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Dietary and psychosocial correlates of nausea and vomiting in pregnancy

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Abstract

Nausea and vomiting during pregnancy (NVP) is a condition that affects women around the world. Previous studies show that NVP is associated with dietary changes and aversions towards certain kinds of food. It has been suggested that these changes could have adaptive functions, such as protecting the embryo from harmful teratogenic substances in certain foods. Here, we used a food frequency questionnaire to record self-reported frequency of consumption of a range of specific food categories by 726 pregnant women. We tested whether the incidence and severity of NVP symptoms varied between women who consumed foods in each category, as well as investigating several potential psychosocial predictors. We found evidence for an association between alcohol, cereals, and (especially) milk consumption on the experience of NVP symptoms. In addition, NVP symptoms were positively correlated with women's self-reported fatigue, stress, and depression, but negatively correlated with perceived level of support from the woman's partner. Finally, NVP symptoms were also associated with use of oral contraceptives during partner choice and we discuss possible reasons for this. Overall, our results contribute to a growing body of evidence for complex and multifactorial effects on the experience of NVP, of which dietary patterns may be a critical component.

Keywords: morning sickness; NVP; maternal and embryo protection hypothesis; food aversion; Rhodes Index; Food Frequency Questionnaire

1. Introduction

Numerous studies have shown specific changes in women's diet during pregnancy, which may be driven by culturally sanctioned beliefs and taboos about food in different societies (Mukhopadhyay & Sarkar, 2009; Placek et al., 2017) as well as individually variable food aversions and cravings (Nyaruhucha, 2009; Yoseph, 2015). These latter changes may be underpinned, at least in part, by the occurrence of nausea and vomiting in pregnancy (NVP) (Ebrahimi et al., 2010; Weigel et al., 2011).

NVP is a common phenomenon affecting women worldwide (Kramer et al., 2013; Lee & Saha, 2011). Symptoms range in severity, but the most severe form, *hyperemesis gravidarum*, is characterised by frequent vomiting and requires hospitalisation since it could be fatal for mother and embryo. Although NVP is also known as "morning sickness", the symptoms appear anytime during the day. NVP occurs most frequently in the first trimester, but women can suffer from NVP at any time of pregnancy. According to a recent meta-analysis (Einarson & Piwko, 2013), almost 70% of women experience some level of NVP and for about 24% this persists into the third trimester. There are, however, some geographical differences. While frequencies are around 5% lower than the meta-analytic average in countries including Australia, UK, USA, Canada, Israel and Sweden, women from East Asia reported higher levels of NVP, ranging from 75–91% (Einarson & Piwko, 2013).

Most women experiencing NVP also report reduced appetite, and sometimes also aversions for hypothesised harmful foods, food cravings and altered odour sensitivity (Weigel et al., 2011). Increased odour sensitivity and irritability (Nordin et al., 2007; Swallow et al., 2005) could be important in driving dietary changes, as women with a food aversion reported that the unpleasant odour of a particular food was the explanation for their aversion in 73% of cases, compared to unpleasant taste in just 5% of cases (Weigel et al., 2011).

Symptoms of NVP are also, to at least some extent, connected with certain psychological and social factors. For example, a higher level of NVP is associated with symptoms of depression (Dekkers et al., 2019) and anxiety (Köken et al., 2008). Furthermore, Iatrakis et al. (1988) found that poor communication with partner was positively associated with symptom severity. Interestingly, it was found that one of the symptoms of NVP - food aversions - occur more often in the company of other people (Reilly, 2009), which points to a

possible social influence on the experience of symptom severity and reporting (Schachtman et al., 2016).

Given its widespread occurrence, we still have limited knowledge about the origin, mechanism and function of NVP. Symptoms of NVP have been considered to be a by-product of intense hormonal changes during pregnancy (Lagiou et al., 2003), which could potentially have harmful effects on the developing embryo or subsequent child health due to undernutrition (Fall et al., 2003). Previous use of terms like "pregnancy sickness" stem from these negative perceptions. However, most evidence indicates that NVP is in fact associated with positive pregnancy outcomes, including lower frequencies of birth defects, pre-term deliveries, miscarriages, and perinatal deaths, as well as higher mean birth weight (for a review see Patil et al., 2012). In light of this, it is now widely accepted that there may be an adaptive function behind NVP.

One such adaptive explanation comes from Huxley (2000), who argued that NVP is a generalised adaptive mechanism to reduce the rate of food intake; this stimulates placental growth in the first trimester which in turn maximises nutrient transfer between mother and embryo in later phases of pregnancy. This hypothesis explains the finding that undernutrition in the first trimester of pregnancy correlates with placental growth (Lumey, 1998), but does not explain the role of specific aversions to food items. The phenomenon of specific food aversions is directly addressed by the embryo protection hypothesis, according to which NVP causes women to avoid foods containing potentially toxic abortifacients and teratogens (which also are often characterised by strong odour and taste). Hook (1976) first proposed this hypothesis with a primary focus on alcohol, caffeine and tobacco, but also suggested that women may avoid other foods including meat, onion and oregano. The hypothesis was then extended by Profet (1992, 1995), who further suggested that women are especially likely to have an aversion for specific plants, such as pungent or bitter vegetables and herbs, that are rich in potential abortifacient or teratogenic phytochemicals. Furthermore, she suggested that women should be less likely to develop aversions for less toxic and more durable foods, such as cereals, grains or starchy carbohydrates, that also all tend to have a faint odour and mild taste. Aversions for food could also be expected with potentially mutagenic compounds such as fried, grilled and roasted foods, which are also characterised by a strong odour. Building on these ideas, Flaxman and Sherman (2000) further argue that protective avoidances should be connected with animal products, especially meat, fish, eggs and milk, because these are quickly perishable (especially so in tropical climates and before widespread use of

refrigerators) and so could easily become a cause of foodborne illnesses and food poisoning. They also proposed that these mechanisms protect not only the developing embryo, but also the mother, as immunosuppression during pregnancy makes women more vulnerable to infections (Flaxman & Sherman, 2000). In support of such protective mechanisms, pregnant women also experience increased disgust sensitivity, especially during the first trimester (Zelaźniewicz & Pawłowski, 2015). In addition to links with a suite of prophylactic behaviours that are unrelated to diet, such as higher risk perception (Mielcarska, Żelaźniewicz, & Pawłowski, 2017) and favouritism of ingroup individuals (Navarrete, Fessler, & Eng, 2007) increased disgust sensitivity in the first trimester can also be connected with diet in terms of avoiding spoiled food and other potential sources of pathogens.

In a test of the embryo protection hypothesis, Pepper & Roberts (2006) studied dietary characteristics and NVP rates in 57 studies across 21 countries on 6 continents, by analysing NVP prevalence against national dietary data. They found a negative relationship between NVP prevalence and the consumption of cereals and pulses, and a positive relationship between NVP rates and the consumption of milk, meat, eggs, sugars and sweeteners, stimulants, alcohol, spices, vegetable oils, vegetables and fruits. However, they recognised that there could be third factors that mediate these correlations, such as variation in the state of development across different geographical regions, their medical infrastructure, economy, and cultural and lifestyle differences. They attempted to minimise these potential confounds in a second analysis which included only North American and European populations, finding a negative relationship between NVP prevalence and cereal consumption, and a positive relationship between NVP and consumption of meat, oil crops, sugars and sweeteners and alcohol.

Pepper & Roberts' (2006) study thus provides support for the maternal and embryo protection hypothesis, but their analyses do not take into account individual women's experience; instead, they compared recorded rates of NVP within a given country and the concurrent national rates of dietary intake of different foodstuffs. Their data also miss any measure of the wide variation between women in the degree of NVP symptom severity. To address these shortfalls, here we aimed to test the relationships between individual women's experience of NVP symptoms and their consumption of specific categories of food. We obtained self-reports of NVP incidence and severity using a robust and sensitive scale, and combined this with a food-frequency questionnaire involving the dietary categories investigated by Pepper & Roberts. We sampled only women from countries of a similar level

of economic development (Western Europe, USA, Canada, Australia), in order to limit possible confounding factors due to cultural differences in diet. Finally, we concurrently investigated some other possible contributory factors to self-reported symptoms, such as fatigue, depression and levels of social and partner support.

2. Material and methods

2.1. Participants

A total of 734 women completed our online questionnaire, but we excluded 8 women who did not provide required information (the month of their pregnancy). Women from our sample were from either the UK (n = 412), other European countries (n = 50), the United States (n = 132), Canada (n = 94) or Australia (n = 38). Mean age was 27.3 (range 16–43 years) and only pregnant women were recruited. Data were collected between December 2008 and February 2009 by advertising the study via Facebook and several online forums for discussion about pregnancy issues. These included Netmums (www.netmums.com), Pregnancy Forum (www.pregnancyforum.co.uk), CafeMom (www.cafemom.com), Baby and Bump (www.babyandbump.com) and Ladies Lounge (http://theladieslounge.forumotion.net).

2.2. Questionnaires

Data collection was anonymous. After providing informed consent, participants completed a short survey including items concerning age, location, ethnicity, parity and current month of pregnancy. To address our main research question, they then completed the Rhodes Index of Nausea, Vomiting and Retching (Koren et al., 2001) and a Food Frequency Questionnaire (FFQ; based on Venter et al., 2006). In addition, for measuring other possible contributory factors, participants also completed the Prenatal Psychosocial Profile (PPP; Curry et al., 1994), The Center for Epidemiologic Studies Depression scale (CES-D; Leander & McMillan, 1975), a Fatigue Symptom Checklist (FSC; Chien & Ko, 2004), items on relationship satisfaction (from Garver-Apgar et al., 2006) and some questions on previous hormonal contraception use. All these scales are described in more detail below.

2.2.1. Rhodes Index of Nausea, Vomiting and Retching

We used the Rhodes Index to identify the level of nausea and vomiting as it has proved to be an efficient measurement of NVP in numerous previous studies (e.g. Köken et al., 2008). The scale contains 8 items, each of which focus on the previous 12 hours and have 5 possible responses. For example, items include: “In the last 12 hours, from nausea/sickness to my stomach, I have felt __ distress” (possible responses: No, Mild, Moderate, Great, Severe), “I threw up __ times” (possible responses: 0, 1–2, 3–4, 5–6, 7 or more), and “I produced a __ amount” (possible responses: I did not throw up, up to ½ cup, ½–1 cup, 2–3 cups, 3 and more cups). Scores on these items were reversed where appropriate and then summed so that the range of possible scores is 0–32, higher scores indicating greater symptom severity.

2.2.2. Food Frequency Questionnaire

Our FFQ was based on a previously used questionnaire from a study of consumption of common food allergens in pregnancy (Venter et al., 2006). Participants were asked to "Please indicate how often you have tended to eat these foods during the past week" by selecting from one of 4 options: “Never”, “Moderate (1–3 times)”, “Frequently (more than 3 times)”, or “Don't Know”. However, in place of common allergens, we included foods that predicted levels of NVP in a previous cross-country study of NVP prevalence (Pepper & Roberts 2006). There were 14 items: milk and milk products, eggs, meat, fish (including shellfish), stimulants (including caffeinated drinks), alcoholic beverages, vegetables, fruit and fruit juices, cereals, starchy roots, sugars/sweeteners/desserts, pulses, oil crops and ethnic, strong or spicy food. For each item, a list of examples was provided to help participants.

2.2.3. Prenatal Psychosocial Profile

The Prenatal Psychosocial Profile (PPP) is a composite measure that enables the assessment of various social and psychological measures on pregnancy experience and outcome (Curry et al., 1994). We used it because it includes separate validated scales of stress, social support from the woman's primary partner, social support from others beyond the partner, and women's self-esteem. Thus, our participants completed the following scales: *(a) Stress scale* - this consisted of 11 items, for each of which participants were asked: “To what extent does this cause you stress/hassle?” Example items include “Financial worries (e.g. food, shelter, health care, transport)”, “Problems related to your family (partner, children etc.)”, “Current pregnancy”, “Work problems (e.g. being laid off)”, and “Feeling generally overloaded”. Participants were asked to indicate how much each of these items was a current stressor by

selecting an answer on a 4-point scale (1 = “no stress”, 2 = “some stress", 3 = “moderate stress”, 4 = “severe stress”). *(b) Support scale* (The Support Behaviors Inventory) also consists of 11 items but is completed twice as participants assess levels of support from their primary partner (where appropriate) and support from other people (Brown, 1986). Participants rated their satisfaction with the support they receive on a 6-point scale anchored by the terms “very dissatisfied” (score of 1) to “very satisfied” (score of 6). The 11 items include “Shares similar experiences as me”, “Helps keep up my morale”, “Shows interest in my daily activities and problems”, and “Let me know that he/she will be around if I need assistance”. *(c) Self-Esteem*. This scale on the PPP consists of the 10-item Self-Esteem Scale (Rosenberg, 1965) plus one additional item: “Feel like you have control over your life”. All 11 items were answered on a 4-point scale (from “Strongly Disagree” to “Strongly Agree“).

2.2.4. Relationship satisfaction and previous hormonal contraception use

For those participants who indicated that they had a current primary partner, we also asked about their relationship length (in years) and 5 items regarding relationship satisfaction. The first item was “How satisfied are you with your partner's *provision of financial resources*?”. The other items were “faithfulness and loyalty”, “intelligence”, “physical attractiveness” and “your partner's ability to arouse you sexually”. These items were selected from Garver-Apgar et al. (2006) as indicative measures of general satisfaction with the partner. We also asked participants about the use of hormonal contraception at relationship formation, because this has been found to affect women's self-reported relationship satisfaction (see Roberts et al. 2012, 2014). To the question "Were you using hormonal contraception when you first began your relationship with your partner?", participants selected one of the following options: “Combined pill”, “Minipill (progestogen-only pill)”, “Hormonal injection”, “Hormonal implant”, or “None of these”.

2.2.5. Fatigue Symptom Checklist

To assess the effect of fatigue, we used the Fatigue Symptom Checklist (FSC; Chien & Ko, 2004). It is a 30-item scale (e.g. “My back hurts”, “I want to lie down”, “I am drowsy”). Participants selected “Yes” (coded 1) or “No” (coded 0), so that possible scores range between 0–30.

2.2.6. Center for Epidemiologic Studies Depression scale

Finally, the Center for Epidemiologic Studies Depression scale (CES-D; Leander & McMillan, 1975) was used to identify the level of depression experienced over the previous week. This scale is comprised of 20 items (e.g. "I talked less than usual", "I had crying spells") with responses being collected on a 4-point scale, where 0 = "Rarely or none of the time (less than 1 day)", 1 = "Some or a little of the time (1–2 days)", 2 = "Occasionally or a moderate amount of time (3–4 days)", 3 = "Most or all of the time (5 7 days)" with possible score range between 0–60.

1.1. Statistical analysis

Due to the non-normal distribution of our data, we used non-parametric Kruskal-Wallis tests and post-hoc Dunn's tests for measuring the relationship between the level of NVP (Rhodes Index score) and frequency of intake for different food types. We report these twice: first for the whole sample, and then in a separate analysis that included only those women in the first to fourth month of pregnancy, when frequency and severity NVP were higher compared to later phases of pregnancy (Fig. 1). For analysing other possible factors, we used non-parametric Spearman's rank correlations or Wilcoxon tests, and for comparing specific food consumption across different phases of pregnancy, chi-squared tests. The statistical program R version 3.6.2 was used for all statistical tests.

2. Results

2.1. Sample characteristics

All women were pregnant when they completed the questionnaire. Of 726 participants, approximately half (365, 50.3%) were pregnant with their first child, 210 (29%) with their second child, 96 (13.2 %) with their third child, and 54 (7.4%) with their fourth (or a subsequent) child. A relatively small number were in the first month of pregnancy, but there was relatively equal representation across the remaining months (see Fig. 1).

As might be expected, the month of pregnancy was negatively correlated with Rhodes Index scores; in other words, NVP symptoms were more common in the early months of pregnancy (rho = -0.339, $p < 0.001$). Although NVP is usually associated with the first

trimester, median scores were highest across months 1–4 and higher in month 4 than month 1. Furthermore, many women reported above-zero scores in months across pregnancy (Wilcoxon test, $z = 9.68$, $p < 0.001$; Figure 1). For these reasons, we investigated associations between NVP and diet both across the whole sample and when restricting analysis only to women in the first 4 months of pregnancy, when NVP symptoms were relatively high.

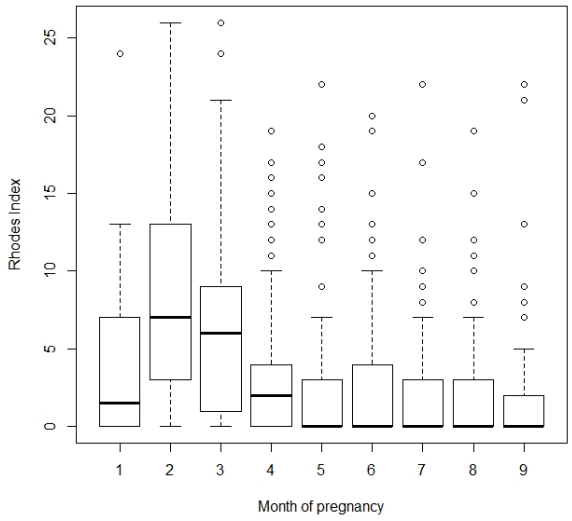

Fig. 1. Rhodes Index scores across the sample of pregnant women. Data show median (horizontal bar), interquartile range (box), upper quartile (whiskers) and outliers (circles). N = 726 women, of whom 11 (1.5%) were in their first month of pregnancy, 59 (8.1%) in month 2, 60 (8.3%) in month 3, 73 (10.1%) in month 4, 137 (18.9%) in month 5, 94 (12.9%) in month 6, 101 (13.9%) in month 7, 98 (13.5%) in month 8, and 93 (12.8%) were in month 9.

2.2. NVP symptoms and diet

First, we compared Rhodes Index scores and recent consumption of dietary components for the whole sample of pregnant women (n = 726; Table 1, see also Fig. S1). We found significant associations between NVP symptoms and the previous week's consumption of milk and milk products, cereals and alcohol (Table 1, Fig. 2). Post hoc tests showed that women who reported "never" consuming milk/milk products had higher Rhodes Index scores than those who reported "moderate" consumption ($p = 0.008$), who in turn had higher scores than those who reported consuming these "frequently" ($p < 0.001$). Women who reported moderate consumption of cereals had higher Rhodes Index scores than women who reported frequent consumption ($p = 0.005$). Finally, women who reported never consuming alcohol

had higher scores than women who reported moderate consumption ($p = 0.021$; note that, although the medians are equal in Table 1, the between-group differences can be visualised in Fig. 2a). No other associations were statistically significant, including between Rhodes Index scores and frequency of consuming meat, seafood or eggs.

Next, we restricted the analysis to women in the first four months of pregnancy only. In this analysis, the previous associations between Rhodes Index score and consumption of alcohol and cereals were not observed (both $p > 0.05$; Fig. S2). However, the association with milk and milk products was still present (Table 2; Fig. S2) and in the same direction, such that women who never consumed milk or milk products had more prevalent NVP symptoms than those who frequently consumed them ($p = 0.045$), but not compared with women who had moderate consumption ($p = 0.284$; the difference between "moderate" and "frequent" was also not statistically significant, $p = 0.052$).

2.3. Dietary differences across pregnancy

Although our primary analysis (above) focused on the association between individual women's NVP symptoms and dietary patterns, we also compared food frequency data between groups of women in the earlier and later months of pregnancy (i.e. months 1 – 4 vs months 5 – 9) of pregnancy, because these groups differ in levels of NVP (Fig. 1). Results of this analysis are shown in Table 3. Women in early pregnancy consumed milk and milk products, cereals, and sugars/sweeteners less often than women in later pregnancy, while there were no statistically significant differences in any of the remaining dietary components.

2.4. Other correlates of NVP symptoms

Finally, we explored some potential social correlates of NVP. Rhodes Index scores were positively correlated with the number of previous children ($rho = 0.075$, $p = 0.042$), as well as with women's scores on the Fatigue Index ($rho = 0.206$, $p < 0.001$), the Stress Scale of the Prenatal Psychosocial Profile ($rho = 0.127$, $p < 0.001$) and CES-D Depression Index ($rho = 0.230$, $p < 0.001$). There was no significant correlation with self-esteem ($rho = -0.004$, $p = 0.913$).

We also found some correlations with support from women's partners. First, Rhodes Index scores were negatively correlated with scores on the Support Behaviors Inventory for

partners (rho = -0.092, p = 0.014), but there was no similar relationship with perceived support from non-partners (rho = -0.015, p = 0.679). This was corroborated by additional items pertaining to partner satisfaction, as women with low Rhodes Index scores tended to be more satisfied with partner's financial provision (rho = -0.094, p = 0.011), faithfulness and loyalty (rho = -0.079, p = 0.033), and intelligence (though this was a non-significant trend: rho = -0.066, p = 0.077). Finally, we found a significant difference in Rhodes Index scores dependent on women's previous use of combined oral contraceptives (COC). Women who used COC when they met their partner had significantly lower Rhodes Index scores compared with those who did not use COC when they met their partner (Wilcoxon test, $z = 2.19$, df = 631.1, p = 0.029.

Table 1. Median Rhodes Index scores for women according to the frequency of consumption of specified dietary components during the previous week (N = 726 women).

Type of food	Frequent	Moderate	Never	X^2	p-value
Alcohol	**0**	**0**	**0**	**6.96**	**0.031**
Cereals	**0**	**1**	**0**	**8.78**	**0.012**
Eggs	1	0	0	1.81	0.404
Ethnic, strong, spicy	0	0	0	4.61	0.090
Fish, seafood	0	0	0	0.68	0.708
Fruits, fruit juices	0	0	0	0.78	0.678
Meat	0	0.5	0	2.19	0.334
Milk and milk products	**0**	**3**	**8**	**19.83**	**<0.001**
Oil crops	2	0	0	3.58	0.167
Pulses	3	0	0	5.85	0.054
Starchy roots	0	0	0	0.16	0.924
Stimulants	0	0	1	2.06	0.357
Sugars and sweeteners	0	1	0	5.91	0.052
Vegetables	0	1	2	4.16	0.125

Fig. 2. Rhodes Index scores for women according to the frequency of consumption of alcohol, cereals and milk during the previous week. Data show medians (horizontal bar), interquartile range (box), upper quartile (whiskers) and outliers (circles). (N = 726). For other dietary components see Supplementary materials.

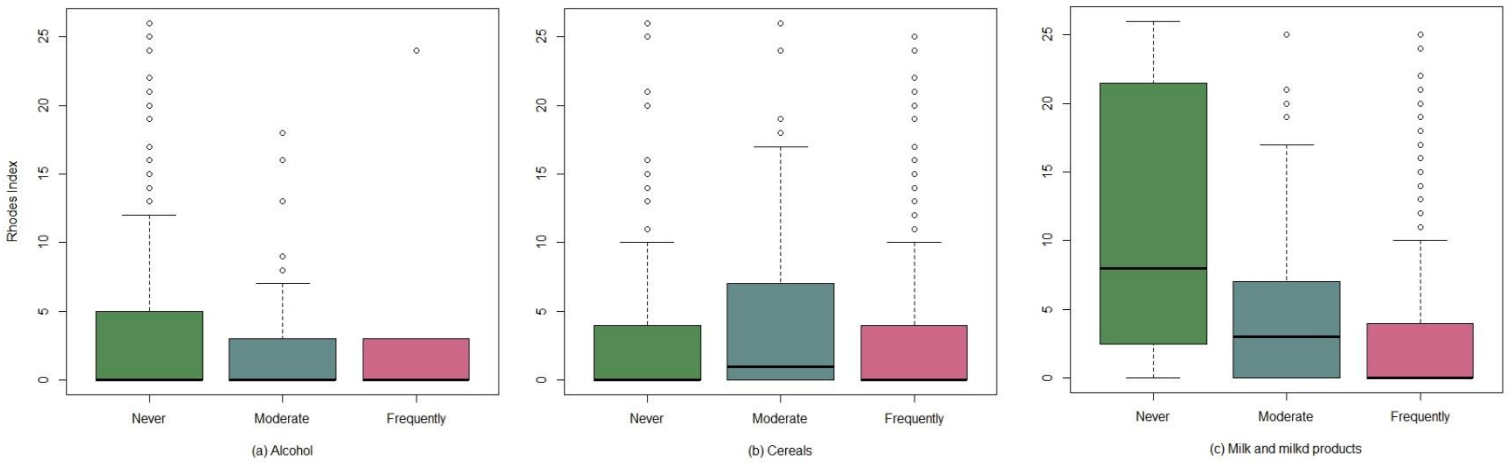

Table 2. Median Rhodes Index scores for women in the first four months of pregnancy only, according to the frequency of consumption of specified dietary components during the previous week (N = 203 women).

Type of food	Frequent	Moderate	Never	X^2	p
Alcohol	13.5	3	4	3.18	0.2
Cereals	3	6	6	2.08	0.353
Eggs	8	3	5	1.34	0.511
Ethnic, strong, spicy	1	3	5	3.51	0.173
Fish, seafood	5.5	3	5	2.08	0.354
Fruits, fruit juices	3	6	3	0.84	0.657
Meat (vegetarians included)	3	4	3.5	0.56	0.755
Meat (vegetarians excluded)	3	4	3.5	0.33	0.847
Milk and milk products	**3**	**6**	**17**	**8.44**	**0.015**
Oil crops	8	3	4	3.77	0.152
Pulses	4	3	4.5	0.87	0.648
Starchy roots	3	5	3	2.59	0.274
Stimulants	3	3.5	4	0.91	0.633
Sugars and sweeteners	3	4	5	2.62	0.27
Vegetables	3	6	5.5	0.78	0.678

Table 3. Differences in reported consumption of different dietary components between pregnancy phases. For ease of interpretation, data show percentages of women in the first trimester (top row) and later trimesters (bottom row), but analysis used counts of observations across frequency categories (N = 203 women in months 1–4 of pregnancy; N = 523 women in months 5–9).

Type of food	Month	Frequent	Moderate	Never	X^2	p
Alcohol	1-4	1	6.7	92.2	4.28	0.118
	5-9	1.6	11.8	86.6		
Cereals	1-4	**49.5**	**40.2**	**10.3**	**9.47**	**0.009**
	5-9	**61.2**	**28.5**	**10.3**		
Eggs	1-4	12	59.2	28.8	2.82	0.245
	5-9	13.2	64.1	22.7		
Ethnic, strong, spicy	1-4	6.8	43.8	49.5	2.86	0.239
	5-9	11	41.6	47.3		
Fish, seafood	1-4	5.2	53.4	41.4	1.72	0.424
	5-9	7.4	55.4	37.2		
Fruits, fruit juices	1-4	76.4	19.5	4.1	4.2	0.123
	5-9	73.6	24.4	2		
Meat (vegetarians included)	1-4	46.7	46.8	8.4	2.51	0.285
	5-9	50.9	40.3	8.8		
Meat (vegetarians excluded)	1-4	47.5	49.2	3.4	4.08	0.13

	5-9	55.1	43.2	1.7		
Milk and milk products	1-4	**74.5**	**22.9**	**2.7**	**16.2**	**<0.001**
	5-9	**86.5**	**12.9**	**0.6**		
Oil crops	1-4	6.3	29.1	64.6	0.81	0.668
	5-9	5	27.3	67.7		
Pulses	1-4	12.6	49.5	37.9	2.97	0.227
	5-9	10.1	56.6	33.3		
Starchy roots	1-4	45.1	46.1	8.8	2.7	0.259
	5-9	45.5	49	5.5		
Stimulants	1-4	33	38.3	28.7	3.87	0.144
	5-9	39.9	37.5	22.6		
Sugars, sweeteners	1-4	**33.3**	**58.9**	**7.8**	**20.69**	**<0.001**
	5-9	**52.1**	**43.8**	**4.1**		
Vegetables	1-4	71.1	25.8	3.1	0.94	0.625
	5-9	73.2	24.9	1.9		

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3. Discussion

Nausea and vomiting have been linked with changes in diet selection and habits in pregnant women. Across our sample, we found that the level of NVP experienced by different women was related to differences in consumption levels of three of our food/drink categories. NVP symptoms were highest in women who reported they had never consumed milk in the previous week and lowest in those who had consumed these frequently. A similar pattern was observed for consumption of alcohol. NVP symptoms also varied with intake of cereals, with symptoms being most prevalent in women who had consumed these in moderate amounts during the preceding week. When we restricted the analysis to women in the first four months of pregnancy, a significant relationship between NVP symptoms and frequency of consumption was found only for consumption of milk, with NVP severity being highest in those who never consumed milk products. No other dietary category was found to be associated with NVP severity in our sample. Comparisons between women in the early and later phases of pregnancy indicated that women tended to consume fewer cereals, milk products and sugars/sweeteners in early pregnancy, when NVP levels were higher.

While we used the same dietary categories in our food frequency questionnaire as those in the previous study by Pepper & Roberts (2006), our results appear to be quite different, at least at first sight. The two studies differ not only in terms of the dietary components that are significantly associated with NVP symptoms, but also in their direction. For example, whereas Pepper & Roberts (2006) reported a positive relationship between NVP prevalence and alcohol consumption, we also found a significant relationship, but in the opposite direction, with NVP symptoms being higher in those who avoided alcohol entirely in the previous week. Similarly, there appeared to be a robust association between experiencing NVP symptoms and non-consumption of milk in our study, whereas milk consumption was positively associated with NVP prevalence in the previous study (at least in their global analysis). Finally, while the previous study indicated that cereal consumption was negatively related to NVP prevalence, NVP symptoms in our study were associated with moderate levels of cereal consumption.

These differences may be explained by considering the differences in design of the two studies. First, while Pepper & Roberts (2006) studied the relationship between average NVP and average consumption of different foodstuffs at the population level, our data address the relationship at the individual level. This allows for a more direct inference of the

relationship between diet and NVP, ruling out the possibility of spurious relationships driven by third factors. Second, our food frequency data refers to women's consumption of food over the previous week. This offers a much greater level of sensitivity, because dietary data at the population level (as used by Pepper & Roberts, 2006) relate to general levels of consumption not just across a year, but across the entire population, including children, men and non-pregnant women.

The individual-level approach of this study allows a degree of speculation about the direction of causality, at least for alcohol. Here, we think it is more likely that the experience of nausea and vomiting leads to an aversion to drinking alcohol, because the alternative (that not drinking alcohol is the cause of nausea and vomiting in pregnancy) seems very unlikely. The chain of causality cannot be similarly addressed for milk, however. It is possible that nausea leads to milk aversion, as for alcohol, but it also possible that not consuming milk or milk products over a long period could lead or contribute to symptoms of NVP. This could occur because such dietary habits might lead to a deficit in some key nutrient that is found at high levels in milk (such as calcium, or vitamin D and B_{12}). Indeed, previous work (Latva-Pukkila et al., 2010) has found that women with NVP have lower dietary intake of vitamin B_{12} and zinc than women without NVP symptoms, although there was no between-group difference in milk intake. However, it should be acknowledged that firmer conclusions on causality could be made only if we were able to know that those women who reported that they did not drink either milk or alcohol were actively avoiding it; in other words, we would need to know their usual consumption levels before pregnancy in order to be sure that they were avoiding it in early pregnancy.

Our results lend some further support for the maternal and embryo protection hypothesis. For example, while milk is no longer as dangerous for mother and embryo as it may have been in the past, protective mechanisms that originated before the advent of refrigeration and pasteurisation may persist even today (Li et al., 2018). A process by which increasing NVP symptoms lead to reduced or complete avoidance of milk intake would then be consistent with the hypothesis. On the other hand, alcohol has a clear and negative influence on health in general and can be particularly harmful to mother and developing embryo. It is thus possible that a protective mechanism exists whereby NVP symptoms lead to an aversion towards alcohol. It is true that in modern times there is broad awareness about the danger of alcohol consumption during pregnancy, and many women would likely avoid alcohol irrespective of NVP (Peadon et al., 2010). However, there is still a certain proportion

of women who drink alcohol during pregnancy; for example, in a recent multinational European study, an average of 15.8% women reported doing so (Mårdby et al., 2017). Indeed, we observed that nearly 12% of our sample consumed alcohol in pregnancy at moderate or frequent levels over the previous week (although it is possible that women drink alcohol in the first trimester before they find out they are pregnant (Muggli et al., 2016), this was not the case in our study, as all participating women were aware of their pregnancy when entering the study). Those women that did drink alcohol in our study tended to have low or no NVP symptoms compared to those who did not. This thus suggests that an aversive role of NVP may still be playing some part in reducing alcohol consumption in at least a proportion of women.

The pattern of NVP symptoms and consumption of some other food types is harder to interpret. We were surprised to find no association between NVP and meat consumption, which is predicted by the maternal and embryo protection hypothesis. Furthermore, although we found lower NVP symptoms in women who consumed cereals frequently than those who did so in moderate amounts, they were also lower in women who never ate cereals. Neither pattern is consistent with Flaxman & Sherman's (2000) suggestion that high NVP levels in industrialised nations may be linked to relatively low cereal (and high meat) consumption. The higher NVP levels in women who consumed moderate amounts of cereals in our study are consistent with a similar pattern in white bread consumption in one study (Crozier et al. 2016). However, the same study also found a negative relationship between NVP symptoms and breakfast cereal consumption. Breakfast cereals may be a specific case because they also contain a relatively high amount of sugar and are usually eaten with milk, which might affect a clear pattern across the different types of cereals. Future studies might therefore address breakfast cereals as a separate category. The results also show that women who reported moderate cereal consumption suffered from higher NVP than women who consumed cereals frequently. This could be interpreted either as a positive influence of eating cereals on decreasing levels of NVP, or conversely, as an effect of NVP on decreasing consumption of food in general, which reveals an effect for cereals because they account for a significant proportion of the diet.

We also compared food frequency data between groups of women in the earlier and later months of pregnancy (i.e. months 1–4 vs months 5–9) of pregnancy, because these groups differ in levels of NVP. We found a reduced frequency of consumption of cereals, milk and sugars/sweeteners in the early phase, which is consistent with results above.

However, sugars may be linked to reduced consumption of cereal and milk (if eaten together as breakfast cereal) and of lower food intake overall in the first trimester (especially of desserts, for example). No change in alcohol (as might have been expected from the above results) may be due to the obscuring effects of social unacceptability of drinking during pregnancy. In other words, the majority of women do not consume alcohol at all through their pregnancy, even after NVP symptoms recede, while those who do (12% in our sample) may be prepared to do so at any stage of their pregnancy.

Finally, we found some relationships between NVP levels and psychosocial factors. There was a positive correlation between NVP and fatigue, stress and depression. As relatively severe nausea and vomiting can significantly affect many aspects of women's lives (including disruption of work, social life and everyday activities), these results are perhaps not surprising: psychosocial context is very important in the experience of NVP (Chou et al., 2006; Munch et al., 2011). But we found some evidence that these effects might be offset by supportive partners, as women with higher partner support reported lower levels of NVP symptoms. This raises the question of whether this is a real effect on the degree of NVP severity, or whether it alters women's subjective perception of their NVP symptoms. We suggest that the latter is more likely (if NVP is hormonally mediated) and that good partner support affects women's perception of their experience, such that they are more resilient to its effects and score their symptoms as less severe than they might do without this support (the converse could also be true, where women with more severe symptoms perceive their partner as less helpful). However, such interpretations assume a causal effect of NVP on fatigue, stress and depression. It is at least possible that the causality is reversed, so that these factors influence NVP symptoms. If so, the effect of good partner support on reducing fatigue, support and depression would ultimately lead to less severe NVP.

Our results also showed that levels of NVP were lower in women who used combined oral contraception at the time when they first met their partners, compared to women who were not using COC when they met their partner. We propose two possible explanations for this. First, it could be related to the previously discussed effects of good partner support. Previous work has indicated that women who meet their partner on oral contraception (OC) are more generally satisfied with their partner (e.g. on measures of financial provision, faithfulness and loyalty) perhaps as a result of effects of OC on women's mate preferences (Roberts et al., 2012, 2014). Second, it is possible that lower NVP severity is influenced by the degree of genetic complementarity between women and the father. The basis for this

suggestion is as follows: if women on OC tend to select a partner who is more HLA-similar than they might otherwise prefer (Havlicek & Roberts, 2009; Wedekind et al., 1995), a resulting foetus would share relatively more of its HLA alleles with the mother. HLA genes play a key role in maternal immune response to the foetus during implantation and subsequent placentation (Havlíček et al., 2020; Moffett & Loke, 2006). Disparity between parental HLA genes (as would be found in offspring of HLA-dissimilar partners) tends to increase the extent of uterine vasculature remodelling, thus increasing blood supply to the foetus and overall size of the placenta (Madeja et al., 2011). This likely leads to greater placental production of human chorionic gonadotropin (hCG, as larger placentae are correlated with higher hCG levels, (Korevaar et al., 2015), which is thought to be the main proximate cause of nausea in early pregnancy (Forbes, 2002; Lee & Saha, 2011). We are currently completing further work in HLA-genotyped couples to test these possibilities.

There are some limitations to our study. First, although we sampled a large number of pregnant women, most of these were in the second half of their pregnancy and were therefore surveyed after the usual peak of NVP severity. Second, although we compare between women in the early and late phases of pregnancy, it is possible that expression of NVP symptoms in different phases of pregnancy are driven by different mechanisms and serve different functions. Third, in order to test the protective avoidance mechanism, future studies need to ask not only about the frequency of current consumption, but also about consumption before the pregnancy and about active avoidance of specific food items. As this study is correlational, all inferences about causality are therefore rather speculative. Ideally, future studies should use a longitudinal design to determine food preferences, avoidance and actual consumption before pregnancy and during pregnancy to ascertain the observed associations' causality. Our study also relies on self-reports, that may for some items such as alcohol consumption, bias the results. Therefore, future studies should complement this approach by using sensory assessment of food-related odours and test for taste and smell sensitivity.

In summary, it seems clear that women's experience of NVP is a complex and multifactorial phenomenon. Whether it arises directly as part of a functional adaptation or indirectly as a by-product of some other physiological mechanism in early pregnancy, our results show that it is associated with both dietary and psychosocial correlates. Gaining a fuller understanding of these factors is key to transforming the experience of pregnancy for women across the world.

Ethical statement

This study was conducted in accordance with the declaration of Helsinki, and procedures were approved by The Ethics Panel of the University of Liverpool's School of Biological Sciences. Informed consent was obtained from all participants.

Conflict of interest

None.

CRediT authorship contribution statement

Kateřina Fiurašková: Formal analysis, Data Curation, Writing - Original Draft, Visualization **Jan Havlíček:** Conceptualisation, Writing - Review & Editing **S. Craig Roberts:** Conceptualisation, Methodology, Investigation, Writing - Review & Editing

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