

The PCA was used to identify dietary patterns before pregnancy. A correlation matrix was constructed to assess the correlation between the food groups. The Kaiser-Meyer-Olkin (KMO) test (greater than 0.6) and Bartlett's Test of Sphericity (p -value < 0.05) were applied to verify whether the PCA assumptions were all met (23,25).

Varimax rotation was applied to obtain orthogonal factors. The foods groups that showed factor loadings > 0.20 and communalities > 0.20 were considered. The factor loading > 0.20 indicates a meaningful strong association with the factor or pattern and has been previously used in other studies (30,31). A positive factor loading indicated that the food group had a positive association with the dietary pattern, while a negative factor loading indicated an inverse association. The food groups were kept in the dietary pattern that have shown the higher factor loading, even if these were higher than 0.20 in other dietary pattern.

The number of factors extracted was based on eigenvalues > 1.5 and Scree test plots (25). The dietary patterns were labeled according to the food items included, the higher factor loading of foods in dietary patterns, and the dietary patterns interpretation. The factor score was obtained with PCA, and each pregnant woman received a factor score for each dietary pattern identified (13).

For some analysis, the pregnant women were classified in a specific pattern only. The high adherence to each dietary pattern was classified according to quintiles. When a woman was classified in the fifth quintile she was considered as having high adherence for that pattern. For example, if a woman was classified in the fifth quintile of the *common-Brazilian* and

healthy patterns, she was kept in the *common-Brazilian* because of the lower range of dietary patterns scores for the *common-Brazilian* (-2.32 to 1.66) vs. *the healthy* pattern (-2.36 to 3.15).

Descriptive and longitudinal analysis

The baseline characteristics of the sample were described using mean and 95% confidence intervals (95% CI) for continuous variables. The categorical variables were described by frequencies. These variables were stratified according to the established dietary patterns identified based on the greater adherence to each dietary pattern. Analysis of variance was employed to compare means of the selected variables, and the chi-square test was applied to compare the frequencies of the categorical variables.

We employed longitudinal mixed-effects (LME) regression models to evaluate the longitudinal associations between dietary patterns before pregnancy and depressive symptoms during pregnancy. Scores for depressive symptoms at the three follow-up waves were the outcomes of LME models. The LME model allows evaluating time-dependent and time-independent covariates and unbalanced time intervals. Furthermore, this model is adequate even if the study data has missing values (32,33). The regression coefficient (β) and standard error (SE) generated by the model provides a combined estimate of the effect between individuals (with respect to the association with time between the independent variables and depressive symptoms) and within individuals (representing the effect of the independent variable variation on changes in depressive symptoms throughout pregnancy) (34).

In all longitudinal models, gestational age (weeks) was included as a random and fixed-effect variable to adjust for all-subject and individual depressive symptoms score variation over time. The dietary pattern scores and all other covariates were analyzed as fixed-effect variables. Dependencies in the data were handled with an unstructured covariance matrix (all variances and co-variances were estimated separately) (32,33).

In the multivariable analyses, we ran an independent LME regression model for each dietary pattern identified. All covariates (age, education, marital status, parity, unplanned pregnancy, pregnancy BMI, total energy intake before pregnancy, and gestational age) were selected based on the biological plausibility of an association with depressive symptoms. Marital status was considered a time-dependent variable because a woman could switch status over pregnancy. All other independent variables included in the models were time-independent. We used the restricted log-likelihood, Akaike's Information Criterion (AIC) and Bayesian Information Criterion (BIC) as global fit criteria to select the best LME model for each dietary pattern. During the modeling process, three types of plots were produced: scatter plots of

residuals to check for specific patterns, quantile-quantile plots to check normality of the residuals, and plots to check the autocorrelation structure (32,33). Interaction terms between gestational age and dietary patterns were tested, with the aim of detecting differences in the variation in depression scores over time for each dietary pattern.

An appropriated statistical analysis was implemented considering that a clinical trial was originally nested within the observational cohort. In this regard, we performed statistical analyses to evaluate whether the data from the 41 women who were enrolled and completed the clinical trial could be included in the modeling process. The aim was to avoid selection bias due to exclusion of women at greater risk of developing depression and also to increase the study's sample size. We fit three longitudinal LME models: (i) Model 1 excluded the information of the pregnant women who were enrolled in the clinical trial only from the third trimester (period when supplementation was effective). We included the data of these women from the first and second trimester follow-up visits. This model excluded the pregnant women at higher risk of depression, creating a selective loss of information bias (**Supplemental Table 2**). (ii) Model 2 included all women (observational cohort and clinical trial) in all pregnancy trimesters in the longitudinal analysis (**Supplemental Table 3**). (iii) Model 3 included all women (observational cohort and clinical trial) in all pregnancy trimesters but adjusted the analysis for a variable that classified the pregnant women based on the type of study in which they were enrolled (observational cohort, treatment group or placebo). The aim was to remove the effect of the supplementation from the analysis. After performing all three models, we compared the model results. We observed a small change across the associations (β coefficients and corresponding p-values) and decided to use model 3, considered the best model for this analysis.

The final model considered only education as a socioeconomic status variable, because the model results did not improve when total family income was included in comparison to the ones without this variable.

The pregnant women were compared regarding the final rate of losses to follow up. This rate was calculated as the proportion between the number of losses to follow-up and the total number of observations at baseline. We calculated this rate for several variables including EPDS (≥ 11 / < 11), age (20-29/ ≥ 30 years), education (≥ 8 / < 8 years), marital status (married/stable partnership), parity (0-1/ ≥ 2) and pre-gestational BMI (≥ 25 / < 25 kg/m²). The chi-square test for proportions was used to assess patterns of nonrandom losses to follow-up.

All analyses were performed using Stata 12.0 (35).

Ethical approval

The study protocol was approved by Ethics Committee of Maternity Hospital (Protocol number: 0023.0.361.000-08) and the Institute of Psychiatry of the Rio de Janeiro Federal University (Protocol number: 0012.0.249.000-09), both from the Rio de Janeiro Federal University, and Ethics Committee of the Municipal Secretary of Rio de Janeiro city (Protocol number: 0139.0.314.000-09). Written consent was obtained from all participants.

Results

A total of 248 pregnant women answered the EPDS and were considered for analysis at baseline. These subjects had a mean age of 26.7 years and an average of 8.8 years of education; 78.6% were married or had a stable partnership, and 22.7% had an unplanned pregnancy. The mean early pregnancy BMI was 25.1 kg/m^2 , the mean total energy intake before pregnancy was 2,250 kcal/d. The mean EPDS score was 9.0 (95% CI: 8.4, 9.6) (**Table 1**).

Three dietary patterns were identified before pregnancy considered data from 251 women who answered the FFQ. The KMO test (0.642) and Bartlett's Test of Sphericity ($P < 0.001$) showed that the correlation in the food groups was sufficient and appropriate for PCA. The first dietary pattern identified was labeled *common-Brazilian*, and consisted of rice, beans, vegetable spices, and meats and eggs. The second pattern was labeled *healthy* and comprised dairy products, fruits and fruit juice, green vegetables and legumes, candies, fish, cakes and cookies-crackers, pasta, roots and tubers, and tea. The third pattern was labeled *processed* and was characterized by positive loadings of bread, fat, fast food and snacks, sugar, sausages and deli meats, soft drinks and coffee. The coffee showed the same factor loading to *healthy* and *processed* patterns, however with negative and positive loading, respectively. The coffee was kept in the *processed* pattern. The percentage of variance explained by each dietary pattern before pregnancy was 15.2%, 11.2%, and 9.8%, respectively. Together, the three dietary patterns explained 36.1% of the percentage of variance. The eigenvalues in each dietary pattern were 2.88 (*common-Brazilian*), 2.12 (*healthy*), and 1.86 (*processed*) (**Supplemental Table 1**). The adherence to the *common-Brazilian* pattern was 36.7%, to the *healthy* pattern was 31.4% and to the *processed* pattern was 31.8% (results not shown in tables).

Pregnant women with higher adherence to the pre-pregnancy *common-Brazilian* pattern had lower age (25.9 years of age) and total energy intake (2,132 kcal/d), and higher early pregnancy BMI (25.5 kg/m^2) and years of education (9.1 years) compared to the *healthy* or *processed pattern*. Women that adhered to the *healthy* pattern were older (27.4 year of age), married or had a stable partnership (85.7%), were less likely to have an unplanned pregnancy

(15.8%) and low depressive symptoms scores (8.3). We observed that women who had higher adherence to the *processed* pattern had higher depressive symptoms scores (10.0), and total energy intake (2,370 kcal/d), and fewer years of education (8.6 years) when compared to the other patterns (**Table 1**).

Depressive symptoms decreased during pregnancy trimesters according to the EPDS scores: 1st: 9.0 (95%CI: 8.4, 9.6); 2nd: 7.2 (95%CI: 6.5, 7.8); 3rd: 7.0 (95%CI: 6.4, 7.7). This trend was confirmed in the longitudinal linear bivariate regression model (β : -0.723; 95% CI: -1.277, -0.169; P = 0.011) (results not shown in tables).

In the linear multiple longitudinal regression model, the pre-pregnancy *healthy* pattern was inversely associated with depressive symptoms during pregnancy (β : -0.723, 95% CI: -1.277, -0.169; P = 0.011). The *common-Brazilian* (β : -0.227; 95% CI: -0.708, 0.253; P = 0.35) and *processed* patterns (β : 0.413; 95% CI: -0.161, 0.986; P = 0.15) were not associated with depressive symptoms during pregnancy (**Table 2**).

The final rate of losses to follow up was 22% (54/245). The analysis of data from the study participants who were lost to follow-up showed no departure from a random process (non-informative) for almost all the variables except marital status and education. The final follow-up rate for pregnant women living without a partner or with higher education was higher than that for married of lower educated women (results not shown in tables).

Interaction terms between gestational age and dietary patterns on depressive symptoms scores were tested, but they were not statistically significantly and were removed from the final models.

Discussion

This prospective cohort study investigated the association between dietary patterns before pregnancy and depressive symptoms during pregnancy and has three main findings. First, three dietary patterns were identified. The patterns were labeled *common-Brazilian*, *healthy* and *processed*. The dietary patterns were labeled according to the main food groups' factorial loadings. Second, we observed that the pre-pregnancy *healthy* pattern showed an inverse association with depressive symptoms measured at three time points during pregnancy. Women that had adhered to this pattern were less likely to report depressive symptoms throughout pregnancy. However, the other two dietary patterns did not show significant associations with EPDS scores. Finally, the study corroborates previous observations that mean EPDS scores decreased progressively during pregnancy. It is worth noting that this is the first

study that has examined the association between pre-pregnancy dietary patterns and prospective depressive symptoms assessed at all three pregnancy trimesters.

There are some limitations to the present study that need to be mentioned. The first relates to the loss of subjects from follow-up. Although this may be considered a limitation, this drawback is commonly observed in prospective studies. Our final rate of losses to follow up was 22%, but there was no departure from a random process for almost all of the variables exception made to marital status and education, variables that were controlled for in the analysis. Another limitation is that the factor analyses used to identify the dietary patterns depends on several decisions made by the researcher, such as food group combinations, number of factors to be retained, and names assigned to the retained factors.

Despite all of these limitations, the present study has important strengths such as the use of high-quality and validated instruments to measure dietary intake, depressive symptoms, social and behavioral data. Another strength includes the employment of the LME procedure, a robust statistical technique for longitudinal analysis that was used to verify the associations. Previous studies that assessed dietary patterns and depression employed cross-sectional designs and only evaluated depressive symptoms during the postpartum period (15,16). The external validity of our study is likely to be high considering that approximately 75% of all pregnant women in Brazil receive pre-natal care from public health centers (36), and the socioeconomic profile of women included in the present study is similar to those of women attended in Brazilian public health centers.

We observed that the pregnant women of our study presented higher depressive symptoms scores when compared to other studies. However, the prevalence of depression from developing countries are usually higher comparing to developed ones (37). Our findings of a decrease in depressive symptoms throughout pregnancy are in line with previous investigations (38-40). Some authors have suggested that a decrease in depression may be due to familiar and social support, coping behavior and skills (41,42).

Some studies have assessed depressive symptoms during the last gestational trimester through the postpartum period (38-40). Micali et al. (38) evaluated depressive symptoms in 11,731 women at 18 and 32 weeks of pregnancy and at 8 weeks and 8 months postpartum based on the EPDS. The authors observed that depression scores decreased significantly over time. These results are consistent with those observed in the current study. Our results are also consistent with those reported by the Obstetrics Out-patients Unit from Porto, Portugal, which have shown a decrease in depressive symptoms and the prevalence of EPDS ≥ 10 , which was 20.0%, 19.6% and 17.4% in the first, second and third gestational trimesters, respectively (39).

A cohort study conducted by Teixeira et al. (40) among Portuguese women reported a significant decrease in depressive symptoms from 6.6 to 6.2 (from the 1st to the 2nd) and further to 5.6 from the 2nd to the 3rd trimesters. Most of the studies observed a decrease of depressive scores, however Evans et al. (43) verified a small increase in the EPDS scores (6.6 to 6.7) from the 18th to the 32nd week of British pregnant women investigated by the Avon Longitudinal Study of Parents and Children (ALSPAC). The difference between the ALSPAC and our study can be attributable to socioeconomic profile. Furthermore the EPDS mean score increase observed in the ALSPAC seems not to be clinically relevant.

The *healthy* pattern identified before pregnancy in our study was composed of prudent foods, such as pasta, roots and tubers, green vegetables and legumes, fruits and fruit juice, dairy products, fish, and tea. This pattern has shown an inverse association with prospective changes in EPDS scores during pregnancy. Similarly, the intake of ‘healthy conscious’ pattern (characterized by vegetables, fruit, pulses, nuts, dairy products and olive oil) prevented depressive symptoms in postpartum women from the ‘Rhea’ project, a prospective cohort study of pregnant women and their children in Crete, Greece (15). However, in pregnant women from the Osaka Maternal and Child Health Study, there was no association between a ‘healthy’ pattern, composed of green and yellow vegetables, seaweeds, white vegetables, potatoes, fish, fruits, shellfish and sea products, and depressive symptoms (16).

In our study, we observed that some factors, such as years of education, marital status and unplanned pregnancy, were risk factors for depressive symptoms in pregnant women. These results agree with those from Hein et al. (44) who evaluated a prospective cohort of women from The Franconian Maternal Health Evaluation Studies and showed that partnership status, previous pregnancies, educational status, income, and accommodation status were risk factors for depressive symptoms during and after pregnancy. Miyake et al. (11) verified in Japanese women from the Kyushu Okinawa Maternal and Child Health Study that the intake of healthy foods rich in EPA and DHA was associated with a lower prevalence of depressive symptoms during pregnancy, and the intake of this dietary pattern was positively associated with age, number of children, unemployment status, household income, and educational level.

The food groups that composed the *healthy* pattern in the present study resulted of a dietary intake rich in several antioxidant compounds (e.g. flavonoids, vitamins, minerals), which are important nutrients to protect the brain from the effects of oxidative stress implicated in depression (45), and long chain essential n-3 polyunsaturated fatty acids (e.g. fish) known as a necessary component for optimal neurological function (46). Thus, it is possible that this

pattern resulted in a healthy diet that possibly prevents neurocognitive impairments that reflect in mood changes during pregnancy such as depressive symptoms.

The two other dietary patterns identified before pregnancy, *common-Brazilian* and *processed*, did not show a significant association with depressive symptoms throughout pregnancy. A higher intake of total fat and saturated fatty acids was associated with an increased prevalence of depressive symptoms in pregnant Japanese women (11).

The *processed* pattern in this study was characterized by a higher intake of fat and carbohydrates and did not show a significant association with EPDS scores, even for the women that adhered more frequently to this pattern. These women had higher mean depressive symptoms scores and number of deliveries, and had fewer years of education and were predominantly single, i.e., risk factors that increase depressive symptoms during pregnancy (1,7,44).

In summary, we observed that depressive symptoms decreased progressively during pregnancy and some risk factors, such as single marital status, increased EPDS scores. We verified that the pre-pregnancy *healthy* pattern was inversely associated with depressive symptoms evaluated prospectively throughout pregnancy.

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TABLE 1 Characteristics of pregnant women followed-up at a Public Health center stratified by dietary patterns at baseline between 5th-13th gestational weeks, Rio de Janeiro/Brazil, 2009-2012¹

	All (n= 248) ³	Dietary patterns ²			p-value ⁴
		Common-Brazilian (n= 90)	Healthy (n= 77)	Processed (n= 78)	
Continuous variables					
Depressive symptoms ⁵ , scores	9.0 (8.4, 9.6)	8.7 (7.7, 9.6)	8.3 (7.2, 9.3)	10.0 (8.9, 11.2)	0.06
Age, years	26.7 (26.1, 27.4)	25.9 (24.9, 27.0)	27.4 (26.2, 28.5)	27.0 (25.6, 28.3)	0.22
Education, years	8.9 (8.5, 9.2)	9.1 (8.5, 9.7)	8.8 (8.2, 9.5)	8.6 (7.9, 9.3)	0.53
Parity, number of deliveries	1.0 (0.8, 1.1)	1.0 (0.8, 1.3)	0.8 (0.6, 1.1)	1.0 (0.8, 1.3)	0.41
Early pregnancy BMI ⁶ , kg/m ²	25.1 (24.5, 25.7)	25.5 (24.5, 26.5)	25.3 (24.3, 26.4)	24.5 (23.3, 25.6)	0.33
Gestational age, weeks	9.6 (9.3, 9.8)	9.6 (9.1, 10.0)	9.5 (9.0, 9.9)	9.6 (9.1, 10.2)	0.85
Total energy intake ⁷ , kcal/d	2250 (2164, 2336)	2132 (2023, 2240)	2267 (2093, 2442)	2370 (2201, 2538)	0.08
Categorical variables					
Marital status, n (%)					0.040
Married or stable partnership	195 (78.6)	72 (80.0)	66 (85.7)	54 (69.2)	
Single	53 (21.4)	18 (20.0)	11 (14.3)	24 (30.8)	
Unplanned pregnancy, n (%)					0.13
No	191 (77.3)	69 (76.7)	64 (84.2)	55 (70.5)	
Yes	56 (22.7)	21 (23.3)	12 (15.8)	23 (29.5)	

¹ Values are mean (95% CI) or n (frequency %) unless indicated otherwise.

² Women were classified in only one dietary pattern considering the highest quintile of each dietary patterns scores.

³ A total of 251 pregnant women had the food intake assessed and a total of 248 women had information about depressive symptoms, however 3 out of the 248 had missing report of food intake.

⁴ p-value refers to ANOVA's test.

⁵ Depressive symptoms were assessed by the Edinburgh Postnatal Depression Scale (EPDS).

⁶ BMI was obtained at baseline.

⁷ 1 kcal/d = 4.184 kJ/d.

⁸ p-value refers to chi-square test.

TABLE 2 Multiple longitudinal regression model with mixed effects between pre-pregnancy dietary patterns and depressive symptoms (EPDS) changes in pregnant women followed-up at a Public Health center in the city of Rio de Janeiro, Brazil, 2009-2012¹

	Dietary patterns					
	Common-Brazilian ²	p-value ³	Healthy ⁴	p-value	Processed ⁵	p-value
Fixed-effect						
Intercept	8.042 (3.797, 12.287)	<0.001	6.779 (2.447, 11.112)	0.002	9.025 (4.631, 13.419)	<0.001
Dietary pattern, scores	-0.227 (-0.708, 0.253)	0.35	-0.723 (-1.277, -0.169)	0.011	0.413 (-0.161, 0.986)	0.16
Age, years	-0.050 (-0.145, 0.044)	0.30	-0.040 (-0.134, 0.053)	0.40	-0.050 (-0.144, 0.044)	0.30
Education, years	-0.013 (-0.187, 0.161)	0.88	-0.010 (-0.183, 0.162)	0.91	-0.019 (-0.193, 0.155)	0.83
Marital status (Married or stable partnership/Single)	2.115 (1.015, 3.215)	<0.001	1.931 (0.829, 3.033)	0.001	2.039 (0.933, 3.145)	<0.001
Parity, number of deliveries	0.503 (0.003, 1.004)	0.05	0.404 (-0.087, 0.896)	0.12	0.475 (-0.018, 0.968)	0.06
Unplanned pregnancy (no/yes)	2.381 (1.216, 3.546)	<0.001	2.402 (1.250, 3.555)	<0.001	2.363 (1.199, 3.527)	<0.001
Pregnancy BMI, kg/m ²	0.059 (-0.036, 0.154)	0.22	0.058 (-0.036, 0.152)	0.23	0.063 (-0.032, 0.157)	0.20
Total energy intake ⁶ , kcal/d	-0.000 (-0.001, 0.001)	0.79	0.000 (-0.000, 0.001)	0.35	-0.001 (-0.001, 0.000)	0.23
Gestational age, weeks	-0.092 (-0.123, -0.061)	<0.001	-0.093 (-0.124, -0.062)	<0.001	-0.093 (-0.124, -0.062)	<0.001
Random-effect						
σ Gestational age	0.005 (0.001, 0.033)	<0.001	0.005 (0.001, 0.034)	<0.001	0.005 (0.001, 0.033)	<0.001
σ Intercept	9.212 (4.751, 17.863)	<0.001	8.468 (4.190, 17.114)	<0.001	8.850 (4.466, 17.538)	<0.001
σ Residual	8.744 (7.178, 10.650)	<0.001	8.758 (7.191, 10.666)	<0.001	8.754 (7.186, 10.664)	<0.001

¹ Values are longitudinal regression coefficients and 95% CI, and were adjusted by a variable that classified the pregnant women in the type of study that they were enrolled (Clinical trial vs observational cohort), number of observations = 627, number of groups = 246, average of 2.5 observations per group. EPDS, Edinburgh Postnatal Depressive Scale; AIC, Akaike Information Criterion; BIC, Bayesian Information Criterion.

² Likelihood = -1744.5, AIC = 3521.0, BIC = 3592.0.

³ p-value refers to restricted maximum likelihood estimator.

⁴ Likelihood = -1741.7, AIC = 3515.4, BIC = 3586.4.

⁵ Likelihood = -1743.9, AIC = 3519.9, BIC = 3590.9.⁶ 1 kcal/d = 4.184 kJ/d.

SUPPLEMENTAL TABLE 1 Factor loadings and communalities (h^2) of the three pre-pregnancy dietary patterns identified ($n= 251$) in pregnant women followed-up at a Public Health center in the city of Rio de Janeiro, Brazil, 2009-2012 ¹

	Factor loadings ²			
	Common-Brazilian	Healthy	Processed	h^2
Rice	0.866	0.032	0.002	0.212
Beans	0.830	-0.042	0.107	0.283
Vegetable spices	0.820	0.119	-0.082	0.297
Meats and eggs	0.318	0.131	0.173	0.562
Dairy products	0.050	0.658	0.137	0.506
Fruit and fruit juice	0.005	0.603	-0.140	0.387
Green vegetables and legumes	0.249	0.595	-0.012	0.392
Candies	-0.037	0.497	0.298	0.506
Fish	0.036	0.437	-0.267	0.632
Cakes and cookies-crackers	-0.041	0.424	0.259	0.645
Pasta, roots and tubers	0.132	0.322	0.063	0.687
Tea	0.076	0.213	-0.052	0.327
Breads	-0.077	0.023	0.720	0.198
Fat	0.076	-0.004	0.692	0.219
Fast food and Snacks	0.088	0.423	0.477	0.435
Sugar	0.174	-0.114	0.472	0.336
Sausages and deli meats	0.012	0.201	0.461	0.647
Soft drinks	-0.080	0.130	0.334	0.577
Coffee	0.042	-0.319	0.319	0.341
Number of groups	4	9	6	
Eigenvalues	2.88	2.12	1.86	
% of variance explained	15.2	11.2	9.8	
% of cumulative variance explained	15.2	26.3	36.1	

SUPPLEMENTAL TABLE 2 Longitudinal regression model with mixed effects between pre-pregnancy dietary patterns and depressive symptoms (EPDS) changes (excluding the information from the third trimester for those enrolled in the clinical trial), in pregnant women followed-up at a Public Health center in the city of Rio de Janeiro, Brazil, 2009-2012 ³

	Dietary patterns					
	Common-Brazilian ⁴	p-value ⁵	Healthy ⁶	p-value	Processed ⁷	p-value
Fixed-effect						
Intercept	7.332 (2.896, 11.767)	0.001	6.330 (1.777, 10.883)	0.006	8.001 (3.413, 12.588)	0.001
Dietary pattern, scores	-0.215 (-0.717, 0.287)	0.40	-0.569 (-1.147, 0.009)	0.05	0.271 (-0.321, 0.863)	0.37
Age, years	-0.035 (-0.134, 0.064)	0.49	-0.026 (-0.124, 0.073)	0.61	-0.034 (-0.133, 0.064)	0.50
Education, years	-0.008 (-0.189, 0.173)	0.93	-0.004 (-0.184, 0.176)	0.97	-0.011 (-0.193, 0.170)	0.90
Marital status (Married or stable partnership/ Single)	2.011 (0.870, 3.153)	0.001	1.854 (0.703, 3.004)	0.002	1.961 (0.810, 3.1120)	0.001
Parity, number of deliveries	0.500 (-0.020, 1.021)	0.06	0.417 (-0.097, 0.930)	0.11	0.471 (-0.043, 0.985)	0.07
Unplanned pregnancy (no/ yes)	2.383 (1.175, 3.591)	<0.001	2.418 (1.218, 3.619)	<0.001	2.390 (1.183, 3.5980)	<0.001
Pregnancy BMI, kg/m ²	0.067 (-0.031, 0.166)	0.18	0.066 (-0.032, 0.165)	0.19	0.070 (-0.029, 0.168)	0.17
Total energy intake ⁸ , kcal/d	0.001 (-0.001, 0.001)	0.72	0.001 (0.000, 0.001)	0.23	0.001 (-0.001, 0.001)	0.73
Gestational age, weeks	-0.094 (-0.126, -0.062)	<0.001	-0.095 (-0.127, -0.063)	<0.001	-0.095 (-0.127, -0.063)	<0.001
Random-effect						
σ Gestational age	0.004 (0.000, 0.065)	<0.001	0.003 (0.000, 0.072)	<0.001	0.004 (0.000, 0.067)	<0.001
σ Intercept	10.694 (5.767, 19.832)	<0.001	10.275 (5.455, 19.354)	<0.001	10.492 (5.608, 19.632)	<0.001
σ Residual	8.903 (7.232, 10.961)	<0.001	8.911 (7.240, 10.967)	<0.001	8.914 (7.240, 10.975)	<0.001

SUPPLEMENTAL TABLE 3 Longitudinal regression model with mixed effects between pre-pregnancy dietary patterns and depressive symptoms (EPDS) changes (in all pregnant women for the observational cohort and clinical trial in all pregnancy trimesters), in pregnant women followed-up at a Public Health center in the city of Rio de Janeiro, Brazil, 2009-2012⁹

	Dietary patterns					
	Common-Brazilian ¹⁰	p-value ⁵	Healthy ¹¹	p-value	Processed ¹²	p-value
Fixed-effect						
Intercept	7.717 (3.302, 12.131)	0.001	6.775 (2.241, 11.309)	0.003	8.354 (3.785, 12.923)	<0.001
Dietary pattern, scores	-0.211 (-0.711, 0.290)	0.41	-0.537 (-1.112, 0.038)	0.07	0.257 (-0.333, 0.847)	0.39
Age, years	-0.037 (-0.135, 0.062)	0.47	-0.028 (-0.126, 0.070)	0.58	-0.036 (-0.134, 0.062)	0.48
Education, years	0.001 (-0.181, 0.181)	0.99	0.003 (-0.177, 0.183)	0.97	-0.003 (-0.185, 0.178)	0.97
Marital status (Married or stable partnership/ Single)	2.022 (0.894, 3.151)	<0.001	1.886 (0.750, 3.0230)	0.001	1.979 (0.841, 3.116)	0.001
Parity, number of deliveries	0.504 (-0.017, 1.025)	0.06	0.424 (-0.091, 0.938)	0.11	0.475 (-0.040, 0.989)	0.07
Unplanned pregnancy (no/ yes)	2.453 (1.248, 3.658)	<0.001	2.482 (1.283, 3.681)	<0.001	2.459 (1.254, 3.665)	<0.001
Pregnancy BMI, kg/m ²	0.060 (-0.039, 0.158)	0.23	0.059 (-0.039, 0.157)	0.24	0.062 (-0.037, 0.161)	0.22
Total energy intake ⁸ , kcal/d	0.000 (-0.001, 0.001)	0.97	0.000 (0.000, 0.001)	0.38	0.000 (-0.001, 0.001)	0.56
Gestational age, weeks	-0.092 (-0.123, -0.061)	<0.001	-0.092 (-0.123, -0.061)	<0.001	-0.092 (-0.123, -0.061)	<0.001
Random-effect						
σ Gestational age	0.005 (0.001, 0.033)	<0.001	0.005 (0.001, 0.034)	<0.001	0.005 (0.001, 0.033)	<0.001
σ Intercept	11.017 (6.210, 19.545)	<0.001	10.572 (5.874, 19.028)	<0.001	10.819 (6.055, 19.331)	<0.001
σ Residual	8.709 (7.154, 10.603)	<0.001	8.716 (7.160, 10.610)	<0.001	8.714 (7.157, 10.609)	<0.001

Notes for supplemental tables 1, 2 and 3

¹ Kaiser Mayer Olkin test= 0.642; Bartlett's Test of Sphericity, p < 0.001.

² The dietary patterns were composed by the food groups with the value of the factor loadings in bold.

³ Values are longitudinal regression coefficients and 95% CI, number of observations = 591; number of groups = 246; average of 2.4 observations per group.

⁴ Likelihood = -1654.8, AIC = 3337.6, BIC = 3398.9.

⁵ p-value refers to restricted maximum likelihood estimator.

⁶ Likelihood = -1653.3, AIC = 3334.6, BIC = 3395.9.

⁷ Likelihood = -1654.7, AIC = 3337.5, BIC = 3398.8.

⁸ 1 kcal/d = 4.184 kJ/d.

⁹ Values are longitudinal regression coefficients and 95% CI, number of observations = 627; number of groups = 246; average of 2.5 observations per group.

¹⁰ Likelihood = -1753.6, AIC = 3535.3, BIC = 3597.5.

¹¹ Likelihood = -1752.3, AIC = 3532.6, BIC = 3594.8.

¹² Likelihood = -1753.6, AIC = 3535.2, BIC = 3597.4.

EPDS, Edinburgh Postnatal Depressive Scale; AIC, Akaike Information Criterion; BIC, Bayesian Information Criterion

6.2 ARTIGO 2. ASSOCIATION OF PRE-PREGNANCY DIETARY PATTERNS AND ANXIETY SYMPTOMS FROM MID-PREGNANCY TO EARLY POSTPARTUM IN A PROSPECTIVE COHORT OF BRAZILIAN WOMEN (Anexo 8)

Abstract

Background: Adherence to unhealthy dietary patterns may alter the risk of mental disorders during pregnancy and postpartum.

Objective: To analyze the association between pre-pregnancy dietary patterns and prospective variations on anxiety symptoms from mid-pregnancy to early postpartum.

Methods: A prospective cohort of 207 healthy pregnant women was followed at 5-13, 20-26, and 30-36 gestational weeks, and once at 30-45 days postpartum. The State-Trait Anxiety Inventory (STAI) was used to evaluate anxiety symptoms at the second and third gestational trimesters and during the postpartum period. Dietary intake was assessed using a food frequency questionnaire administered in the first trimester of pregnancy that referred to the six months before pregnancy. Principal components analysis was used to identify dietary patterns and three pre-pregnancy dietary patterns were identified: *common-Brazilian*, *healthy*, and *processed*. Three longitudinal mixed-effect models were estimated to verify the association between dietary patterns and anxiety symptoms, adjusted for confounding variables.

Results: The mean anxiety symptom scores were 40.4, 40.5, and 37.2 for the 2nd trimester, 3rd trimester, and postpartum, respectively. The rate of variation of the STAI score was 0.535 (95% CI: -0.035, 1.107, p=0.066) and -0.010 (95% CI: -0.018, -0.002, p=0.019) when accounting for gestational age and quadratic gestational age, respectively. The *common-Brazilian* pattern, comprised mainly of rice, and beans ($\beta = -1.200$, 95%CI: -2.220, -0.181, p=0.021), and the *healthy* pattern comprised mostly of vegetables, fruits, fish, and tea ($\beta = -1.290$, 95%CI: -2.438, -0.134, p=0.029), were negatively associated with prospective changes in anxiety symptoms.

Conclusions: High adherence to the *common-Brazilian* or *healthy* patterns was negatively associated with higher anxiety symptom scores from mid-pregnancy to early postpartum in this group of Brazilian women.

Keywords: Anxiety; Food consumption; Factor Analysis - Statistical; Pregnancy; Cohort study.

Introduction

Anxiety is considered a common mental health disorder during pregnancy and has been associated with adverse outcomes for the mother and the fetus, such as inadequate weight gain, premature birth, obstetric complications and postpartum depression¹⁻⁴. The prevalence of anxiety during pregnancy may vary from 9% to 33.3% worldwide⁵⁻⁸. In Brazil, it ranges from 16.9% to 33.3%⁷⁻⁹. The mean prevalence of anxiety symptoms in Brazilian pregnant women is higher than the prevalence in other countries. For instance, in Peruvian women, anxiety during pregnancy ranges from 8.1 to 19.6%¹⁰, for North Americans¹¹ and Swedish pregnant women¹², the mean prevalence is 13% and 11.4%, respectively. Prospective studies have shown that anxiety symptoms increase during pregnancy and decrease after birth^{3,13,14}.

Some studies have reported that socio-economic, demographic, nutritional and lifestyle factors are associated with the occurrence of anxiety during pregnancy^{15,16}. A cross-sectional study with 165 pregnant women from Athens, Greece found a positive association between unfavorable social conditions (low level of education and unstable marital status) and anxiety¹⁷. Hurley et al.¹⁸ showed that the high intake of carbohydrates, fats, and protein were positively associated with anxiety symptoms in pregnant women from Baltimore. These studies have assessed maternal diet by micro- and macronutrient intake^{19,20}. However, in nutritional epidemiology, dietary patterns have been used in some studies to assess the relationship between diet and health outcomes^{21,22}.

Dietary habits have been associated with several outcomes, including psychological illness²³⁻²⁵. The Avon Longitudinal Study of Parents and Children (ALSPAC) conducted in South West, England, with women at 32 weeks of gestation, found that high adherence to ‘health-conscious’ and ‘traditional’ patterns, consisting of healthy foods such as vegetables, fruits, fish, and red meat, were shown to be inversely associated with anxiety symptoms²⁴. Adherence to the ‘Western’ pattern characterized by processed or fried foods, refined grains, sugary products, and beer, was shown to have a positive association with anxiety symptoms in Norwegian adults and elderly women²⁶. Furthermore, the consumption of processed foods was associated with state and trait anxieties in adult women aged 18-35 years living in Tehran, Iran²⁷.

Therefore, considering the high prevalence of anxiety symptoms during pregnancy/postpartum and the association of dietary intake with this outcome, the aim of this study was to evaluate the association between pre-pregnancy dietary patterns and anxiety symptoms from mid-pregnancy to early postpartum using a prospective cohort study design. We hypothesized that adherence to dietary patterns with healthy foods would be associated with lower anxiety

symptoms during the study period. In a recent study from our research group, we observed that the higher adherence to the ‘healthy’ pattern before pregnancy was associated with lower depressive symptoms during pregnancy²⁸, but little is known about the influence of diet on other mental illnesses during gestation, including anxiety. Findings from the current study may contribute to closing this gap and provide insights to guide the enriching of maternal nutrition, in order to improve mental health during the perinatal period.

Methods

Design and study population

This study included a prospective cohort of pregnant women from the Heitor Beltrão public health care center, located in the city of Rio de Janeiro, Brazil. Recruitment occurred between November 2009 and October 2011, and women who had an immune positive pregnancy test and met the following eligibility criteria were invited to participate in the study: (a) were between 5 and 13 weeks of pregnancy at the time of recruitment; (b) were aged between 20 and 40 years; (c) were free from any chronic diseases (except obesity, that was determined from self-reported pre-pregnancy weight and measured height at baseline; women with a pre-pregnancy BMI of $\geq 30 \text{ kg/m}^2$ were classified as obese); and (d) were free from infectious diseases.

The pregnant women were evaluated at the following periods during pregnancy: 5-13, 20-26 and 30-36 gestational weeks, and once between 30-45 days postpartum. A total of 299 pregnant women were recruited for this study. However, after entering the study, we excluded women who gave birth to twins ($n = 4$), changed their prenatal care health unit ($n = 11$), abandoned the prenatal care and follow-up ($n = 19$), were diagnosed with an infectious or non-communicable disease ($n = 12$), were identified as more than 13 weeks of pregnancy based on the ultrasound at baseline ($n = 16$), had missing data at baseline ($n = 15$), had a miscarriage ($n = 25$), or had a stillbirth ($n = 1$). Following these exclusions, the final sample included 196 pregnant women at the second trimester.

Assessment of dietary intake

The food frequency questionnaire (FFQ) used on our study was validated in a sample of 88 employees from Rio de Janeiro State University who completed four 24-hour recalls, which is considered the gold standard. The authors observed that the correlation coefficients ranged from 0.18 (vitamin A) to 0.55 (calcium). The coefficients for energy, carbohydrate, protein and

fat were 0.44, 0.34, 0.44 and 0.41, respectively. Except for vitamin A, all the other nutrients have high significant agreements²⁹.

Dietary intake was assessed using this validated FFQ²⁹ administered in the first trimester of pregnancy. The time frame to which the FFQ referred was six months before pregnancy. The FFQ included 82 food items and had eight frequency options: (i) more than three times a day; (ii) two to three times a day; (iii) once a day; (iv) five to six times a week; (v) two to four times a week; (vi) once a week; (vii) one to three times a month; and (viii) never or hardly ever. These data were transformed into daily frequencies by multiplying those quantities by: (i) 4; (ii) 2.5; (iii) 1; (iv) 0.79; (v) 0.43; (vi) 0.14; (vii) 0.07; and (viii) 0, respectively. Daily energy intake (in kilocalories) was obtained using DietSys software, version 4.02³⁰. The Brazilian Food Composition Table (TACO)³¹ was the database used in this analysis, and we used the United States Department of Agriculture (USDA)³² food composition table for those foods that were not found in TACO.

To identify the dietary patterns, 77 of 82 items listed in the FFQ were grouped into 19 food groups. The food groupings were based on their nutritional characteristics. Items that were consumed by 80% or more of the subjects or had different nutritional composition were kept separate³³, even if they had a nutritional composition similar to other items (rice, beans, bread, and sugar). Lard, wine, beer, vodka, and dried meat/codfish had a lower consumption (< than 20% percent of frequency), so they were excluded from the dietary pattern analysis. The foods were grouped as follows: (i) rice; (ii) beans; (iii) breads; (iv) cakes and cookies-crackers; (v) pasta, roots and tubers - pasta; gnocchi/lasagna/ravioli; baked/mashed potato; cassava/yam; cassava flour; and polenta; (vi) meats and eggs - pork; beef; chicken; barbecue; giblets (gizzard, heart, liver, stomach/tripe, kidneys); and eggs; (vii) vegetable spices - onion; garlic; and red/green/yellow pepper; (viii) dairy products - cheese; milk; cottage cheese; and yogurt; (ix) green vegetables and legumes - lentils/peas/chickpeas; lettuce; cabbage; kale; cauliflower/broccoli; tomato; cucumber; chayote; squash; zucchini; carrots; beets; okra; and pea pods; (x) fruit and fruit juice - orange/ tangerine; banana; papaya; apple; watermelon/melon; pineapple; grape; mango; and fruit juices/pulp; (xi) fish; (xii) sausages and deli meats - sausage/frankfurter; cold cuts (bologna, ham, fatty ham, and salami); and bacon; (xiii) fat - butter and margarine; (xiv) fast food and snacks - pizza; hamburgers; French fries/chips/straw potatoes; mayonnaise; snacks; popcorn; fried/baked salted pastries; canned vegetables; and peanuts; (xv) coffee; (xvi) tea; (xvii) sodas; (xviii) candies - ice cream; candies/caramels; chocolate powder; chocolate bars/bonbon; fruit jam/jelly; and sweet dairy; and (xix) sugar²⁸.

Dietary patterns were extracted using principal component analysis (PCA). Initially, the Kaiser-Meyer-Olkin (KMO) test was used to measure sampling adequacy ($KMO > 0.6$) and Bartlett's Test of Sphericity ($p\text{-value} < 0.05$) was used to verify that the PCA assumptions were all met^{34,35}. Then, orthogonal Varimax rotation of the factors was applied to improve interpretation, and eigenvalues (> 1.5) and the Cattell's scree plot test were calculated to identify the number of factors that have to be retained. Factor loadings greater than 0.20 were used to verify the correlation between the food group and its pattern. The participants received a factor score for each dietary pattern identified, so the women adhered (in a higher or lower degree) to all identified dietary patterns. Finally, the dietary patterns were labeled according to the food items that were included, the higher factor loading of foods in dietary patterns, and the dietary patterns interpretation.

Three pre-pregnancy dietary patterns were derived on a previous study and labeled *common-Brazilian*, *healthy*, and *processed*²⁸. The *common-Brazilian* pattern consisted of rice, beans, meats and eggs, and vegetable spices. The *healthy* pattern was comprised of roots and tubers, green vegetables and legumes, fruits and fruit juice, dairy products, fish, tea, pasta, cakes and cookies-crackers, candies and was inversely related with coffee intake. The *processed* pattern was characterized by positive loadings of bread, sugar, fat, fast food and snacks, soft drinks, and sausages and deli meats.

Anxiety symptoms

Anxiety symptoms were measured with the State-Trait Anxiety Inventory (STAI)³⁶ at three time points, i.e., in the second and third pregnancy trimesters and at postpartum. The cross-cultural adaptation of the instrument consisted of 4 steps that were detailed in Biaggio et al.³⁷. This instrument was then translated and adapted for use in Brazil by Biaggio & Natalício³⁸. Recently, Tendais et al.³⁹ have validated the instrument in the pregnancy and postnatal periods. This inventory consists of two distinct scales to measure the two concepts of anxiety (state and trait anxiety). In this study, we analyzed only the state anxiety scale, which refers to a transitory emotional state that is characterized by subjective feelings at momentary episodes.

This STAI has 20 items with four response options: almost never, sometimes, often, and almost always. These responses range from 1 (less anxious) to 4 (very anxious), depending on the anxiety level⁴⁰. Therefore, for the STAI, the minimum score is 20 points and the maximum is 80 points. Higher scores on the STAI indicate more anxiety symptoms.

Covariates assessment

A structured questionnaire was used during all trimesters of pregnancy and once at postpartum to obtain the following variables: age (years), education (years), marital status (married/stable partnership or single/others), desire to become pregnant (yes/no), parity (number of deliveries), current alcohol consumption (no/yes) and current smoking habit (never, smokers and ex-smokers). We collected these data in all follow-up visits in order to check for consistency throughout the pregnancy, with the exception of age, education, unplanned pregnancy, and parity, which are variables that do not change.

Weight and height were measured according to standardized procedures and recorded by trained interviewers⁴¹. Weight was assessed at each wave of follow-up with an electronic scale (Filizzola PL 150, Filizzola Ltda, Brazil) with a 150 kg capacity and 0.1 kg precision. Height was measured in duplicate using a portable stadiometer (Seca Ltd., Hamburg, Germany). When the measurements differed by more than 0.5 cm, a third measurement was performed, and the mean of the two similar measurements was used. Body Mass Index [BMI = weight (kg)/height (m)²] was calculated, and the initial nutritional statuses of the women were classified as underweight/ normal weight ($BMI < 25 \text{ kg m}^{-2}$) or overweight/ obese ($BMI \geq 25 \text{ kg m}^{-2}$), which is based on the cutoff points proposed by the Institute of Medicine⁴². The total pre-pregnancy energy intake estimated by the FFQ was used as a co-variable in all three independent models.

Gestational age (weeks) was preferentially measured using the first obstetric ultrasonography ($n = 188$, 95.9%) performed prior to 26 weeks of pregnancy. When this information was not available, we used the reported date of the last menstrual period ($n = 8$, 4.1%) to calculate the gestational age.

Statistical analysis

The characteristics of pregnant women at the second trimester (20-26 gestational weeks) were described as means and standard deviations ($\pm \text{SD}$) for continuous variables and as a frequency for categorical variables. Mean and 95% confidence intervals (95% CI) were used to describe the anxiety symptom scores at the second and third trimesters of pregnancy and the early postpartum period according to selected variables gathered at baseline. These variables were categorized as follows: age (< 30/ ≥ 30 years), education ($\leq 8/ > 8$ years), parity (0-1/ ≥ 2 number of deliveries), early pregnancy BMI ($< 25/ \geq 25 \text{ kg/m}^2$), and total energy intake (1st and 2nd tertile/3rd tertile).

We employed linear mixed-effects (LME) regression models to analyze the longitudinal associations between the dietary patterns identified and anxiety symptom scores from mid-

pregnancy (2nd and 3rd trimesters) to the early postpartum period (30-45 days), adjusted for covariates. The LME model can capture changes both between and within individuals, and allows the inclusion of time-dependent and time-independent covariates and unbalanced time intervals^{43,44}. Moreover, this model is appropriate when the study has missing data at some points in the follow-up. Gestational age (weeks) was included both as a random and fixed-effect. All other variables were treated as fixed effects.

Quadratic gestational age was included in all longitudinal models because the change in the anxiety symptom scores was not linear. Interaction terms between gestational age and dietary patterns were tested, with the aim of detecting differences in the variation in anxiety scores over time for each dietary pattern.

Different models were constructed for each dietary pattern identified. The degree of adherence to each dietary pattern was the exposure variable and anxiety symptom scores was the outcome variable. The covariates were chosen for the final model according to biological plausibility and p-value < 0.2. We used the likelihood ratio test, Akaike Information Criterion (AIC) and Bayesian Information Criterion (BIC) as global criteria to select the best fitting LME models for each dietary pattern. During the modeling process, scatter plots of residuals, and quantile-quantile plots were constructed to check for specific patterns in residuals, to verify the normality of the residuals, and to check the autocorrelation structure, respectively^{43,44}.

Statistical analyses were performed using Stata Data Analysis and Statistical Software (STATA) version 12.0⁴⁵.

Ethical approval

The present study was approved by Ethics Committee of Maternity Hospital (Protocol number: 0023.0.361.000-08) and the Institute of Psychiatry of the Rio de Janeiro Federal University (Protocol number: 0012.0.249.000-09), both from the Rio de Janeiro Federal University (UFRJ), and Ethics Committee of the Municipal Secretary of Rio de Janeiro city (Protocol number: 0139.0.314.000-09). Written consent was obtained from all participants.

Results

We collected data describing anxiety symptoms for 196 women in the second trimester, 197 women in the third trimester and 185 women during the postpartum period (11/196, 5.6% of losses of follow-up). We observed that 10 women did not have available data in the third trimester wave of the follow-up due to the following reasons: missing data (n = 9) and stillbirth (n = 1). Eleven women were absent in the second trimester follow-up and returned to the cohort

at the third trimester visit. At the postpartum visit 22 women were lost, due to: missing data about anxiety symptoms ($n = 2$), outlier score of anxiety ($n = 1$), missing data ($n = 16$), and reported stillbirth ($n = 3$). However, ten women that were absent in the third trimester follow-up returned to the cohort at the postpartum visit (**Figure 1**).

The socio-economic, demographic, lifestyle and obstetrics data can be seen in **Table 1**.

The mean anxiety score observed in the second trimester [40.4 (± 9.3)] did not show a statistically significant change in comparison to the third trimester [40.5 (± 8.6)]. However, we observed a statistically significant decrease between the third gestational trimester and early postpartum [37.2 (± 8.1)]. The rate of change on STAI scores increased 0.535 points/week (95% CI: -0.035, 1.107, $p = 0.066$) from the second to the third gestational trimester, and decreased 0.010/week (95% CI: -0.018, -0.002, $p = 0.019$) from the third trimester to the early postpartum (**Figure 2**).

We observed higher mean of STAI scores at the second gestational trimester among women who had higher adherence to the *processed* pattern (second and third tertiles) when compared to women in the first tertile ($p = 0.018$). Single women had higher mean of STAI scores in the postpartum period when compared to those who were married or had a stable partnership ($p = 0.013$). Women with two or more deliveries had higher mean of STAI scores from the third trimester to the postpartum period when compared to nulliparous or primiparous women. Women with unplanned pregnancy had higher mean of STAI scores in the second trimester ($p = 0.057$), as did those who consumed alcohol ($p = 0.008$) when compared to those who planned the pregnancy or did not consume alcohol, respectively (**Table 2**).

In the multivariate longitudinal regression, after adjustment for potential confounders, we observed that the high adherence to the *common-Brazilian* ($\beta = -1.200$; 95%CI: -2.220, -0.181) and the *healthy* patterns ($\beta = -1.290$; 95%CI: -2.438, -0.134) were negatively associated with the anxiety symptom scores throughout the studied period. We did not find a significant association between the adherence to the *processed* pattern and anxiety symptoms (**Table 3**). Interaction terms between gestational age and each of the three dietary patterns were tested, but they were not statistically significantly associated with anxiety symptom scores and were excluded from the final models.

Discussion

This study investigated the prospective association between pre-pregnancy dietary patterns and changes in anxiety symptom scores from mid-pregnancy to early postpartum in a sample of Brazilian women. The anxiety symptom scores showed a small increase from the

second to the third gestational trimester and a strong decrease from the third trimester to postpartum. Women with higher adherence to the *common-Brazilian* or to the *healthy* patterns had lower anxiety scores from mid-pregnancy to early postpartum compared to those with lower adherence to these patterns. The *processed* pattern did not show a significant association with anxiety symptoms during the assessed period, but we verified higher anxiety scores in women who adhered to this pattern, when compared with the other dietary patterns. To our knowledge, this is the first study to evaluate the association between dietary patterns and anxiety symptoms from mid-pregnancy to early postpartum.

Some studies with pregnant women have identified similar dietary patterns to those observed in our study using PCA. Northstone et al.⁴⁶ defined five dietary patterns in the third trimester of pregnancy from ALSPAC. The similar patterns were ‘health conscious’, composed of salad, fruit, rice, pasta, oat/bran-based breakfast cereals, fish, pulses, fruit juices and non-white bread, and ‘traditional’, consisting of all types of vegetables, red meat and poultry. These patterns are similar to a mix of our *common-Brazilian* and *healthy* patterns. Castro et al.⁴⁷ identified two dietary patterns in Brazilian pregnant women: ‘healthy’, characterized by fruits, green vegetables, vegetables, fish, roots/corn/and potato, milk/dairy, and herbal tea mate, and negative loadings for alcohol and coffee, which is extremely similar to our pattern also called *healthy*. The ‘mixed’ pattern was composed of rice, beans, flour/pasta, breads, cake/cookies, soda/juice, sugar/sweets, fatty foods, meats, chicken, and eggs, and had food groups contained in the three dietary patterns identified in our study. Although our study has identified three dietary patterns before the pregnancy period, they were similar to other studies that derived patterns during pregnancy^{46,47}.

Our study has a higher total variance explained by patterns when compared with previous studies, which reported 31.3% and 23.5% of variance explained, respectively. These data explain the percentage of variability of dietary in a specific population²¹, i.e., the *common-Brazilian* pattern was the most consumed in our sample because it had a higher percentage of variance explained, and all patterns together represent 36.2% of dietary variability of our population.

The anxiety symptom scores assessed from mid-pregnancy to early postpartum showed no change from the second to the third trimester. However, we observed a statistically significant decrease between the third gestational trimester and early postpartum. Figueiredo and Conde¹³ conducted a study in Porto, Portugal and assessed anxiety symptoms at five time points: the first, second, and third gestational trimesters, childbirth (between days 1 and 3) and 3-months postpartum using the STAI instrument. These authors verified that anxiety symptoms

decreased from the first to the second trimesters, increased at the third trimester and at childbirth, and decreased considerably at the postpartum visit. Liou et al.¹⁴ evaluated trends in the mental health of pregnant women from Taiwan and observed that anxiety symptoms increased from 25-29 to 30-34 gestational weeks, remained the same at 34 gestational weeks until birth and declined dramatically after birth (4-6 weeks after postpartum). Although the pattern of variation was similar, the Zung Self-Rating Anxiety Scale was used to assess the anxiety symptoms, which was a different instrument from the one employed in the current study. Both studies found similar results as ours.

The pre-pregnancy dietary patterns employed in the current study has been previously derived in an investigation between the association of dietary patterns and depressive symptoms during pregnancy²⁸. These authors observed that the *healthy* dietary pattern was inversely associated with depressive symptoms and the current study has shown that the *healthy* dietary pattern may reduce the risk of anxiety. Anxiety and depression are common mental illnesses during pregnancy and postpartum that deserves attention, because can affect the maternal and child health^{48,49}.

Pregnant women with high adherence to the *common-Brazilian* or the *healthy* patterns were more likely to have lower anxiety symptom scores from mid-pregnancy to early postpartum when compared to those with high adherence to the *processed* pattern. These results are consistent with previous studies that assessed dietary patterns and anxiety during pregnancy in British²⁴, Australian²⁶ and Norwegian women⁵⁰. In a cross-sectional analysis of the ALSPAC, the authors verified that lower consumption of ‘health-conscious’ and ‘traditional’ patterns was associated with higher anxiety symptoms during pregnancy²⁴. These dietary patterns were composed of foods groups similar to the *common-Brazilian* and *healthy* patterns from the present study. Adherence to dietary patterns composed of rice and beans in Brazil is known as *common-Brazilian*, and subjects who were low-income, had low educational attainment, or low social position, which was the majority of our sample, were more likely to consume a *common-Brazilian* pattern^{33,47} because these foods are cheaper, compared to other dietary items. The low educational attainment and low social position are considered risk factors for anxiety symptoms. However, the women who chose the *common-Brazilian* pattern tended to eat a balanced and more appropriate diet for gestation, thus reducing the risk of anxiety⁵¹.

The *healthy* pattern, mainly composed of healthy foods, such as green vegetables and legumes, fruits and fruit juice, dairy products, fish, and tea, showed a significant association with lower anxiety symptom scores. Our finding is consistent with Jacka et al.²⁶, who studied 1,046 Australian women aged 20-93 years, and observed that the “traditional” pattern

comprised of vegetables, fruit, beef, lamb, fish, and whole-grain foods was associated with a lower likelihood of anxiety disorders. Although these analyses were performed adjusting for age and other confounders, the wide age range should be taken into consideration when comparisons are made. The consumption of fish and other foods with a high content of n-3 polyunsaturated fatty acids (PUFAs), such as meat, eggs, vegetable oils, nuts and seeds can reduce the risk of anxiety symptoms^{24,52}.

We observed a statistically significant higher STAI score among women in the second and third tertiles of adherence to the *processed* pattern when compared to women in the first tertile, but only in the second trimester of pregnancy. In contrast, in the fully adjusted longitudinal models, we found no association between the *processed* pattern and the repeated measures of anxiety symptoms. Therefore, we hypothesize that the sample size is an explanation for the lack of a longitudinal association.

To our knowledge, this is the first study that has investigated the association between dietary patterns and anxiety symptoms in pregnant women with a longitudinal design. For this reason the discussion of our results took into account cross-sectional studies, some of them that have investigated not only pregnant women but adults and even elderly's.

In a study conducted with pregnant women from Baltimore, researchers observed that the intake of foods composed of carbohydrates and fats, such as those in typical *processed* patterns, increased anxiety symptom scores during pregnancy¹⁸. Yannakoulia et al.⁵³ investigated the association between dietary patterns and trait anxiety in a sample of Greek adults from the ATTICA Study. The authors verified that two dietary patterns, one composed of meat and meat products and the other composed of sweets were positively associated with anxiety scores in women aged 26-48 years of age, after adjusting for potential confounders. The researchers of The Hordaland Health Study conducted with Norwegian women found a positive association between the 'Western' pattern (comprised of meat and liver, processed meats, pizza, salty snacks, chocolates, sugar and sweets, soft drinks, margarine, mayonnaise and other dressings, French fries, beer, coffee, cake, and ice cream) and anxiety symptoms in older adults and elderly⁵⁰.

The limitations of this study include the loss of subjects during the study follow-up period, a common drawback in cohort studies, but this loss was small. The anxiety symptom scores were not assessed at baseline, which would have allowed analysis of the change in anxiety symptom scores throughout the study. Another limitation was the unmeasured variables, which may also be related to dietary patterns and/or anxiety. However, we included

the most common factors risk in our analysis such age, education, number of deliveries, marital status, and unplanned pregnancy.

The analytical procedure employed to account for the prospective nature of the data is one of the main strengths of the current study. The diagnosis of mental health disorders is more accurate when it is performed at different times in the same woman, which may provide information about the prevalence and mean scores of psychiatric disorders of interest at several time points and provide information on stability and potential variations⁵⁴. Furthermore, the instruments used to measure dietary intake, mental health, social, and behavioral data are highly accurate and were previously validated in other studies^{29,38}.

In summary, our study revealed that higher adherence to either the *common-Brazilian* or the *healthy* pattern was associated with lower risk of anxiety during mid-pregnancy and early postpartum. Our study suggests that adherence to healthier foods in the pre-gestational period may reduce the risk of anxiety symptoms during the study period.

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Table 1. Characteristics of pregnant women followed at 20-26 gestational weeks (n = 196) in a public health center in the city of Rio de Janeiro, Brazil, 2009-2012^a.

Characteristics	Values
Anxiety symptoms (STAI) ^b , <i>mean of scores</i>	40.4 (\pm 9.3)
Age, <i>mean of years</i>	26.7 (\pm 5.5)
Education, <i>mean of years</i>	8.7 (\pm 2.9)
Parity (at baseline), <i>mean of number of deliveries</i>	1.0 (\pm 1.1)
BMI ^c , <i>mean of kg/m²</i>	27.2 (\pm 4.5)
Pre-pregnancy total energy intake, <i>mean of kcal/d</i>	2,308 (\pm 676)
Marital status, n (%)	
Married or stable partnership	164 (83.7)
Single	32 (16.3)
Unplanned pregnancy (at baseline), n (%)	
No	147 (75.0)
Yes	49 (25.0)
Smoking, n (%)	
Never smoked	145 (74.0)
Current smoker	38 (19.4)
Ex-smoker	13 (6.6)
Alcohol consumption, n (%)	
No	164 (83.7)
Yes	32 (16.3)

^a Values are mean (\pm Standard Deviation) or n (frequency %) unless indicated otherwise.^b STAI refers to State-Trait Anxiety Inventory.^c BMI was obtained at all follow up period.

Table 2. Mean and 95% confidence intervals (95% CI) of changes in anxiety symptoms scores (STAI)^a of selected variables in pregnant and postpartum women followed at a public health center in the city of Rio de Janeiro, Brazil, 2009-2012.

Selected variables ^b	Follow up period					
	20-26 gestational weeks		30-36 gestational weeks		30-45 days postpartum	
	Anxiety symptoms scores					
	n	Mean (95 CI%)	n	Mean (95 CI%)	n	Mean (95 CI%)
Anxiety symptoms scores	196	40.4 (39.1 - 41.7)	197	40.5 (39.3 - 41.7)	185	37.2 (36.0 - 38.4)
Common-Brazilian pattern						
1 st tertile	65	40.9 (38.5 - 43.3)	66	41.6 (39.2 - 44.0)	57	37.4 (35.1 - 39.7)
2 nd and 3 rd tertile	130	40.1 (38.5 - 41.7)	130	39.91 (38.5 - 41.3)	128	37.3 (35.8 - 38.8)
Healthy pattern						
1 st tertile	65	40.2 (38.1 - 42.3)	62	41.6 (39.5 - 43.6)	61	37.9 (35.7 - 40.2)
2 nd and 3 rd tertile	130	40.5 (38.8 - 42.2)	134	40.0 (38.5 - 41.5)	124	37.1 (35.6 - 38.6)
Processed pattern						
1 st tertile	64	38.4 (36.2 - 40.6)*	64	39.2 (37.3 - 41.2)	65	36.8 (34.9 - 38.7)
2 nd and 3 rd tertile	131	41.4 (39.7 - 43.0)*	132	41.1 (39.6 - 42.6)	120	37.7 (36.0 - 39.3)
Age (years)						
< 30	136	40.2 (38.7 - 41.7)	138	40.0 (38.6 - 41.4)	131	36.89 (35.5 - 38.1)
≥ 30	60	40.8 (38.0 - 43.6)	59	41.6 (39.2 - 44.0)	54	38.2 (35.6 - 40.7)
Education (years)						
≤ 8	86	40.6 (38.7 - 42.6)	88	40.4 (38.7 - 42.1)	82	37.4 (35.6 - 39.2)
> 8	110	40.2 (38.4 - 42.0)	109	40.5 (38.8 - 42.2)	103	37.0 (35.4 - 38.6)
Marital status						
Married or stable partnership	164	40.0 (38.6 - 41.4)	174	40.4 (39.1 - 41.6)	166	36.7 (35.5 - 37.8)
Single	32	42.3 (38.5 - 46.0)	23	41.0 (36.7 - 45.4)	19	41.5 (35.8 - 47.2)*

Table 2 (continuation). Mean and 95% confidence intervals (95% CI) of changes in anxiety symptoms scores (STAI)^a of selected variables in pregnant and postpartum women followed at a public health center in the city of Rio de Janeiro, Brazil, 2009-2012.

Selected variables ^b	Follow up period					
	20-26 gestational weeks		30-36 gestational weeks		30-45 days postpartum	
	Anxiety symptoms scores					
Parity (number of deliveries)	n	Mean (95 CI%)	n	Mean (95 CI%)	n	Mean (95 CI%)
0-1	74	38.2 (36.4 - 40.1)*	74	38.9 (36.9 - 40.8)*	68	35.6 (34.0 - 37.1)*
≥ 2	122	41.7 (39.9 - 43.4)	123	41.4 (39.9 - 42.9)	117	38.1 (36.5 - 39.7)
Unplanned pregnancy						
No	49	42.4 (39.0 - 45.7)*	44	42.1 (39.4 - 44.9)	43	38.2 (35.2 - 41.2)
Yes	147	39.7 (38.4 - 41.1)	151	40.0 (38.7 - 41.4)	141	36.9 (35.6 - 38.2)
Smoking (at baseline)						
Never smoked	145	40.0 (38.6 - 41.5)	146	40.1 (38.7 - 41.4)	137	36.9 (35.6 - 38.2)
Current smoker	38	41.6 (37.9 - 45.3)	37	40.8 (37.5 - 44.1)	35*	38.9 (35.1 - 42.8)
Ex-smoker	13	40.5 (35.0 - 45.9)	14	43.7 (38.5 - 48.9)	14	38.4 (33.5 - 43.4)
Alcohol consumption (at baseline)						
No	150	39.6 (38.1 - 40.9)*	167	40.2 (38.8 - 41.5)	158	37.1 (35.7 - 38.4)
Yes	46	43.3 (40.2 - 46.4)	30	42.1 (39.1 - 45.2)	28	39.2 (35.5 - 42.9)
Early pregnancy BMI (kg/m ²) ^c						
< 25	112	39.3 (37.6 - 40.9)	116	40.1 (38.5 - 41.7)	106	37.6 (36.0 - 39.1)
≥ 25	84	41.9 (39.7 - 43.9)	81	40.9 (39.1 - 42.8)	79	36.7 (34.9 - 38.4)
Total energy intake (Kcal)						
1 st and 2 nd tertile (1,056 - 2,400)	131	40.0 (38.4 - 41.5)	130	41.0 (39.5 - 42.5)	126	37.4 (35.9 - 38.9)
3 rd tertile (2,400 - 5,159)	65	41.2 (38.8 - 43.6)	97	39.9 (37.4 - 41.5)	59	36.7 (34.8 - 38.6)

^a STAI refers to State-Trait Anxiety Inventory; ^b Total energy intake was categorized in tertile, the first category refers to the first and second tertiles combined; ^c BMI was obtained in the first wave of the follow up (5-13 gestational weeks).

* refers to significant difference of Student's *t* test (*p* < 0.05).

Table 3. Multiple longitudinal regression models between dietary patterns and anxiety symptoms scores (STAI)^a changes during pregnant and postpartum women followed at a public health center in the city of Rio de Janeiro, Brazil, 2009-2012.

Fixed-effect ^b	Common-Brazilian			Dietary patterns			Processed		
	β^c	95% CI	p-value ^d	β	95% CI	p-value	β	95% CI	p-value
Intercept	27.616	15.426 - 39.807	<0.001	25.478	13.074 - 37.882	<0.001	29.528	17.029 - 42.026	<0.001
Dietary pattern (scores)	-1.200	-2.220 - -0.181	0.021	-1.290	-2.438 - -0.134	0.029	0.742	-0.462 - 1.947	0.227
Age (years)	-0.046	-0.248 - 0.155	0.652	-0.010	-0.211 - 0.192	0.925	-0.029	-0.231 - 0.175	0.788
Education (years)	0.184	-0.171 - 0.543	0.308	0.196	-0.162 - 0.554	0.283	0.183	-0.178 - 0.544	0.320
Marital status (Married or stable partnership/Single)	1.361	-1.200 - 3.921	0.298	1.170	-1.414 - 3.754	0.375	1.230	-1.309 - 3.901	0.330
Parity (number of deliveries)	1.317	0.259 - 2.374	0.015	1.022	-0.022 - 2.066	0.055	1.129	0.076 - 2.182	0.036
Unplanned pregnancy (no/yes)	1.021	-1.413 - 3.455	0.411	1.058	-1.380 - 3.496	0.395	1.034	-1.426 - 3.494	0.410
Smoking									
Current smoker (no/yes)	0.692	-1.822 - 3.205	0.589	1.05	-1.459 - 3.558	0.412	1.013	-1.515 - 3.541	0.432
Ex-smoker (no/yes)	-0.080	-3.930 - 3.769	0.967	-0.277	-4.144 - 3.589	0.888	-0.056	-3.824 - 3.936	0.977
Alcohol consumption (no/yes)	1.865	0.105 - 3.626	0.038	1.612	-0.150 - 3.375	0.073	1.729	-0.034 - 3.491	0.055
Pregnancy BMI (kg/m ²)	0.102	-1.413 - 3.455	0.411	0.092	-0.115 - 0.300	0.383	0.105	-0.105 - 0.314	0.328
Total energy intake (Kcal)	0.001	-0.0181 - 0.002	0.462	0.001	-0.0004 - 0.003	0.082	-0.0004	-0.002 - 0.001	0.682
Gestational age (weeks)	0.465	-0.147 - 1.078	0.136	0.463	-0.149 - 1.075	0.138	0.442	-0.162 - 1.065	0.149
Gestational age quadratic (weeks)	-0.009	-0.018 - 0.0002	0.056	-0.009	-0.018 - 0.0002	0.056	-0.009	-0.022 - 0.001	0.062
Likelihood		-1942.92			-1943.17			-1944.81	
Akaike's information criterion		3921.85			3922.35			3925.62	
Bayesian Information Criterion		3999.97			4000.47			4003.75	
Random-Effect		β^2 (95% CI)			β^2 (95% CI)			β^2 (95% CI)	
σ Gestational age		0.0001 (6.44e-06 - 0.094)			0.001 (0.00002 - 0.642)			0.001 (0.00001 - 0.066)	
σ Intercept		49.260 (24.109 - 100.649)			51.643 (26.840 - 99.366)			52.178 (27.224 - 100.005)	
σ Residual		33.427 (28.884 - 38.684)			33.369 (28.839 - 38.611)			33.369 (28.838 - 38.613)	

^a STAI refers to State-Trait Anxiety Inventory; ^b The first category of the dichotomous variable is the reference and the second is the exposure; ^c β refers to longitudinal linear regression coefficient; ^d p-value refers to maximum likelihood estimator.

Note: Number of women for each follow-up: 1st = 196; 2nd = 197; 3rd = 185 Number of observations= 567; Number of groups= 207; Average of 2.7 observations per group.

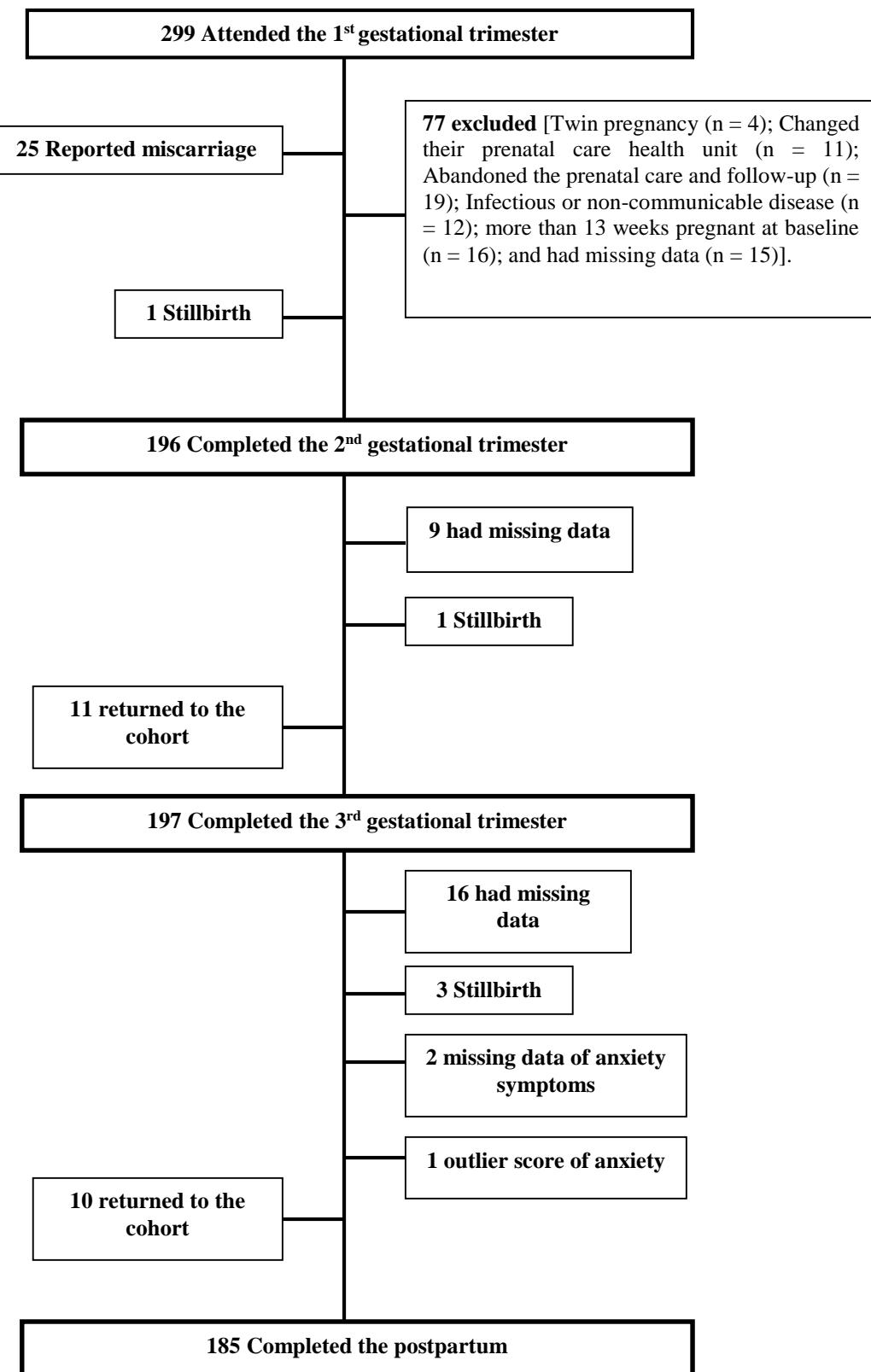


Figure 1. Flowchart illustrating the process of recruitment and follow-up of women attending at a public prenatal care in Rio de Janeiro, Brazil 2009-2011.

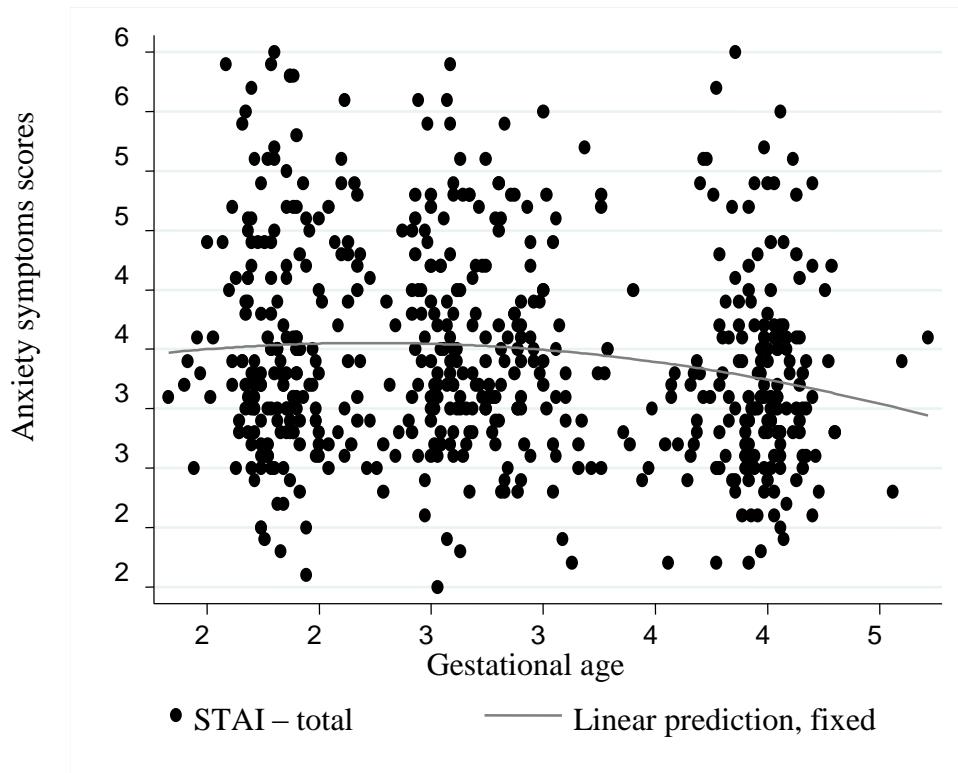


Figure 2. Changes in anxiety symptoms scores during pregnancy trimesters of women followed at a public health center in Rio de Janeiro city, Brazil, 2009 - 2012.

Notes: STAI refers to State-Trait Anxiety Inventory.

a) Mean score of STAI (\pm Standard Deviation) at pregnancy trimesters: 2nd (n = 196): 40.4 (\pm 9.3); 3rd (n = 197): 40.5 (\pm 8.6); and postpartum (n = 185): 37.2 (\pm 8.1). Longitudinal linear regression coefficient according to gestational age (95% confidence interval) = 0.535 (-0.035 - 1.107), p-value = 0.066; and gestational age quadratic (β - 95% confidence interval) = -0.010 (-0.018 - -0.002), p-value = 0.019.

6.3 ARTIGO 3. DIETARY PATTERNS BY CLUSTERS ANALYSIS IN PREGNANT WOMEN: RELATIONSHIP WITH NUTRIENT INTAKES AND DIETARY PATTERNS IN 7 YEARS OLD OFFSPRING

Abstract

Background: Little is known about the tracking of dietary patterns of mothers and their children over time.

Objective: To obtain dietary patterns in pregnancy using clusters analysis, to examine women's mean nutrient intakes in each cluster and to compare the dietary patterns of mothers with those of their children.

Methods: Pregnant women ($n = 12,195$) from the Avon Longitudinal Study of Parents and Children reported their frequency of consumption 50 foods and food groups. These data were used to obtain dietary patterns during pregnancy by clusters analysis. The absolute and energy-adjusted nutrient intakes were compared between clusters. Women's dietary pattern clusters were compared with those of their children. Multinomial logistic regression was performed to evaluate the association between maternal and childhood clusters.

Results: Three dietary pattern clusters were obtained: 'fruit and vegetables', 'meat and potatoes' and 'white bread and coffee'. After energy adjustment the highest mean nutrient intakes were observed in women in the 'fruit and vegetables' cluster. The mothers in the 'fruit and vegetables' cluster during pregnancy were more likely than mother in the other two clusters to have children in a 'plant-based' cluster and less likely to have children in a 'processed' cluster in childhood.

Conclusion: Three distinct dietary pattern clusters were obtained in pregnancy. Women in the 'fruit and vegetables' cluster consumed a diet with a better nutrient profile than women in the other two clusters. Mothers' dietary patterns showed a tendency towards influencing childhood dietary patterns.

Key words: Dietary patterns; Cluster analysis; Pregnancy, Children; ALSPAC.

Introduction

Energy and nutrient requirements during pregnancy are increased due to maternal metabolic demands to achieve optimally length of gestation and fetal development (Ramakrishnan et al., 2012; Grieger and Clifton, 2015). An unhealthy diet and inadequate nutrient intakes during pregnancy may influence weight gain during pregnancy (Maslova et al., 2015), hypertensive disorders of pregnancy (Schoenaker et al., 2014), maternal (Chatzi et al., 2011) and infant (Jacka et al., 2013) mental health, birthweight and fetal growth (Ramakrishnan et al., 2012; Grieger and Clifton, 2015, Okubo et al., 2012).

Adequate nutrient intake during pregnancy is influenced by the consumption of a balanced diet, which needs to be composed of a range of food items providing an adequate supply of macronutrients and bioavailable micronutrients (Black, 2001). Dietary patterns have been commonly used in epidemiological studies of diet, as a method of assessing the combination of the usual foods consumed. Dietary patterns describe the habitual diet as one overall dietary exposure, accounting for the fact that people do not eat isolated nutrients or foods (Hu, 2002; Newby and Tucker, 2004; Wifält et al., 2013). Clusters analysis can be used to derive dietary patterns, which separate the individuals into mutually exclusive and non-overlapping clusters consuming similar foods (Bailey et al., 2006; Devlin et al., 2012; Wifält et al., 2013) and allows detailed comparison of the nutrient quality of the diet between the clusters (Okubo et al., 2011).

Dietary patterns may be used to assess the stability of dietary intake or to follow changes in intake over time (Newby and Tucker, 2004). The tracking of dietary patterns has been described in the literature, although never between a mother and her child. Tracking has been observed in different periods of life, during adulthood (Mishra et al., 2006), from before to during pregnancy (Crozier et al., 2009), from pregnancy to post-partum (Northstone and Emmett, 2008) and from mid childhood to early adolescence (Northstone et al., 2008). Most of the studies found small changes in dietary patterns over time with the ‘healthy’ diet having a greater agreement than other types of diet.

There are currently very few studies which use cluster analysis to derive dietary patterns during pregnancy in diverse settings (Okubo et al., 2011; Okubo et al., 2012; Hoffmann et al., 2013; McGowan et al., 2013) and there are no studies that track dietary patterns between mothers and their children. Therefore, the purpose of this study was to obtain dietary patterns in pregnancy using clusters analysis, to examine the mean nutrients intake of women in each cluster and to compare the dietary patterns of mothers with those of their children.

Methods

Sample

The Avon Longitudinal Study of Parents and Children (ALSPAC) is a longitudinal birth cohort designed to investigate the determinants of health and disease during pregnancy, childhood and beyond (Golding et al., 2001, Fraser et al., 2013). Pregnant women residing in the former county of Avon health area in Southwest England and who had an estimated date of delivery between 1 April 1991 and 31 December 1992 were eligible and invited for this study. A total of 14,541 pregnancies were enrolled and 13,988 infants survived to 1 year of age. Ethical approval for the study was granted by ALSPAC Law and Ethics Committee and Local Research Ethics Committees. More details about ALSPAC are available at the website (<http://www.bristol.ac.uk/alspac/>).

Assessment of dietary intake

The dietary intake was estimated by an unquantified food frequency questionnaire (FFQ) self-completed at approximately 32 weeks' gestation, covering the main foods consumed in the UK (Rogers and Emmett, 1998). The FFQ was composed of 43 food types with five frequency options, which were assigned into weekly frequencies as follows: (i) never or rarely - 0 times per week (pw); (ii) once in 2 weeks - 0.5 times pw; (iii) 1-3 times a week - 2 times pw; (iv) 4-7 times a week - 5.5 times pw; and (v) more than once a day - 10 times pw. For 8 other foods normally consumed daily there were more detailed questions, e.g. number of cups of tea, coffee or milk, number of slices of bread, type of bread (white or other) and milk (full-fat or other) normally consumed (Rogers and Emmett, 1998). Pregnant women with more than 10 missing dietary items were excluded from the analysis, if 10 or less items were missing, it was assumed that the women never consumed that food item.

Nutrients

Daily nutrient intakes were estimated from the FFQ using the nutrient content of foods from the 5th edition of McCance and Widdowsons 'The Composition of Foods' and supplements (The Royal Society of Chemistry 1988 - 1993) and standard portion sizes (Ministry of Agriculture, 1993). The weekly frequencies were divided by seven to obtain the daily nutrient values (Rogers and Emmett, 1998).

Childhood dietary patterns

The FFQ administered when the children were aged 7 years had previously been used to derive dietary clusters describing the child's diet (Smith, et al., 2011). Three dietary pattern clusters had been obtained in childhood, which were labelled 'plant-based', 'traditional British' and 'processed' clusters. The first cluster was composed mainly by healthy foods as brown/wholemeal bread, fruit, vegetables, meat substitutes, vegetarian foods and fish. The second cluster contained children who had highest consumption of full-fat milk, oat-based cereals, meat and potatoes. The last and largest cluster was composed by children that present higher consumption of processed food as white bread, processed meat, fizzy drinks, squash, and snack foods, and less consumption fruit and vegetables, potatoes, bran and oat-based cereals.

Socio-demographic variables

The socio-demographic and lifestyle variables were obtained by self-completed postal questionnaires at 8, 18 and 32 weeks gestation. Maternal education, housing, crowding at home, stressful life events, maternal age, financial difficulty, partner present, maternal smoking in pregnancy, maternal alcohol use in pregnancy, parity, pre-pregnancy body mass index (BMI) and ethnic origin were the selected variables included in this study. Maternal education was classified as low (no academic examinations or a vocational level training), medium (O level - academic examination usually taken at age 16 years) and high (A level - academic examination usually taken at age 18 years or degree). Financial difficulty was obtained based on a list of five items (food, clothing, heating, rent/mortgage and things for child) with four answers' options of difficulty to afford (very, fairly, some and no). The maximum score that could be obtained was 20, which was categorized as no financial difficulty (score = 0), some (score = 1-5) or many (score = 6 or more). Pre-pregnancy Body Mass Index (BMI) [weight (kg)/height (m^2)] was calculated from the self-reported weight and height at 12 weeks gestation. The cut-off points proposed by the Institute of Medicine (IOM, 2009) were used to classify the pre-pregnancy nutritional status: underweight ($<18.5\text{ kg}/m^2$), normal weight ($18.5 - 24.9\text{ kg}/m^2$), overweight ($25.0 - 29.9\text{ kg}/m^2$) or obese ($\geq 30.0\text{ kg}/m^2$).

Statistical Analysis

Cluster analysis was applied to obtain dietary patterns using 47 standardized food items as used in Northstone et al. (2008), with the addition of full-fat milk, other milk and alcohol. Some foods, such as tea, coffee, bread and milk were measured on a different scale to the other variables, therefore all the dietary data were standardized by subtracting the mean and dividing

by the range for each variable, which is an appropriate method of standardization for clusters analysis (Gnanadesikan et al., 1995). Cluster analysis combines individuals into subgroups (or clusters) non-overlapping in which food consumption is relatively homogeneous. The k-means clustering is the main method used in cluster analysis in dietary studies (Newby and Tucker, 2004), it minimises the sum of squares of distances between each woman's food intake and the mean of her cluster. The standard k-means algorithm may not find the correct cluster solution that minimizes this sum of squares (Everitt et al., 2001), therefore the algorithm was run 100 times, with different starting positions, to find the solution with the smallest sum of squares differences.

The analyses were performed for 2 to 7 clusters, and the best cluster solution was chosen considering the amount of variation explained by the solution, the size and interpretation of each cluster, and the linear discriminant analysis. The analysis of variance (ANOVA) and the Tukey-Kramer method were applied to test differences between the cluster means for each food item.

The socio-demographic and life style variations between women in each cluster were compared using the chi-square test. The absolute and energy-adjusted nutrient intakes were described according to the clusters and the ANOVA and the Tukey-Kramer method were used to verify the differences among the nutrients mean. The dietary patterns of the mothers and their children (Smith et al., 2011) were compared by cross-tabulating clusters solutions and the proportion of similar clusters between mother and child were calculated. Multinomial logistic regression with relative risk ratios (RRR) was performed to verify the association between maternal and childhood clusters.

All analyses were performed with the use of statistical software package STATA v13.1.

Results

A total of 12,436 (85.5%) women returned the questionnaire at 32 weeks gestation, and 12,195 (98.1%) of these had sufficient dietary intake data to obtain the clusters solution.

The three cluster solution was found to give the best fit, explaining 14.9% of the variation in the sample. A total of 534 (4.4%) women were reclassified to a different cluster when linear discriminant analysis was applied. Fresh fruit, biscuits, chocolate bars, non-white bread, chocolate and salad were the foods that discriminated most between the clusters. Equivalent data for the 2-7 cluster solutions are shown in Supplemental tables 1-5.

The cluster 1 ($n = 4,478$) was labelled the 'fruit and vegetables' cluster and characterised by having the highest consumption of non-white bread, bran- and oat-based breakfast cereals,

crispbreads/crackers, poultry, fish, eggs, cheese, meat substitutes, pulses, nuts, potatoes (not fried), pasta, rice, vegetables, fruit, fruit juice, herbal tea, low-fat milk, and alcohol compared to the other clusters. The women in this cluster had the lowest intakes of white bread, other breakfast cereal, meat pies, sausages/burgers, fried foods, fried potatoes, roast potatoes, baked beans, cola, tea, coffee, sweets, chocolates, crisps, and full-fat milk.

The second cluster with the lowest number of subjects ($n = 2,469$), was labelled the ‘meat and potatoes’ cluster due to the highest consumption of fried potatoes, roast potatoes, potatoes (not fried), poultry, red meat, meat pies and sausages/burgers, in addition to white bread, other breakfast cereal, biscuits, puddings, cakes/buns, fried foods, pizza, eggs, baked beans, peas, cola, tea, sweets, chocolates, savoury snacks and full-fat milk than the other clusters. This cluster had the lowest intake of meat substitutes and herbal tea.

The largest and the last cluster ($n = 5,248$) was composed of subjects with high consumption of white bread, coffee, cola and full-fat milk, and the lowest intakes of all foods which characterised the ‘fruit and vegetables’ cluster as well as biscuits, puddings, cakes/buns, red meat, pizza, peas and chocolates. It was called the ‘white bread and coffee’ cluster (Table 1).

The main difference in the characteristics of the women with dietary data compared to those without were the percentage with high educational attainment (35.4% vs 32.3%), with a mortgaged or owned housing (75.7% vs. 56.0%), likely to be in a stable partnership (97.3% vs. 93.5%), age ≥ 30 years (39.3% vs. 25.7%) and with a parity of less than 2 (80.3% vs. 74.1%, respectively) (data not shown). Women in the ‘fruit and vegetables’ cluster were more likely to have high educational attainment, mortgaged or owned housing, a stable partnership, no financial difficulty, be non-smokers, of older age, of normal weight pre-pregnancy and nulliparous compared to women in the other clusters. In the ‘meat and potatoes’ cluster women were more likely to be white, to drink alcohol during pregnancy and be underweight pre-pregnancy. The women who were in the ‘white bread and coffee’ cluster were more likely to have low education, a non-stable partnership, many financial difficulties, to smoke during pregnancy, be younger, overweight or obese pre-pregnancy and have had 2 deliveries or more, when compared with the women who were in the other dietary clusters (Table 2).

For absolute mean intakes, women in the ‘white bread and coffee’ cluster had the lowest intake of energy and all nutrients, while those in the ‘meat and potatoes’ cluster had the highest absolute mean intakes of energy and most macronutrients except n-3 fatty acids and fibre and most micronutrients except magnesium, carotene, folate, vitamins C, and D (Table 3). Women in the ‘fruit and vegetables’ cluster had the highest absolute mean intakes of n-3 fatty acids,

DHA, EPA, fibre, magnesium, carotene, folate, vitamin C and D (Table 3). After energy adjustment, the mean intakes of almost all of the nutrients were higher in the ‘fruit and vegetables’ cluster showing that this was the most nutrient dense dietary pattern. Conversely the ‘white bread and coffee’ pattern was the least nutrient dense (Table 4).

There were 7,874 children with dietary pattern data available to compare with their mothers, representing 95.2% (7,874/8,274) of dietary data of children at 7 years of age and 64.6% (7,874/12,195) of eligible pregnancy data. Foods associated with the maternal ‘fruit and vegetables’ cluster were very similar to those in the childhood ‘plant-based’ cluster. Some foods that characterised the ‘meat and potatoes’ cluster during pregnancy characterised the ‘traditional British’ cluster in childhood. Foods characterizing the ‘processed’ cluster in childhood were a mixture of foods from both the ‘meat and potatoes’ and ‘white bread and coffee’ clusters during pregnancy. The ‘processed’ cluster dominated the diets of the children, overall more than half the children were in this cluster, however, mother’s dietary clusters were associated with some variations in children’s dietary clusters. For women who were in the ‘fruit and vegetables’ cluster during pregnancy a third of their children were in the ‘plant-based’ cluster compared with less than a fifth of children with mothers in the other two clusters. For women in the ‘meat and potatoes’ and ‘white bread and coffee’ clusters during pregnancy more than half of their children were in the ‘processed’ cluster in childhood compared with two fifths if the mothers were in the ‘fruit and vegetables’ cluster. For all three maternal diet clusters around a quarter of the children were in the ‘traditional British’ cluster in childhood (Table 5).

The multinomial logistic regression found associations between similar maternal and children dietary patterns over time. Women who were in the ‘meat and potatoes’ and ‘white bread and coffee’ clusters during pregnancy were more than twice as likely to have children in the ‘traditional British’ or ‘processed’ clusters during childhood, when compared with women in the ‘fruit and vegetables’ cluster and children in the ‘plant-based’ cluster. Similar results were observed for women in the ‘fruit and vegetables’ cluster during pregnancy, they were more than twice as likely to have children in the ‘plant-based’ cluster compared with women in the ‘meat and potatoes’ and ‘white bread and coffee’ clusters and children in the ‘processed’ cluster. These associations were slightly attenuated after adjustment for confounders (Table 6).

Discussion

Three dietary patterns during pregnancy were obtained by cluster analysis in this cohort of women: the ‘fruit and vegetables’, ‘meat and potatoes’ and ‘white bread and coffee’ clusters. Women in the ‘meat and potatoes’ cluster had the highest absolute mean intakes of energy and

many nutrients, however after energy adjustment the highest mean nutrient intakes were observed in women in the ‘fruit and vegetables’ cluster. The women in the ‘fruit and vegetables’ cluster during pregnancy were more likely to have children in the ‘plant-based’ cluster and less likely to have children in the ‘processed’ cluster in childhood compared to women in the other two clusters.

The most important limitation of this study was the loss of subjects during the follow-up which is a common problem in cohort studies. We observed only a small loss of data during the pregnancy [16.1% (12,195/14,541) and of these 717 were miscarriages prior to completion of the FFQ], however the loss to follow up was lower than others cohort studies (Okubo et al., 2012; McGowan et al., 2013; Vilela et al., 2014). The FFQ is the instrument most used in epidemiological studies of diet, but memory bias and under- or over-estimation of consumption frequency by untrained individuals are common in this instrument. Women were asked to report their current food intake to minimize recall bias. There was no portion size information collected in the FFQ therefore standard portion sizes were used to estimate nutrient intakes, thus nutrient estimates were totally reliant on the accuracy of the frequency data.

The present study had important strengths such as large sample size, the use of cluster analysis to obtain dietary patterns which allowed each individual to be categorised exclusively into one dietary pattern, the availability of estimates of energy and nutrient intakes and the cohort design which made it possible to compare the dietary intakes of mother and child pairs.

Northstone et al. (2008) obtained dietary patterns using principal component analysis (PCA) in this sample of pregnant women. They identified five dietary patterns named; ‘health conscious’, ‘traditional’, ‘processed’, ‘confectionery’ and ‘vegetarian’. The foods characterising the ‘health conscious’ and ‘vegetarian’ components are combined in the ‘fruit and vegetables’ cluster of the present study, while foods characterising the other three components are combined in the ‘meat and potatoes’ cluster. The foods which composed the ‘white bread and coffee’ cluster except white bread, had low factor loading in the PCA, thus they did not contribute to the components in the Northstone et al. (2008) study.

Of the few studies which derived dietary patterns using cluster analysis during pregnancy, only Hoffmann et al. (2013) in Brazil used an FFQ to measure the dietary intake, reporting the frequency intake according to the median and 25th and 75th percentiles. Other studies used a diet history questionnaire in Japan (Okubo et al., 2011; Okubo et al., 2012) or a 3 days food diary in Ireland (McGowan et al., 2013).

The three clusters identified by Hoffmann et al. (2013) were related to Brazilian dietary habits therefore were substantially different from those in British women. The authors named

the clusters ‘restricted’, ‘varied’ and ‘common-Brazilian’ and the ‘varied’ cluster was the one with the highest intakes of fish, fruits and vegetables so was the cluster most similar to our ‘fruit and vegetables’ cluster. Okubo et al. (2011) obtained 3 cluster solutions in pregnant Japanese women labelled ‘meat and eggs’, ‘wheat products’, ‘rice, fish and vegetables’. The last cluster was characterised by higher median intakes of rice, potatoes, pulses, fruit, green and yellow vegetables, white vegetables, pickled vegetables, and fish, thus was fairly similar to the ‘fruit and vegetables’ cluster found in the current study. McGowan et al. (2012) identified two clusters in the diets of Irish women; ‘Unhealthy’ associated with higher median intakes of white bread, refined breakfast cereals, confectionery, chips, processed meats and high-energy beverages, showing some similarities with our ‘meat and potatoes’ cluster; the second was labelled ‘Health Conscious’, and was characterised by higher intakes of wholegrain breads and breakfast cereals, fruit, vegetables, fruit juice, fish, low-fat milk and white meat consistent with the ‘fruit and vegetables’ cluster of our study.

Crozier et al. (2006) obtained two dietary patterns by cluster analysis in young non-pregnant women from Southampton, UK, these were similar to the dietary patterns of our study. The first one labelled ‘less healthy’ was characterised by higher intakes of white bread, full-fat spread, processed meat, roast potatoes and chips, crisps, added sugar, confectionery and high-energy soft drinks and had similar foods to those in our ‘meat and potatoes’ and ‘white bread and coffee’ clusters combined. The second was called ‘more healthy’ and was characterized by higher intakes of wholemeal bread, breakfast cereals, yoghurt, cheese, reduced-fat spread, cooking and salad oils, fruits and vegetables when compared to the ‘less healthy’ cluster. It was similar to the ‘fruit and vegetables’ cluster of our study. These results suggest that the diet in young British women is similar, whether pregnant or not.

The nutritional profile of the diet of the current cohort of pregnant women was previously reported (Rogers and Emmett, 1998), as well as the correlation between nutrient intakes and dietary patterns obtained by PCA (Northstone et al., 2008). The ‘meat and potatoes’ cluster was characterised by food groups with higher energy-density, when compared with the ‘fruit and vegetables’ and ‘white bread and coffee’ clusters, so this cluster had the highest mean energy intake and absolute intake of many nutrients. A similar dietary pattern to our ‘meat and potatoes’ pattern was derived by PCA in pregnant women of Pregnancy, Infection, and Nutrition (PIN) Study in North Carolina, the highest quartile of this pattern was associated with a higher energy intake than the highest quartile of a pattern characterised by foods similar to our ‘fruit and vegetables’ cluster (Martin et al., 2015).

Nutrients intakes adjusted for energy intake in each cluster, showed different results when compare with absolute nutrient intakes. The highest mean intakes of long-chain polyunsaturated fatty acids (PUFA), fibre and most micronutrients were observed in the ‘fruit and vegetables’ cluster, however mean intakes of some less desirable macronutrients were lowest in this cluster (fat, monounsaturated and saturated fat, carbohydrate, sugar and free sugar). Similarly Northstone et al. (2008), showed that high scores on the PCA ‘processed’ and ‘confectionery’ patterns were associated with increased intakes of sugar and fats after energy adjustment. Okubo et al. (2011) observed the median of daily energy-adjusted nutrient intakes in their ‘rice, fish and vegetables’ pattern was similar to our study, with higher intakes of most nutrients in this cluster, except carbohydrate, total fat, saturated fat, cholesterol and n-3 PUFA. The median intakes of n-3 (6.4 vs. 6.7) and n-6 (1.5 vs. 1.4) PUFA were similar between the ‘rice, fish and vegetables’ and ‘meat and eggs’ patterns.

To the best of our knowledge, this is the first study to compare the dietary patterns by cluster analysis between women during pregnancy and their children. In this study, we observed that a child’s dietary cluster was partially influenced by the mother’s dietary cluster during pregnancy, although the ‘processed’ dietary cluster dominated the children’s diets whatever type of diet the mother had eaten in pregnancy. In a previously study in ALSPAC children obtained cluster dietary patterns using diet diaries and investigated the changes over time in children’s dietary clusters from 7 to 13 years of age. Four dietary clusters were obtained and again the ‘processed’ cluster contained the largest number of children. The ‘healthy’ cluster and the ‘processed’ cluster were the most stable over time suggesting that the types of diet consumed by children at younger ages are likely to track at least over childhood (Northstone et al., 2013).

In Southampton Women’s Survey diet was obtained when the women were not pregnant (Crozier et al., 2006) and a prudent dietary pattern identified by PCA. In the offspring associations between maternal and family factors and quality of pre-school children’s diet were explored and the quality of the mother’s diet, characterized by higher scores on a prudent diet, was the most important determinant of the child’s diet (Fisk et al. 2011). The similarity in clusters dietary patterns over time was also observed in adult subjects from the Netherlands who were followed for 6 months 66.2% of them remained in the same cluster, 11.9% changed to an unhealthier cluster, while 21.9% moved to a healthier cluster (Walthouwer et al., 2014).

In conclusion, we obtained three dietary pattern clusters during pregnancy. Diets of women in the ‘fruit and vegetables’ cluster, showed a better nutrient profile after energy adjustment than those of women in the ‘meat and potatoes’ and ‘white bread and coffee’

clusters. The type of diet consumed by the mother during pregnancy was associated with the type of diet consumed by her offspring in childhood. This study adds to the evidence that improving the diets of pregnant women can have the added advantage of improving the diets of their children.

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Table 1. Mean (standard deviation) frequency of weekly intakes of foods across clusters dietary patterns for 12,195 pregnant women.

Cluster	Fruit and vegetables	Meat and potatoes	White bread and coffee	
Cluster size	4,478	2,469	5,248	F (p-value) ¹
White bread (slices)	2.8 (5.4)^a	8.4 (8.8)^b	8.6 (8.7)^b	769 (<0.001)
Non-white bread (slices)	13.6 (9.6)^a	7.4 (8.6) ^b	5.1 (7.0)^c	1290 (<0.001)
Bran-based cereal	3.4 (2.6)^a	2.1 (2.5) ^b	1.4 (2.0)^c	845 (<0.001)
Oat-based cereal	2.6 (2.7)^a	1.8 (2.5) ^b	1.2 (1.9)^c	471 (<0.001)
Other breakfast cereal	<u>1.5 (2.1)^a</u>	3.1 (2.7)^b	2.2 (2.3) ^c	405 (<0.001)
Biscuits	2.2 (2.0) ^a	6.4 (2.8)^b	1.9 (1.6)^c	4711 (<0.001)
Crispbreads/crackers	0.7 (1.4)^a	0.5 (1.2) ^b	0.3 (0.8)^c	138 (<0.001)
Puddings	1.3 (1.5) ^a	2.0 (1.9)^b	0.9 (1.1)^c	472 (<0.001)
Cakes/buns	1.4 (1.3) ^a	2.6 (2.1)^b	1.2 (1.1)^c	893 (<0.001)
Poultry	1.8 (1.3)^a	1.9 (1.3)^a	1.5 (1.1)^b	127 (<0.001)
Red meat	2.3 (1.9) ^a	2.9 (2.0)^b	2.1 (1.6)^c	184 (<0.001)
Meat pies	<u>0.4 (0.6)^a</u>	0.7 (0.9)^b	0.6 (0.8) ^c	238 (<0.001)
Offal	0.1 (0.4) ^a	0.1 (0.5) ^a	0.1 (0.4) ^a	0.65 (0.524)
Sausages, burgers	0.4 (0.6) ^a	0.7 (0.9)^b	0.7 (0.8) ^c	221 (<0.001)
Fried foods (e.g. fish, eggs, bacon)	<u>0.4 (0.7)^a</u>	0.9 (1.4)^b	0.7 (1.0) ^c	285 (<0.001)
Pizza	0.5 (0.7) ^a	0.6 (0.9)^b	0.4 (0.7)^c	51.0 (<0.001)
Fish	2.5 (1.9)^a	1.9 (1.8) ^b	1.5 (1.5)^c	364 (<0.001)
Eggs	1.5 (1.3)^a	1.5 (1.4)^a	1.2 (1.2)^b	90.7 (<0.001)
Cheese	4.0 (2.3)^a	3.6 (2.3) ^b	2.3 (1.9)^c	742 (<0.001)
Meat substitutes (soya, tofu, etc.)	0.3 (1.0)^a	<u>0.1 (0.9)^b</u>	<u>0.1 (0.7)^c</u>	60.7 (<0.001)
Pulses	0.5 (1.0)^a	0.2 (0.7) ^b	0.1 (0.5)^c	361 (<0.001)
Nuts	0.5 (1.1)^a	0.3 (0.8) ^b	<u>0.2 (0.5)^c</u>	217 (<0.001)
Fried potatoes (chips)	<u>0.8 (0.9)^a</u>	1.7 (1.4)^b	1.5 (1.2) ^c	601 (<0.001)
Roast potatoes	<u>0.7 (0.9)^a</u>	1.3 (1.1)^b	1.1 (1.0) ^c	376 (<0.001)
Potatoes (not fried)	3.2 (1.9)^a	3.3 (1.9)^a	2.3 (1.6)^b	352 (<0.001)
Pasta	1.5 (1.2)^a	1.1 (1.1) ^b	0.9 (1.0)^c	446 (<0.001)
Rice	1.5 (1.2)^a	1.1 (1.2) ^b	0.9 (1.0)^c	377 (<0.001)
Baked beans	<u>1.3 (1.1)^a</u>	1.6 (1.3)^b	1.3 (1.1) ^c	72.6 (<0.001)
Leafy green vegetables	2.2 (1.7)^a	1.9 (1.5) ^b	1.6 (1.2)^c	249 (<0.001)
Other green vegetables	2.5 (1.7)^a	2.0 (1.5) ^b	1.6 (1.1)^c	453 (<0.001)
Carrots	2.6 (1.8)^a	2.2 (1.7) ^b	1.6 (1.2)^c	487 (<0.001)
Other root vegetables	1.1 (1.3)^a	0.9 (1.2) ^b	<u>0.6 (0.9)^c</u>	173 (<0.001)
Peas	2.1 (1.5) ^a	2.2 (1.6)^b	1.7 (1.2)^c	145 (<0.001)
Salad	3.5 (2.4)^a	2.3 (2.0) ^b	1.6 (1.4)^c	1148 (<0.001)
Fresh fruit	8.2 (2.3)^a	5.8 (3.0) ^b	2.9 (2.1)^c	5974 (<0.001)
Fruit juice	5.1 (3.9)^a	3.6 (3.6) ^b	2.1 (2.6)^c	949 (<0.001)
Cola (cups)	<u>0.8 (2.1)^a</u>	1.9 (3.4)^b	1.9 (3.4)^b	165 (<0.001)
Tea (cups)	<u>19.5 (15.1)^a</u>	22.6 (17.7)^b	21.5 (19.6) ^c	27.2 (<0.001)
Coffee (cups)	<u>7.2 (10.4)^a</u>	9.2 (12.3) ^b	10.1 (13.3)^c	69.1 (<0.001)
Herbal tea (cups)	8.9 (26.8)^a	<u>2.9 (15.0)^b</u>	1.9 (10.8)^b	175 (<0.001)
Sweets	<u>0.7 (1.3)^a</u>	1.9 (2.5)^b	0.8 (1.4) ^c	521 (<0.001)
Chocolate	<u>0.9 (1.1)^a</u>	2.6 (2.5)^b	<u>0.9 (1.1)^a</u>	1253 (<0.001)
Chocolate bars	<u>1.3 (1.4)^a</u>	4.1 (2.7)^b	1.6 (1.5) ^c	2154 (<0.001)
Savoury snacks (crisps)	<u>1.4 (1.7)^a</u>	3.1 (2.5)^b	1.9 (2.0) ^c	606 (<0.001)
Full-fat milk (l)	<u>0.8 (1.4)^a</u>	1.6 (1.8)^b	1.5 (1.6)^b	276 (<0.001)
Low-fat milk (l)	1.8 (1.5)^a	1.4 (1.6) ^b	1.0 (1.4)^c	307 (<0.001)
Alcohol	1.1 (2.9)^a	<u>0.9 (2.8)^{ab}</u>	<u>0.9 (3.0)^b</u>	4.27 (0.014)

Total variance = 14.9%. The highest and lowest mean in each row are bold and underlined, respectively.

¹ F values refers to difference between the clusters according to ANOVA F-test statistic and p-value refers to ANOVA's test.^{abc} Where superscripts differ there is a significant difference between cluster means (Tukey–Kramer method).

Table 2. Characteristics of pregnant women from ALSPAC according to clusters dietary patterns.

Confounding factors	Total	Fruit and vegetables	Meat and potatoes	White bread and coffee	P-value ¹
	n (%)	n (%)	n (%)	n (%)	
Maternal education					<0.001
Low	3,622 (29.9)	670 (15.0) ^a	727 (29.6) ^b	2,225 (42.8) ^c	
Middle	4,210 (34.7)	1,319 (29.6) ^a	972 (39.5) ^b	1,919 (36.9) ^c	
High	4,292 (35.4)	2,474 (55.4) ^a	761 (30.9) ^b	1,057 (20.3) ^c	
Housing					<0.001
Mortgaged/owned	8,934 (75.7)	3,724 (85.1) ^a	1,875 (78.4) ^b	3,335 (66.2) ^c	
Public housing	1,508 (12.8)	208 (4.7) ^a	265 (11.1) ^b	1,035 (20.6) ^c	
Other	1,360 (11.5)	446 (10.2) ^a	251 (10.5) ^b	663 (13.2) ^c	
Crowding at home					<0.001
< 1 person/room	8,725 (75.0)	3,630 (83.9) ^a	1,788 (75.6) ^b	3,307 (66.9) ^c	
> 1 person/room	2,905 (25.0)	696 (16.1) ^a	576 (24.4) ^b	1,633 (33.1) ^c	
Financial difficulty					<0.001
None (0)	4,356 (35.9)	1,992 (44.7) ^a	848 (34.5) ^b	1,516 (29.1) ^c	
Some (1-5)	5,346 (44.1)	1,843 (41.3) ^a	1,133 (46.2) ^b	2,370 (45.4) ^c	
Many (> 6)	2,429 (20.0)	626 (14.0) ^a	474 (19.3) ^b	1,329 (25.5) ^c	
Life events					0.007
0-7	10,296 (91.8)	3,862 (92.8) ^a	2,109 (92.1) ^{ab}	4,325 (90.9) ^b	
8-18	915 (8.2)	302 (7.2) ^a	182 (7.9) ^a	431 (9.1) ^{ba}	
Partner					<0.001
No	326 (2.7)	82 (1.9) ^a	49 (2.0) ^a	195 (3.8) ^b	
Yes	11,586 (97.3)	4,330 (98.1) ^a	2,364 (98.0) ^a	4,892 (96.2) ^b	
Maternal age					<0.001
< 20 years	464 (3.8)	64 (1.4) ^a	98 (4.0) ^b	302 (5.8) ^c	
20 – 30 years	6,927 (56.9)	2,075 (46.4) ^a	1,491 (60.5) ^b	3,361 (64.1) ^c	
≥ 30 years	4,787 (39.3)	2,333 (52.2) ^a	876 (35.5) ^b	1,578 (30.1) ^c	
Maternal smoking in pregnancy					<0.001
Non-smoker	5,971 (50.4)	2,503 (56.9) ^a	1,269 (52.8) ^b	2,199 (43.5) ^c	
Stopped	3,607 (30.4)	1,474 (33.5) ^a	705 (29.3) ^b	1,428 (28.3) ^c	
Still smoking	2,275 (19.2)	419 (9.6) ^a	430 (17.9) ^b	1,426 (28.2) ^c	
Maternal alcohol use in pregnancy					<0.001
Non-drinker	910 (7.7)	246 (5.6) ^a	177 (7.4) ^b	487 (9.7) ^c	
Stopped	4,454 (37.6)	1,737 (39.4) ^a	856 (35.5) ^b	1,861 (36.9) ^c	
Still drinking	6,491 (54.7)	2,420 (55.0) ^a	1,376 (57.1) ^b	2,695 (53.4) ^c	
Parity (number of deliveries)					<0.001
0	5,264 (44.8)	2,239 (51.3) ^a	928 (38.9) ^b	2,097 (42.0) ^c	
1	4,172 (35.5)	1,404 (32.2) ^a	983 (41.3) ^b	1,785 (35.7) ^c	
≥ 2	2,307 (19.7)	723 (16.5) ^a	472 (19.8) ^b	1,112 (22.3) ^c	
Pre-pregnancy BMI					<0.001
Underweight	520 (4.8)	167 (4.1) ^a	146 (6.6) ^b	207 (4.6) ^c	
Normal weight	8,057 (74.7)	3,294 (80.5) ^a	1,667 (75.9) ^b	3,096 (68.9) ^c	
Overweight	1,624 (15.1)	489 (11.9) ^a	301 (13.7) ^b	834 (18.6) ^c	
Obese	582 (5.4)	144 (3.52) ^a	83 (3.8) ^b	355 (7.9) ^c	
Ethnic origin					<0.001
White	11,732 (97.4)	4,305 (97.2) ^a	2,405 (98.6) ^b	5,022 (97.0) ^c	
Black	127 (1.1)	43 (1.0) ^a	13 (0.5) ^b	71 (1.4) ^c	
Asian	185 (1.5)	81 (1.8) ^a	22 (0.9) ^b	82 (1.6) ^c	

¹P-values refer to chi-square test

abc Where superscripts differ there is a significant difference among confounder variables according to the clusters.

Table 3. Mean (standard deviation) of daily absolute nutrient intakes according to clusters dietary patterns of 12,195 pregnant women.

Nutrients	Total	Fruit and vegetables	Meat and potatoes	White bread and coffee	P-value ¹
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	
Energy (MJ)	7.24 (2.01)	7.27 (1.69) ^a	9.02 (2.02) ^b	6.39 (1.69) ^c	<0.001
Carbohydrate (g)	212 (62.8)	214 (50.7) ^a	268 (63.3) ^b	186 (54.2) ^c	<0.001
Protein (g)	69.4 (19.7)	75.0 (18.2) ^a	79.6 (19.3) ^b	59.9 (16.7) ^c	<0.001
Fat (g)	71.8 (23.4)	69.3 (20.5) ^a	91.4 (24.2) ^b	64.7 (20.0) ^c	<0.001
Monounsaturated fat (g)	24.2 (7.99)	23.3 (7.00) ^a	31.0 (8.30) ^b	21.7 (6.80) ^c	<0.001
Polyunsaturated fat (g)	12.3 (4.58)	13.0 (4.49) ^a	14.4 (4.64) ^b	10.7 (4.06) ^c	<0.001
Saturated fat (g)	30.1 (11.5)	27.9 (9.96) ^a	39.7 (12.1) ^b	27.5 (10.1) ^a	<0.001
n-3 fatty acid (g)	0.15 (0.15)	0.19 (0.16) ^a	0.14 (0.15) ^b	0.11 (0.13) ^c	<0.001
DHA (g)	0.07 (0.07)	0.09 (0.08) ^a	0.06 (0.07) ^b	0.05 (0.06) ^c	<0.001
EPA (g)	0.05 (0.05)	0.07 (0.05) ^a	0.05 (0.05) ^b	0.04 (0.04) ^c	<0.001
Sugar (g)	96.0 (39.0)	92.8 (27.5) ^a	130.7 (41.4) ^b	82.5 (36.4) ^c	<0.001
Free sugar (g)	60.6 (34.6)	51.0 (23.0) ^a	91.9 (38.1) ^b	54.1 (32.7) ^c	<0.001
Fibre (g)	14.9 (5.13)	18.0 (4.70) ^a	16.4 (4.44) ^b	11.5 (3.51) ^c	<0.001
Calcium (mg)	939 (287)	991 (263) ^a	1093 (289) ^b	823 (258) ^c	<0.001
Iron (mg)	10.2 (3.32)	11.8 (3.02) ^a	11.7 (3.09) ^a	8.2 (2.48) ^b	<0.001
Zinc (mg)	8.17 (2.38)	9.01 (2.18) ^a	9.35 (2.30) ^b	6.91 (1.94) ^c	<0.001
Sodium (mg)	2195 (647)	2322 (605) ^a	2541 (645) ^b	1925 (569) ^c	<0.001
Magnesium (mg)	247 (74.6)	285 (67.9) ^a	280 (67.5) ^b	199 (53.4) ^c	<0.001
Potassium (mg)	2882 (738)	3061 (652) ^a	3315 (725) ^b	2528 (644) ^c	<0.001
Retinol (μg)	367 (362)	353 (319) ^a	432 (380) ^b	349 (384) ^a	<0.001
Carotene (μg)	2133 (1177)	2578 (1292) ^a	2279 (1173) ^b	1686 (876) ^c	<0.001
Riboflavin (mg)	1.70 (0.56)	1.80 (0.51) ^a	1.99 (0.58) ^b	1.48 (0.50) ^c	<0.001
Folate (μg)	243 (73.4)	279 (66.2) ^a	273 (68.3) ^b	199 (55.7) ^c	<0.001
Iodine (μg)	148 (48.5)	157 (46.3) ^a	172 (48.4) ^b	129 (42.9) ^c	<0.001
Niacin (mg)	16.0 (5.19)	17.9 (4.87) ^a	18.1 (5.05) ^a	13.3 (4.25) ^b	<0.001
Thiamine (mg)	1.43 (0.42)	1.60 (0.39) ^a	1.63 (0.40) ^b	1.19 (0.33) ^c	<0.001
Vitamin B6 (mg)	1.89 (0.54)	2.07 (0.49) ^a	2.17 (0.53) ^b	1.60 (0.44) ^c	<0.001
Vitamin B12 (μg)	4.88 (2.70)	5.38 (2.66) ^a	5.33 (2.76) ^a	4.24 (2.57) ^b	<0.001
Vitamin C (mg)	79.7 (35.3)	103 (32.0) ^a	84.6 (31.4) ^b	57.1 (23.2) ^c	<0.001
Vitamin D (μg)	3.83 (2.11)	4.46 (2.23) ^a	4.08 (2.08) ^b	3.17 (1.81) ^c	<0.001
Vitamin E (mg)	8.54 (4.12)	9.99 (4.16) ^a	9.84 (4.02) ^a	6.69 (3.33) ^b	<0.001

¹ P value refers to ANOVA's test.² P value refers to Kruskal-Wallis tests^{abc} Where superscripts differ there is a significant difference between cluster means (Tukey-Kramer method and Kruskal-Wallis tests).

Table 4. Mean (standard deviation) of daily nutrient intake adjusting for energy intake according to clusters dietary patterns of 12,195 pregnant women.

Nutrients	Total	Fruit and vegetables	Meat and potatoes	White bread and coffee	P-value ¹
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	
Carbohydrate (g)	212 (22.5)	213 (21.3) ^a	216 (24.4) ^b	211 (22.3) ^c	<0.001
Protein (g)	69.4 (11.4)	74.8 (10.3) ^a	65.4 (12.21) ^b	66.8 (10.1) ^c	<0.001
Fat (g)	71.8 (8.78)	69.1 (8.34) ^a	72.2 (9.19) ^b	73.9 (8.32) ^c	<0.001
Monounsaturated fat (g)	24.2 (3.18)	23.2 (3.01) ^a	24.5 (3.35) ^b	24.9 (3.03) ^c	<0.001
Polyunsaturated fat (g)	12.3 (3.29)	12.9 (3.25) ^a	11.6 (3.48) ^b	12.1 (3.15) ^c	<0.001
Saturated fat (g)	30.1 (6.26)	27.8 (5.94) ^a	31.1 (6.48) ^b	31.6 (5.82) ^c	<0.001
n-3 fatty acid (g)	0.15 (0.15)	0.19 (0.16) ^a	0.11 (0.14) ^b	0.12 (0.12) ^c	<0.001
DHA (g)	0.07 (0.07)	0.09 (0.08) ^a	0.05 (0.07) ^b	0.06 (0.06) ^c	<0.001
EPA (g)	0.05 (0.05)	0.07 (0.05) ^a	0.04 (0.05) ^b	0.04 (0.04) ^c	<0.001
Sugar (g)	96.0 (25.8)	92.4 (20.9) ^a	104 (28.6) ^b	94.9 (27.2) ^c	<0.001
Free sugar (g)	60.6 (25.7)	50.7 (19.1) ^a	71.5 (28.8) ^b	63.9 (26.3) ^c	<0.001
Fibre (g)	14.9 (4.03)	18.0 (3.57) ^a	13.6 (3.48) ^b	12.9 (2.87) ^c	<0.001
Calcium (mg)	939 (174)	988 (167) ^a	891 (182) ^b	920 (166) ^c	<0.001
Iron (mg)	10.2 (2.27)	11.7 (2.00) ^a	9.54 (2.10) ^b	9.22 (1.83) ^c	<0.001
Zinc (mg)	8.17 (1.40)	8.98 (1.20) ^a	7.65 (1.45) ^b	7.72 (1.21) ^c	<0.001
Sodium (mg)	2195 (332)	2315 (305) ^a	2049 (358) ^b	2161 (307) ^c	<0.001
Magnesium (mg)	247 (47.6)	284 (40.5) ^a	229 (41.7) ^b	223 (34.3) ^c	<0.001
Potassium (mg)	2882 (422)	3053 (390) ^a	2780 (444) ^b	2786 (390) ^b	<0.001
Retinol (μg)	367 (344)	351 (302) ^a	330 (352) ^b	398 (369) ^c	<0.001
Carotene (μg)	2134 (1132)	2574 (1258) ^a	1993 (1146) ^b	1824 (859) ^c	<0.001
Riboflavin (mg)	1.70 (0.39)	1.80 (0.37) ^a	1.64 (0.42) ^b	1.65 (0.38) ^b	<0.001
Folate (μg)	243 (52.2)	278 (45.8) ^a	227 (49.7) ^b	221 (41.2) ^c	<0.001
Iodine (μg)	148 (32.4)	156 (33.0) ^a	140 (32.7) ^b	144 (30.1) ^c	<0.001
Niacin (mg)	16.0 (3.84)	17.8 (3.54) ^a	15.0 (4.03) ^b	14.8 (3.35) ^c	<0.001
Thiamine (mg)	1.43 (0.27)	1.60 (0.24) ^a	1.34 (0.28) ^b	1.33 (0.22) ^c	<0.001
Vitamin B6 (mg)	1.89 (0.36)	2.06 (0.32) ^a	1.81 (0.38) ^b	1.78 (0.31) ^c	<0.001
Vitamin B12 (μg)	4.88 (2.42)	5.36 (2.42) ^a	4.27 (2.44) ^b	4.75 (2.34) ^c	<0.001
Vitamin C (mg)	79.7 (33.0)	103 (30.4) ^a	73.5 (30.2) ^b	62.4 (22.7) ^c	<0.001
Vitamin D (μg)	3.83 (1.92)	4.45 (2.03) ^a	3.30 (1.89) ^b	3.55 (1.67) ^c	<0.001
Vitamin E (mg)	8.54 (3.51)	9.96 (3.54) ^a	7.93 (3.50) ^b	7.61 (3.07) ^c	<0.001

¹ P value refers to ANOVA's test.² P value refers to Kruskal-Wallis tests^{abc} Where superscripts differ there is a significant difference between cluster means (Tukey-Kramer method and Kruskal-Wallis tests).

Table 5. Cross-tabulation between clusters dietary patterns of mothers during pregnancy and children at 7 years of age

Child's clusters dietary patterns	Maternal cluster dietary patterns							
	Fruit and vegetables	Meat and potatoes	White bread and coffee				Total	
	n	%	n	%	n	%	n	%
Plant-based	1,134	35.3	322	19.4	517	17.3	1,973	25.1
Traditional British	743	23.1	445	26.7	738	24.6	1,926	24.4
Processed	1,338	41.6	896	53.9	1,741	58.1	3,975	50.5
Total	3,215	100.0	1,663	100.0	2,996	100.0	7,874	100.0

* Chi-square test <0.001 between maternal and children clusters dietary patterns

Table 6. Unadjusted and adjusted associations between child and maternal clusters dietary patterns estimated by multinomial logistic regression.

Child's clusters dietary patterns	Maternal clusters dietary patterns		
	Fruit and vegetables	Meat and potatoes	White bread and coffee
	Unadjusted	RRR (95% CI) ¹	RRR (95% CI) ¹
Plant-based	1.00 (reference)	1.00 (reference)	1.00 (reference)
Traditional British	1.00 (reference)	2.11 (1.78, 2.50)**	2.18 (1.88, 2.52)**
Processed	1.00 (reference)	2.36 (2.03, 2.74)**	2.85 (2.52, 3.24)**
Plant-based	2.36 (2.03, 2.74)**	1.00 (reference)	0.83 (0.70, 0.97)*
Traditional British	1.12 (0.97, 1.29)	1.00 (reference)	0.85 (0.74, 0.98)*
Processed	1.00 (reference)	1.00 (reference)	1.00 (reference)
Plant-based	2.85 (2.52, 3.24)**	1.21 (1.03, 1.42)*	1.00 (reference)
Traditional British	1.31 (1.16, 1.48)**	1.17 (1.02, 1.35)*	1.00 (reference)
Processed	1.00 (reference)	1.00 (reference)	1.00 (reference)
Adjusted ²	RRR (95% CI) ¹	RRR (95% CI) ¹	RRR (95% CI) ¹
Plant-based	1.00 (reference)	1.00 (reference)	1.00 (reference)
Traditional British	1.00 (reference)	1.78 (1.47, 2.15)**	1.67 (1.41, 1.99)**
Processed	1.00 (reference)	2.00 (1.69, 2.36)**	2.18 (1.87, 2.53)**
Plant-based	2.00 (1.69, 2.36)**	1.00 (reference)	0.92 (0.77, 1.10)
Traditional British	1.13 (0.96, 1.32)	1.00 (reference)	0.86 (0.74, 1.01)
Processed	1.00 (reference)	1.00 (reference)	1.00 (reference)
Plant-based	2.18 (1.87, 2.53)**	1.09 (0.91, 1.30)	1.00 (reference)
Traditional British	1.30 (1.12, 1.51)**	1.16 (0.99, 1.36)	1.00 (reference)
Processed	1.00 (reference)	1.00 (reference)	1.00 (reference)

* p-value <0.05; ** p-value <0.001

¹ Relative risk ratios and 95 % confidence intervals² The analysis was adjusted by maternal education, housing, crowding at home, stressful life events, maternal age, financial difficulty, partner, maternal smoking and alcohol use in pregnancy, parity, pre-pregnancy BMI, ethnic origin and gender. We included only the models with great associations in unadjusted and adjusted analysis models.

Supplemental table 1. Mean (standard deviation) frequency of weekly intakes of foods across clusters dietary patterns for 12,195 pregnant women.

Cluster	Solution 1	Solution 2
Cluster size	5,684	6,511
White bread (slices)	3.5 (6.1) ^a	9.0 (8.9)^b
Non-white bread (slices)	12.9 (9.6)^a	5.0 (7.0) ^b
Bran-based cereal	3.2 (2.6)^a	1.4 (2.0) ^b
Oat-based cereal	2.6 (2.8)^a	1.2 (2.0) ^b
Other breakfast cereal	1.8 (2.3) ^a	2.4 (2.4)^b
Biscuits	3.2 (2.8)^a	2.7 (2.5) ^b
Crispbreads/crackers	0.6 (1.4)^a	0.3 (0.8) ^b
Puddings	1.5 (1.7)^a	1.1 (1.3) ^b
Cakes/buns	1.7 (1.6)^a	1.4 (1.4) ^b
Poultry	1.8 (1.3)^a	1.5 (1.1) ^b
Red meat	2.5 (1.9)^a	2.2 (1.6) ^b
Meat pies	0.4 (0.7) ^a	0.7 (0.8)^b
Offal	0.1 (0.4)^a	0.1 (0.4) ^a
Sausages, burgers	0.4 (0.7) ^a	0.7 (0.8)^b
Fried foods (e.g. fish, eggs, bacon)	0.5 (0.9) ^a	0.8 (1.1)^b
Pizza	0.5 (0.7)^a	0.5 (0.7) ^b
Fish	2.4 (1.9)^a	1.5 (1.6) ^b
Eggs	1.5 (1.4)^a	1.3 (1.2) ^b
Cheese	4.0 (2.3)^a	2.5 (2.0) ^b
Meat substitutes (soya, tofu, etc.)	0.2 (1.0)^a	0.1 (0.7) ^b
Pulses	0.5 (1.0)^a	0.1 (0.4) ^b
Nuts	0.5 (1.0)^a	0.2 (0.5) ^b
Chips	0.9 (1.1) ^a	1.5 (1.3) ^b
Roast potatoes	0.8 (1.0) ^a	1.2 (1.0)^b
Potatoes (not chips)	3.3 (1.9)^a	2.4 (1.7) ^b
Pasta	1.5 (1.2)^a	0.9 (1.0) ^b
Rice	1.5 (1.3)^a	0.9 (1.0) ^b
Baked beans	1.3 (1.1) ^a	1.4 (1.2)^b
Leafy green vegetables	2.2 (1.7)^a	1.6 (1.2) ^b
Other green vegetables	2.4 (1.7)^a	1.6 (1.2) ^b
Carrots	2.6 (1.8)^a	1.7 (1.2) ^b
Other root vegetables	1.1 (1.3)^a	0.6 (0.9) ^b
Peas	2.2 (1.5)^a	1.8 (1.3) ^b
Salad	3.3 (2.4)^a	1.6 (1.5) ^b
Fresh fruit	8.1 (2.3)^a	3.2 (2.2) ^b
Fruit juice	5.0 (3.9)^a	2.2 (2.7) ^b
Cola (cups)	0.9 (2.2) ^a	1.9 (3.5)^b
Tea (cups)	20.1 (15.7) ^a	21.8 (19.3)^b
Coffee (cups)	7.6 (10.6) ^a	10.0 (13.2)^b
Herbal tea (cups)	7.9 (25.2)^a	1.9 (11.1) ^b
Sweets	0.9 (1.7) ^a	1.1 (1.7)^b
Chocolate	1.3 (1.6) ^a	1.3 (1.7)^a
Chocolate bars	1.8 (2.0) ^a	2.1 (2.1)^b
Crisps	1.7 (2.0) ^a	2.2 (2.2)^b
Full-fat milk (l)	0.9 (1.5) ^a	1.6 (1.6)^b
Other milk (ml)	1.8 (1.5)^a	1.0 (1.4) ^b
Alcohol	1.0 (2.7)^a	0.9 (3.1) ^b

Total variance = 10.4%. The highest mean in each row are bold. Linear discriminant analysis = 2.14% (n = 261)

^{ab} Where superscripts differ there is a significant difference between cluster means (Student's T-Test).

Supplemental table 2. Mean (standard deviation) frequency of weekly intakes of foods across clusters dietary patterns for 12,195 pregnant women.

Cluster	Solution 1	Solution 2	Solution 3	Solution 4
Cluster size	2,049	3,416	4,676	2,054
White bread (slices)	<u>3.2 (5.7)^a</u>	<u>3.5 (6.1)^a</u>	8.8 (8.8) ^b	9.1 (8.9)^b
Non-white bread (slices)	12.4 (9.5)^a	13.0 (9.6)^a	<u>4.7 (6.8)^b</u>	6.6 (8.4) ^c
Bran-based cereal	<u>3.6 (2.7)^a</u>	2.9 (2.5) ^b	<u>1.3 (1.9)^c</u>	1.9 (2.3) ^d
Oat-based cereal	6.0 (1.4)^a	<u>0.7 (0.8)^b</u>	1.0 (1.7) ^c	1.5 (2.3) ^d
Other breakfast cereal	<u>1.6 (2.3)^a</u>	<u>1.7 (2.1)^a</u>	2.2 (2.2) ^b	3.1 (2.7)^c
Biscuits	2.6 (2.3) ^a	2.4 (2.1) ^b	<u>1.8 (1.6)^c</u>	6.6 (2.8)^d
Crispbreads/crackers	0.7 (1.4)^a	0.6 (1.3) ^b	<u>0.3 (0.7)^c</u>	0.4 (1.2) ^d
Puddings	1.5 (1.7) ^a	1.2 (1.5) ^b	<u>0.9 (1.1)^c</u>	1.9 (1.9)^d
Cakes/buns	1.6 (1.5) ^a	1.5 (1.4) ^b	<u>1.1 (1.1)^c</u>	2.7 (2.1)^d
Poultry	1.8 (1.3)^a	1.8 (1.3)^a	<u>1.4 (1.1)^b</u>	1.8 (1.2)^a
Red meat	2.2 (1.8) ^a	2.5 (1.9) ^b	<u>2.1 (1.6)^c</u>	2.8 (1.9)^d
Meat pies	0.4 (0.7) ^a	<u>0.4 (0.6)^a</u>	0.6 (0.8) ^b	0.8 (1.0)^c
Offal	0.1 (0.6) ^a	0.1 (0.4) ^a	0.1 (0.4) ^a	0.1 (0.4) ^a
Sausages, burgers	<u>0.4 (0.6)^a</u>	<u>0.4 (0.6)^a</u>	0.7 (0.8) ^b	0.7 (0.9)^c
Fried foods (e.g. fish, eggs, bacon)	<u>0.4 (0.8)^a</u>	<u>0.4 (0.7)^a</u>	0.7 (1.0) ^b	1.0 (1.4)^b
Pizza	0.5 (0.7) ^a	0.5 (0.6) ^b	<u>0.4 (0.7)^c</u>	0.6 (0.9)^d
Fish	2.5 (2.2)^a	2.3 (1.8) ^b	<u>1.5 (1.5)^c</u>	1.8 (1.7) ^d
Eggs	1.5 (1.3)^a	1.5 (1.3)^a	<u>1.2 (1.2)^b</u>	1.5 (1.5)^a
Cheese	3.9 (2.3)^a	3.8 (2.3)^a	<u>2.3 (1.9)^b</u>	3.4 (2.3) ^c
Meat substitutes (soya, tofu, etc.)	0.3 (1.3)^a	0.2 (0.8) ^b	<u>0.1 (0.7)^c</u>	<u>0.1 (0.6)^c</u>
Pulses	0.6 (1.1)^a	0.4 (0.9) ^b	<u>0.1 (0.5)^c</u>	<u>0.2 (0.6)^c</u>
Nuts	0.6 (1.2)^a	0.4 (0.9) ^b	<u>0.2 (0.5)^c</u>	0.3 (0.8) ^d
Chips	0.9 (1.0) ^a	0.9 (0.9) ^a	1.5 (1.2) ^b	1.8 (1.5)^c
Roast potatoes	<u>0.7 (0.9)^a</u>	<u>0.7 (0.9)^a</u>	1.2 (1.0)^b	1.3 (1.1) ^c
Potatoes (not chips)	3.1 (1.9)^a	3.2 (1.9)^a	<u>2.3 (1.6)^b</u>	3.1 (1.9)^a
Pasta	1.5 (1.2)^a	1.4 (1.2) ^a	<u>0.8 (0.9)^b</u>	1.1 (1.0) ^c
Rice	1.5 (1.3)^a	1.4 (1.2) ^a	<u>0.8 (1.0)^b</u>	1.0 (1.1) ^c
Baked beans	<u>1.3 (1.1)^a</u>	<u>1.3 (1.1)^a</u>	1.4 (1.1) ^{ab}	1.6 (1.3)^{bc}
Leafy green vegetables	2.3 (1.7)^a	2.1 (1.7) ^b	<u>1.6 (1.2)^c</u>	1.8 (1.5) ^d
Other green vegetables	2.4 (1.7)^a	2.4 (1.6)^a	<u>1.6 (1.1)^b</u>	1.9 (1.5) ^c
Carrots	2.5 (1.8)^a	2.5 (1.8)^a	<u>1.6 (1.2)^c</u>	2.1 (1.6) ^c
Other root vegetables	1.1 (1.3)^a	0.9 (1.2) ^b	<u>0.6 (0.9)^c</u>	0.8 (1.1) ^d
Peas	2.1 (1.5) ^a	2.1 (1.5) ^a	<u>1.7 (1.2)^b</u>	2.2 (1.6)^c
Salad	3.2 (2.3)^a	3.3 (2.4)^a	<u>1.5 (1.4)^b</u>	2.1 (1.9) ^c
Fresh fruit	7.5 (2.7) ^a	8.1 (2.3)^b	<u>2.7 (1.9)^c</u>	5.2 (2.9) ^d
Fruit juice	5.1 (3.8)^a	4.8 (3.8) ^b	<u>2.0 (2.5)^c</u>	3.3 (3.5) ^d
Cola (cups)	<u>0.8 (2.1)^a</u>	<u>0.9 (2.3)^a</u>	1.9 (3.4) ^b	2.0 (3.6)^b
Tea (cups)	<u>20.6 (15.4)^a</u>	<u>19.4 (15.1)^a</u>	<u>21.6 (19.9)^{ab}</u>	22.7 (18.3)^b
Coffee (cups)	<u>7.1 (10.0)^a</u>	<u>7.6 (10.8)^a</u>	10.3 (13.4)^b	9.4 (12.6) ^c
Herbal tea (cups)	9.4 (28.1)^a	6.9 (23.1) ^b	<u>1.9 (10.9)^c</u>	<u>2.5 (14.0)^c</u>
Sweets	<u>0.7 (1.3)^a</u>	<u>0.7 (1.3)^a</u>	<u>0.8 (1.3)^a</u>	2.1 (2.6)^b
Chocolate	1.0 (1.3) ^a	<u>1.0 (1.1)^a</u>	<u>0.9 (1.1)^b</u>	2.8 (2.6)^c
Chocolate bars	1.5 (1.6) ^a	<u>1.4 (1.4)^b</u>	1.5 (1.5) ^a	4.4 (2.7)^c
Crisps	<u>1.5 (1.9)^a</u>	<u>1.5 (1.8)^a</u>	1.9 (1.9) ^b	3.2 (2.5)^c
Full-fat milk (l)	1.1 (1.7) ^a	<u>0.8 (1.3)^b</u>	1.5 (1.6) ^c	1.7 (1.8)^d
Other milk (l)	2.1 (1.7)^a	1.6 (1.3) ^b	<u>1.0 (1.4)^c</u>	1.2 (1.5) ^d
Alcohol	1.0 (2.9) ^a	1.0 (2.7) ^a	0.9 (3.1) ^a	<u>0.9 (2.8)^a</u>

Total variance = 17.3%. The highest and lowest mean in each row are bold and underlined, respectively.

Linear discriminant analysis = 6.22% (n = 758).

abcd Where superscripts differ there is a significant difference between cluster means (Tukey–Kramer method).

Supplemental table 3. Mean (standard deviation) frequency of weekly intakes of foods across clusters dietary patterns for 12,195 pregnant women.

Cluster	Solution 1	Solution 2	Solution 3	Solution 4	Solution 5
Cluster size	3,387	2,451	1,915	1,718	2,724
White bread (slices)	8.6 (8.7)^a	<u>2.3 (4.7)^b</u>	2.9 (5.4) ^b	8.9 (8.9)^a	8.3 (8.7)^a
Non-white bread (slices)	5.2 (7.2) ^a	15.5 (9.5)^b	12.9 (9.4) ^c	7.0 (8.6) ^d	<u>4.9 (6.3)^a</u>
Bran-based cereal	1.4 (2.0) ^a	3.7 (2.5)^b	3.8 (2.7)^b	1.9 (2.4) ^c	<u>1.1 (1.7)^d</u>
Oat-based cereal	1.1 (1.8) ^a	<u>0.7 (0.9)^b</u>	6.0 (1.4)^c	1.6 (2.4) ^d	0.9 (1.6) ^e
Other breakfast cereal	2.0 (2.2) ^a	<u>1.3 (1.9)^b</u>	1.6 (2.3) ^c	3.1 (2.7) ^d	2.7 (2.4) ^e
Biscuits	<u>1.9 (1.7)^a</u>	2.6 (2.3) ^b	2.7 (2.4) ^b	67.0 (2.7)^c	<u>2.0 (1.7)^a</u>
Crispbreads/crackers	<u>0.3 (0.7)^a</u>	0.7 (1.4)^b	0.7 (1.5)^b	0.5 (1.2) ^c	<u>0.3 (0.9)^a</u>
Puddings	<u>0.9 (1.1)^a</u>	1.3 (1.5) ^b	1.5 (1.7) ^c	2.0 (2.0)^d	1.0 (1.3) ^e
Cakes/buns	<u>1.2 (1.1)^a</u>	1.5 (1.4) ^b	1.6 (1.5) ^b	2.8 (2.1)^c	1.3 (1.2) ^d
Poultry	<u>1.4 (1.1)^a</u>	1.8 (1.3)^b	1.8 (1.3) ^b	1.8 (1.2) ^b	1.6 (1.1) ^c
Red meat	<u>2.1 (1.6)^a</u>	2.5 (2.0) ^b	<u>2.2 (1.8)^a</u>	2.9 (2.0)^c	2.3 (1.7) ^b
Meat pies	0.7 (0.8) ^a	0.3 (0.6) ^b	0.4 (0.7) ^b	0.8 (1.0)^c	0.6 (0.7) ^d
Offal	0.1 (0.4) ^a	0.1 (0.3) ^a	0.1 (0.6) ^a	0.1 (0.4) ^a	0.1 (0.4) ^a
Sausages, burgers	0.7 (0.8) ^a	<u>0.4 (0.6)^b</u>	<u>0.4 (0.6)^b</u>	0.8 (0.9)^c	0.6 (0.7) ^d
Fried foods (e.g. fish, eggs, bacon)	0.7 (1.0) ^a	<u>0.3 (0.7)^b</u>	<u>0.4 (0.8)^b</u>	1.0 (1.4)^c	0.6 (0.9) ^d
Pizza	0.4 (0.7) ^{ab}	0.5 (0.6) ^{ac}	0.5 (0.7) ^c	0.7 (0.9)^d	<u>0.4 (0.6)^b</u>
Fish	<u>1.5 (1.6)^a</u>	2.5 (1.8)^b	2.5 (2.2)^b	1.8 (1.7) ^c	1.7 (1.6) ^c
Eggs	<u>1.2 (1.2)^a</u>	1.6 (1.3)^{bc}	1.5 (1.3)^b	1.5 (1.5)^c	<u>1.3 (1.2)^a</u>
Cheese	<u>2.3 (1.9)^a</u>	4.1 (2.2)^b	4.0 (2.3) ^c	3.6 (2.3) ^d	<u>2.4 (1.9)^a</u>
Meat substitutes (soya, tofu, etc.)	<u>0.1 (0.8)^a</u>	0.2 (0.9)^b	0.3 (1.4)^b	<u>0.1 (0.6)^a</u>	<u>0.1 (0.4)^a</u>
Pulses	<u>0.1 (0.5)^a</u>	0.5 (1.0)^b	0.6 (1.1)^b	<u>0.2 (0.6)^a</u>	<u>0.1 (0.5)^a</u>
Nuts	<u>0.2 (0.5)^a</u>	0.5 (1.0) ^b	0.6 (1.2)^b	0.3 (0.8) ^b	<u>0.2 (0.5)^a</u>
Chips	1.4 (1.2) ^a	0.7 (0.8) ^b	0.9 (1.0) ^c	1.9 (1.5)^d	1.3 (1.1) ^e
Roast potatoes	1.2 (1.0) ^a	<u>0.6 (0.8)^b</u>	0.7 (0.9) ^c	1.3 (1.1)^d	1.1 (1.0) ^e
Potatoes (not chips)	<u>2.3 (1.6)^a</u>	3.3 (1.9)^b	3.1 (1.9) ^c	3.2 (2.0)^{bc}	2.5 (1.7) ^d
Pasta	<u>0.8 (1.0)^a</u>	1.5 (1.2)^b	1.5 (1.2)^b	1.1 (1.1) ^c	1.0 (1.0) ^d
Rice	<u>0.8 (1.0)^a</u>	1.5 (1.2)^b	1.5 (1.3)^b	1.0 (1.2) ^c	1.0 (1.1) ^c
Baked beans	1.4 (1.1) ^a	<u>1.2 (1.1)^b</u>	<u>1.3 (1.1)^{ab}</u>	1.6 (1.4)^d	<u>1.3 (1.1)^{ab}</u>
Leafy green vegetables	<u>1.6 (1.2)^a</u>	2.2 (1.7)^b	2.3 (1.7) ^c	1.9 (1.5) ^d	<u>1.7 (1.3)^a</u>
Other green vegetables	<u>1.6 (1.2)^a</u>	2.5 (1.7)^b	2.5 (1.7) ^b	2.0 (1.5) ^c	1.7 (1.2) ^d
Carrots	<u>1.6 (1.2)^a</u>	2.6 (1.8)^b	2.6 (1.8)^b	2.1 (1.7) ^c	1.8 (1.3) ^d
Other root vegetables	<u>0.6 (0.9)^a</u>	1.0 (1.2) ^b	1.2 (1.3)^c	0.8 (1.1) ^d	<u>0.7 (0.9)^a</u>
Peas	<u>1.7 (1.2)^a</u>	2.1 (1.5) ^b	2.1 (1.5) ^b	2.2 (1.6)^b	1.8 (1.3) ^c
Salad	<u>1.4 (1.3)^a</u>	3.7 (2.4)^b	3.3 (2.3) ^c	2.1 (2.0) ^d	2.0 (1.7) ^d
Fresh fruit	<u>1.5 (0.8)^a</u>	8.1 (2.3)^b	7.6 (2.6) ^c	5.1 (3.0) ^d	6.6 (1.9) ^d
Fruit juice	<u>1.8 (2.4)^a</u>	5.1 (3.8) ^b	5.2 (3.8) ^c	3.4 (3.5)^d	3.1 (3.2) ^e
Cola (cups)	1.9 (3.6) ^a	<u>0.8 (2.0)^b</u>	<u>0.8 (2.1)^b</u>	2.1 (3.6)^c	1.6 (2.9) ^d
Tea (cups)	22.3 (21.1)^a	<u>19.4 (14.9)^b</u>	20.4 (15.5) ^c	22.8 (18.4)^a	19.9 (16.3)^a
Coffee (cups)	10.5 (13.7)^a	7.4 (10.6) ^b	<u>6.9 (9.7)^b</u>	9.4 (12.6)^c	9.1 (12.2) ^c
Herbal tea (cups)	<u>1.9 (10.8)^a</u>	8.1 (23.7)^b	9.9 (29.0)^b	2.3 (12.0) ^c	2.8 (16.7) ^c
Sweets	0.8 (1.3) ^a	<u>0.7 (1.3)^b</u>	0.7 (1.3) ^{ab}	2.2 (2.7)^c	0.9 (1.4) ^a
Chocolate	<u>0.9 (1.1)^a</u>	<u>1.0 (1.1)^a</u>	<u>1.0 (1.3)^a</u>	3.0 (2.7)^b	<u>0.9 (1.1)^a</u>
Chocolate bars	1.6 (1.6) ^a	<u>1.4 (1.5)^b</u>	1.5 (1.6) ^{ab}	4.7 (2.7)^c	1.6 (1.5) ^{ab}
Crisps	1.8 (1.9) ^a	<u>1.4 (1.7)^b</u>	<u>1.5 (1.9)^b</u>	3.3 (2.6)^c	2.1 (2.0) ^d
Full-fat milk (l)	1.6 (1.6)^a	<u>0.7 (1.2)^b</u>	1.1 (1.7) ^c	1.6 (1.8)^a	1.3 (1.5) ^d
Other milk (l)	<u>1.0 (1.4)^a</u>	1.7 (1.3) ^b	2.1 (1.7)^c	1.3 (1.6) ^d	<u>1.1 (1.4)^a</u>
Alcohol	0.9 (3.0) ^a	1.1 (2.9) ^b	1.1 (3.0) ^{ab}	0.9 (2.9) ^a	0.8 (2.8) ^a

Total variance = 19.2%. The highest and lowest mean in each row are bold and underlined, respectively.

Linear discriminant analysis = 5.60% (n = 683).

abcde Where superscripts differ there is a significant difference between cluster means (Tukey–Kramer method).

Supplemental table 4. Mean (standard deviation) frequency of weekly intakes of foods across clusters dietary patterns for 12,195 pregnant women.

Cluster	Solution 1	Solution 2	Solution 3	Solution 4	Solution 5	Solution 6
Cluster size	1,485	2,951	1,223	2,853	2,166	1,517
White bread (slices)	5.4 (7.2) ^a	8.7 (8.7) ^b	11.0 (9.3)^c	7.3 (8.4) ^d	<u>1.7 (4.2)^e</u>	4.3 (6.4) ^f
Non-white bread (slices)	8.1 (8.0) ^a	<u>5.1 (7.3)^b</u>	4.4 (6.9) ^b	6.2 (7.2) ^c	16.2 (9.7)^d	13.3 (9.6) ^e
Bran-based cereal	3.5 (2.7)^a	<u>1.2 (1.9)^b</u>	<u>1.3 (2.0)^{bc}</u>	1.4 (1.9) ^c	3.7 (2.6) ^d	3.4 (2.6)^a
Oat-based cereal	5.8 (1.6)^a	<u>0.6 (1.1)^b</u>	1.3 (2.2) ^c	<u>0.6 (1.0)^b</u>	2.5 (2.6) ^d	2.0 (2.5) ^e
Other breakfast cereal	2.1 (2.4) ^a	2.0 (2.2) ^a	3.3 (2.8)^b	2.6 (2.4) ^c	<u>1.0 (1.7)^d</u>	2.1 (2.3) ^a
Biscuits	2.2 (1.8) ^a	1.9 (1.7) ^b	6.0 (2.9) ^c	2.0 (1.5) ^b	<u>1.7 (1.4)^c</u>	6.9 (2.3)^e
Crispbreads/crackers	0.5 (1.1) ^a	<u>0.2 (0.7)^b</u>	0.4 (1.1) ^{ac}	0.4 (0.9) ^c	0.8 (1.6)^d	0.6 (1.3) ^e
Puddings	1.3 (1.5) ^a	<u>0.8 (1.1)^b</u>	1.8 (1.9) ^c	1.0 (1.3) ^d	1.1 (1.4) ^d	2.1 (2.0)^e
Cakes/buns	1.4 (1.3) ^a	<u>1.1 (1.1)^b</u>	2.6 (2.1) ^c	1.3 (1.2) ^a	1.3 (1.3) ^a	2.6 (2.0)^c
Poultry	1.7 (1.2) ^a	<u>1.4 (1.1)^b</u>	1.7 (1.2) ^a	1.7 (1.1) ^a	1.7 (1.3) ^a	2.0 (1.3)^c
Red meat	<u>2.2 (1.7)^a</u>	2.0 (1.5) ^b	2.7 (1.9) ^c	<u>2.4 (1.7)^a</u>	<u>2.1 (1.9)^{ab}</u>	3.1 (2.0)^d
Meat pies	0.5 (0.8) ^a	0.6 (0.8) ^b	0.9 (1.0)^c	0.5 (0.7) ^a	<u>0.3 (0.5)^d</u>	0.5 (0.8) ^a
Offal	0.1 (0.5)^a	0.1 (0.4) ^{ab}	0.1 (0.5) ^{ab}	0.1 (0.4) ^{ab}	<u>0.1 (0.4)^b</u>	0.1 (0.4) ^{ab}
Sausages, burgers	0.5 (0.7) ^a	0.7 (0.8) ^b	0.8 (1.0)^c	0.6 (0.7) ^a	<u>0.3 (0.5)^d</u>	0.5 (0.8) ^a
Fried foods (e.g. fish, eggs, bacon)	0.6 (0.9) ^a	0.7 (1.0) ^b	1.2 (1.6)^c	0.6 (0.9) ^a	<u>0.3 (0.6)^d</u>	0.5 (1.0) ^a
Pizza	0.5 (0.7) ^a	<u>0.4 (0.7)^b</u>	0.6 (0.9)^c	0.4 (0.6) ^b	0.5 (0.7) ^a	0.6 (0.7)^{ac}
Fish	2.1 (1.9) ^a	<u>1.4 (1.6)^b</u>	<u>1.6 (1.7)^b</u>	1.8 (1.6) ^c	2.6 (2.0)^d	2.4 (1.9) ^e
Eggs	1.4 (1.2) ^a	<u>1.2 (1.2)^b</u>	1.6 (1.5) ^c	1.3 (1.2) ^a	1.6 (1.3)^c	1.6 (1.4) ^c
Cheese	3.0 (2.0) ^a	<u>2.3 (1.9)^b</u>	3.2 (2.3) ^a	2.7 (2.0) ^c	4.4 (2.3)^d	4.3 (2.3)^d
Meat substitutes (soya, tofu, etc.)	0.1 (1.0) ^a	0.1 (0.7) ^a	0.1 (0.5) ^a	<u>0.1 (0.4)^a</u>	0.4 (1.3)^b	0.1 (1.0) ^a
Pulses	0.3 (0.7) ^a	<u>0.1 (0.5)^b</u>	<u>0.1 (0.4)^b</u>	<u>0.1 (0.5)^b</u>	0.8 (1.3)^c	0.4 (0.9) ^d
Nuts	0.3 (0.7) ^a	<u>0.1 (0.4)^b</u>	0.3 (0.8) ^{ac}	0.2 (0.5) ^c	0.7 (1.3)^d	0.4 (0.9) ^e
Chips	1.2 (1.1) ^a	1.5 (1.2) ^b	2.1 (1.7)^c	1.3 (1.1) ^{ad}	<u>0.6 (0.8)^e</u>	1.1 (1.0) ^a
Roast potatoes	1.0 (1.0) ^a	1.2 (1.0) ^b	1.4 (1.1)^b	1.0 (1.0) ^a	<u>0.5 (0.8)^b</u>	0.9 (0.9) ^a
Potatoes (not chips)	2.7 (1.7) ^a	<u>2.3 (1.6)^b</u>	2.8 (1.9) ^{ae}	2.6 (1.7) ^{af}	3.2 (2.0) ^c	3.8 (1.9)^d
Pasta	1.2 (1.1) ^a	<u>0.8 (0.9)^b</u>	0.9 (1.1) ^c	1.0 (1.0) ^c	1.7 (1.2)^d	1.4 (1.1) ^e
Rice	1.2 (1.2) ^a	<u>0.8 (1.0)^b</u>	0.9 (1.1) ^b	1.1 (1.2) ^c	1.6 (1.3)^e	1.4 (1.1) ^f
Baked beans	1.4 (1.1) ^a	1.3 (1.1) ^a	1.7 (1.4)^b	1.3 (1.1) ^a	<u>1.2 (1.1)^c</u>	1.4 (1.1) ^a
Leafy green vegetables	2.0 (1.4) ^a	<u>1.5 (1.2)^b</u>	1.7 (1.4) ^c	1.7 (1.3) ^c	2.5 (1.9)^d	2.2 (1.6) ^e
Other green vegetables	2.0 (1.3) ^a	<u>1.5 (1.1)^b</u>	1.7 (1.4) ^c	1.8 (1.2) ^c	2.8 (1.9)^d	2.4 (1.6) ^e
Carrots	2.0 (1.5) ^a	<u>1.6 (1.2)^b</u>	1.7 (1.4) ^c	1.9 (1.4) ^c	2.8 (1.9)^d	2.7 (1.8)^d
Other root vegetables	1.0 (1.1) ^a	<u>0.6 (0.9)^b</u>	<u>0.7 (1.0)^b</u>	<u>0.7 (0.9)^b</u>	1.1 (1.3)^c	1.1 (1.3)^c
Peas	2.0 (1.3) ^a	<u>1.7 (1.2)^b</u>	2.0 (1.5) ^a	1.9 (1.3) ^{ad}	2.1 (1.5) ^a	2.4 (1.6)^c
Salad	2.1 (1.8) ^a	1.4 (1.4) ^b	<u>1.7 (1.7)^c</u>	2.2 (1.8) ^a	4.2 (2.5) ^d	2.9 (2.2)^e
Fresh fruit	4.7 (2.4) ^a	<u>1.5 (0.8)^b</u>	4.1 (2.7) ^c	6.8 (2.0) ^d	8.9 (2.0)^e	7.6 (2.6) ^f
Fruit juice	3.6 (3.4) ^a	<u>1.7 (2.4)^b</u>	2.6 (3.1) ^c	3.2 (3.2) ^d	5.8 (4.0)^e	4.9 (3.7) ^f
Cola (cups)	1.2 (2.4) ^a	2.0 (3.7) ^b	2.6 (4.2)^c	1.6 (2.9) ^d	<u>0.6 (1.9)^e</u>	0.9 (1.9) ^e
Tea (cups)	21.9 (17.0)^a	22.1 (20.8)^a	23.5 (21.2)^a	19.6 (16.1) ^b	<u>18.9 (14.7)^c</u>	21.4 (14.8)^{ad}
Coffee (cups)	8.5 (11.7) ^a	10.6 (13.7)^b	10.4 (13.7)^b	9.1 (12.1) ^a	<u>6.5 (9.5)^c</u>	<u>7.6 (10.4)^{ac}</u>
Herbal tea (cups)	4.0 (16.1) ^a	<u>1.8 (10.0)^b</u>	<u>1.5 (9.6)^b</u>	3.0 (17.0) ^{ab}	12.6 (31.6)^c	5.4 (19.0) ^d
Sweets	0.8 (1.4) ^a	0.8 (1.3) ^a	2.5 (2.8)^b	0.9 (1.4) ^a	<u>0.6 (1.2)^c</u>	1.2 (1.9) ^d
Chocolate	0.9 (1.1) ^a	<u>0.9 (1.0)^b</u>	3.6 (2.8)^b	0.9 (1.1) ^a	0.9 (1.1) ^a	1.6 (1.7) ^c
Chocolate bars	1.5 (1.6) ^a	1.4 (1.4) ^a	5.5 (2.6)^b	1.5 (1.4) ^a	<u>1.2 (1.3)^c</u>	2.5 (2.1) ^d
Crisps	1.6 (1.9) ^a	1.7 (1.8) ^a	3.7 (2.7)^b	2.0 (2.0) ^c	<u>1.1 (1.5)^d</u>	2.3 (2.2) ^e
Full-fat milk (ml)	1.6 (2.0) ^a	1.5 (1.6) ^a	1.9 (1.8)^b	1.2 (1.5) ^c	<u>0.6 (1.3)^d</u>	1.1 (1.6) ^c
Other milk (ml)	1.7 (1.8)^a	<u>1.0 (1.3)^b</u>	<u>1.0 (1.5)^b</u>	1.2 (1.3) ^c	1.8 (1.4)^a	1.8 (1.6)^a
Alcohol	1.0 (3.1) ^a	0.9 (3.1) ^{ab}	0.9 (3.0) ^{ab}	0.8 (2.8) ^{abd}	1.2 (2.8) ^{acf}	1.0 (2.6) ^{abcdef}

Total variance = 20.7%. The highest and lowest mean in each row are bold and underlined, respectively. Linear discriminant analysis = 6.42% (n = 783).

abcdef Where superscripts differ there is a significant difference between cluster means (Tukey–Kramer method).

Supplemental table 5. Mean (standard deviation) frequency of weekly intakes of foods across clusters dietary patterns for 12,195 pregnant women.

Cluster	Solution 1	Solution 2	Solution 3	Solution 4	Solution 5	Solution 6	Solution 7
Cluster size	874	1,186	2,556	1,355	1,375	2,854	1,995
White bread (slices)	4.9 (7.2) ^a	11.2 (9.4)^b	7.7 (8.5) ^c	5.7 (7.3) ^a	4.1 (6.2) ^a	8.7 (8.7) ^d	<u>1.5 (3.8)^e</u>
Non-white bread (slices)	10.5 (9.1) ^a	<u>4.2 (6.7)^b</u>	5.6 (6.7) ^c	7.7 (7.7) ^d	13.4 (9.6) ^e	5.1 (7.3) ^c	16.8 (9.6)^f
Bran-based cereal	3.1 (2.7) ^a	1.3 (1.9) ^b	<u>1.3 (1.8)^b</u>	3.3 (2.7) ^{ac}	3.4 (2.6)^c	<u>1.3 (1.9)^b</u>	3.6 (2.5)^c
Oat-based cereal	2.4 (2.7) ^a	1.3 (2.2) ^b	<u>0.6 (1.0)^c</u>	5.8 (1.5)^d	2.0 (2.5) ^e	<u>0.6 (1.0)^f</u>	2.4 (2.5) ^a
Other breakfast cereal	2.1 (2.4) ^a	3.4 (2.7)^b	2.6 (2.4) ^c	2.1 (2.5) ^a	2.0 (2.3) ^a	1.9 (2.1) ^a	<u>0.9 (1.6)^d</u>
Biscuits	2.5 (2.1) ^a	6.0 (2.9) ^b	2.0 (1.6) ^c	2.2 (1.9) ^c	7.1 (2.3)^d	1.9 (1.7) ^e	<u>1.7 (1.4)^f</u>
Crispbreads/crackers	0.7 (1.5)^a	0.4 (1.1) ^b	0.3 (0.9) ^b	0.5 (1.1) ^{bd}	0.6 (1.3)^a	<u>0.2 (0.7)^c</u>	0.7 (1.4)^a
Puddings	1.5 (1.8) ^a	1.8 (1.9)^b	1.0 (1.3) ^c	1.3 (1.4) ^a	2.0 (1.9)^b	<u>0.8 (1.1)^d</u>	1.1 (1.4) ^c
Cakes/buns	1.6 (1.5) ^a	2.7 (2.1)^b	1.3 (1.2) ^c	1.4 (1.3) ^{ac}	2.5 (2.0) ^b	<u>1.1 (1.1)^d</u>	1.3 (1.3) ^c
Poultry	2.4 (1.8)^a	1.7 (1.2) ^b	1.6 (1.1) ^b	1.6 (1.1) ^b	1.9 (1.2) ^c	<u>1.4 (1.1)^d</u>	1.6 (1.2) ^b
Red meat	3.2 (2.3)^a	2.7 (1.9) ^b	2.4 (1.7) ^c	2.2 (1.6) ^d	2.9 (1.9) ^e	2.0 (1.5) ^f	<u>1.9 (1.7)^f</u>
Meat pies	0.5 (1.0) ^a	0.9 (1.0)^b	0.6 (0.7) ^a	0.5 (0.8) ^{ac}	0.5 (0.7) ^{ad}	0.6 (0.8) ^e	<u>0.2 (0.5)^f</u>
Offal	0.2 (0.7)^a	0.1 (0.5) ^b	0.1 (0.4) ^b	0.1 (0.5) ^{bc}	0.1 (0.3) ^b	0.1 (0.4) ^b	0.1 (0.3) ^{bd}
Sausages, burgers	0.5 (0.8) ^a	0.8 (1.0)^b	0.6 (0.7) ^a	0.5 (0.7) ^a	0.5 (0.7) ^a	0.7 (0.8) ^c	<u>0.3 (0.5)^d</u>
Fried foods (e.g. fish, eggs, bacon)	0.6 (1.1) ^a	1.2 (1.5)^b	0.6 (0.9) ^{ad}	0.5 (0.9) ^{ad}	0.5 (0.9) ^{ad}	0.7 (1.0) ^{ae}	<u>0.3 (0.6)^c</u>
Pizza	0.5 (0.8) ^a	0.6 (0.9)^b	0.4 (0.6) ^{ac}	0.5 (0.7) ^{ab}	0.6 (0.7) ^{ab}	<u>0.4 (0.7)^c</u>	0.5 (0.7) ^{ab}
Fish	2.8 (2.6)^a	1.6 (1.6) ^{be}	1.7 (1.6) ^b	2.1 (1.8) ^c	2.3 (1.6) ^d	<u>1.4 (1.5)^e</u>	2.5 (1.9) ^f
Eggs	1.8 (1.7)^a	1.6 (1.5) ^b	1.3 (1.2) ^c	1.3 (1.1) ^c	1.5 (1.3) ^b	<u>1.2 (1.2)^c</u>	1.6 (1.3) ^b
Cheese	3.8 (2.3) ^a	3.1 (2.3) ^b	2.6 (1.9) ^c	2.9 (2.0) ^d	4.3 (2.2)^e	<u>2.3 (1.9)^f</u>	4.4 (2.3)^e
Meat substitutes (soya, tofu, etc.)	0.3 (1.5)^a	<u>0.1 (0.5)^b</u>	<u>0.1 (0.4)^b</u>	<u>0.1 (1.0)^b</u>	<u>0.1 (0.6)^b</u>	<u>0.1 (0.7)^b</u>	0.4 (1.3)^a
Pulses	0.5 (1.2) ^a	<u>0.1 (0.4)^b</u>	<u>0.1 (0.4)^b</u>	0.2 (0.6) ^c	0.4 (0.8) ^d	0.1 (0.5) ^b	0.7 (1.2)^e
Nuts	0.5 (1.1) ^a	0.3 (0.7) ^b	0.2 (0.5) ^b	0.3 (0.7) ^b	0.4 (0.9) ^{ab}	<u>0.1 (0.4)^c</u>	0.7 (1.3)^d
Chips	1.1 (1.3) ^a	2.1 (1.6)^b	1.3 (1.1) ^c	1.2 (1.1) ^{ac}	1.1 (1.0) ^{ac}	1.5 (1.2) ^d	<u>0.6 (0.7)^e</u>
Roast potatoes	1.1 (1.2) ^a	1.4 (1.1)^b	1.0 (0.9) ^a	1.0 (1.0) ^{ac}	<u>0.9 (0.9)^c</u>	1.1 (1.0) ^a	0.5 (0.7) ^d
Potatoes (not chips)	4.2 (2.1)^a	2.8 (1.9) ^b	2.5 (1.7) ^c	2.6 (1.7) ^c	3.6 (1.9) ^d	<u>2.2 (1.6)^e</u>	3.0 (1.9) ^b
Pasta	1.5 (1.4) ^a	0.9 (1.0) ^b	1.0 (1.0) ^{bd}	1.2 (1.1) ^c	1.4 (1.1) ^a	<u>0.8 (0.9)^b</u>	1.6 (1.2)^a
Rice	1.6 (1.6)^a	<u>0.8 (1.0)^b</u>	1.0 (1.1) ^c	1.2 (1.1) ^d	1.3 (1.1) ^e	<u>0.8 (1.0)^b</u>	1.5 (1.2)^a
Baked beans	1.5 (1.4) ^a	1.7 (1.4)^b	1.3 (1.0) ^{cd}	1.4 (1.1) ^{ac}	1.4 (1.1) ^a	1.3 (1.1) ^d	<u>1.2 (1.0)^e</u>
Leafy green vegetables	5.1 (1.6)^a	1.7 (1.3) ^b	<u>1.5 (1.1)^c</u>	1.8 (1.2) ^b	1.8 (1.2) ^b	<u>1.5 (1.1)^c</u>	1.8 (1.2) ^b
Other green vegetables	5.2 (1.5)^a	1.7 (1.3) ^b	1.6 (1.0) ^b	1.7 (1.0) ^{be}	2.0 (1.3) ^c	<u>1.5 (1.0)^d</u>	2.1 (1.3) ^c
Carrots	5.0 (1.8)^a	1.8 (1.4) ^b	1.7 (1.2) ^b	1.8 (1.2) ^b	2.3 (1.5) ^c	<u>1.5 (1.1)^d</u>	2.2 (1.5) ^c
Other root vegetables	2.3 (2.1)^a	<u>0.7 (1.0)^b</u>	<u>0.6 (0.8)^b</u>	0.9 (1.0) ^c	0.9 (1.0) ^c	<u>0.6 (0.8)^b</u>	0.8 (0.9) ^c
Peas	3.1 (2.1)^a	2.0 (1.5) ^b	1.8 (1.3) ^c	1.9 (1.2) ^{bc}	2.2 (1.4) ^d	<u>1.6 (1.2)^e</u>	1.9 (1.3) ^{bc}
Salad	4.0 (2.6)^a	1.7 (1.7) ^b	2.1 (1.7) ^c	2.0 (1.7) ^c	2.8 (2.2) ^d	<u>1.4 (1.3)^e</u>	3.9 (2.4)^a
Fresh fruit	7.4 (2.8) ^a	4.0 (2.7) ^b	6.7 (2.0) ^c	4.4 (2.3) ^d	7.6 (2.6) ^a	<u>1.5 (0.8)^e</u>	8.7 (2.1)^f
Fruit juice	4.8 (4.1) ^a	2.6 (3.1) ^b	3.1 (3.2) ^c	3.4 (3.3) ^c	4.9 (3.7) ^a	<u>1.7 (2.3)^d</u>	5.7 (3.9)^e
Cola (cups)	1.2 (2.9) ^a	2.6 (4.2)^b	1.6 (2.8) ^c	1.3 (2.5) ^a	<u>0.9 (1.9)^d</u>	2.0 (3.7) ^e	<u>0.6 (1.8)^d</u>
Tea (cups)	22.3 (17.4)^a	23.5 (21.1)^a	19.6 (16.0)^b	21.5 (16.9)^a	21.0 (14.4)^a	22.2 (20.9)^a	18.6 (14.8)^b
Coffee (cups)	8.8 (11.4)^a	10.2 (13.7)^{ab}	9.1 (12.1) ^{ad}	8.6 (12.0) ^a	7.4 (10.4) ^a	10.6 (13.7) ^b	<u>6.5 (9.6)^c</u>
Herbal tea (cups)	7.4 (23.4) ^a	<u>1.5 (9.6)^b</u>	<u>2.8 (16.6)^b</u>	3.9 (16.3) ^c	5.2 (17.5) ^{ac}	1.8 (10.0) ^b	12.1 (31.5)^d
Sweets	1.1 (1.8) ^a	2.5 (2.7)^b	0.9 (1.4) ^{ac}	0.8 (1.4) ^c	1.2 (1.9) ^a	0.8 (1.3) ^{ac}	<u>0.5 (1.1)^d</u>
Chocolate	1.2 (1.5) ^a	3.5 (2.8)^b	<u>0.9 (1.1)^c</u>	<u>0.9 (1.1)^c</u>	1.6 (1.7) ^d	<u>0.9 (1.0)^c</u>	0.9 (1.1) ^c
Chocolate bars	1.6 (1.8) ^a	5.5 (2.6)^b	1.5 (1.4) ^a	1.6 (1.6) ^a	2.6 (2.1) ^c	1.4 (1.4) ^a	<u>1.1 (1.3)^d</u>
Crisps	1.8 (2.2) ^a	3.7 (2.7)^b	2.0 (2.0) ^a	1.6 (1.8) ^a	2.2 (2.1) ^c	1.7 (1.8) ^a	<u>1.1 (1.5)^c</u>
Full-fat milk (ml)	1.4 (1.8) ^a	1.9 (1.8)^b	1.2 (1.5) ^{ae}	1.6 (1.9) ^a	1.0 (1.5) ^c	1.5 (1.6) ^a	<u>0.6 (1.2)^d</u>
Other milk (ml)	1.5 (1.6) ^a	<u>1.0 (1.5)^b</u>	1.1 (1.3) ^c	1.7 (1.8)^d	1.9 (1.6)^d	<u>1.0 (1.3)^b</u>	1.8 (1.3)^d
Alcohol	0.9 (2.6) ^a	0.9 (3.1) ^{ab}	0.9 (2.9) ^a	0.9 (2.7) ^a	1.0 (2.4) ^a	0.9 (3.0) ^{ab}	1.2 (3.2) ^{ac}

Total variance = 22.2%. The highest and lowest mean in each row are bold and underlined, respectively. Linear discriminant analysis = 7.35% (n = 896).

abcdefg Where superscripts differ there is a significant difference between cluster means (Tukey-Kramer method).

6.4 ARTIGO 4. MATERNAL DIETARY PATTERNS DURING PREGNANCY AND INTELLIGENCE QUOTIENT IN THE OFFSPRING AT 8 YEARS OF AGE: FINDINGS FROM THE ALSPAC COHORT

Abstract

Background: The dietary intake during pregnancy may influence the gestational and childhood health.

Objective: To obtain dietary patterns in pregnancy and investigate the association between these patterns and intelligence quotient (IQ) in offspring at 8 years of age.

Methods: Pregnant women enrolled on the Avon Longitudinal Study of Parents and Children completed a food frequency questionnaire at 32 weeks' gestation. Dietary patterns were obtained by clusters analysis. The child's IQ was assessed using the Wechsler Intelligence Scale for Children. Imputed models were performed for missing values. Linear regressions models were applied to investigate the associations between the maternal dietary patterns and IQ in childhood.

Results: Three dietary pattern clusters best described women's diets during pregnancy: 'fruit and vegetables' (non-white bread, fish, vegetables, fruit, herbal tea, and low-fat milk), 'meat and potatoes' (meat, potatoes and some processed foods), 'white bread and coffee' (white bread, coffee, and lower intakes of healthy foods). The children of women who were in the 'meat and potatoes' and 'white bread and coffee' clusters during pregnancy had lower average verbal, performance and full scale IQ at 8 years of age, when compared to children of mothers in the 'fruit and vegetables' cluster, even after adjustment for known confounders.

Conclusion: The pregnant women who were in the 'fruit and vegetables' cluster had offspring with higher average IQ than children of mothers in the 'meat and potatoes' and 'white bread and coffee' clusters.

Key words: Dietary patterns, Cluster analysis, Intelligence Quotient, Pregnancy, Children, ALSPAC.

Introduction

General intellectual functioning is described by the intelligence quotient (IQ), which refers to general mental capacity, such as learning ability, reasoning and problem solving (DSM IV, 1994). Brain development occurs at different stages of life, however its fastest growth occurs in the first two years after conception therefore this is a critical period. Brain function affects cognitive development and behavioural performance over-time (Thompson & Nelson, 2001).

During pregnancy important neurologic functions are in development. Research has shown long-term positive associations of maternal diet with offspring neurodevelopment (Hibbeln et al., 2007; Anjos et al., 2013; Gil & Gil, 2015; Starling et al., 2015). Intakes of individual foods and nutrients during pregnancy have been shown to be associated with neurodevelopment outcomes in childhood (Anjos et al., 2013; Gil & Gil, 2015; Starling et al., 2015). Breastfeeding and diet in early infancy are also associated with neurodevelopment outcomes in children (Anderson et al., 1999; Auestad et al., 2003; Michaelsen et al., 2009).

The study of isolated nutrient or food intakes is of limited value because people do not consume nutrients or foods singly but in complex combinations. The derivation of dietary patterns is considered an appropriate way to assess dietary intake, because this method allows the evaluation of a combination of different types of food consumed together. Dietary patterns can be used to assess the habitual dietary intake of population groups in a meaningful way (Hu, 2002; Newby and Tucker, 2004).

Studies have examined the association between dietary patterns and cognitive outcomes at different stages of life; in childhood, adolescence and old age (Gale et al., 2009; Northstone et al., 2012; Nyaradi et al., 2014; Kim et al., 2015). These studies have shown that higher scores on dietary patterns characterised by ‘healthy’ foods are associated with better cognitive outcomes, including higher childhood IQ. In addition, higher scores on an ‘unhealthy’ dietary pattern are associated with poorer cognitive outcomes in childhood and adolescence (Gale et al., 2009; Northstone et al., 2012; Smithers et al., 2012; Smithers et al., 2013; Nyaradi et al., 2014; Kim et al., 2015).

The effects of maternal dietary patterns during pregnancy on neurodevelopment outcomes in childhood are unknown. Therefore, the purpose of the present study was to obtain maternal dietary patterns during pregnancy and investigate the association between these dietary patterns and IQ evaluated in offspring at 8 years of age.

Methods

Sample

The Avon Longitudinal Study of Parents and Children (ALSPAC) is a prospective cohort of pregnant women and their partners and offspring residing in the former county of Avon in Southwest England. It is designed to investigate the development of health and disease during pregnancy, childhood and beyond (Golding et al., 2001; Boyd et al., 2013). Pregnant women who had an estimated date of delivery between 1 April 1991 and 31 December 1992 were eligible and invited for this study. A cohort of 14,541 pregnancies was established and 13,988 infants survived to 1 year of age. Ethical approval for the study was obtained by ALSPAC Law and Ethics Committee and Local Research Ethics Committees. More details about ALSPAC are available at website (<http://www.bristol.ac.uk/alspac/>).

Dietary data

Dietary data was obtained at approximately 32 weeks' gestation by a self-completed unquantified food frequency questionnaire (FFQ), which reported the frequency of consumption of 50 foods or food groups regularly consumed in UK (Rogers and Emmett, 1998). The five frequency options of the FFQ were transformed into weekly frequencies as follows: (i) never or rarely - 0 times per week (pw); (ii) once in 2 weeks - 0.5 times pw; (iii) 1-3 times a week - 2 times pw; (iv) 4-7 times a week - 5.5 times pw; and (v) more than once a day - 10 times pw. Pregnant women were excluded from the analysis when had more than 10 missing dietary items. However, if 10 or less items were missing, each was given a value 0, since it was assumed that the women never consumed that food item. Detailed information about the FFQ and dietary intake is published in Rogers and Emmett (1998).

Intelligence quotient (IQ) data

At 8 years of age, all children enrolled in ALSPAC were invited to attend a research clinic where trained psychologists measured their IQ using an adapted form of the Wechsler Intelligence Scale for Children (WISC) - III (Wechsler et al., 1992). The raw scores were age adjusted (Joinson et al., 2007). In this study we included singleton and first-twins births as proposed in previous study from ALSPAC (Hibbeln et al., 2007).

Confounding variables

Variables which had previously been shown to be associated with diet and neurodevelopmental outcomes in childhood were selected (Hibbeln et al., 2007). The maternal

and child characteristics were obtained by self-completed postal questionnaires answered by the mother at 8, 18 and 32 weeks gestation, and 6 months postpartum. Confounding variables included maternal education, housing, crowding at home, partner present, maternal age, maternal smoking in pregnancy, maternal alcohol use in pregnancy, parity, ethnic origin, pre-pregnancy body mass index (BMI), breastfeeding, child gender, child diet at 7 years and age at IQ measurement. Maternal education was classified as low (no academic examinations or a vocational level training), medium (O level - academic examination usually taken at age 16 years) and high (A level - academic examination usually taken at age 18 years or degree). Pre-pregnancy Body Mass Index [weight (kg)/height (m²)] was calculated from the self-reported weight and height at 12 weeks gestation.

Statistical analysis

The dietary patterns were obtained by cluster analysis using 47 standardized food items, which were the same food groups used in Northstone et al. (2008) to obtain dietary patterns by principal component analysis, with the addition of full-fat milk, other milk and alcohol. All dietary data were standardized by subtracting the mean and dividing by the range for each variable. K-means clustering was used to obtain the dietary patterns. The best solution of cluster dietary patterns, with the smallest sum of squares differences, was found after running the algorithm 100 times. The analysis of variance (ANOVA) and the Tukey-Kramer methods were applied to test the differences between the cluster means for each food item.

The confounder variables included in this study were compared between children with and without IQ data using Student's T test and the chi-square test for continuous and categorical variables, respectively. The ANOVA, the Tukey-Kramer method and chi-square test were applied to test the differences in confounding variable structures between clusters.

Multiple imputation

Considering the loss of follow-up in longitudinal studies, multiple imputation can be used as an alternative to applying listwise deletion to missing data which reduces statistical power and introduces biases if those with missing data show systematic differences to those with complete data. In ALSPAC, there is substantial information regarding the pattern of missing data and we used this to impute for missing data. Multiple Imputation by Chained Equations (MICE) is a common method used to handle missing data (Sterne et al., 2009; White et al., 2011). This method relies on the 'missing at random' (MAR) assumption where missing data is predictable from observed data. Therefore, the first step of imputation in this study was

to verify the correlation between the IQ data and different neurodevelopment outcomes in childhood for which we had more complete data. Variables with correlations greater than 0.2 were used in the MICE models: vocabulary scores and grammar scores at 24 months, verbal and performance IQ at 49 months, fine motor at 42 months and hyperactivity scores at 81 months (data not shown). The correlated variables of neurodevelopment outcomes were included in all models of imputation.

For those with dietary intake data during pregnancy two models of imputation were constructed. In the first model, we imputed missing confounding variables data for the children with complete IQ measurements at 8 years and correlated neurodevelopment outcomes, which were presented before (6,817). In the second model, the missing data of IQ and all confounders were imputed (12,039). One hundred imputed datasets were generated and all variables used in this study were imputed simultaneously, using adequate multivariate imputation methods. The fraction of missing information (FMI) was used to justify if the number of imputations was sufficient for the analysis. The rule of thumb suggests that the number of imputations (m) should be at least equal to the percentage of incomplete cases in the dataset, which can be assessed by the following equation: $m \geq 100 * FMI$ (White et al., 2011).

Figure 1 presented a flow chart for this cohort showing the number of subjects included in each step of this study. Unadjusted and adjusted linear regression models were performed to evaluate the association between dietary patterns during pregnancy and IQ at 8 years of age. Verbal, performance and full scale of IQ were assessed in separate models. The ‘fruit and vegetables cluster’ was designated as the reference group since this cluster was defined by foods considered to be ‘healthy’. The multiple linear regressions were adjusted for all confounding variables listed previously. The linear regression models were performed in three different models: (i) all available data without imputation; (ii) imputations for missing data of IQ and all confounders, only up to the sample for complete the IQ scale at 8 years or another correlated neurodevelopment outcomes (6,817); (iii) imputations for missing data of IQ and all confounders included all subjects with eligible dietary intake data (12,039).

All analyses were performed with the use of statistical software package STATA v13.1.

Results

Three maternal cluster dietary patterns during pregnancy were obtained which explaining 14.9% of the variation in the sample. The cluster solutions were labelled as ‘fruit and vegetables’ ($n = 4,478$), ‘meat and potatoes’ ($n = 2,469$) and ‘white bread and coffee’ ($n = 5,248$) clusters (Table 1).

The ‘fruit and vegetables’ cluster women had the highest frequency of consumption of non-white bread, fish, cheese, pulses, nuts, pasta, rice, vegetables, salad, fruit, fruit juice, when compared to the other clusters. The ‘meat and potatoes’ cluster women had the highest frequency of consumption of all types of potatoes, red meat, meat pies, sausages/burgers, pizza, baked beans, peas and fried foods than the other clusters. In the largest cluster ‘white bread and coffee’ the women consumed many of the foods associated with the other two clusters less frequently with white bread, coffee, cola and full-fat milk being the foods that most characterised this cluster pattern. Table 1 provides a full list of the food consumption frequencies in each cluster.

Table 2 shows the main maternal characteristics for children with and without IQ data at age 8 years as well as those for mothers in each dietary pattern cluster. For children with IQ data compared to those without the mothers were more likely to have high educational attainment (43.3% vs. 25.7%), a mortgaged or owned housing (84.2% vs. 65.0%), a stable partnership (98.4% vs. 95.8%), to be non-smokers (55.8% vs. 43.6%), nulliparous (46.6% vs. 42.9%), and to have breastfed their children (81.9% vs. 67.1%). The women in the ‘fruit and vegetables’ cluster were more likely than those in the other clusters to have high education, mortgaged or owned housing, a stable partnership, to be of older age (≥ 30 years), non-smokers and to have breastfed their children. Women in the ‘white bread and coffee’ cluster, were more likely to show less favourable socioeconomic indicators when compared to those in the other two clusters (Table 2).

The average IQ scores for verbal, performance and full scale IQ, and the child characteristics for all children and for children of mothers in each of the dietary pattern clusters are presented in table 3. Children of women in ‘fruit and vegetables’ cluster had the highest average verbal, performance and full scale IQ scores in childhood compared to children with mothers in the other two clusters; while children of women in ‘white bread and coffee’ had the lowest average scores (Figure 2).

The results of the linear regression analysis with and without imputation are shown in table 4. In both the unadjusted and adjusted models, children of women in the ‘meat and potatoes’ and ‘white bread and coffee’ clusters during pregnancy had lower average IQ scores at 8 years of age when compared with children of women in the ‘fruit and vegetables’ cluster, whether multiple imputations were applied or not. However adjustment for the potential confounders greatly attenuated the associations in each case; for example for full scale IQ in model 1 attenuation was from 8.13 IQ points deficit unadjusted to 3.19 IQ points deficit adjusted between the ‘fruit and vegetables’ cluster and the ‘white bread and coffee’ cluster.

Considering the largest FMI of the models, which range from 0.027 (Verbal IQ, model 2 - unadjusted) to 0.773 (Verbal IQ, model 3 - adjusted), the one-hundred imputations were adequate for our analyses.

Discussion

The three dietary patterns during pregnancy obtained using cluster analysis were named 'fruit and vegetables', 'meat and potatoes', 'white bread and coffee' clusters. The women who were placed in the 'meat and potatoes' and 'white bread and coffee' clusters during pregnancy had children with lower average verbal, performance and full scale IQ at 8 years of age, when compared to children of women in the 'fruit and vegetables' cluster in pregnancy. Adjusting for socio-economic factors, breastfeeding and child diet attenuated but did not abolish these associations and imputation did not change the associations greatly. To our knowledge, this is the first study to investigate the association between dietary pattern clusters during pregnancy and offspring IQ in childhood.

A limitation of this study is the loss to follow-up of subjects from the original sample and missing data for some of the confounding variables, common problems in cohort studies. We used multiple imputations to try to account for this and found that the relationships were very similar with and without imputation. Another potential limitation refers to the memory bias when completing a FFQ which may lead to under- or over-estimation of the dietary intake however in this study we asked women to recall their current diet over one month and used only the frequency of intake of each food thus avoiding memory bias and that due to inaccurate estimation of portion size. The FFQ was designed to capture the intake of a UK population in 1990s there may have been some changes to the types of diets consumed by pregnant women in the ensuing years.

The strengths of this study include the large sample size, the long-term follow-up from pregnancy to childhood, the standardised instrument used to collect the IQ data, and the availability of a large number of prospectively collected confounding variables.

The children evaluated in this cohort presented with higher average IQ scores when compared with children from some other studies. The WISC-III was applied in children age 6 years and older from a prospective study of pregnant women living in towns of Kosovo, former Yugoslavia in 1984-1985. The mean of full scale, performance and verbal IQ were 75.5, 75.3 and 79.4, respectively (Wasserman et al., 1997). In New York City, the WISC-IV was administered at age 7 years in a longitudinal birth cohort of African American or Dominican pregnant women and the mean IQ scores were in the same order as above 97.1, 99.3, 94.4,

respectively (Factor-Litvak et al., 2014). When the intelligence of children from Chile was assessed using the WISC-revised and the IQ medians from 7 to 11 years of age were 103.5, 102.0 and 105.0 for full-scale, verbal IQ and performance IQ, respectively (Iglesias et al., 2011) very similar to results in ALSPAC.

Individual parts of maternal diet during pregnancy have been investigated with respect to childhood neurological development. Nutrients such as iron and zinc, have been found to be associated with infant neurological development (Anjos et al., 2013; Gil & Gil, 2015; Starling et al., 2015). Adequate supplementation with folic acid during pregnancy was associated with neurological developmental in children under 18 months in two studies (Chatzi et al., 2012; Valera-Gran et al., 2014). Investigations relating to particular foods have focussed on fish which is a good source of many nutrients such as long-chain polyunsaturated fatty acid, iodine and many vitamins. In a previous study from ALSPAC, children of mothers who had lower intakes of fish/seafood during pregnancy were more likely to have suboptimum neurodevelopmental outcomes, including verbal and full scale IQ at 8 years of age (Hibbeln et al., 2007). Furthermore in a sub-sample of pregnant ALSPAC women in early gestation urinary iodine concentrations were associated with child cognitive development; low maternal iodine status was associated with an increased risk of sub optimum scores for verbal IQ at 8 years of age (Bath et al., 2013). In a mother-child cohort from North Eastern Italy, the intake of fresh fish during pregnancy showed slightly positive association with full scale and performance IQ, while the intake of canned fish was negatively associated with verbal, performance and full scale IQ at 7 years of age (Deroma et al., 2013). These results suggest that consuming a nutrient dense diet in pregnancy is important for an offspring's neurological development. This is supported by our previous study (to be submitted), which found that women in the 'fruit and vegetables' cluster had a diet which was more nutrient dense than that of women in the other two clusters. In the current study we have shown that this better quality diet is associated with better neurological development in the offspring.

It is likely that mothers' diet will influence the diet of their children and in our previous study we found this to be the case (to be submitted) in particular children of mothers in the 'fruit and vegetables' cluster were more likely than those of mothers in the other two clusters to be in a 'plant-based' cluster, which was characterised by very similar foods (Smith et al., 2011). There are a few studies that have assessed dietary patterns in childhood in relation to neurological outcomes (Gale et al., 2009; Northstone et al., 2012; Smithers et al., 2012; Smithers et al., 2013). Using principal component analysis (PCA) to obtain dietary patterns in at 6 and 12 month old infants from the Southampton Women's Survey Gale et al. (2009), found

an association between higher scores on an '*Infant guidelines*' dietary pattern and higher full-scale and verbal IQ at 4 years of age. In ALSPAC, Smithers et al. (2012) found that the high scores on PCA derived dietary patterns in infancy which included fruits, vegetables and breastfeeding were associated with higher average IQ at 8 years of age, furthermore the high scores on dietary patterns which included processed foods were associated with lower average IQ at 8 years of age.

In older children, in ALSPAC Northstone et al. (2012) observed a negative association with a '*processed*' dietary pattern at 3 years of age and a positive association with a '*health-conscious*' dietary pattern' at 8 years of age of IQ measured at 8 years of age. In Australia, Nyaradi et al. (2014) assessed adolescents from the Western Australian Pregnancy Cohort (Raine) Study and found that higher scores on a '*Western dietary pattern*' at 14 years of age were associated with lower cognitive performance at 17 years of age. A study with older subjects from rural areas of South Korea identified two dietary patterns using the K-means cluster analysis and found that subjects in a cluster composed by multigrain rice, fish, dairy products, and fruits and fruit juices, presented lower cognitive impairment, when compared with those in a cluster constituted by white rice, noodles, and coffee (Kim et al., 2015). These results suggest that the dietary pattern of the person themselves is also influential in determining their cognitive status. In this study controlling for child's cluster pattern at 7 years of age did not remove the association with maternal diet in pregnancy

In summary, the women whose food habits during pregnancy placed them in the '*meat and potatoes*' and '*white bread and coffee*' clusters had children with lower average IQ at 8 years of age, when compared with children of mothers whose food habits placed them in the '*fruit and vegetables*' cluster. Therefore, further large-scale prospective studies are required to verify the effects maternal dietary during pregnancy patterns and infant neurodevelopmental.

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Table 1. Mean (standard deviation) frequency of weekly intakes of foods across clusters dietary patterns for 12,195 pregnant women.

Cluster	Fruit and vegetables	Meat and potatoes	White bread and coffee
Cluster size	4,478	2,469	5,248
White bread (slices)	<u>2.8 (5.4)^a</u>	8.4 (8.8)^b	8.6 (8.7)^b
Non-white bread (slices)	13.6 (9.6)^a	7.4 (8.6) ^b	<u>5.1 (7.0)^c</u>
Bran-based cereal	3.4 (2.6)^a	2.1 (2.5) ^b	<u>1.4 (2.0)^c</u>
Oat-based cereal	2.6 (2.7)^a	1.8 (2.5) ^b	<u>1.2 (1.9)^c</u>
Other breakfast cereal	<u>1.5 (2.1)^a</u>	3.1 (2.7)^b	2.2 (2.3) ^c
Biscuits	2.2 (2.0) ^a	6.4 (2.8)^b	<u>1.9 (1.6)^c</u>
Crispbreads/crackers	0.7 (1.4)^a	0.5 (1.2) ^b	<u>0.3 (0.8)^c</u>
Puddings	1.3 (1.5) ^a	2.0 (1.9)^b	<u>0.9 (1.1)^c</u>
Cakes/buns	1.4 (1.3) ^a	2.6 (2.1)^b	<u>1.2 (1.1)^c</u>
Poultry	1.8 (1.3)^a	1.9 (1.3)^a	<u>1.5 (1.1)^b</u>
Red meat	2.3 (1.9) ^a	2.9 (2.0)^b	<u>2.1 (1.6)^c</u>
Meat pies	<u>0.4 (0.6)^a</u>	0.7 (0.9)^b	0.6 (0.8) ^c
Offal	0.1 (0.4) ^a	0.1 (0.5) ^a	0.1 (0.4) ^a
Sausages, burgers	<u>0.4 (0.6)^a</u>	0.7 (0.9)^b	0.7 (0.8) ^c
Fried foods (e.g. fish, eggs, bacon)	<u>0.4 (0.7)^a</u>	0.9 (1.4)^b	0.7 (1.0) ^c
Pizza	0.5 (0.7) ^a	0.6 (0.9)^b	<u>0.4 (0.7)^c</u>
Fish	2.5 (1.9)^a	1.9 (1.8) ^b	<u>1.5 (1.5)^c</u>
Eggs	1.5 (1.3)^a	1.5 (1.4)^a	<u>1.2 (1.2)^b</u>
Cheese	4.0 (2.3)^a	3.6 (2.3) ^b	<u>2.3 (1.9)^c</u>
Meat substitutes (soya, tofu, etc.)	<u>0.3 (1.0)^a</u>	<u>0.1 (0.9)^b</u>	<u>0.1 (0.7)^b</u>
Pulses	<u>0.5 (1.0)^a</u>	0.2 (0.7) ^b	<u>0.1 (0.5)^c</u>
Nuts	<u>0.5 (1.1)^a</u>	0.3 (0.8) ^b	<u>0.2 (0.5)^c</u>
Fried potatoes (chips)	<u>0.8 (0.9)^a</u>	1.7 (1.4)^b	1.5 (1.2) ^c
Roast potatoes	<u>0.7 (0.9)^a</u>	1.3 (1.1)^b	1.1 (1.0) ^c
Potatoes (not fried)	3.2 (1.9)^a	3.3 (1.9)^a	<u>2.3 (1.6)^b</u>
Pasta	1.5 (1.2)^a	1.1 (1.1) ^b	<u>0.9 (1.0)^c</u>
Rice	1.5 (1.2)^a	1.1 (1.2) ^b	<u>0.9 (1.0)^c</u>
Baked beans	<u>1.3 (1.1)^a</u>	1.6 (1.3)^b	1.3 (1.1) ^c
Leafy green vegetables	2.2 (1.7)^a	1.9 (1.5) ^b	<u>1.6 (1.2)^c</u>
Other green vegetables	2.5 (1.7)^a	2.0 (1.5) ^b	<u>1.6 (1.1)^c</u>
Carrots	2.6 (1.8)^a	2.2 (1.7) ^b	<u>1.6 (1.2)^c</u>
Other root vegetables	1.1 (1.3)^a	0.9 (1.2) ^b	<u>0.6 (0.9)^c</u>
Peas	2.1 (1.5) ^a	2.2 (1.6)^b	<u>1.7 (1.2)^c</u>
Salad	3.5 (2.4)^a	2.3 (2.0) ^b	<u>1.6 (1.4)^c</u>
Fresh fruit	8.2 (2.3)^a	5.8 (3.0) ^b	<u>2.9 (2.1)^c</u>
Fruit juice	5.1 (3.9)^a	3.6 (3.6) ^b	<u>2.1 (2.6)^c</u>
Cola (cups)	<u>0.8 (2.1)^a</u>	1.9 (3.4)^b	1.9 (3.4)^b
Tea (cups)	<u>19.5 (15.1)^a</u>	22.6 (17.7)^b	21.5 (19.6) ^c
Coffee (cups)	<u>7.2 (10.4)^a</u>	9.2 (12.3) ^b	10.1 (13.3)^c
Herbal tea (cups)	8.9 (26.8)^a	<u>2.9 (15.0)^b</u>	<u>1.9 (10.8)^b</u>
Sweets	<u>0.7 (1.3)^a</u>	1.9 (2.5)^b	0.8 (1.4) ^c
Chocolate	<u>0.9 (1.1)^a</u>	2.6 (2.5)^b	<u>0.9 (1.1)^a</u>
Chocolate bars	<u>1.3 (1.4)^a</u>	4.1 (2.7)^b	1.6 (1.5) ^c
Savoury snacks (crisps)	<u>1.4 (1.7)^a</u>	3.1 (2.5)^b	1.9 (2.0) ^c
Full-fat milk (l)	<u>0.8 (1.4)^a</u>	1.6 (1.8)^b	1.5 (1.6)^b
Low-fat milk (l)	1.8 (1.5)^a	1.4 (1.6) ^b	<u>1.0 (1.4)^c</u>
Alcohol	1.1 (2.9)^a	<u>0.9 (2.8)^{ab}</u>	<u>0.9 (3.0)^b</u>

Total variance = 14.9%. The highest and lowest mean in each row are bold and underlined, respectively.

^{abc} Where superscripts differ there is a significant difference between cluster means (Tukey-Kramer method).

Table 2. Maternal characteristics of children with and without intelligence quotient (IQ) data at 8 years of age and according to maternal clusters dietary patterns.

Confounding	Without IQ data	With IQ data ¹		Fruit and vegetables	Meat and potatoes	White bread and coffee	P-value ³
	Mean (SD)	Mean (SD)	P-value ²	Mean (SD)	Mean (SD)	Mean (SD)	
Continuous							
Pre-pregnancy BMI	22.9 (4.0)	22.9 (3.7)	0.329	22.4 (3.2) ^a	22.6 (3.5) ^a	23.7(4.2) ^b	<0.001
Categorical	n (%)	n (%)	P-value ⁴	n (%)	n (%)	n (%)	P-value ³
Maternal education			<0.001				<0.001
Low	2,146 (39.9)	1,430 (21.7)		662 (15.0) ^a	719 (29.5) ^b	2,195 (42.8) ^b	
Middle	1,856 (34.5)	2,299 (34.9)		1,304 (29.6) ^a	961 (39.5) ^b	1,890 (36.9) ^b	
High	1,383(25.7)	2,854 (43.3)		2,442 (55.4) ^a	754 (31.0) ^b	1,041 (20.3) ^b	
Housing			<0.001				<0.001
Mortgaged/owned	3,364 (65.0)	5,454(84.2)		3,681 (85.0) ^a	1,856 (78.4) ^b	3,281 (66.1) ^c	
Public housing	988 (19.1)	504 (7.8)		206 (4.8) ^a	262 (11.1) ^b	1,024 (20.6) ^c	
Other	826 (15.9)	522 (8.1)		441 (10.2) ^a	248 (10.5) ^b	659 (13.3) ^c	
Crowding at home			<0.001				<0.001
< 1 person/room	3,425 (67.5)	5,187 (80.9)		3,585 (83.8) ^a	1,769 (75.6) ^b	3,258 (66.9) ^c	
> 1 person/room	1,650 (32.5)	1,226 (19.1)		691 (16.2) ^a	571 (24.4) ^b	1,614 (33.1) ^c	
Partner			<0.001				<0.001
No	219 (4.2)	104 (1.6)		82 (1.9) ^a	49 (2.1) ^a	192 (3.8) ^b	
Yes	5,011 (95.8)	6,431 (98.4)		4,279 (98.1) ^a	2,339 (97.9) ^a	4,824 (96.2) ^b	
Maternal age			<0.001				<0.001
< 20 years	350 (6.5)	113 (1.70)		64 (1.4) ^a	98 (4.0) ^b	301 (5.8) ^c	
20 – 30 years	3,411 (62.9)	3,440 (52.1)		2,052 (46.5) ^a	1,477 (60.6) ^b	3,322 (64.3) ^c	
≥ 30 years	1,659 (30.6)	3,049 (46.2)		2,301 (52.1) ^a	864 (35.4) ^b	1,543 (29.9) ^c	
Maternal smoking in pregnancy			<0.001				<0.001
Non-smoker	2,268 (43.6)	3,632 (55.8)		2,476 (57.0)a	1,258 (52.9)b	2,166 (43.5)c	
Stopped	1,564 (30.1)	1,994 (30.7)		1,455 (33.5)a	695 (29.2)b	1,408 (28.3)c	
Still smoking	1,370 (26.3)	877 (13.5)		414 (9.5)a	425 (17.9)b	1,408 (28.3)c	

Table 2 (continuation). Maternal characteristics of children with and without intelligence quotient (IQ) data at 8 years of age and according to maternal clusters dietary patterns.

Confounders	Without IQ data	With IQ data ¹	Fruit and vegetables	Meat and potatoes	White bread and coffee	
Categorical	n (%)	n (%)	P-value ⁴	n (%)	n (%)	n (%) P-value ³
Maternal alcohol use in pregnancy			<0.001			<0.001
Non-drinker	513 (9.9)	384 (5.9)		241 (5.5) ^a	177 (7.4) ^b	479 (9.6) ^c
Stopped	1,909 (36.8)	2,485 (38.1)		1,7150(39.4) ^a	846 (35.5) ^b	1,833 (36.9) ^c
Still drinking	2,769 (53.3)	3,648 (56.0)		2,396 (55.1) ^a	1,361 (57.1) ^b	2,660 (53.5) ^c
Parity (number of deliveries)			<0.001			<0.001
0	2,207 (42.9)	3,003 (46.6)		2,216 (51.4) ^a	921 (39.1) ^b	2,073 (42.1) ^c
1	1,795 (34.9)	2,313 (35.9)		1,383 (32.1) ^a	968 (41.1) ^b	1,757 (35.7) ^c
≥ 2	1,146 (22.2)	1,133 (17.5)		716 (16.5) ^a	468 (19.9) ^b	1,095 (22.2) ^c
Ethnic origin			<0.001			<0.001
White	5,138 (96.4)	6,443 (98.2)		4,252 (97.2) ^a	2,380 (98.6) ^b	4,949 (97.0) ^a
Black	79 (1.5)	46 (0.7)		42 (1.0) ^a	12 (0.5) ^b	71 (1.4) ^a
Asian	112 (2.1)	71 (1.1)		81 (1.8) ^a	22 (0.9) ^b	80 (1.6) ^a
Breastfeeding			<0.001			<0.001
Yes	2,766 (67.1)	5,073 (81.9)		3,513 (87.7) ^a	1,550 (73.2) ^b	2,776 (66.2) ^c
No	1,358 (32.9)	1,124 (18.1)		493 (12.3) ^a	569 (26.8) ^b	1,420 (33.8) ^c
Gender			<0.001			0.717
Boy	2,898 (53.5)	3,290 (49.8)		2,283 (51.7) ^a	1,245 (51.1) ^a	2,660 (51.5) ^a
Girl	2,522 (46.5)	3,311 (50.2)		2,133 (48.3) ^a	1,194 (48.9) ^a	2,506 (48.5) ^a

¹ At least one IQ data (verbal or performance)²P-values refer to Student's T test³P-values refer to ANOVA test.⁴P-values refer to chi-square test.

abc Where superscripts differ there is a significant difference among confounder variables according to the clusters(Tukey–Kramer method).

Table 3. Infant characteristics of children with and without intelligence quotient (IQ) data at 8 years of age and according to maternal clusters dietary patterns.

Confounding variables	Without IQ data		With IQ data ¹		Fruit and vegetables	Meat and potatoes	White bread and coffee	P-value ³
	Mean (SD)	Mean (SD)	P-value ²	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	
Continuous								
Verbal IQ	--	107.5(16.7)	--	111.6 (16.7) ^a	106.6 (16.1) ^b	103.3(16.0) ^c	<0.001	
Performance IQ	--	99.9 (17.1)	--	102.9(16.8) ^a	99.1(17.0) ^b	97.1 (16.9) ^c	<0.001	
Full scale IQ	--	104.5 (16.4)	--	108.6 (16.1) ^a	103.5 (16.2) ^b	100.5 (15.9) ^c	<0.001	
Child's diet at 7 years (kJ)	7,743 (1930)	7,637 (1,776)	0.010	7,610 (1,700) ^a	7,984 (2,282) ^b	7,461 (2,486) ^c	<0.001	
Child's age at IQ (months)	105.4 (5.1)	103.4(3.3)	<0.001	103.3(3.1) ^a	103.3 (3.1) ^a	103.7 (3.7) ^b	<0.001	

¹ At least one IQ data (verbal or performance)²P-values refer to Student's T test³ P-values refer to ANOVA test.

abc Where superscripts differ there is a significant difference among confounder variables according to the clusters(Tukey–Kramer method).

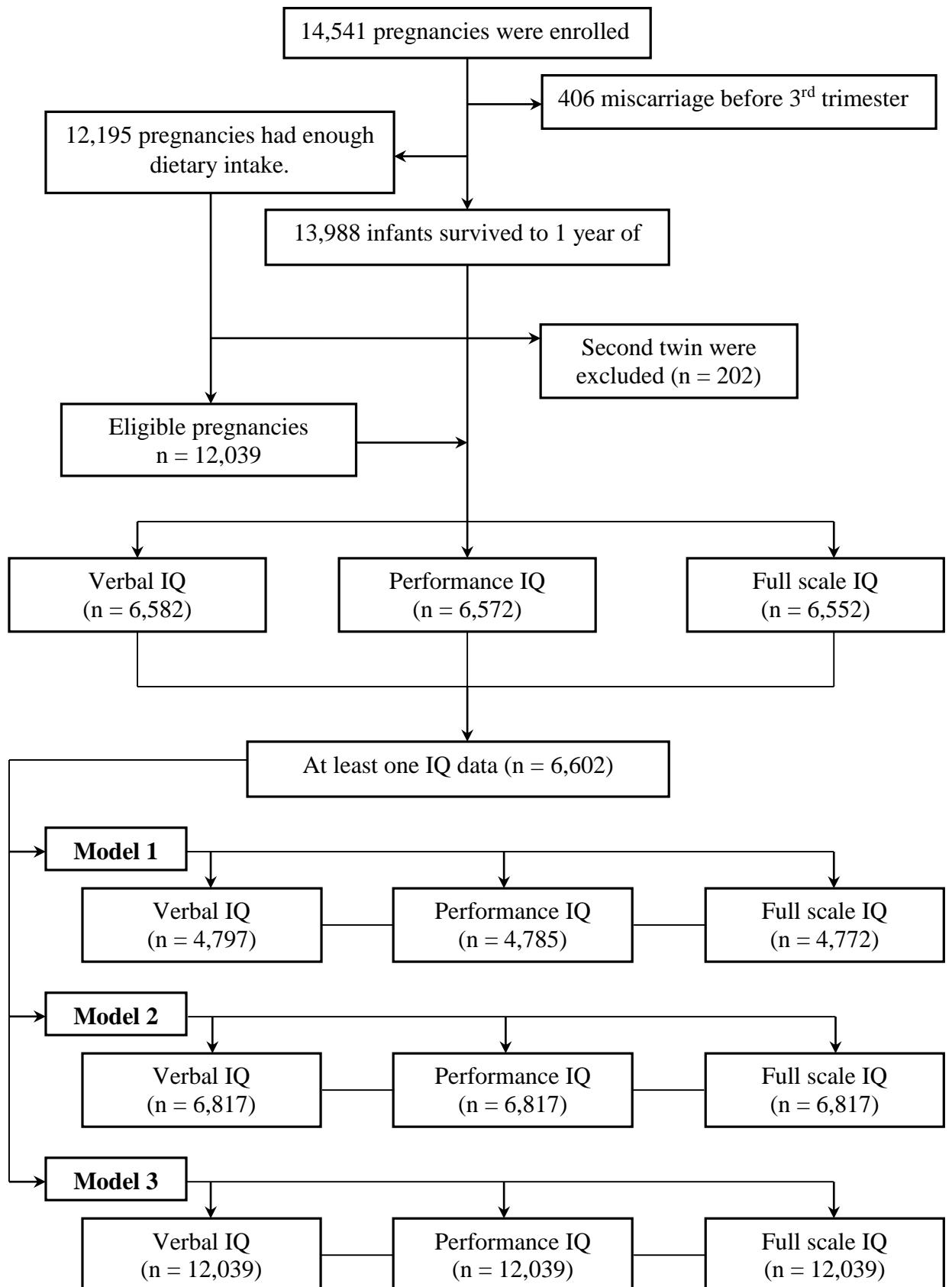
Table 4. Unadjusted and adjusted models of linear regression between clusters dietary patterns during pregnancy and verbal, performance and full scale of intelligence quotient (IQ) at 8 years of age.

	Verbal IQ				Performance IQ				Full scale IQ			
	N	β	95% CI	P	n	β	95% CI	P	n	β	95% CI	P
Model 1– Unadjusted	6,582				6,572				6,552			
Fruit and vegetables			Reference				Reference				Reference	
Meat and potatoes	-5.00	-6.05; -3.95	<0.001		-3.77	-4.86; -2.68	<0.001		-5.08	-6.11; -4.04	<0.001	
White bread and coffee	-8.34	-9.23; -7.45	<0.001		-5.75	-6.67; -4.83	<0.001		-8.13	-9.00; -7.25	<0.001	
Model 1–Adjusted*	4,797				4,785				4,772			
Fruit and vegetables			Reference				Reference				Reference	
Meat and potatoes	-2.04	-3.22; -0.86	0.001		-1.96	-3.21; -0.72	0.002		-2.35	-3.51; -1.20	<0.001	
White bread and coffee	-3.62	-4.71; -2.53	<0.001		-1.80	-2.95; -0.65	0.002		-3.19	-4.25; -2.13	<0.001	
Model 2– Unadjusted ¹	6,817				6,817				6,817			
Fruit and vegetables			Reference				Reference				Reference	
Meat and potatoes	-4.97	-6.02; -3.93	<0.001		-3.67	-4.76; -2.59	<0.001		-4.97	-6.00; -3.93	<0.001	
White bread and coffee	-8.36	-9.24; -7.48	<0.001		-5.73	-6.65; -4.82	<0.001		-8.09	-8.96; -7.22	<0.001	
Model 2 –Adjusted ^{*2}	6,817				6,817				6,817			
Fruit and vegetables			Reference				Reference				Reference	
Meat and potatoes	-1.88	-2.89; -0.87	<0.001		-1.52	-2.60; -0.43	0.006		-1.96	-2.95; -0.96	<0.001	
White bread and coffee	-3.02	-3.93; -2.12	<0.001		-1.69	-2.66; -0.71	0.001		-2.74	-3.63; -1.84	<0.001	
Model 3 – Unadjusted ³	12,039				12,039				12,039			
Fruit and vegetables			Reference				Reference				Reference	
Meat and potatoes	-5.44	-6.39; -4.49	<0.001		-3.91	-4.93; -2.88	<0.001		-5.36	-6.30; -4.42	<0.001	
White bread and coffee	-9.12	-10.01; -8.22	<0.001		-6.36	-7.21; -5.51	<0.001		-8.88	-9.70; -8.05	<0.001	
Model 3 – Adjusted ^{*4}	12,039				12,039				12,039			
Fruit and vegetables			Reference				Reference				Reference	
Meat and potatoes	-1.75	-2.70; -0.81	<0.001		-1.29	-2.31; -0.27	0.013		-1.76	-2.69; -0.83	<0.001	
White bread and coffee	-3.05	-3.95; -2.16	<0.001		-1.76	-2.68; -0.84	<0.001		-2.80	-3.65; -1.95	<0.001	

Model 1-All available data; Model 2 - Imputations for missing data of IQ and all confounders, only up to the sample for complete the IQ scale at 8 years and correlated child neurodevelopment variables; Model 3- Imputations for missing data of IQ and all confounders.

*All models were adjusted for maternal education, housing tenure, crowding at home, partner present, maternal age, maternal smoking in pregnancy, maternal alcohol use in pregnancy, parity, ethnic origin, pre-pregnancy BMI, breastfeeding, child gender, child's diet at 7 years of age, and child's age at IQ measurement.

Largest FMI:¹Verbal IQ = 0.032, Performance IQ = 0.034, Full scale IQ = 0.032; ²Verbal IQ = 0.109, Performance IQ = 0.118, Full scale IQ = 0.105;³Verbal IQ = 0.445, Performance IQ = 0.457, Full scale IQ = 0.440; ⁴Verbal IQ = 0.711, Performance IQ = 0.771, Full scale IQ = 0.746.

**Figure 1.** Flow chart illustrating the participant data of study.

Model 1- All available data; **Model 2** - Imputations for missing data of IQ and all confounders, only up to the sample for complete the IQ scale at 8 years and correlated child neurodevelopment variables; **Model 3** - Imputations for missing data of IQ and all confounders.

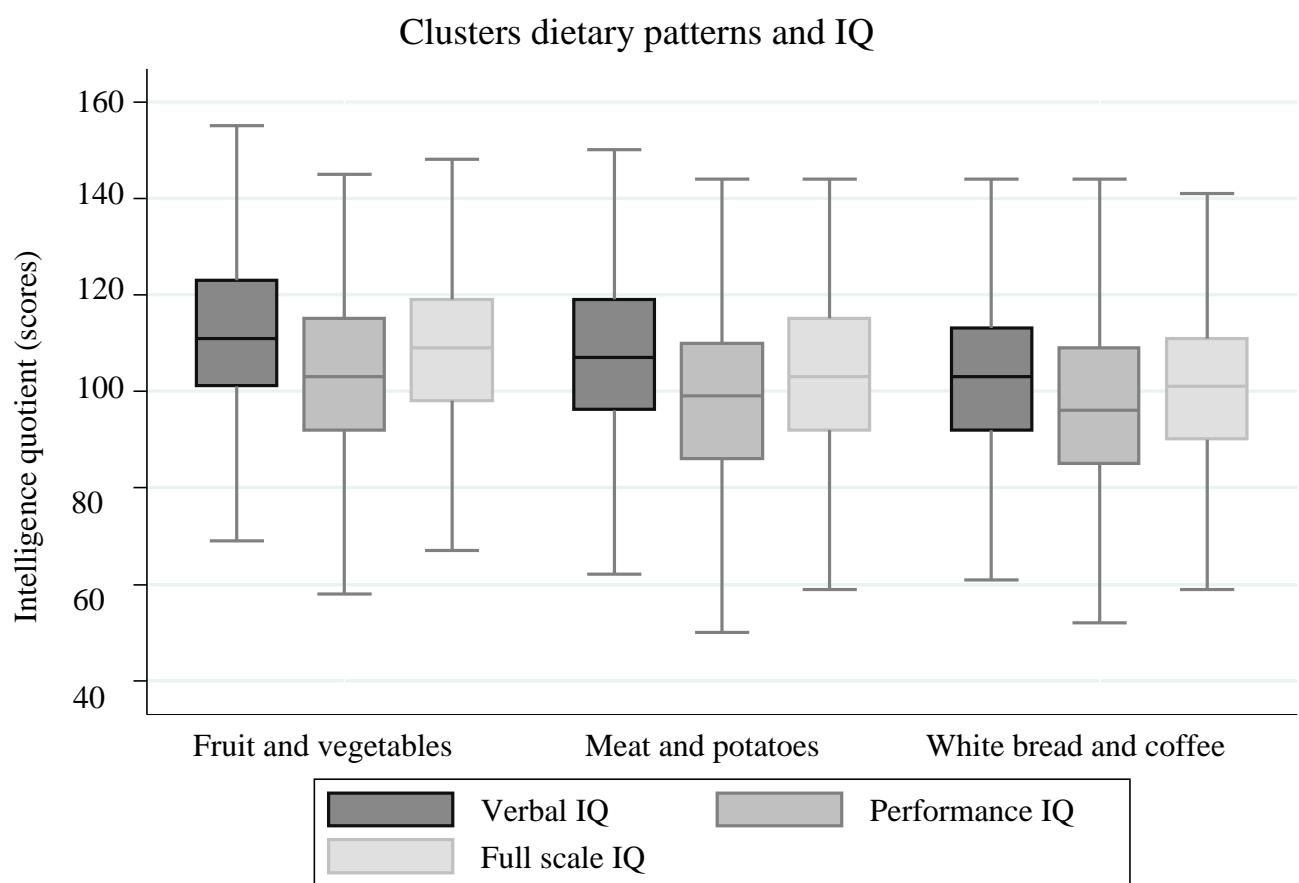


Figure 2. Mean and 95% confidential interval (95% CI) of verbal, performance and full scale of intelligence quotient (IQ) at 8 years of age according to clusters dietary patterns during pregnancy.

Fruit and vegetables cluster - mean score (95% CI): Verbal IQ = 111.6 (111.0 to 112.2); Performance IQ = 102.9 (102.2 to 103.5); Full scale IQ = 108.6 (108.0 to 109.2).

Meat and potatoes cluster - mean score (95% CI): Verbal IQ = 106.6 (105.8 to 107.5); Performance IQ = 99.1 (98.2 to 100.0); Full scale IQ = 103.5 (102.7 to 104.4).

White bread and coffee cluster - mean score (95% CI): Verbal IQ = 103.3 (102.6 to 103.9); Performance IQ = 97.1 (96.4 to 97.8); Full scale IQ = 100.5 (99.9 to 101.1).

7 CONCLUSÕES

A presente tese teve quatro artigos científicos como principais produtos. As principais conclusões desses produtos foram:

- i) Três padrões alimentares foram obtidos no período pré-gestacional da coorte brasileira e intitulados '*comum brasileiro*', '*saudável*' e '*processado*'. Mulheres que aderiram mais ao padrão '*saudável*' tiveram menores sintomas de depressão. Não houve associação significativa dos demais padrões alimentares com os sintomas de depressão ao longo da gestação;
- ii) Mulheres que aderiram mais aos padrões alimentares '*comum brasileiro*' e '*saudável*' tiveram menores sintomas de ansiedade durante a gestação e início do pós-parto;
- iii) Três padrões alimentares foram obtidos na coorte de gestantes britânicas, que foram intitulados: '*frutas e vegetais*', '*carnes e batatas*' e '*pão branco e café*'. O padrão '*frutas e vegetais*' apresentou o melhor perfil nutricional para quase todos os nutrientes após o ajuste por energia. E ainda, os filhos durante a infância aderiram a padrões alimentares semelhantes aos que as mães aderiram durante a gestação, principalmente os padrões alimentares compostos por alimentos saudáveis;
- iv) As mulheres que aderiram aos padrões '*carnes e batatas*' e '*pão branco e café*' tiveram maior risco de ter filhos com menor QI aos 8 anos quando comparadas as mulheres que aderiram o padrão '*frutas e vegetais*' durante a gestação.

8 CONSIDERAÇÕES FINAIS

A escolha de uma dieta inadequada, juntamente com hábitos não saudáveis, como a inatividade física, o tabagismo e o etilismo têm aumentado o risco de DCNT ao longo da vida. A saúde materna e consumo alimentar antes e durante a gestação são importantes para o desenvolvimento gestacional, fetal, infantil e também ao longo da vida.

Os resultados obtidos nessa tese de doutorado são inéditos, uma vez que não foram identificados estudos que avaliaram padrão pré-gestacional e sintomas de depressão e ansiedade ao longo da gestação e início do pós-parto, comparação entre o padrão alimentar materno durante a gestação e seus filhos na infância, e a associação dos padrões alimentares maternos durante a gestação e o QI na infância.

Nesta perspectiva, sugerimos que são necessários novos estudos com análises longitudinais para avaliar o impacto da dieta no período pré-gestacional e gestacional sobre os desfechos de saúde mental ao longo da gestação e no pós-parto, assim como no neurodesenvolvimento infantil.

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ANEXOS

TESE DE DOUTORADO

ANEXO 1

GRÁFICOS DE SCREE PLOT

PADRÕES ALIMENTARES

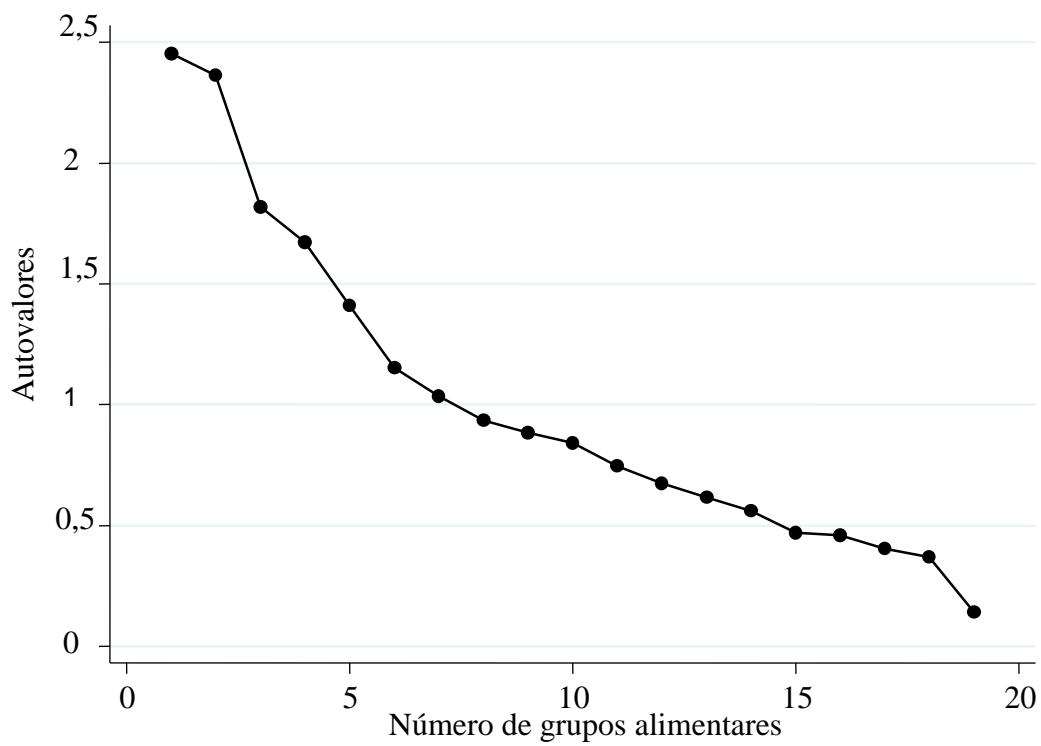


Figura 1. *Scree plot* dos autovalores dos agrupamentos alimentares dos fatores extraídos para identificação dos padrões alimentares no período pré-gestacional de 251 mulheres atendidas em uma unidade de saúde pública do Rio de Janeiro.

ANEXO 2

GRÁFICOS PARA SELEÇÃO DOS MODELOS LONGITUDINAIS

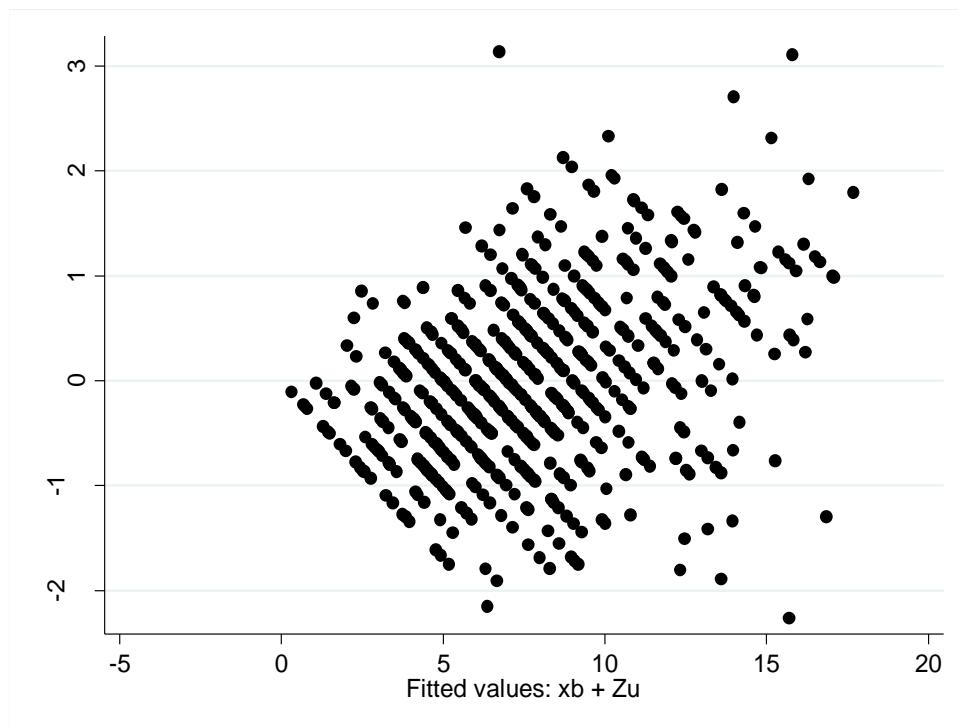


Figura 1. Gráficos de dispersão dos resíduos para avaliar a qualidade do ajuste do modelo final para o padrão *comum brasileiro* e o risco de depressão durante a gestação.

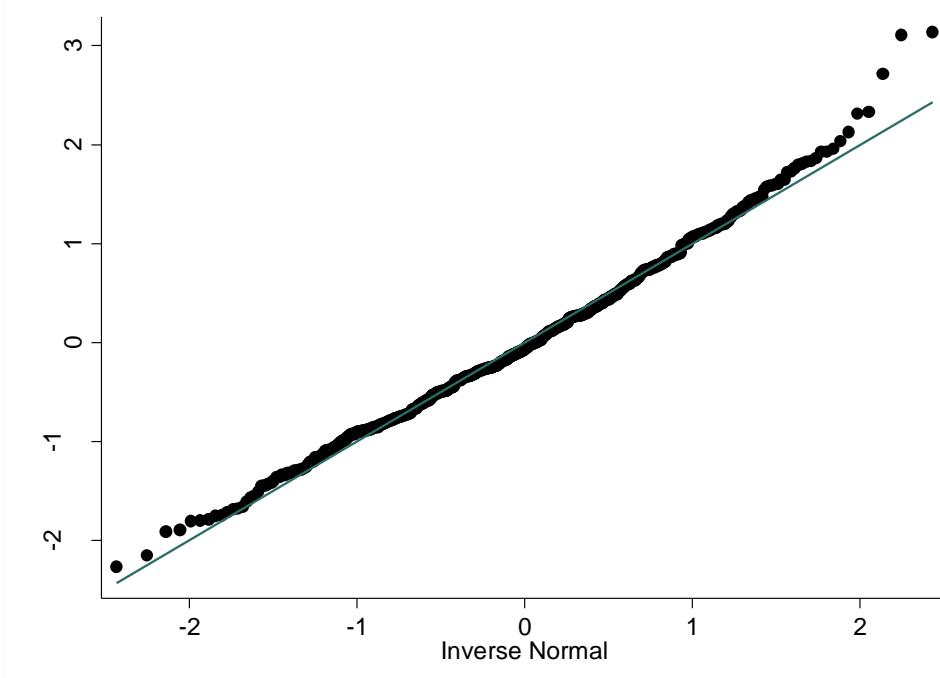


Figura 2. *Quantile-quantile plot* para verificar normalidade dos resíduos do modelo final para modelo final para o padrão *comum brasileiro* e o risco de depressão durante a gestação.

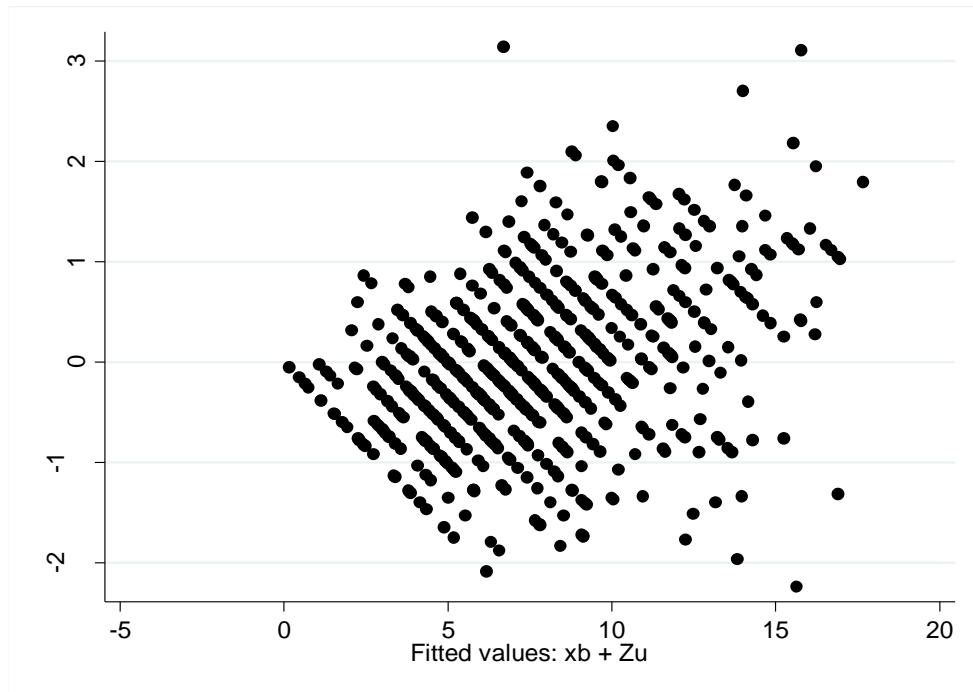


Figura 3. Gráficos de dispersão dos resíduos para avaliar a qualidade do ajuste do modelo final para o padrão saudável e o risco de depressão durante a gestação.

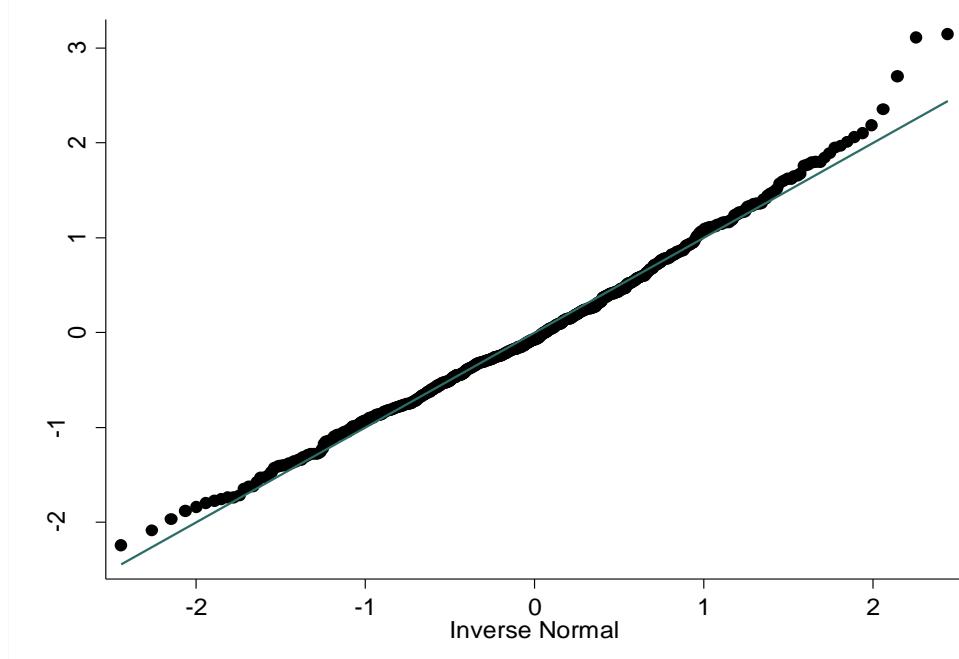


Figura 4. Quantile-quantile plot para verificar normalidade dos resíduos do modelo final para modelo final para o padrão saudável e o risco de depressão durante a gestação.

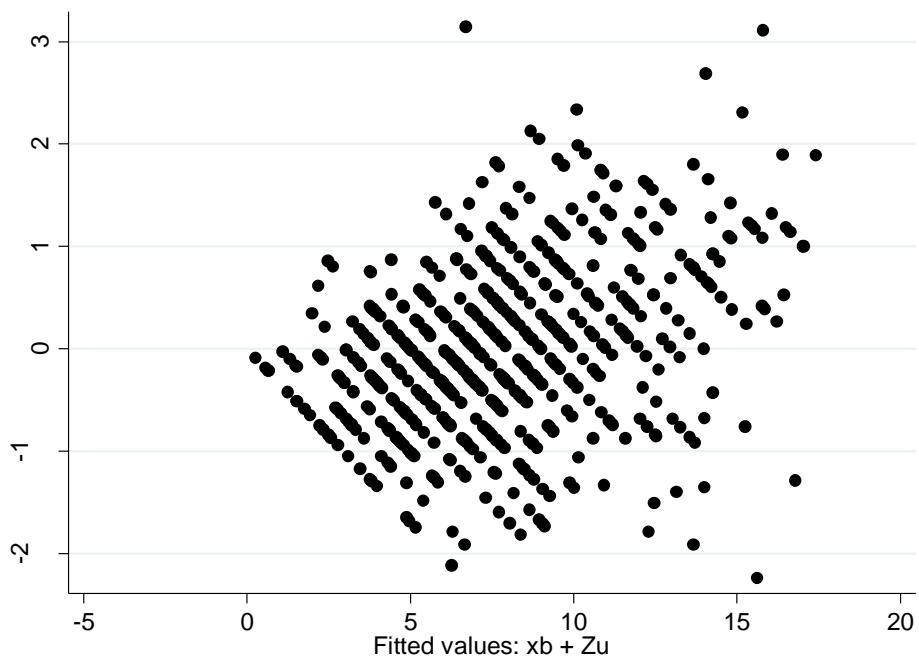


Figura 5. Gráficos de dispersão dos resíduos para avaliar a qualidade do ajuste do modelo final para o padrão *processado* e o risco de depressão durante a gestação.

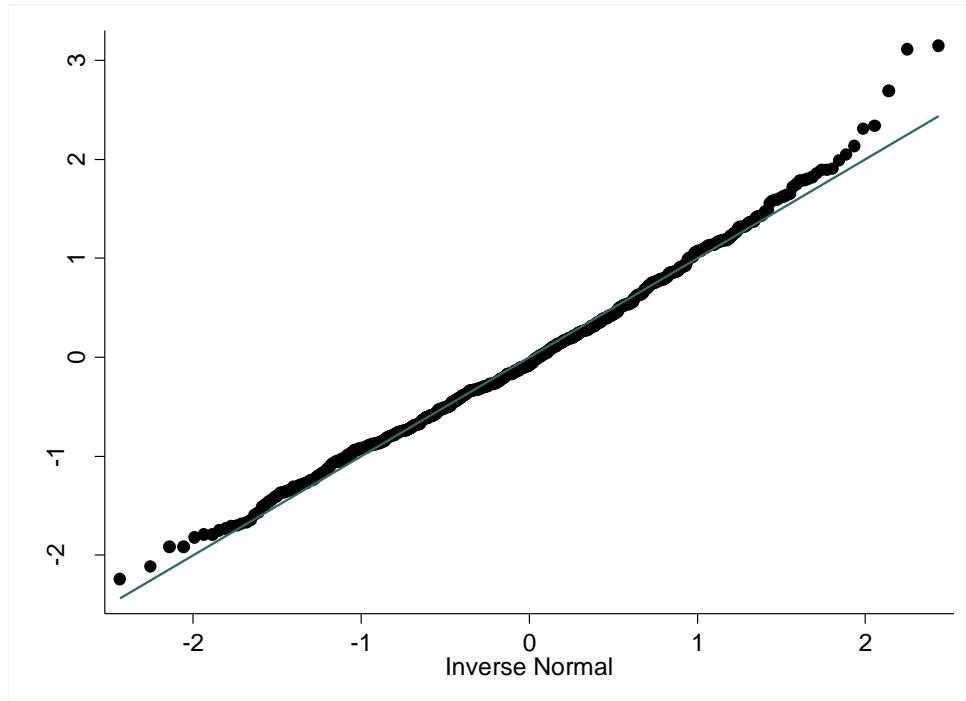


Figura 6. *Quantile-quantile plot* para verificar normalidade dos resíduos do modelo final para o padrão *processado* e o risco de depressão durante a gestação.

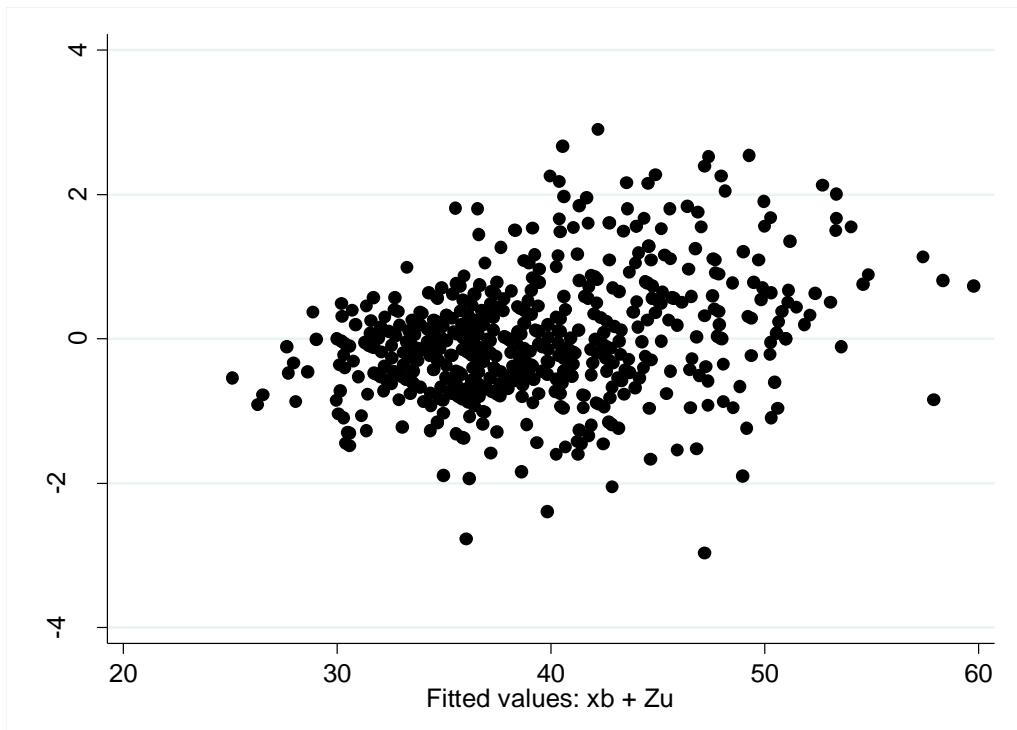


Figura 7. Gráficos de dispersão dos resíduos para avaliar a qualidade do ajuste do modelo final para o padrão *comum brasileiro* e risco de ansiedade na gestação e no pós-parto.

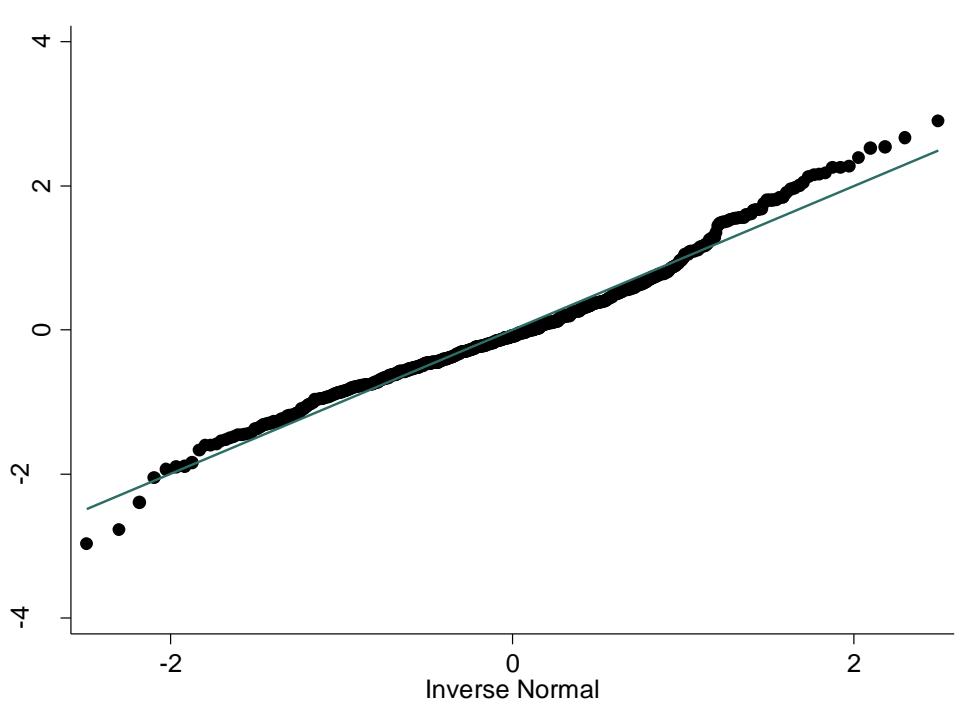


Figura 8. *Quantile-quantile plot* para verificar normalidade dos resíduos do modelo final para o padrão *comum brasileiro* e risco de ansiedade na gestação e no pós-parto.

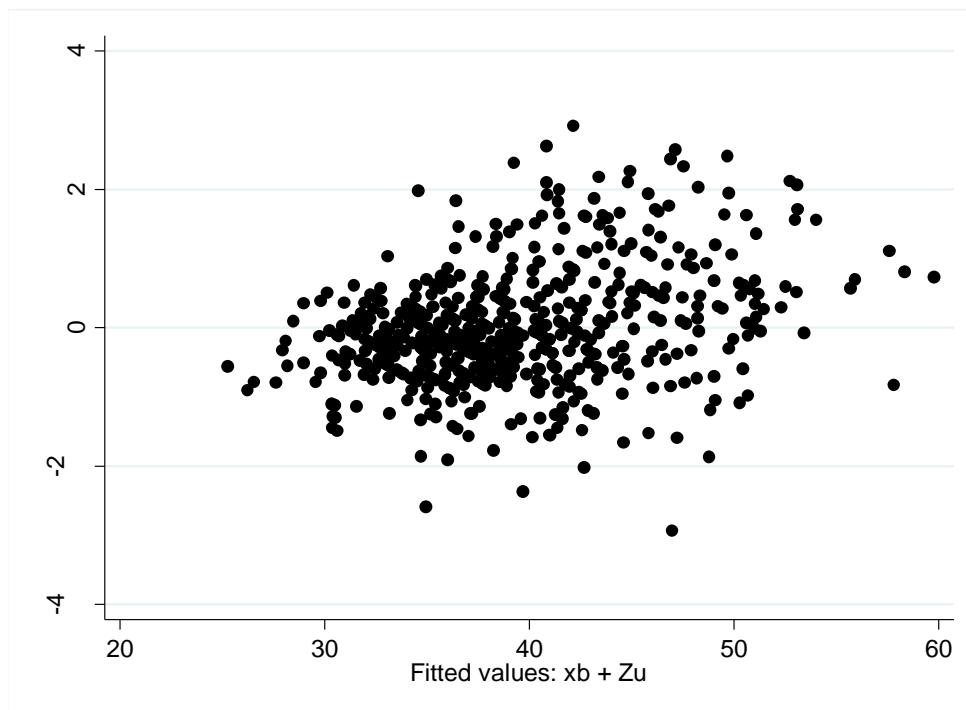


Figura 9. Gráficos de dispersão dos resíduos para avaliar a qualidade do ajuste do modelo final para o padrão *saudável* e risco de ansiedade na gestação e no pós-parto.

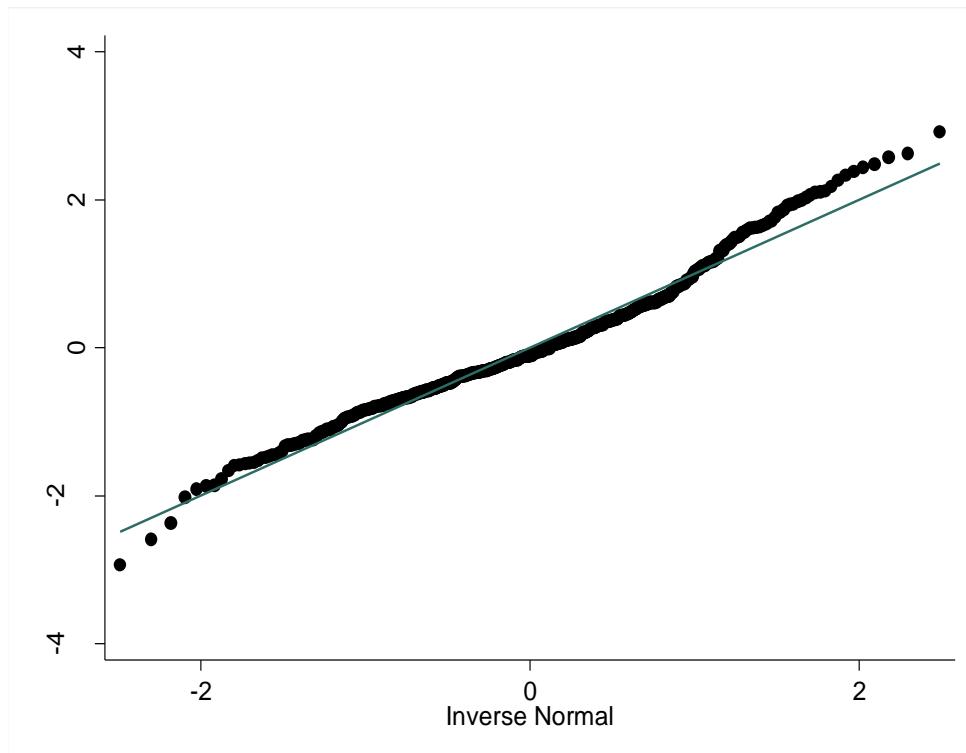


Figura 10. Quantile-quantile plot para verificar normalidade dos resíduos do modelo final para o padrão *saudável* e risco de ansiedade na gestação e no pós-parto.

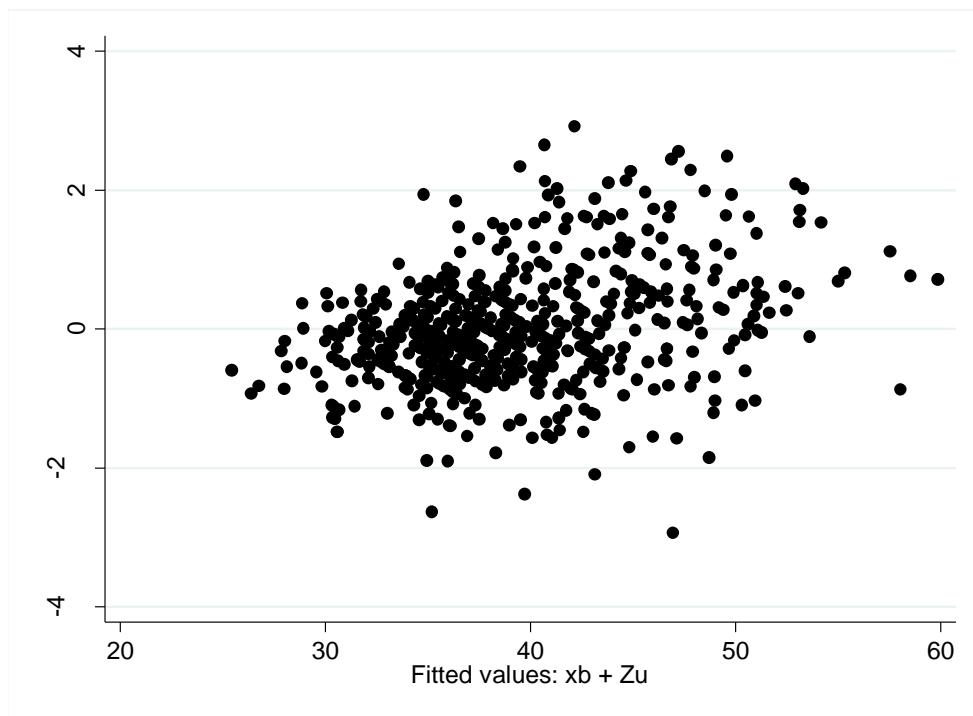


Figura 11. Gráficos de dispersão dos resíduos para avaliar a qualidade do ajuste do modelo final para o padrão *processado* e risco de ansiedade na gestação e no pós-parto.

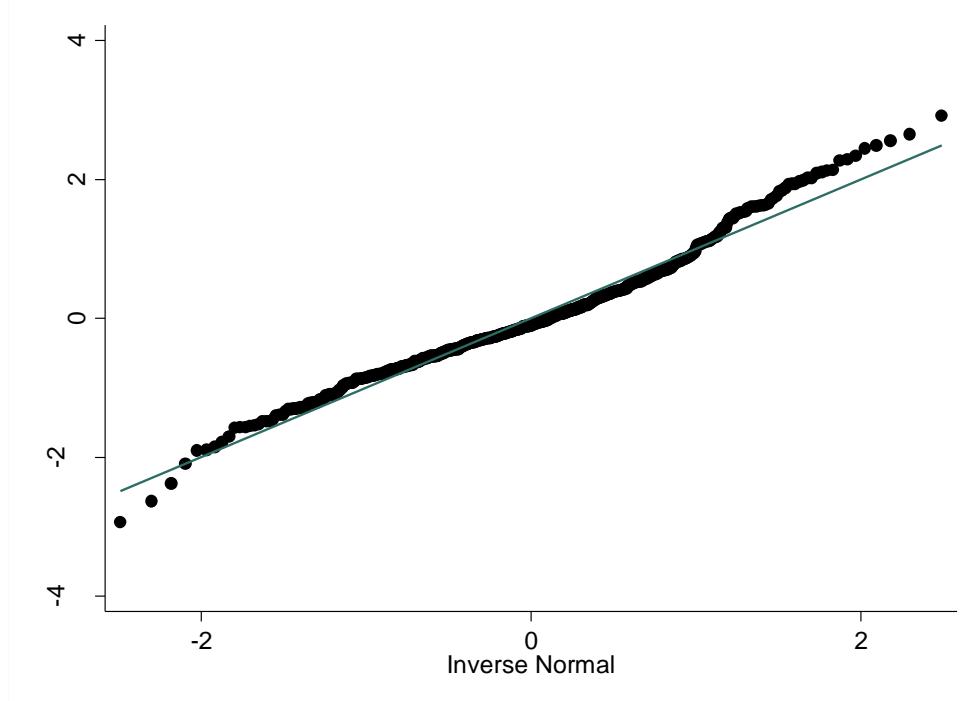


Figura 12. *Quantile-quantile plot* para verificar normalidade dos resíduos do modelo final para o padrão *processado* e risco de ansiedade na gestação e no pós-parto.

ANEXO 3

APROVAÇÃO DO COMITÊ DE ÉTICA

COORTE BRASILEIRA



Comitê de Ética em Pesquisa

Parecer nº 168A/2009

Rio de Janeiro, 10 de agosto de 2009.

Sr(a) Pesquisador(a),

Informamos a V.Sa. que o Comitê de Ética em Pesquisa da Secretaria Municipal de Saúde e Defesa Civil - CEP SMSDC-RJ, constituído nos Termos da Resolução CNS nº 196/96 e, devidamente registrado na Comissão Nacional de Ética em Pesquisa, recebeu, analisou e emitiu parecer sobre a documentação referente ao Protocolo de Pesquisa, conforme abaixo discriminado:

<p>Coordenadora: Salésia Felipe de Oliveira</p> <p>Vice-Coordenadora: Suzana Alves da Silva</p> <p>Membros: Andréa Estevam de Amorim Alice de C. A. Vinhaes Bráulio dos Santos Júnior Carlos Alberto Pereira de Oliveira Elisete Casotti José M. Salame Jucema Fabrício Vieira Márcia Constância P. A. Gomes Maria Alice Gunzburger Mônica Amorim de Oliveira Nara Saraiva Pedro Paulo Magalhães Chrispim Rafael Aron Abitbol Rondineli Mendes da Silva Sandra Regina Victor</p> <p>Secretárias Executivas: Carla Costa Vianna Renata Guedes Ferreira</p>	<p>PROTOCOLO DE PESQUISA Nº 121/09 CAAE: 0139.0.314.000-09</p> <p>TÍTULO: Saúde mental e estado nutricional na gestação e no pós-parto: estudo prospectivo com ensaio clínico randomizado aninhado.</p> <p>PESQUISADOR RESPONSÁVEL: Gilberto Kac.</p> <p>UNIDADE (S) ONDE SE REALIZARÁ A PESQUISA: CMS Heitor Beltrão.</p> <p>DATA DA APRECIAÇÃO: 13/08/2009.</p> <p>PARECER: APROVADO.</p>
---	--

Ressaltamos que o pesquisador responsável por este Protocolo de Pesquisa deverá apresentar a este Comitê de Ética um relatório das atividades desenvolvidas no período de 12 meses a contar da data de sua aprovação (*item VII. 13.d., da Resolução CNS/MS Nº 196/96*).

Esclarecemos, ainda, com relação aos Protocolos, que o CEP/SMSDC deverá ser informado de fatos relevantes que alterem o curso normal do estudo, devendo o pesquisador apresentar justificativa, caso o projeto venha a ser interrompido e/ou os resultados não sejam publicados.

Salésia Felipe de Oliveira
Coordenadora
Comitê de Ética em Pesquisa

ANEXO 4

TERMO DE CONSENTIMENTO LIVRE E ESCLARECIDO

COORTE BRASILEIRA

TERMO DE CONSENTIMENTO LIVRE E ESCLARECIDO PARA PARTICIPAR DA PESQUISA

“Estado nutricional e saúde mental na gestação e no pós-parto: Estudo prospectivo com ensaio clínico randomizado”

Você está sendo convidada a fazer parte de uma pesquisa que tem por objetivo entender melhor a relação entre a alimentação e a ocorrência de problemas como a ansiedade e o estresse durante a gestação e após o parto. Neste estudo, também avaliaremos se o ômega-3 (um composto natural presente em vários alimentos, como peixes e alguns vegetais) protege as gestantes de tais problemas.

Você não é obrigada a participar e, mesmo aceitando fazer parte do estudo, poderá desistir e retirar o seu consentimento a qualquer momento. Sua recusa em participar do estudo não trará nenhum prejuízo em sua relação com o pesquisador, com o seu médico ou com a maternidade; ou seja, você poderá seguir normalmente com o seu atendimento nesta unidade de saúde.

Como irei participar?

Você fará uma avaliação completa e detalhada sobre sua saúde. No total, você terá 4 consultas com nossa equipe: 4 durante o pré-natal (com **até 13 semanas**, na **24^a e 34^a semanas**) e uma de **30 a 45 dias após o nascimento de seu filho**. **Todas estas consultas serão preferencialmente marcadas em dias em que você já tenha que vir ao hospital**. O tempo aproximado destas consultas é de 30-45 minutos.

Durante as consultas, você irá **responder a perguntas e preencher questionários** para obtermos informações como: sua identificação (endereço e telefone), dados demográficos (nome, estado civil, idade), situação social e econômica, história obstétrica, uso de álcool, fumo e outras drogas, violência familiar, estresse e ansiedade, atividade física e como você se alimenta. Em todas as 4 consultas iremos também avaliar seu peso e altura e coletar amostras de sangue para avaliarmos o açúcar, gorduras, colesterol e níveis de hormônios.

Além disso, em cada consulta, deixaremos com você dois aparelhos por um período de **24 horas (1 dia)**: um chamado de “frequencímetro polar” que mede a freqüência cardíaca (batimentos do coração) e o outro “pedômetro” que conta o número de passos que você dará durante este dia. No dia seguinte, um pesquisador do projeto irá até a sua casa recolher esses equipamentos, **não sendo necessário, portanto, que você retorne ao hospital apenas para devolvê-los**.

A partir da **18^a semana** de gestação, um grupo de mulheres que estiverem participando do estudo serão convidadas a integrar uma parte diferente do estudo e serão orientadas a fazer uso de um suplemento na forma de cápsulas, contendo **ômega-3**. Se você fizer parte deste grupo, você deverá fazer uso de **5-6 cápsulas por dia** junto das refeições (almoço), todos os dias **até 30 dias após o parto**. Você não precisará comprar ou pagar por este suplemento, ou seja, **você vai recebê-lo de graça**.

É importante você saber que esta suplementação é composta unicamente de óleo de peixes marinhos, porém sem qualquer sabor ou cheiro característico de peixe. Além do óleo, o outro ingrediente presente é uma pequena quantidade de vitamina E. **O uso desta suplementação durante a gestação não traz nenhum risco ou efeito colateral para a sua saúde e a do bebê**. No entanto, já foram relatados a **ocorrência passageira** de diarréia, regurgitação e refluxo. Consumir o óleo na forma de cápsula torna apenas mais prático.

Todas as informações que você fornecer serão mantidas em segredo e utilizadas apenas para a pesquisa. Nenhuma outra pessoa ou profissional terá acesso a suas informações, somente os pesquisadores que trabalham para esta pesquisa. Quando divulgarmos os resultados deste trabalho, seu nome em momento algum irá aparecer, bem como qualquer outra informação fornecida, ou resultado de exame de sangue. Portanto, não há riscos em participar desta pesquisa, apenas a necessidade de coletar sangue e o tempo que você irá gastar com as avaliações durante as consultas. Por ocasião da coleta de sangue, você poderá observar a formação pequeno hematoma na região do braço onde ocorreu a picada da agulha. Sempre usaremos materiais descartáveis.

Quais as vantagens?

Ao participar deste estudo, você terá a **oportunidade de realizar uma avaliação mais completa e detalhada da sua saúde**. O acompanhamento de seus hábitos durante a gestação, como o seu ganho de peso e sua alimentação, são medidas importantes para garantir a saúde do seu bebê ao nascer. Este acompanhamento também é importante para que você tenha uma vida mais saudável, prevenindo problemas futuros como a obesidade, ansiedade e depressão. **Você terá acesso a todos os seus resultados se assim desejar.**

Este termo de consentimento é um documento importante e você irá receber uma cópia na qual consta o telefone e o endereço do pesquisador principal, **podendo tirar suas dúvidas sobre o projeto e sua participação, agora ou a qualquer momento**.

Meu consentimento:

Minha participação é de livre e espontânea vontade, ou seja, não fui pressionada por ninguém para participar desta pesquisa. Tenho liberdade para continuar ou recusar, em qualquer momento, a participar da pesquisa. O meu atendimento e de meu(minha) filho(a), nesta unidade não será, em momento algum, afetado pela minha recusa. Desta forma, concordo em participar deste estudo estando totalmente esclarecida dos objetivos, riscos e benefícios desta pesquisa, uma vez que tive em mãos este documento e a oportunidade de lê-lo antes de assinar.

Nome e assinatura do pesquisador

data

Nome do sujeito da pesquisa

Telefones: _____

Assinatura do sujeito da pesquisa

data

Contato do coordenador da pesquisa:

Professor Dr. Gilberto Kac
Universidade Federal do Rio de Janeiro - UFRJ
Telefones: 25626595 / 93152301
E-mail: kacetal@gmail.com

Juliana dos Santos Vaz
Nutricionista, doutoranda UFRJ
Telefones: 74221922
E-mail: juliana.vaz@gmail.com

Secretaria Municipal de Saúde e Defesa Civil / Comitê de Ética em Pesquisa
Rua Afonso Cavalcanti, 455 Bloco 1 - Sala 715
Email: cepsms@rio.rj.gov.br

ANEXO 5

PROJETO PROPOSTO PARA O ALSPAC

Project Proposals

Reference:

B2354



Title

Dietary patterns during pregnancy by cluster analysis and childhood neurodevelopment

Date(s)

11/12/2014 (approved) / 09/12/2014 (received)

Outline

Dietary patterns during pregnancy and childhood neurodevelopmental. This work is to be the international part of a PhD based in Brazil during this time experience will be gained working in Bristol.

The maternal diet can affect the infant neurodevelopmental (del Río García et al., 2009; Bernard et al., 2013). The ALSPAC study was explored and there are some studies that assessed the maternal dietary intake of fatty acids (Hibbeln et al., 2007; Hibbeln and Davis, 2009) and 'healthy' and 'unhealthy' food groups (Barker et al., 2013) with childhood neurodevelopmental deficiencies. Dietary patterns have been used in some studies to assess the relationship between diet and health outcomes, because they represent an overview of food and nutrient consumption (Slattery, 2010; Tucker, 2010).

Aim: To obtain clusters of dietary patterns during pregnancy and to examine the association between these dietary patterns and neurodevelopmental outcomes in childhood.

Hypotheses: The adherence to dietary patterns composed by healthy foods can reduce the risk of neurodevelopmental outcomes during the childhood, while the patterns composed by processed food can increase the risk of neurodevelopmental outcomes.

Exposure variable(s): Dietary patterns during pregnancy obtained by cluster analysis.

Outcome variable(s): Neurodevelopmental outcomes in child previously explored in Hibbeln et al. (2007) study. Including clinic measured IQ and parental questionnaire assessed Denver Developmental Screening Test and Strengths & Difficulties.

Confounding variable(s): Maternal education, social class, age at delivery, parity, energy intake, BMI. Child's date of birth, birth weight, sex, gestational age, breastfeeding, child diet at the time of assessment.

We plan to write at least 2 papers as a result of this work. We also have a comparable Brazilian cohort and aim to do some work comparing outcomes in Brazil with ALSPAC outcomes as appropriate.

PI | Affiliation Vilela, Ana Amélia Freitas () | *Federal University of Rio de Janeiro (UFRJ)*

Co-applicants

- , | Not used 0 (Not used 0)
- , | Not used 0 (Not used 0)
- , | Not used 0 (Not used 0)
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- , | Not used 0 (Not used 0)
- , | Not used 0 (Not used 0)
- , | Not used 0 (Not used 0)

Keywords

Cognitive Function Diet Pregnancy

Next action:

Main menu >>> ▾

Continue



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of Parents and Children**

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Bristol BS8 2BN, UK**

**T. 0117 331 0010
E. info@childrenofthe90s.ac.uk**

ANEXO 6

APROVAÇÃO DO COMITÊ DE ÉTICA

COORTE BRITÂNICA

Avon Longitudinal Study of Parents and Children

University of Bristol

LREC Approval References

Please note that all self-completion Questionnaire content is approved by the ALSPAC Ethics and Law Committee

Initial Approval:

Bristol and Weston Health Authority: E1808 Children of the Nineties: Avon Longitudinal Study of Pregnancy and Childhood (ALSPAC). (28th November 1989)

Southmead Health Authority: 49/89 Children of the Nineties - "ALSPAC". (5th April 1990)

Frenchay Health Authority: 90/8 Children of the Nineties. (28th June 1990)

Children in Focus or “The 10% Club”

Southmead Health Services: 48/89: ALSPAC – “The 10% Club” (25th August 1992)

7 Year Clinic:

United Bristol Healthcare Trust: E4168 ALSPAC Hands on Assessments at Age Seven. (30th September 1998)

Southmead Health Services: 67/98 Avon Longitudinal Study of Pregnancy and Childhood (ALSPAC) - Hands on Assessments at Age Seven. (14th September 1998)

Frenchay Healthcare Trust: 98/52 Avon Longitudinal Study of Pregnancy and Childhood (ALSPAC). Hands on Assessments at Age Seven.(8th December 1998)

8 Year Clinic:

United Bristol Healthcare Trust: E4445 ALSPAC Focus at Eight. (28th January 2000)

Southmead (North Bristol Trust): Project 084/99 ALSPAC Assessments at Age Eight. (November 1999)

Frenchay (North Bristol Trust): Project 99/42 Avon Longitudinal Study of Parents and Children (ALSPAC). Assessments at Age Eight (ALSPAC Focus at Eight). (15th December 1999)

Weston Area Health Trust: E177 Avon Longitudinal Study of Parents and Children (ALSPAC). Assessments at Age Eight (21st September 1999)

9 Year Clinic:

United Bristol Healthcare Trust: E5018 Avon Longitudinal Study of Parents and

**Children – Assessments at Age Nine (ALSPAC Focus@9). [Reciprocal Arrangement]
(7th February 2002)**

Southmead (North Bristol Trust): 008/01 ALSPAC Assessments at Age Nine. (20th March 2001)

Frenchay (North Bristol Trust): 2001/35 Avon Longitudinal Study of Parents and Children (ALSPAC) Assessments at Age Nine. (9th May 2001)

10 Year Clinic:

United Bristol Healthcare Trust: E5215 ALSPAC – Focus at 10+. [Reciprocal]. (31st January 2002)

Southmead (North Bristol Trust): 138/01 ALSPAC – Focus 10+. (18th January 2002)

Frenchay (North Bristol Trust): 2001/90 Avon Longitudinal Study of Parents and Children (ALSPAC) Assessments at Age Ten Plus. (28th January 2002)

Weston Area Health Trust: E280R – ALSPAC Focus 10+. (12th December 2001)

11 Year Clinic:

Southmead (North Bristol Trust): 137/02: ALSPAC – Focus at 11+. (17th April 2003)

United Bristol Healthcare Trust: E5691 ALSPAC Focus @ 11+. [Reciprocal] (29th May 2003)

Frenchay (North Bristol Trust): 2002/110 Avon Longitudinal Study of Parents and Children (ALSPAC) Assessments at Age Eleven Plus. (23rd June 2003)

Weston Area Health Trust: E325 (R) – 137/02 Avon Longitudinal Study of Parents and Children (ALSPAC) Assessments at Age Eleven Plus. (28th February 2003)

12 Year Clinic:

Central & South Bristol Research Ethics Committee (UBHT): E5806 ALSPAC Teen Focus 1. (19th February 2004) Confirmation of Site Specific Approval (Southmead and North Somerset) (26th May 2004)

Southmead Research Ethics Committee: Project 030/04 ALSPAC Hands on Assessments: Teen Focus 1. (26th April 2004)

Frenchay Local Research Ethics Committee: 2004/18 Avon Longitudinal Study of Parents and Children (ALSPAC) Hands on Assessments: Teen Focus 1. (22nd April 2004)

North Somerset Research Ethics Committee (Weston): 04/Q2003/5 Avon Longitudinal Study of Parents and Children (ALSPAC) Hands on Assessments: Teen Focus 1. (7th April 2004)

12 Year Clinic Amendment (TF1 Fast-track):

Central & South Bristol Research Ethics Committee (UBHT): E5806 ALSPAC Teen Focus 1 fasttrack Amendment. (16th February 2005)

13 Year Clinic:

Central & South Bristol Research Ethics Committee (UBHT): 04/Q2006/168 Avon Longitudinal Study of Parents and Children (ALSPAC), Hands on Assessments: Teen Focus 2 (Focus 13+). (11th March 2005)

Approval for use of Biosamples (8th June 2007)

15 Year Clinic:

Central & South Bristol Research Ethics Committee (UBHT): 06/Q2006/53 Avon Longitudinal Study of Parents and Children (ALSPAC), Hands on Assessments: Teen Focus 3 (Focus 15+). (7th August 2006) (Confirmed 15th September 2006)

17 year clinic:

North Somerset & South Bristol Research Ethics Committee: 08/H0106/9 Avon Longitudinal Study of Parents and Children (ALSPAC), Hands on Assessments: Teen Focus 4 (Focus 17+) (18th November 2008)

NAFLD:

North Somerset & South Bristol Research Ethics Committee: 09/H0106/53 Evaluating the prevalence, causes and biomarkers for identifying non-alcoholic fatty liver disease (NAFLD) in young adults. (7th August 2009)

Mothers Clinic:

North Somerset & South Bristol Research Ethics Committee: 08/H0106/96 Avon Longitudinal Study of Parents and Children (ALSPAC); Focus on Mothers (2nd September 2008, Confirmed 8th September 2008).

Enrolment of Partners:

North Somerset & South Bristol Research Ethics Committee: 09/H0106/82. Avon Longitudinal Study of Parents and Children (ALSPAC); Enrolment of Partners (26 October 2009, Questionnaire approval 18 October 2010).

Home Visits:

South West 3 Research Ethics Committee: 10/H0106/74 Avon Longitudinal Study of Parents and Children (ALSPAC); Home Visits (22nd December 2010)

PEARL project

North West 5 Research Ethics Committee: 10/H1010/70 (protocol Number 1278). Project to Enhance ALSPAC through Record Linkage (PEARL): phenotypic enrichment of the ALSPAC Cohort through linkage to primary care electronic patient records and other databases. (3rd February 2011)

Mothers Clinic 2&3:

National Research Ethics Service Committee South West – Central Bristol: 11/SW/0110 Avon Longitudinal Study of Parents and Children (ALSPAC); Focus on Mothers 2 and 3 (1st June 2011, Confirmed 20th June 2011)

Fathers Clinic:

National Research Ethics Service Committee North West – Haydock: 11/NW/0369 Avon Longitudinal Study of Parents and Children (ALSPAC); Focus on Fathers (3rd August 2011)

ANEXO 7

ARTIGO 1. PRE-PREGNANCY HEALTHY DIETARY PATTERN IS INVERSELY ASSOCIATED WITH DEPRESSIVE SYMPTOMS AMONG PREGNANT BRAZILIAN WOMEN

Prepregnancy Healthy Dietary Pattern Is Inversely Associated with Depressive Symptoms among Pregnant Brazilian Women^{1–3}

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Abstract

Dietary patterns before pregnancy may be associated with depressive symptomatology during pregnancy. The aim of this study was to identify dietary patterns before pregnancy and to examine the association between these dietary patterns and depressive symptoms during pregnancy. A prospective cohort of 248 healthy pregnant women were followed at 5–13, 20–26, and 30–36 gestational weeks. Dietary intake was obtained by using a food-frequency questionnaire administered between 5 and 13 gestational weeks, which referred to the 6 mo preceding gestation, and factor analysis (principal components) was applied to identify dietary patterns. The Edinburgh Postnatal Depressive Scale (EPDS) was used to evaluate depressive symptoms during 3 follow-up pregnancy points. A multiple linear mixed-effects model was applied to verify the association between dietary patterns and depressive symptoms adjusted for obstetric factors, socioeconomic status, and energy intake. Three prepregnancy dietary patterns were identified: common-Brazilian, healthy, and processed. Together, these patterns explained 36.1% of the total percentage of variance; the eigenvalues were 2.88, 2.12, and 1.86, respectively. Mean depressive symptom scores were 9.0 (95% CI: 8.4, 9.6), 7.2 (95% CI: 6.5, 7.8), and 7.0 (95% CI: 6.4, 7.7) for trimesters 1, 2, and 3, respectively. The rate of decrease in depressive symptoms was $-0.088/\text{wk}$ (95% CI: -0.115 , -0.061 ; $P < 0.001$). In the multiple longitudinal linear regression model, the healthy dietary pattern before pregnancy was inversely associated with depressive symptoms ($\beta = -0.723$; 95% CI: -1.277 , -0.169 ; $P = 0.011$). High adherence to the healthy pattern before pregnancy was associated with lower EPDS scores during pregnancy in women from Rio de Janeiro, Brazil. *J. Nutr.* 144: 1612–1618, 2014.

Introduction

During pregnancy, women undergo environmental, psychological, and metabolic changes, increasing the likelihood of mental health disorders (1). The prevalence of depressive symptoms during pregnancy varies from 10% to 20% in developed and developing countries (2). Depressive symptoms increase the risk of maternal and fetal adverse outcomes, such as inadequate

prenatal care, insufficient gestational weight gain, low birth weight, and postpartum depression (PPD)¹⁰ (3–5).

Sociodemographic factors such as poverty and lack of a partner have been shown to be risk factors for depressive symptoms during pregnancy (1,6,7). In addition, nutrient and energy requirements often increase during pregnancy and many nutrients are critically important during this period (8,9), with deficiencies associated with depressive symptoms (10–13).

Different from the single-nutrient-based approach, the evaluation of dietary patterns identifies dietary habits on the basis of an assessment of food group intake. This method enables a broader analysis of the diet, including the associations and interactions between nutrients (13,14). In this way, this type of

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³ Supplemental Tables 1–3 are available from the “Online Supporting Material” link in the online posting of the article and from the same link in the online table of contents at <http://jn.nutrition.org>.

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¹⁰ Abbreviations used: ALSPAC, Avon Longitudinal Study of Parents and Children; EPDS, Edinburgh Postnatal Depressive Scale; LME, longitudinal mixed-effects; PCA, principal components analysis; PPD, postpartum depression.

ANEXO 8

**ARTIGO 2. ASSOCIATION OF PRE-PREGNANCY DIETARY PATTERNS AND
ANXIETY SYMPTOMS FROM MID-PREGNANCY TO EARLY POSTPARTUM IN A
PROSPECTIVE COHORT OF BRAZILIAN WOMEN**

Association of Prepregnancy Dietary Patterns and Anxiety Symptoms from Midpregnancy to Early Postpartum in a Prospective Cohort of Brazilian Women



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ABSTRACT

Background Adherence to unhealthy dietary patterns may alter the risk of mental disorders during pregnancy and the postpartum period.

Objective To analyze the association between prepregnancy dietary patterns and prospective variations on anxiety symptoms from midpregnancy to early postpartum.

Methods A prospective cohort of 207 healthy pregnant women was followed at 5 to 13, 20 to 26, and 30 to 36 gestational weeks, and once at 30 to 45 days postpartum. The State-Trait Anxiety Inventory was used to evaluate anxiety symptoms at the second and third gestational trimesters and during the postpartum period. Dietary intake was assessed using a food frequency questionnaire administered during the first trimester of pregnancy that referred to the 6 months before pregnancy. Principal components analysis was used to identify dietary patterns and three prepregnancy dietary patterns were identified: common-Brazilian, healthy, and processed. Three longitudinal mixed-effect models were estimated to verify the association between dietary patterns and anxiety symptoms, adjusted for confounding variables.

Results The mean anxiety symptom scores were 40.4, 40.5, and 37.2 for the second trimester, third trimester, and postpartum, respectively. The rate of variation of the State-Trait Anxiety Inventory score was 0.535 (95% CI -0.035 to 1.107; $P=0.066$) and -0.010 (95% CI -0.018 to -0.002; $P=0.019$) when accounting for gestational age and quadratic gestational age, respectively. The common-Brazilian pattern, comprised mainly of rice and beans ($\beta=-1.200$, 95% CI -2.220 to -0.181; $P=0.021$), and the healthy pattern comprised mostly of vegetables, fruits, fish, and tea ($\beta=-1.290$, 95% CI -2.438 to -0.134; $P=0.029$), were negatively associated with prospective changes in anxiety symptoms.

Conclusions High adherence to the common-Brazilian or healthy patterns was negatively associated with higher anxiety symptom scores from mid-pregnancy to early postpartum in this group of Brazilian women.

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ANXIETY IS CONSIDERED A COMMON MENTAL health disorder during pregnancy and has been associated with adverse outcomes for the mother and the fetus, such as inadequate weight gain, premature birth, obstetric complications, and postpartum depression.¹⁻⁴ The prevalence of anxiety during pregnancy may vary from 9% to 33.3% worldwide.⁵⁻⁸ In Brazil, it ranges from 16.9% to 33.3%.⁷⁻⁹ The mean prevalence of anxiety symptoms in Brazilian pregnant women is higher than the prevalence in other countries. For instance, in Peruvian women, anxiety during pregnancy ranges from 8.1% to 19.6%;¹⁰ for North Americans¹¹ and Swedish pregnant women,¹² the mean prevalence is 13% and 11.4%, respectively. Prospective studies have shown that anxiety symptoms increase during pregnancy and decrease after birth.^{3,13,14}

Some studies have reported that socioeconomic, demographic, nutrition-related, and lifestyle factors are associated with the occurrence of anxiety during pregnancy.^{15,16} A cross-sectional study with 165 pregnant women from Athens, Greece, found a positive association between unfavorable social conditions (ie, low level of education and unstable marital status) and anxiety.¹⁷ Hurley and colleagues¹⁸ showed that the high intake of carbohydrates, fats, and protein were positively associated with anxiety symptoms in pregnant women from Baltimore, MD. These studies have assessed maternal diet by micro- and macronutrient intake.^{19,20} However, in nutritional epidemiology, dietary patterns have been used in some studies to assess the relationship between diet and health outcomes.^{21,22}