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The relationship between diet, supplement use, and the prevalence and severity of nausea and vomiting during the 1st and 2nd trimesters of pregnancy

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Abstract

Nausea and vomiting during pregnancy (NVP) are common conditions experienced by women throughout the world. However, despite their widespread occurrence, the prevalence and severity of symptoms range significantly, with the exact aetiology underpinning this variation relatively unclear. Several studies propose that NVP may serve as an adaptive function, protecting the embryo from harmful foodstuffs, implying that diet is implicated within the pathogenesis of the condition. However, there is limited literature focusing on this topic, specifically with regards to supplement use. Therefore, the aim of the present research was to examine the relationship between diet, both pre-pregnancy and current diet, including supplement use, and the prevalence and severity of NVP. Women completed an online questionnaire involving two food frequency questionnaires (FFQ), one to assess their pre-pregnancy diet and the other their current diet, alongside questions regarding supplement use. Women experiencing NVP also completed the Pregnancy Unique Quantification of Emesis Scoring System (PUQESS) to assess their severity of symptoms. Results indicated that pre-pregnancy consumption of pulses was significantly associated with the severity of NVP ($p=0.046$), with all current diet food stuffs, apart from meat consumption also significantly associated ($p=<0.05$). Vitamin D supplementation ($p=0.002$), as well as first trimester folic acid supplementation ($p=<0.001$) were also associated. The present study therefore indicates that current diet and supplement use are associated with the severity of NVP to a greater extent than pre-pregnancy diet. Subsequently, if conducted amongst larger, more diverse populations, these findings may contribute to improving the management of NV amongst pregnant women.

Key Words: Nausea and Vomiting during Pregnancy (NVP), Pregnancy Sickness, Severity, Pre-pregnancy Diet, Current Diet, Food Frequency Questionnaire (FFQ), Supplements, Pregnancy Unique Quantification of Emesis Scoring System (PUQESS), Embryo Protection Hypothesis (EPH).

Introduction

Nausea and vomiting during pregnancy (NVP) are common phenomenon affecting 70-80% of pregnant women worldwide (Einarson et al., 2013; Kramer et al., 2013). Such conditions typically establish between 4-6 weeks gestation (Deuchar, 2000; Sherman and Flaxman, 2002), and thus is often the initial symptom of early pregnancy (Lee and Saha, 2011). NVP is commonly referred to as 'morning sickness', although such terminology is thought to trivialise the condition (Gadsby et al., 2020) since symptoms can occur at any time of day, with a minimal 1.8% of women thought to experience sickness only in the mornings (Lacroix et al., 2000). Although the severity of NVP ranges significantly between women, the condition is typically isolated to the first trimester (T1) of pregnancy, with symptoms often peaking between 8-16weeks gestation and generally resolving by 20-22 weeks gestation (Lee and Saha, 2011; Lacroix *et al.,* 2000; Weigel and Weigel, 1989).

However, although only affecting around 1.5% of pregnant women in the United Kingdom (Fiaschi *et al.,* 2016), a severe form of NVP, known as Hyperemesis Gravidarum (HG) persists throughout pregnancy, with debilitating symptoms occurring up until birth (Furneaux *et al.,* 2001; Lee and Saha, 2011). Although clinical practice lacks a universal definition of this disorder (Maltepe and Koren, 2013), it is typically characterised by persistent and intractable nausea and vomiting (NV) resulting in fluid, electrolyte, and acid-base imbalance, nutritional deficiency (Verberg *et al.,* 2005), and weight loss of >5% of pre-pregnancy body weight (Golberg *et al.,* 2007; Maltepe and Koren, 2013). Subsequently, if left untreated, HG can result in significant maternal and fetal morbidity (Lee and Saha, 2011) and thus is the most common cause of hospitalisation in early pregnancy (Gazmararian *et al.,* 2002).

Despite its widespread occurrence, NVP is an enigmatic feature of human reproduction (Forbes, 2017), with the exact aetiology not well understood (Fiurašková *et al.,* 2021; Lacasse *et al.,* 2009). However, one of the most widely accepted pathogenesis is that it is a by-product of the intense hormonal changes occurring during early pregnancy (Lagiou *et al.,* 2003; Masson *et al.,* 1985); more specifically the rising levels of the human chorionic gonadotropin (hCG) hormone (Lee and Saha, 2011). This paradigm is supported by the fact that peak NVP and peak hCG production occur concurrently between 12-14 weeks gestation; postulating that a temporal relationship exists between the two (Lee and Saha, 2011). In support of this, women experiencing molar pregnancies, multiple gestations, or are pregnant with a baby with Down syndrome often have elevated levels of hCG and subsequently more severe NV (Banerjee *et al.,* 2005, Davis, 2004).

Despite the evidence to support this hormonal aetiology, if NVP is driven predominately by hormones, then such condition should be ubiquitous given that all women experience these hormonal changes during pregnancy. However, this does not appear the case since 20-30% of women do not experience any NVP, with racial, ethnic, and geographical disparities in the prevalence of the phenomenon also widely reported in the literature (Einarson *et al.,* 2013; Lacasse *et al.,* 2009; Semmens, 1971). Subsequently, this raises the question as to what other factors are implicated within the aetiology of NVP, particularly given that the phenomenon has been associated with favourable outcomes, including a reduced risk of birth defects, pre-term births, perinatal deaths, miscarriages, and a higher mean birth weight (Hinkle *et al.,* 2016; Weigel and Weigel, 1989; Patil *et al.,* 2012).

Subsequently, maternal diet is one factor which has been proposed to be implicated within the pathogenesis of this multifactorial phenomenon. Several adaptative explanations for NVP have been suggested, with the two most widely acknowledged advocating associations between nutritional intake and the consumption of specific dietary components (Pepper and Roberts, 2006). Of these adaptive explanations, is the theory proposed by Huxley (2000) which postulates that the beneficial effects of NVP arise from such symptoms indirectly inducing higher levels of placental growth in the T1 through lowering maternal energy intake and levels of insulin and insulin growth factors IGF-1, ultimately shunting nutrients towards the developing placenta and away from maternal tissue synthesis (Fiurašková *et al.,* 2021). Such theory is supported by research reporting that a reduction in maternal energy intake during pregnancy is associated with increased placental weight (Schuster *et al.,* 1985; Lunney, 1998). Nevertheless, such hypothesis only addresses the role of energy intake, providing little insight into the aetiology of food aversions which typically arise alongside NVP.

However, an alternative theory, known as the embryo protection hypothesis (EPH), provides an explanation for this temporal relationship between the development of food aversions and the onset of NVP (Bayley *et al.,* 2002). The first evidence for this theory was proposed by Hook (1976, p. 173) who stated that NVP causes women to avoid or expel foods which may be teratogenic or contain potentially toxic abortifacients. Flaxman and Sherman (2000) expand on this through postulating that women tend to have the greatest aversions to meats, fish, poultry, and eggs, as these animal products can cause food poisoning and foodborne illnesses; of which can detrimentally effect developing embryos (Williamson, 2006). Pepper and Roberts (2006) extend on and provide complementary evidence to support the EPH through investigating the association between the prevalence of NVP obtained from 56 studies across 21 countries, and national dietary characteristics. It was concluded that high intakes of cereals and pulses were negatively correlated with NVP, whilst high macronutrient consumption, alongside high intakes of meat, milk, eggs, sugars, and stimulants were positively correlated (Peppers and Roberts, 2006).

Nevertheless, Pepper and Roberts (2006) utilised quantitative estimates per capita for these dietary categories and thus their findings represent the dietary patterns of the entire population, including non-pregnant women, men, and children. Subsequently, their analysis does not account for individual variation in dietary habits, nor does it reflect specifically pregnant women or the association between the severity of the condition and diet; of which may be a more sensitive measure given the widespread prevalence of NVP. However, a recent study by Fiurašková *et al.,* (2021) sought to address these limitations through adopting an individual-level approach to assess the relationship between the incidence and severity of NVP and the consumption of these foodstuffs. From a sample of 726 women, Fiurašková *et al.,* (2021) concluded that cow's milk and alcohol consumption were negatively associated with NVP symptoms, with moderate amounts of cereals positively associated.

Despite Fiurašková *et al.,* (2021) overcoming the previous limitations of Pepper and Robert's (2006) research, women's pre-pregnancy diets were not assessed. Consequently, it was unknown whether women were actively avoiding specific foods, meaning the protective avoidance mechanism was not tested. Furthermore, neither

Pepper and Roberts (2006) or Fiurašková *et al.,* (2021) collected data on supplements, of which tend to be key aspects of women's diets both preconception and during pregnancy (Tsui *et al.,* 2001). Subsequently there is a requirement to investigate the relationship between supplement use and NVP, particularly given the evidence to support the efficacy of the vitamin pyridoxine in alleviating NV symptoms amongst pregnant women (Scharifzadeh *et al.,* 2018; Babaei and Foghaha, 2014). Consequently, due to the paucity of studies involving pre-pregnancy dietary data and supplement use, the aim of this present research was to examine the relationship between both pre-pregnancy and current dietary factors, including supplement use, and the prevalence and severity of NVP.

Methodology

Participants

Prior to recruitment, ethical approval was obtained from the University of Plymouth's Faculty of Science and Engineering Research Ethics and Integrity Committee. Women were eligible to participate if they were >18years of age and were currently pregnant in either their T1 or second trimester (T2) with a singleton pregnancy. Criteria for exclusion were known diagnosis of Type 1 Diabetes, Type 2 Diabetes, or Gestational Diabetes. Women were recruited via advertisement of the online questionnaire (Appendix 1) on social media platforms, predominately Facebook and Instagram between the 5th of November 2021, and the 3rd of January 2022, with written informed consent provided prior to completing the questionnaire.

Questionnaire

All data collection was anonymous, with participants first providing their descriptive characteristics, including their age, weight, height, ethnicity, and gestational age. To address the main research question, the questionnaire was then divided into two predominant sections. One to obtain data on NVP symptoms, and the other, to assess women's diets and supplement use (Appendix 1).
Regarding quantification of the severity of NVP, the Pregnancy-Unique Quantification of Emesis and Nausea Scoring System (PUQESS) was adopted, of which has been widely utilised in recent literature yielding significant findings (Heitmann *et al.,* 2017; Sathiyabama and Meraklinsofey, 2021). Such system has also been validated against four independent clinical outcomes of direct importance and relevance for NVP (Koren *et al.,* 2005) and is proven to be a robust indicator of severe HG (Birkeland *et al.,* 2015).

The PUQESS is based on 3 items, including number of daily vomiting episodes, the length of nausea per day in hours, and the number of retching episodes occurring within the previous 12 hours (Koren *et al.,* 2002). Within this research, the PUQESS was modified to ask participants to rate their NVP with respect to when their symptoms were at their worst, rather than during the previous 12 hours. For example, nausea was assessed by means of asking women "At its worst, how long would you feel nauseous or sick to your stomach in a 12-hour period", rather than the original question of "In the last 12 hours, how long have you felt nauseated or sick to your stomach". This modification was more sensitive to variations in the severity of NV symptoms and allowed for women who were no longer experiencing NV but had done so in the previous days/weeks to be included within the analysis. The scoring system remained the same as the traditional PUQESS, with symptoms perceived as less severe obtaining a score of 1, and most severe scoring 5. Total scores could therefore potentially range from 3, indicating no symptoms, to 15,

implying maximal symptoms. However, since only women with NVP completed the PUQESS, the score range in the present study was 4-15.

Regarding dietary assessment, women completed two identical food frequency questionnaires (FFQ) to assess both their current diet, and their diet pre-pregnancy. This FFQ was adapted from that used by Fiurašková *et al.,* (2021) and shortened to assess the weekly consumption of three animal products of which Flaxman and Sheerman (2000) reported were likely to be associated with NVP. These included meat and eggs which were quantified through asking participants to state whether they consumed these foods and if so, whether it was on average "1-2", "3-4", "5-6", or "≥7 times per week". Cow's milk consumption was also assessed by asking participants to state whether they consume this and if so on how many days per week, selecting from "1-2 days", "3-5 days", or "everyday". Regarding fruit and vegetables (F&V), pulses, and wholegrain consumption, participants stated how many daily portions they consume of these foods from either "none", "1-2", "3-4", or ">5". Examples were provided for the latter two foods groups to ensure participants understood the foods which align with these categories. Participants also provided their type of diet, both currently and pre-pregnancy, choosing from 4 categories: I consume meat, I follow a pescatarian diet, I am vegetarian, or I am vegan. Finally, to assess supplement use, women stated if they were currently taking a vitamin D supplement, had taken folic acid pre-conception, and whether they took or are intending to take folic acid for the first 12 weeks of pregnancy.

Statistical analysis

Prior to statistical analysis, participants' total sickness severity scores were derived from calculating the sum scores of the three questions from the PUQESS. Body Mass Index (BMI) was calculated for each participant by converting height into metres and dividing weight (kg) by height $(m)^2$. All data was statistically analysed using Minitab® Statistical Software (Minitab, LLC, USA) version 21.1.0. Descriptive statistics are displayed as Mean ± Standard Deviation for continuous variables and percentages for categorical variables. All maternal characteristics were non-normally distributed and thus Mann-Whitney tests were adopted to compare the median values for continuous variables between women who had NVP and those who did not, including, age, height, weight, BMI, and gestational age. For categorical variables such as the trimester of pregnancy and pre-pregnancy smoking status, Chi-squared tests were used to compare the distributions between the two groups. Non-parametric Spearman's Rank correlations were used when analysing continuous variables against the severity of NVP, however, when analysing the prevalence of NVP against these variables, Kruskal-Wallis tests were used to compare the median values between women who had NVP and those who did not.

To address the main research question, Kruskal-Wallis tests were utilised to establish the relationship between the severity of NVP and the type of diet, as well as the frequency of consuming various foods. When statistically significant findings were evident, a Mann-Whitney test was used to identify between which categories these differences existed, as well as for comparing the severity of NVP across binary categories with non-parametric data; for example, the relationship between vitamin D supplementation status and the severity of NVP. Due to the limited number of women who reported having no NVP, there was not sufficient statistical power to detect true associations between the prevalence of NVP and the type of diet or dietary factors. However, the association between the prevalence of NVP and supplement use was analysed using a Chi-Squared test. Finally, when analysing the

relationship between changes in women's diets from pre-pregnancy and the severity of NVP, a Mann-Whitney test was adopted. The level of significance was set to $p<0.05$ for all statistical tests performed.

Results

Participant Characteristics.

As shown in Figure 1, after excluding women who were <18years of age, were in their third trimester of pregnancy, had been diagnosed with Gestational Diabetes, or Type 2 Diabetes, the final sample for analysis comprised of 313 women who were currently pregnant.

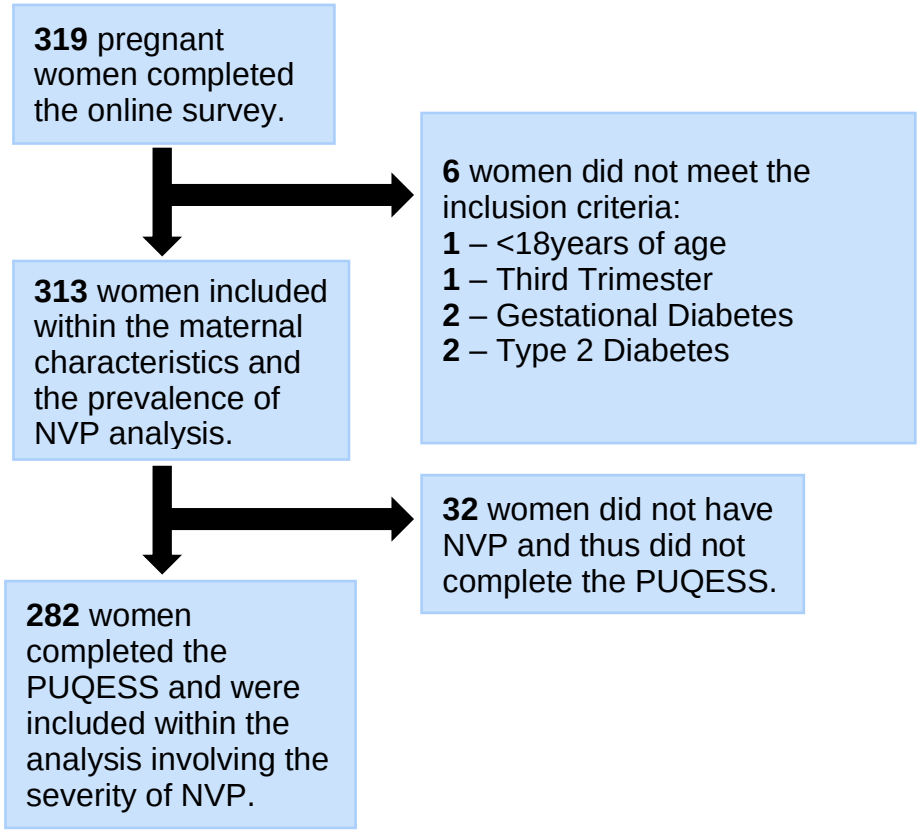

Figure 1: Study Flow Diagram.

The characteristics of the 282 women who had NVP and the 31 women who did not, are displayed in **Table 1.** The age range for women who had NVP was 20-40 years, with the mean age being 30.0±4.1 years, and the mean gestational age 16.1±6.4 weeks. For women who had not suffered with NVP, the age range was 22-42 years, with the mean age being 32.1±4.6 years and the mean gestational age 17.1±6.4 weeks. Although there were no significant differences in most characteristics between the two groups (p=>0.05), it was revealed that women experiencing NVP were significantly younger than women who were not (p=0.023). Regarding ethnicity, the majority of women identified as either English/Welsh/Scottish/Northern Irish or British in both groups (76.0% and 64.5%).

Table 1: Displaying the Maternal Characteristics.

Participant Characteristic	Women with NVP *n*=282	Women without NVP *n*=31	*p* value
Age (years)	30.0 ± 4.1	32.1 ± 4.6	0.023*
Height (cm)	165.3 ± 7.2	166.5 ± 7.4	0.333
Weight (kg)	72.3 ± 14.2	76.5 ± 12.6	0.084
BMI (kg/m^2)	26.5 ± 5.1	27.7 ± 4.6	0.139
Gestational Age (weeks)	16.1 ± 6.4	17.1 ± 6.4	0.421
	***n*(%)**		
1st Trimester	111(39.4)	9(29.0)	0.253
2nd Trimester	171(60.6)	22(71.0)	
Diagnosed with Hyperemesis Gravidarum	86(30.5)	0(0)	-
Smoker Pre-pregnancy	21(7.5)	2(6.5)	0.837
Current Smoker	2(9.5)	0	-
Nulliparous	148(52.5)	-	-
Ethnic Origin			
English/Welsh/Scottish/Northern Irish/British	216(76.0)	20(64.5)	-
Irish	10(3.6)	-	-
White and Black Caribbean	1(0.4)	-	-
African	3(1.1)	-	-
White and Asian	3(1.1)	-	-
Indian	1(0.4)	1(3.2)	-
Pakistani	2(0.7)	-	-
Chinese	1(0.4)	1(3.2)	-
Arab	2(0.7)	-	-
Other	43(15.3)	9(29.0)	-

*Denotes a statistically significant finding

A non-parametric Spearman's Rank correlation revealed maternal age to be negatively correlated with the severity of NVP (r=-0.156; p=0.009), with younger women experiencing more severe symptoms than older women. Although a Kruskal Wallis test showed there were no statistically significant associations between gestational age and the prevalence of NVP (p=0.420), surprisingly, a non-parametric Spearman's Rank correlation revealed that the severity of NVP was positively correlated with both the trimester of pregnancy (r=0.167; p=0.005) and gestational age (r=0.194; p=0.001); with women in their T2 experiencing more severe symptoms compared to those in their T1. Furthermore, there was a statistically significant difference in the severity of NVP between parity groups, with nulliparous women

experiencing less severe symptoms than multiparous women (median sickness severity score: 10.0 vs.11.0; p=0.006). There were no statistically significant correlations between maternal weight, height, and BMI and the severity of NVP, as well as associations between these variables and the prevalence of NVP (p=>0.05 for all).

The Prevalence of Nausea and Vomiting and Supplement Use.

A Chi-squared test revealed there were no statistically significant associations between the prevalence of NVP and vitamin D supplementation (p=0.653), pre-conception folic acid supplementation (p=0.414), and T1 folic acid supplementation (p=0.811).

The Severity of Nausea and Vomiting Symptoms and Pre-pregnancy Diet.

As shown in **Table 2,** a Kruskal-Wallis test revealed there were no statistically significant associations between the type of maternal diet both pre-pregnancy and currently and the severity of NVP (p=0.537 and 0.122).

Table 2: Displaying the median PUQE scores according to the type of diet followed both pre-pregnancy and currently

Diet	*n* (%)	Median Sickness Severity Score (Interquartile Range)	p value
Pre-pregnancy Diet:			
Consumed meat	248(79.2)	11.0 (6.0)	
Pescatarian	16 (5.1)	8.5 (6.8)	0.537
Vegetarian	26(8.3)	10.0 (4.0)	
Vegan	23(7.3)	11.0 (7.0)	
Current Diet:			
Consume meat	246(78.6)	10.0 (6.0)	0.122
Pescatarian	14(4.5)	9.5 (6.5)	
Vegetarian	32(10.2)	12.0 (6.3)	
Vegan	21(6.7)	10.0 (6.8)	

Statistical test performed: Kruskal-Wallis test.

However, as shown in **Table 3**, when analysing the consumption of pre-pregnancy dietary components against NV severity scores using the Kruskal-Wallis test, a statistically significant association was identified between the severity of NVP and the consumption of pulses (p=0.046). Mann-Whitney tests revealed this significant difference existed between the consumption categories of “1-2” and “3-4 portions” of pulses per day **(Figure 2)**, with the median NV severity score significantly higher amongst women who consumed “3-4 portions” a day pre-pregnancy, compared to those who consumed “1-2 portions” of pulses a day (13 vs.10; p=0.036). There were no statistically significant associations between the remaining pre-pregnancy food stuffs and the severity of NVP (p=<0.05 for all).

Table 3: Displaying the median PUQE scores according to the frequency of consumption of various dietary components pre-pregnancy.

Pre-pregnancy diet: Food Stuffs	Frequency Median Sickness Severity Score (Interquartile Range)					p value
	Never	**1-2**	**3-4**	**5-6**	**≥7**	
Meat (times per week)	10.0 (5.5)	11.0 (8.0)	10.0 (5.0)	12.0 (5.0)	9.0 (6.0)	0.484
Eggs (times per week)	10.0 (6.6)	11.0 (5.0)	10.0 (6.0)	9.0 (5.0)	8.0 (7.0)	0.587
Fruit and Vegetables (portions per day)	**None**	**1-2**	**3-4**	**≥5**	**-**	
	13.5 (6.0)	11.0 (6.0)	11.0 (6.0)	10.0 (6.0)		0.479
Pulses (portions per day)	11.0 (6.0)	10.0 (6.0)	13.0 (6.5)	-		0.046*
Wholegrains (portions per day)	11.0 (5.3)	10.0 (6.0)	11.0 (6.5)	11.0 (6.5)		0.963
Cow's Milk (days per week)	**None**	**1-2**	**3-5**	**7**	**-**	
	10.0 (6.0)	11.0 (5.3)	10.0 (6.0)	11.0 (6.0)		0.550

*Denotes a statistically significant finding.

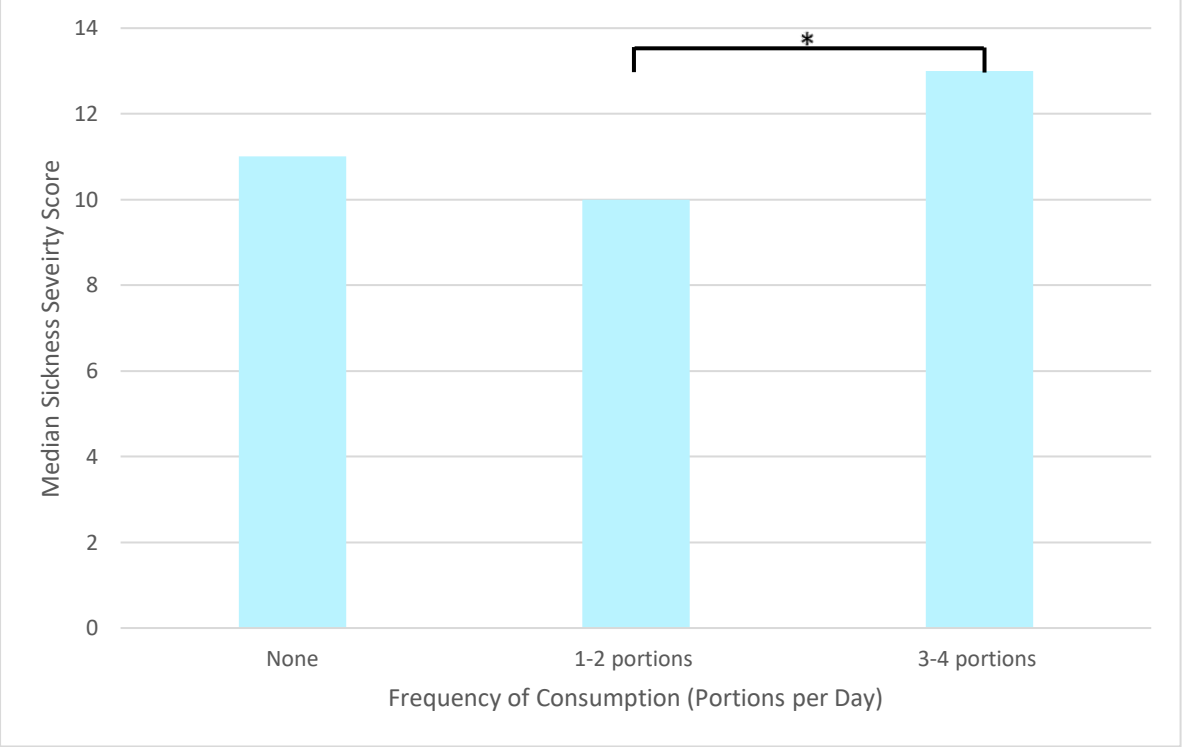

Figure 2: A bar chart displaying the statistically significant differences between median sickness severity scores according to the consumption categories for pre-pregnancy pulses. *p=<0.05.

The Severity of Nausea and Vomiting Symptoms and Current Diet.

Regarding women's current diets **(Table 4),** although a Kruskal-Wallis test revealed that current meat consumption was not statistically associated with the severity of NVP (p=0.230), the remaining dietary components were of statistical significance (p=<0.05 for all). As displayed in **Figure 3.0,** Mann-Whitney tests revealed that women who reported currently consuming cow's milk "everyday" had significantly lower NV severity scores than women who were only consuming milk "1-2 days per week" (9 vs. 12; p=0.007), as well as compared to women who reported "never" consuming milk (9 vs. 11; p= 0.044). Furthermore, women who reported consuming milk on "3-5d/wk" also had less severe NVP than women who consumed milk on "1-2d/wk" (10 vs. 12; p=0.009). Regarding egg consumption **(Figure 3.1),** women who reported consuming eggs "1-2 times/wk" had significantly higher NV scores than women consuming eggs "5-6 times/wk" (11 vs. 5; p=0.013), with significant differences also evident between women consuming eggs "1-2 times/wk" and "3-4 times/wk" (11 vs. 9; p=0.011). Furthermore, women who reported "never" consuming eggs had statistically more severe NVP compared to women who consumed eggs "3-4 times/wk" (11 vs. 9; p=<0.001) and "5-6 times/wk" (11 vs. 5; p=0.004). In terms of F&V consumption **(Figure 3.2)**, women who were consuming "≥5 portions per day" had significantly less severe NV than women consuming no F&V (8 vs. 14; p=0.001), as well as "1-2 portions per day" (8 vs. 11; p=0.001).

Table 4: Displaying the median PUQE scores according to the frequency of consumption of various dietary components as part of participants' current diets.

Current Diet: Food Stuffs	**Frequency**					**p value**
	Median Sickness Severity Score (Interquartile Range)					
	Never	**1-2**	**3-4**	**5-6**	**≥7**	**0.230**
Meat (times per week)	**11.0 (7.0)**	**11.0 (6.0)**	**10.0 (6.0)**	**10.5 (6.0)**	**9.0 (4.5)**	
Eggs (times per week)	**11.0 (6.0)**	**11.0 (6.0)**	**9.0 (4.0)**	**5.0 (6.0)**	**10.5 (7.3)**	**0.001***
Fruit and Vegetables (portions per day)	**None**	**1-2**	**3-4**	**≥5**	**-**	**<0.001***
	14.0 (3.0)	**11.0 (6.0)**	**10.0 (6.0)**	**8.0 (5.5)**		
Pulses (portions per day)	**12.0 (5.0)**	**9.0 (6.0)**	**10.5 (8.5)**	**-**		**0.002***
Wholegrains (portions per day)	**12.5 (4.6)**	**10.0 (6.0)**	**11.0 (5.0)**	**10.0 (9.0)**		**0.001***
Cow's Milk (days per week)	**Never**	**1-2**	**3-5**	**7**	**-**	**0.010***
	11.0 (6.0)	**12.0 (6.0)**	**10.0 (6.0)**	**9.0 (6.0)**		

*Denotes a statistically significant finding

Additionally, women consuming "3-4 portions" also had statistically less severe NVP compared to women consuming "none" (10 vs. 14; p=<0.001), with even women consuming a minimal "1-2 portions per day" having less severe NVP compared to women consuming "none" (11 vs. 14; p= 0.001). Regarding pulses **(Figure 3.3)**, women who reported consuming "1-2 portions a day" had significantly less severe NV compared to women who reported consuming "none" (9 vs. 12; p=<0.001), and for wholegrain consumption **(Figure 3.4)**, those women who reported consuming "1-2 portions per day" had lower NV severity

scores than women who reported consuming “none” (10 vs. 12.5; *p*=<0.001), as well as women consuming “3-4 portions” compared to “none” (11 vs. 12.5; *p*=0.026).

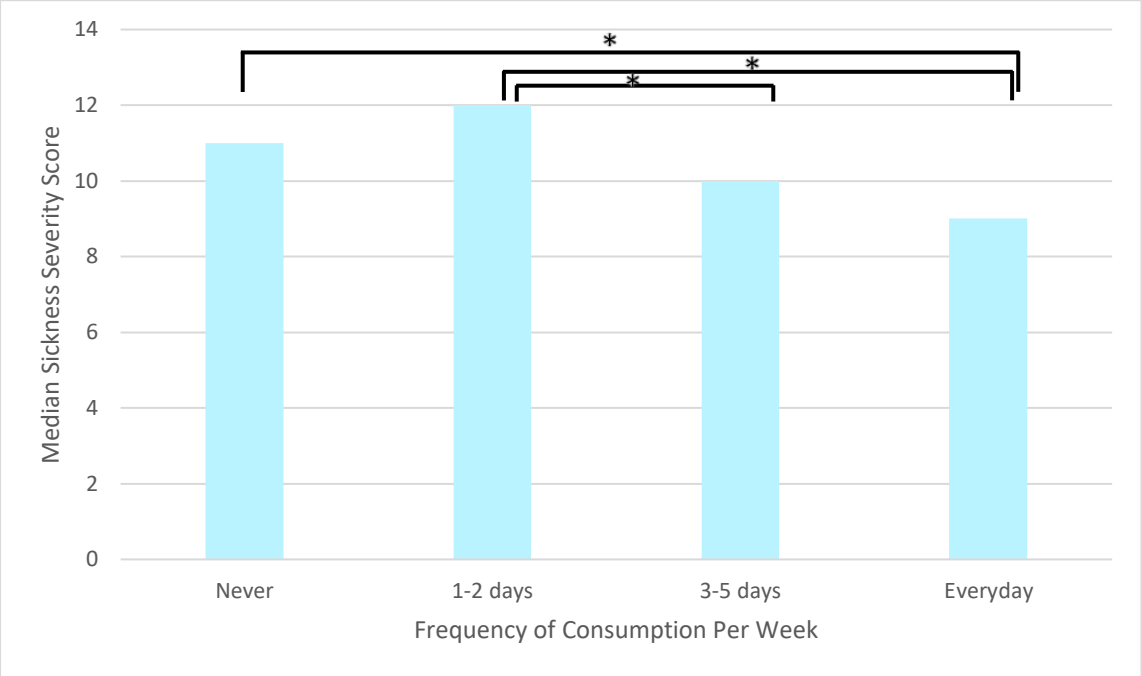

Figure 3.0: A bar chart displaying the statistically significant differences between median sickness severity scores according to the consumption categories for cow’s milk. **p*=<0.05.

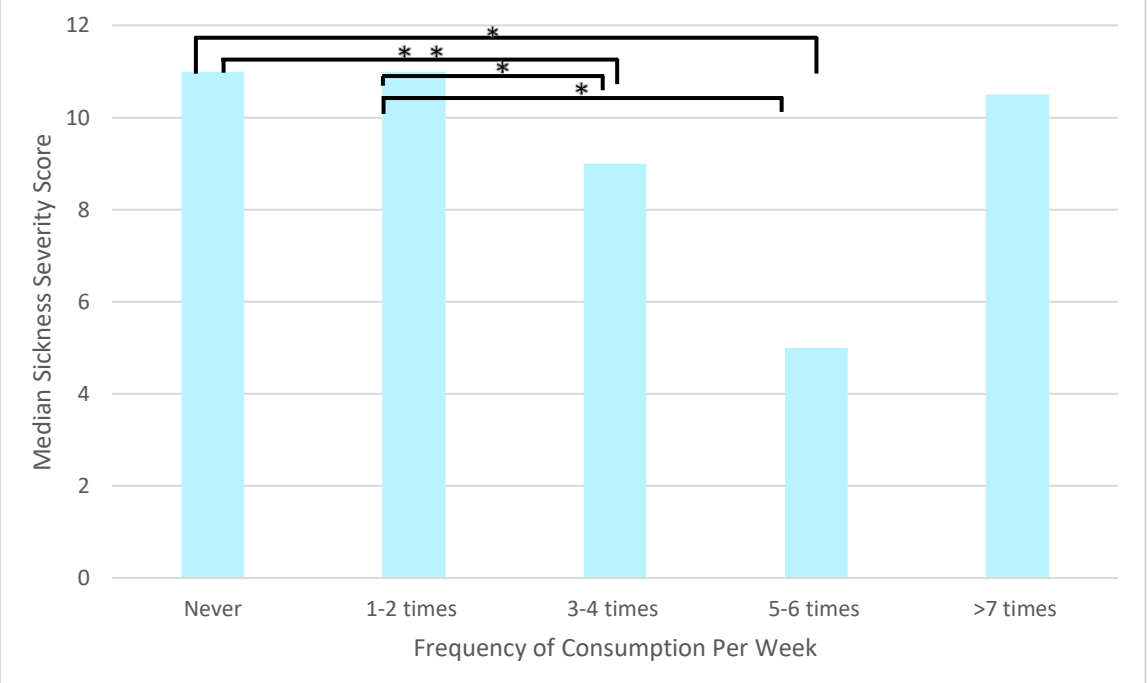

Figure 3.1: A bar char displaying the statistically significant differences between median sickness severity scores according to the consumption categories for egg. **p*=<0.05, ***p*=<0.001.

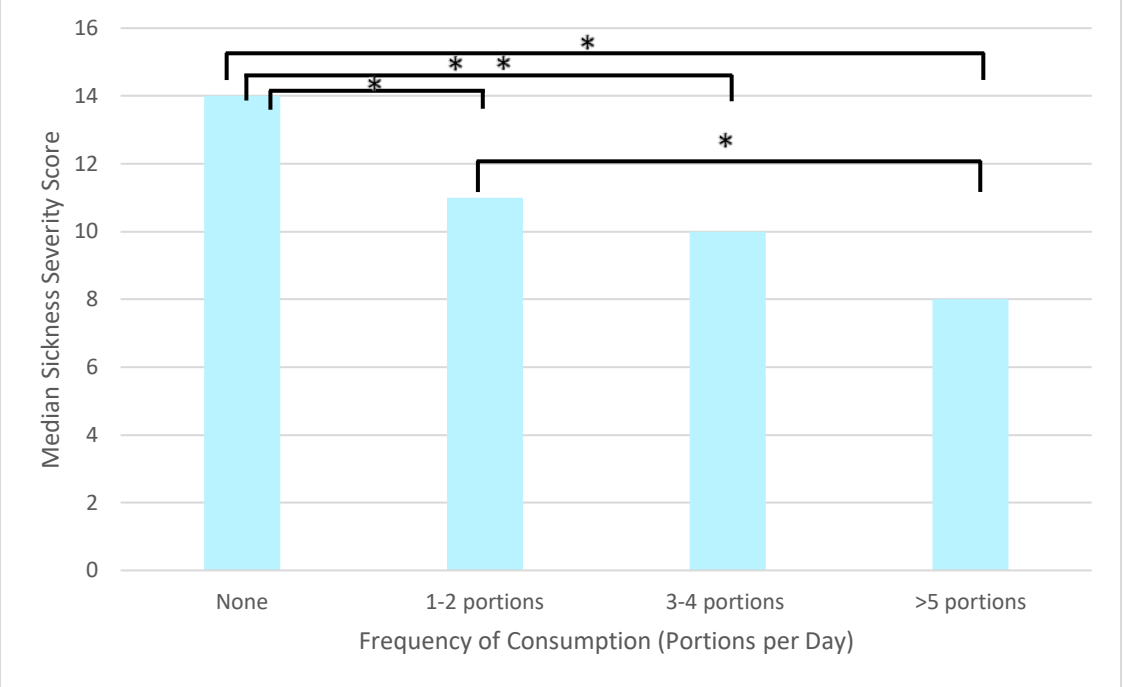

Figure 3.2: A bar char displaying the statistically significant differences between median sickness severity scores according to the consumption categories for fruits and vegetables. *p=<0.05, **p=<0.001.

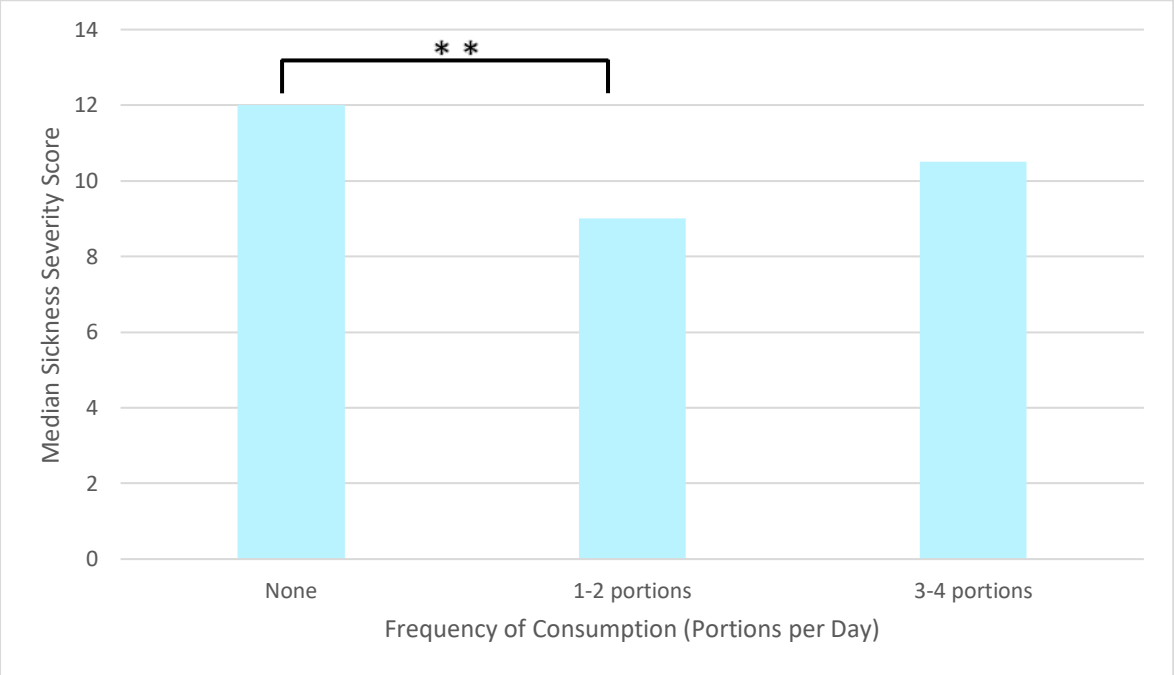

Figure 3.3. A bar char displaying the statistically significant differences between the median sickness severity scores according to the consumption categories for pulses. **p=<0.001.

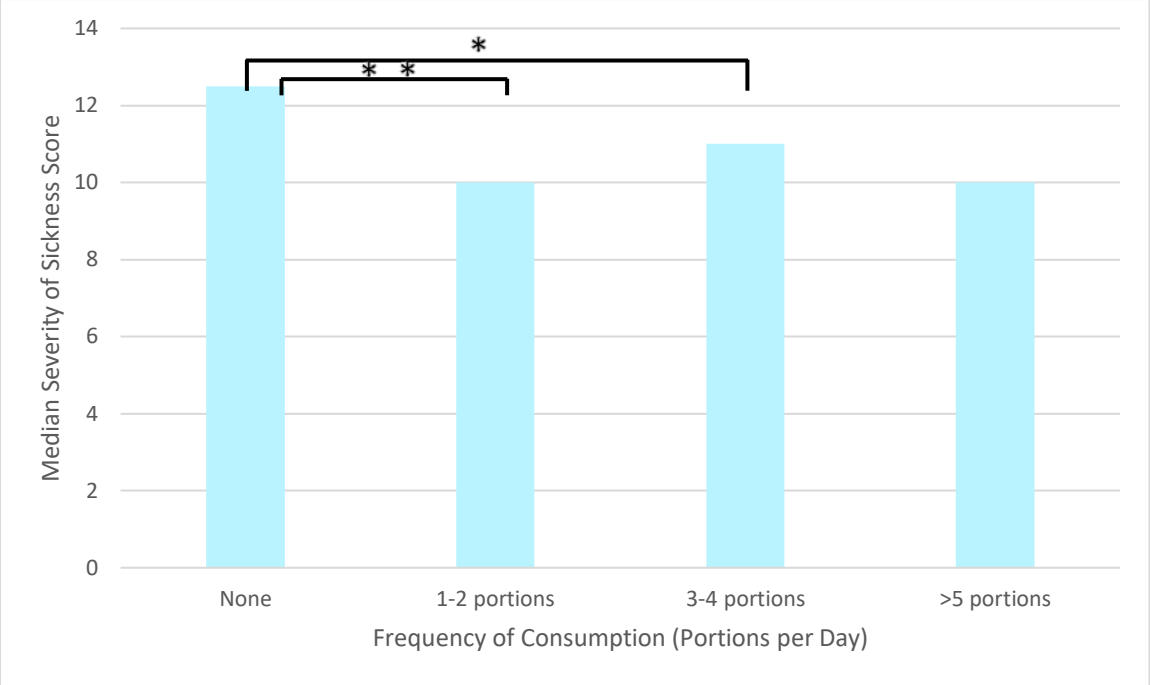

Figure 3.4: A bar char displaying the statistically significant differences between the consumption categories for wholegrains. *p=<0.05, **p=<0.001.

Dietary Changes During Pregnancy and The Severity of Nausea and Vomiting.

Mann-Whitney tests revealed that for cow's milk consumption, women who decreased their intake compared to pre-pregnancy experienced more severe NVP than women who increased their intake (13 vs. 9; p=<0.001), or did not change their intake (13 vs. 10; p=<0.001). Similarly, for eggs, women who decreased their consumption had statistically more severe NVP than women who increased their intake (12 vs. 9; p=0.005), or did not change their intake (12 vs. 10; p=0.001). Regarding F&V, again women who decreased their consumption had statistically more severe NVP than women who increased their consumption (12 vs. 10.5; p=0.042) or did not change their consumption (12 vs. 10; p=<0.001). The same trend was also apparent for wholegrain consumption since a decrease in intake was associated with statistically higher NVP scores compared to an increase in intake (13 vs. 9; p=0.005), as well as compared to no change in intake (13 vs. 10; p=<0.001). However, for pulses, the only statistically significant difference was between women who decreased their consumption and those who did not change their consumption (12 vs. 10; p=<0.001). There were no statistically significant differences in the median sickness severity scores according to changes in the frequency of consuming meat (p=>0.05).

The Severity of Nausea and Vomiting Symptoms and Supplement Use.

As shown in **Table 5,** when analysing supplement use and the severity of NVP, Mann-Whitney tests revealed that for vitamin D, women who reported currently taking this supplement had significantly less severe NVP compared to women who were not currently taking this supplement (10 vs. 12; p=0.002). For T1 folic acid supplementation, women who were >12weeks gestation and had taken folic acid until this point in their pregnancy had statistically lower NV severity scores than those who did not take this supplement (11 vs. 14; p=0.001). Moreover, women who were <12weeks gestation but were currently taking folic acid and intended to continue until this point in their pregnancy had less severe NV symptoms than women not taking this supplement (9 vs. 14; p=<0.001), as well as

compared to women who were >12weeks gestation and had taken folic acid for their T1 but were currently no longer taking this supplement (9 vs. 11; *p*=<0.001).

Table 5. Displaying the median PUQE scores according to women's supplement use

Supplement	**Median Sickness Severity Score (Interquartile Range)**			***p* value**
	Yes		**No**	
Currently taking Vitamin D	10.0 (6.0)		12.0 (5.8)	0.002*
Pre-conception Folic Acid	10.0 (6.0)		11.0 (7.0)	0.133
Folic Acid until 12weeks gestation	**Yes[a]**	**Yes[b]**	**No**	
	11.0 (5.0)	9.0 (6.0)	14.0 (5.0)	<0.001*

*Denotes a statistically significant finding.
Yes[a] – Women over 12weeks gestation who took Folic Acid until 12weeks.
Yes[b] – Women under 12weeks gestation who are currently taking Folic Acid and intend to continue until 12weeks.

Discussion

The present study illustrates that individual food stuffs, rather than the type of diet are associated with the severity of NVP, with the consumption of specific foods as part of women's current diets implicated within this association to a more significant extent than components of women's pre-pregnancy diets. For pre-pregnancy diet, only the consumption of pulses was statistically associated with the severity of NVP, whilst for current diet, all food stuffs apart from meat were statistically associated; with symptoms most severe amongst women consuming eggs, milk, F&V, pulses, and wholegrains less frequently. Moreover, women who decreased their intake of all foodstuffs apart from meat, experienced more severe NVP compared to women who increased or did not change their intake. Regarding supplements, women who were currently taking vitamin D, as well as those who took or were intending to continue taking folic acid for their T1 had statistically less severe NVP compared to women not taking these supplements. Subsequently, such findings indicate that both current maternal diet and supplement use are associated with the severity of NVP.

Regarding pre-pregnancy diet, the fact that the consumption of "3-4 portions" of pulses per day was associated with the greatest severity of NVP suggests that consuming such foods in high quantities pre-conception may predispose women to more severe NVP. Such paradigm is difficult to interpret, although one explanation could be associated with the fact that pulses are high in saponins (Mudryi *et al.,* 2014). Despite such compounds being linked to several health benefits (Singh et al., 2017), research suggests they can alter the integrity of intestinal epithelial cells (Samtiya et al., 2020) and inhibit the activity of several digestive enzymes (Ali et al., 2006; Ercan and El, 2016; Lee et al., 2015). Subsequently, this, accompanied by the fact that rising levels of progesterone and oestrogen during pregnancy decrease smooth muscle contractility, slowing digestion and altering gastric emptying (Lee and Saha, 2011) may lead to the regular consumption of pulses pre-pregnancy increasing women's susceptibility to these gastrointestinal side effects, potentially contributing to more severe NVP. Nevertheless, such paradigm should be taken with caution

since further research is required to delineate the exact relationship between pre-pregnancy consumption of pulses and the severity of NVP.

In terms of the wider field of literature, research is equivocal regarding the association between NVP and current maternal diet. Pepper and Roberts (2006) reported that the intake of pulses was negatively associated with the prevalence of NVP (r=0.160; p=0.004), whereas the present study found that although consuming "none" was associated with the most severe NVP, consuming "1-2 portions" of pulses per day was associated with the lowest NVP severity score. Moreover, Pepper and Roberts (2006) also concluded that meat (r=0.315), cow's milk (r=0.257), and egg (r=0.489) consumption were positively correlated to the prevalence of NVP (p=<0.001 for all). Whilst the present research found no associations for meat intake, with those women consuming cow's milk and eggs less frequently experiencing more severe NVP compared to women regularly consuming these foods. These differences may be accountable to variations in the collection of dietary data. Pepper and Roberts (2006) investigated the relationship between the prevalence of NVP and dietary factors at a population level, whereas the present research adopted an individual level approach. Subsequently, the findings from the present research more accurately reflect specifically pregnant women than those reported in the study by Pepper and Roberts (2006). However, it is important to consider that comparison between Pepper and Robert's (2006) study should be taken with caution since the present research did not analyse the association between the prevalence of NVP and diet.

Despite these discrepancies, recent research by Fiurašková *et al.,* (2021) reports congruent findings to the present study in that significant associations were evident between the severity of NVP and the consumption of cow's milk (p=<0.001), with no associations for meat consumption (p=0.334). However, on closer examination, it appears that the exact relationship between the frequency of consuming milk and the severity of NVP differs slightly to the present study. Fiurašková *et al.,* (2021) concluded an inverse association between milk consumption and the severity of NVP since women who reported "never" consuming milk had statistically higher NVP severity scores compared to those who consumed milk 1-3 times/wk (p=0.008), who in turn had higher scores compared to women consuming milk >3 times/wk (p=<0.001). Whereas, in the present study, women who reported "never" consuming cow's milk did not have statistically more severe NVP compared to women consuming milk "1-2d/wk", however these women did have more severe NVP compared to women consuming milk "3-5d/wk" and "everyday". Subsequently, although Fiurašková *et al.,* (2021) supports the trend that a high consumption of cow's milk is associated with less severe NVP, a dose response relationship was not evident within the present research. Nevertheless, it is likely this discrepancy is accountable to differences in the categorisation of consumption used within the studies.

Moreover, the present study also reported that the frequency of consuming eggs, F&V, pulses, and wholegrains was statistically associated with the severity of NVP (p=<0.05 for all), however, the research by Fiurašková *et al.,* (2021) failed to report any significant findings for these food stuffs. Such inconsistencies may be explained by differences in the assessment of NV severity. Fiurašková *et al.,* (2021) utilised the Rhodes Index, which although is considered the 'gold standard' measure of NV, was initially formulated to quantify the severity of such symptoms amongst patients receiving chemotherapy for cancer (Rhodes, 1984). Whereas the present study

adopted the PUQESS, which was developed specifically for assessing the severity of NV amongst pregnant women. Subsequently, although the PUQESS has been found to be tightly correlated to the Rhodes Index (r=0.904; p=<0.001) (Koren *et al.,* 2002), it is likely to be a more sensitive scale to adopt when investigating the severity of NVP and thus may explain why significant findings were observed for these foodstuffs in the present study, yet not in the research by Fiurašková *et al.,* (2021).

Regarding changes in women's diets compared to pre-pregnancy, it appears the present research predominately contradicts the protective avoidance mechanism outlined by Hook's (1976, p. 173) EPH. If the present study were to support this theory, then it would be anticipated that reducing the consumption of cow's milk, eggs and meat during pregnancy would be associated with less severe NVP, however this did not appear the case. Although there was no association for meat, the fact that women who increased their consumption of cow's milk and eggs had less severe NVP compared to women who decreased their consumption may suggest that NVP does not cause women to expel potentially teratogenic foods. However, due to the nature of this observational study, it is impossible to determine whether these associations are causal since women who decreased their consumption did not justify their reasoning for doing so. Nevertheless, Croizer *et al.,* (2017) reported amongst 2270 pregnant women, that a decreased intake of vegetables, pulses, and citrus fruit was associated with more severe NVP (p=<0.01 for all); with 66% of women stating that their reason for decreasing their consumption was due to NV symptoms. Subsequently, such research allows for speculation around the direction of causality, suggesting it is likely that greater NVP symptoms lead to a reduced intake of these foods; however, such topics warrant further investigation.

In terms of supplement use, given the present study reported that vitamin D supplementation was associated with significantly less severe NVP, it could be implied that vitamin D deficiency may play a role in worsening the severity of the condition. However, although the relationship between vitamin D deficiency and pregnancy complications such as preterm births, pre-eclampsia, and high blood pressure has been extensively researched (Dovnik and Mujezinović, 2018; Dror, 2011; Tuan *et al.,* 2019), there is a lack of literature investigating the exact effects of vitamin D on NVP. Despite this, Jomah *et al.,* (2020) supports the paradigm to an extent through reporting amongst 150 pregnant women in either their 1st or T2, that those experiencing NVP had significantly decreased serum vitamin D3 levels compared to women with no symptoms (p=<0.05); however, the severity of NVP was not assessed in this study. Nevertheless, to confirm that vitamin D deficiency does worsen the severity of NVP, serum blood levels would be required, of which were not obtained in the present study.

Similarly, regarding T1 folic acid supplementation, the fact that this was also associated with reduced NVP severity, implies that a deficiency of such vitamin may also contribute to the onset of more severe NVP. Czeizel and Dudas (1992) provide support for this paradigm through concluding that a significant reduction in the prevalence of HG and moderate NVP was observed amongst women taking a periconceptual multivitamin, which included folic acid, compared to women not supplementing. However, despite such study being placebo-controlled, since a multivitamin was consumed it cannot be ascertained that such effects were elicited solely by folic acid, with a synergistic interaction likely responsible for this outcome.

Nevertheless, the fact that in the present study, women who were in their T1 and currently taking folic acid had less severe NVP compared to women who were >12weeks gestation and had previously taken folic acid until this point in their pregnancy, implies that actively taking this supplement may reduce the severity of NVP. In support, Twigt *et al.,* (2011) postulates that folic acid supplementation can alter hormonal responses, of which in turn may contribute to reducing the severity of NVP. Such study reported that women not consuming folic acid had higher estradoil responses during ovarian stimulation treatment compared to women not supplementing. This is of particular importance since Lagiou *et al.,* (2003) concluded that higher levels of estradoil can contribute to the occurrence of NVP, with Depue *et al.,* (1987) reporting amongst women diagnosed with HG, that estradoil levels were 26% higher compared to women without NVP. Subsequently, it is plausible that a biological mechanism underpins this association between folic acid supplementation and reduced NV severity since such supplement may attenuate levels of estradoil, in turn mediating the severity of NVP.

Notwithstanding this, it is difficult to infer the direction of causality with regards to supplement use, since although it could be argued that women who do not take supplements experience more severe NVP, it is also plausible that severe NVP leads to women being unable to take supplements. Ebrahimi *et al.,* (2009) provides support for this latter concept through concluding that the severity of NVP was significantly associated with the tendency to not take multivitamins, with 25% of women with severe NVP reporting taking no multivitamins compared to 0% amongst women with mild NVP (p=<0.001). Subsequently, to determine the exact direction of causality, a randomised controlled trial would be necessary, although given the overwhelming evidence to support the role of both pre-conception and T1 folic acid supplementation in significantly reducing the prevalence of neural tube defects (Czeizel *et al.,* 2013; Czeizel and Dudas, 1992; Milunsky *et al.,* 1989), such study design would be deemed unethical. Therefore, observational research like that performed in the present study are the most suitable to quantify the effects of supplement use on the severity of NVP.

A primary strength of the present research is the fact that pre-pregnancy dietary data was collected, of which both Pepper and Roberts (2006) and Fiurašková *et al.,* (2021) did not assess. The collection of such data allowed for the investigation into how women's diets change during pregnancy and whether the severity of NVP is implicated within this association (Croizer *et al.,* 2017). Nevertheless, the way in which the assessment of women's pre-pregnancy diets was performed is vulnerable to critique. A retrospective approach was adopted since women completed the FFQ when they were in either their T1 or T2, which is a limitation given there was large variation in gestational age and thus the ability for women to accurately recall their pre-pregnancy diets would have differed accordingly. Subsequently, it would be most accurate to adopt a longitudinal study design whereby women complete the FFQ pre-conception as well as during pregnancy, like that conducted by Croizer *et al.,* (2017).

Additionally, there are limitations associated with utilising FFQ in general, especially amongst pregnant women. Research postulates that pregnant women tend to overestimate their food intake to align with that of antenatal dietary advice (Suitor *et al.,* 1989), creating a social desirability bias. Therefore, since women often gain

awareness of the importance of nutrition whilst pregnant (Blondin *et al.,* 2018) and understand how nutrition can affect fetal development (Borge *et al.,* 2017; Morrison *et al.,* 2016), it is plausible that women may have inaccurately reported their diet and supplement use to align with antenatal advice. Subsequently, to enhance the validity of such data, further research should consider obtaining serum blood levels to quantify biomarkers of specific vitamins. Finally, the fact that 75.4% of women identified as either English, Welsh, Scottish, Northern Irish or British, limits the generalisability of these findings to women of other ethnicities. This is a particular limitation since research suggests that ethnicity is implicated with both the likelihood of reporting NV symptoms (Lacasse *et al.,* 2009) and the prevalence of the condition (Fiaschi *et al.,* 2019). Subsequently, future studies should be conducted amongst more diverse populations to ensure these findings are applicable to women of other ethnic origins.

Conclusion

In conclusion, the present study illustrates that both diet and supplement use are associated with the severity of NVP. However, it appears that current dietary habits are implicated within this association to a greater extent than pre-pregnancy dietary habits. Subsequently, these findings suggest that the composition of women's diets pre-pregnancy, alongside the tendency to take a pre-conception folic acid supplement have minimal influence on the severity of NV experienced in future pregnancies. Nevertheless, while it is likely this condition arises as a biproduct of hormonal changes, since current diet and supplement use were associated with the severity of NVP, it could be hypothesised that dietary and supplement modifications during pregnancy may alleviate the severity of the condition. Consequently, if such research is conducted amongst larger, more diverse populations, and incorporates more extensive dietary components and supplements, these findings may contribute to improving the understanding and optimising the care provided to women experiencing NVP.

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