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## ***Helicobacter pylori* infection: a predictor of vomiting severity in pregnancy and adverse birth outcome**

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### **Abstract**

**Background**—Nausea and occasional vomiting in early pregnancy is common. Why some women experience severe nausea and occasional vomiting in early pregnancy is unknown. Causes are multifactorial and only symptomatic treatment options are available, although adverse birth outcomes have been described. *Helicobacter pylori* infection has been implicated in the cause of nausea and occasional vomiting in early pregnancy.

**Objective**—The purpose of this study was to investigate the association of *H pylori* with vomiting severity in pregnancy and its effect on birth outcome.

**Study Design**—We assembled a population-based prospective cohort of pregnant women in The Netherlands. Enrolment took place between 2002 and 2006. *H pylori* serology was determined in mid gestation. Women reported whether they experienced vomiting in early, mid, and late gestation. Maternal weight was measured in the same time periods. Birth outcomes were obtained from medical records. Main outcome measures were vomiting frequency (no, occasional, daily) and duration (early, mid, late gestation), maternal weight gain, birthweight, small for gestational age, and prematurity. Data were analyzed with the use of multivariate regression.

**Results**—We included 5549 Women, of whom 1932 (34.8%) reported occasional vomiting and 601 (10.8%) reported daily vomiting. Women who were *H pylori*-positive (n=2363) were more likely to report daily vomiting (adjusted odds ratio, 1.44; 95% confidence interval, 1.16-1.78). *H pylori* positivity was associated with a reduction of total weight gain in women with daily

vomiting (adjusted difference, -2.1 kg; 95% confidence interval, -2.7 to -1.5); infants born to women with *H pylori* and daily vomiting had slightly reduced birthweight (adjusted difference -60g; 95% confidence interval, -109 - -12) and an increased risk of being small for gestational age (adjusted odds ratio, 1.49; 95% confidence interval, 1.04-2.14). *H pylori* and daily vomiting did not significantly affect prematurity rate.

**Conclusion**—This study suggests that *H pylori* is an independent risk factor for vomiting in pregnancy. In women with daily vomiting, *H pylori* is also associated with low maternal weight gain, reduced birth weight, and small for gestational age. Because effective treatments for severe nausea and occasional vomiting in early pregnancy are currently lacking, the effect of *H pylori* eradication therapy on nausea and occasional vomiting in early pregnancy symptom severity should be the target of future studies.

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## Introduction

Nausea and occasional vomiting in early pregnancy (NVP) affects 50-90% of pregnant women in the first half of gestation,<sup>1</sup> and can impact greatly maternal wellbeing and quality of life.<sup>2</sup> When vomiting is severe or protracted or is accompanied by weight loss, dehydration, electrolyte disturbances, or hospitalization, it is referred to as hyperemesis gravidarum (HG).<sup>3</sup> In the absence of an internationally recognized definition, HG and severe NVP are likely to overlap in studies.<sup>4</sup>

In the Western world, severe NVP more often affects socially disadvantaged women and those of non-Western ethnicity.<sup>5</sup> To date, there is no clear explanation for the risk differences between Western and non-Western ethnic groups. In a recent metaanalysis, colonization with the gastric bacterium *Helicobacter pylori* was positively associated with severe NVP (odds ratio (OR) 3.34, 95% confidence interval (CI) 2.92–4.81).<sup>6</sup> Interestingly, the *H pylori* prevalence in pregnant women of Western ethnicity is much lower than in women of non-Western ethnicity.<sup>7</sup> The association between *H pylori* and severe NVP has been replicated in several studies, but mainly in non-Western populations in which the prevalence of *H pylori* is high.<sup>8–10</sup> Three small studies on this topic have been conducted in a Western setting but reported conflicting findings.<sup>11–13</sup> Furthermore, some have suggested that more pathogenic variants of *H pylori*, such as cytotoxin associated gene A (CagA)-positive strains are more often found among women with severe NVP.<sup>14</sup> Several small studies have suggested that *H pylori* infection is not only associated with the presence of severe NVP, but also associated positively with symptom severity<sup>8</sup> and persistence.<sup>10</sup>

Severe NVP has been associated repeatedly with adverse birth outcome, which includes low birthweight, small for gestational age (SGA), and prematurity;<sup>15</sup> however, the mechanism by which severe NVP may lead to adverse birth outcomes is not well understood. Weight loss or insufficient weight gain during pregnancy has been suggested to play a role,<sup>16, 17</sup> although other factors such as the presence of *H pylori* on birth outcome has not been investigated.

In the present study, we investigated the hypothesis that *H pylori* is associated with vomiting severity in pregnancy and contributes to adverse birth outcomes in women with severe NVP. Furthermore, we investigated whether *H pylori* explains the marked ethnic differences in

maternal daily vomiting incidence. The study was performed in a large prospective multiethnic cohort study in the Netherlands, the Generation R study.

## Methods

### Study population

This study was embedded in the Generation R study, which is a population-based, prospective cohort study from early pregnancy until young adulthood. Approval of the Generation R Study was obtained from the Central Committee on Research that involves Human Subjects in the Netherlands via the Medical Ethics Committee of the Erasmus Medical Center, Rotterdam. All participants provided written informed consent. The study is still ongoing and conducted in Rotterdam, which is the second largest city of the Netherlands with a multiethnic community. Study design and aims have been described in detail elsewhere. 18 In brief, 8879 pregnant women were enrolled from 2002-2006. Women underwent physical examinations (measurement of height and weight) and filled out questionnaires in early, mid, and late gestation. These questionnaires contained information on medical history, socioeconomic background, lifestyle, and current pregnancy. The number of physical examinations and questionnaires received was dependent on the gestational age at enrolment. Serum samples were obtained during mid gestation. 19

In this study, 5549 women with complete data on vomiting status in early gestation and *H pylori* serology in mid gestation were included. Women enrolled after 22 weeks gestation with no information on previous vomiting status were excluded, because vomiting that starts after this gestational age is likely to have other underlying causes. Women were also excluded if they participated multiple times in subsequent pregnancies or delivered at <23 weeks gestation (Figure 1).

### Definition of daily vomiting

There is no internationally recognized definition for severe NVP or HG. In this study, women were asked in every questionnaire whether they experienced vomiting for the past 3 months. Answers ranged from “never” to “daily” on a 1-5 scale (never, less than once a week, once a week, few times a week, daily). If daily vomiting has been present for 3 months at study enrollment, women were considered to have severe NVP. When vomiting occurred <1 time each week, once a week, or few times a week, women were considered to have occasional vomiting. Because occasional vomiting in pregnancy is considered physiological, women with no vomiting and occasional vomiting were considered the reference group, despite the fact there were some statistical differences in baseline characteristics between women with no vomiting and occasional vomiting (Table 1).

### Symptom severity

Symptom severity was explored according to vomiting frequency (no, occasional, daily vomiting) and vomiting duration. When daily vomiting for the past 3 months was reported in both the first and second questionnaire, women were considered to have daily vomiting that persisted into mid gestation. Similarly, when daily vomiting was reported in all 3 questionnaires, women were considered to have daily vomiting that persisted into late

gestation. Because inadequate weight gain is often part of severe NVP, the association of *H pylori* and daily vomiting with total maternal weight gain (kilograms) was also investigated. Weight gain was based on self-reported prepregnancy weight and measured weight in late gestation.

### ***H pylori* serology**

Mid pregnancy (18-25 weeks) serum samples were used to determine *H pylori* serology. *H pylori* immunoglobulin G (IgG) antibody levels were examined by enzyme-linked immunosorbent assay (ELISA), with the use of whole cell antigens.<sup>20</sup> A separate ELISA was performed to determine serum IgG antibodies against CagA protein.<sup>21</sup> Both ELISAs were validated locally, by adaption of the ELISA properties based on positive and negative controls.

### **Pregnancy outcomes**

Gestational age at birth, birthweight, and neonatal sex were obtained from medical records. Prematurity was defined as birth at <37 weeks gestation; SGA was defined as gestational age-adjusted birthweight at <10th percentile in this study's population, based on the reference standard by Niklasson et al.<sup>22</sup>

### **Covariates**

**General characteristics**—Maternal age was assessed at enrolment. Prepregnancy body mass index (kilograms per square meter) was calculated with the use of self-reported prepregnancy weight and height measured at enrolment. All sociodemographic characteristics were self-reported. Ethnicity was determined according to the definition of Statistics Netherlands<sup>23</sup> by country of birth of the pregnant woman and her parents. Based on the urban population of Rotterdam, the following ethnic groups were identified: Dutch, "other Western" (women who originated from Europe, North America, Oceania, Japan, or Indonesia), Surinamese, Turkish, Cape Verdean/Dutch Antilles, Moroccan and "other non-Western" (women who originated from Africa, Asia, or South or Central America). Dutch and "other Western" ethnic groups were classified as Western, all other ethnic groups that were described were classified as non-Western. Educational level served as a proxy for socioeconomic status and was based on the highest completed education (none or primary school, secondary school, higher education). Smoking during pregnancy was also self-reported.

**Pregnancy characteristics**—All major pregnancy characteristics and outcomes were obtained from medical records<sup>18</sup> that included parity, twin pregnancy, diabetes mellitus gravidarum, and information on hypertensive disorders in pregnancy (pregnancy-induced hypertension, preeclampsia, and hemolysis, elevated liver enzymes, low platelets (HELLP) syndrome).

### **Data analysis**

Differences in subject characteristics between groups were evaluated with the use of chi-square tests for proportions and 1-way analysis of variance or Kruskal Wallis for continuous

variables. Logistic regression analysis was performed to study associations between *H pylori* seropositivity and vomiting frequency and persistence. We adjusted for maternal age, parity, ethnicity (ethnic groups), education level, and smoking (model 2). Effects of *H pylori* and daily vomiting on maternal weight gain and birth outcomes were explored with linear regression analysis. These analyses were adjusted for neonatal sex, gestational age at birth, twin pregnancy, maternal age, parity, diabetes mellitus gravidarum, hypertensive disorders, ethnicity, education level, prepregnancy body mass index, and smoking. Sensitivity analyses were performed by including maternal weight gain based on measured weight in early and late gestation, additional adjustment for gestational age at time of measured weight in late gestation, and the exclusion of twin pregnancies. We also investigated whether *H pylori* explained ethnic differences in daily vomiting. Using logistic regression analysis, we first explored the association of ethnicity and daily vomiting, followed by adjustment for *H pylori* (model 2). We then further adjusted for maternal age, parity, education level, and smoking (model 3). Possible strain-specific effects on vomiting frequency were assessed among women who were *H pylori*-positive (CagA-positive and -negative). Because of small numbers, analyses on birth outcomes were not repeated in this subgroup. Last, sensitivity analyses were performed to examine whether the associations between *H pylori*, vomiting severity, and birth outcomes were similar for Dutch women only (largest ethnic group). Possible confounders were identified with directed acyclic graphs, <sup>24</sup> based on known risk factors for HG. Missing data of covariates were input with the use of multiple imputations (5 datasets). The percentages of missing values within the population for analysis were <2%, except for prepregnancy weight (10.8%) and total weight gain (14.1%). All analyses were performed with the use of IBM SPSS Statistics for Windows (version 21.0; SPSS, IBM, Armonk, NY).

## Results

### Baseline characteristics of women with and without daily vomiting

The study population consisted of 5549 pregnant women, of which 601 women experienced daily vomiting in early gestation (10.8%). Compared with women excluded from the analysis (n=3330; Figure 1), women who were included were slightly more often nulliparous, of Western ethnicity, and more highly educated (data not shown). Table 1 describes sociodemographic and clinical characteristics of women who were included and infants according to vomiting frequency. Women with daily vomiting were younger, more often of non-Western ethnicity, less highly educated, and with a higher body mass index than women with no or occasional vomiting. Women with daily vomiting were more often *H pylori* positive (64.4%), compared with women with no vomiting (36.5%) and occasional vomiting (45.2%;  $P<.001$ ), and more often infected by CagA-positive strains.

### Does *H pylori* underlie symptom severity?

After adjustment for confounders, the association between *H pylori* and daily vomiting was still present (Table 2). *H pylori* was also associated positively with symptom duration: 39.9% of women with no or occasional vomiting were *H pylori* positive, compared with 62.4% of women with daily vomiting in early pregnancy, 66.4% of women with daily vomiting persistent into mid pregnancy, and 72.1% of women with daily vomiting persistent

into late pregnancy ( $P < .001$ ). Logistic regression for the association of *H pylori* and daily vomiting duration is shown in Figure 2. After adjustment for confounders, the association was reduced, but a similar trend was seen. Furthermore, women with daily vomiting had reduced weight gain in pregnancy (Table 3). The presence of *H pylori* further reduced weight gain in these women.

### **Does *H pylori* underlie the association between daily vomiting and poor pregnancy outcome?**

We also examined the effects of *H pylori* and daily vomiting on pregnancy outcome (Table 3). After adjustment for confounders, there was no significant association between *H pylori* or daily vomiting and SGA or prematurity. However, in infants born to women with *H pylori*, birthweight was slightly reduced. In infants born to women with both *H pylori* and daily vomiting, birthweight was further reduced, and the risk for SGA was increased. Maternal weight gain was associated significantly with birthweight (for every kilogram of maternal weight gain adjusted birthweight difference was 18g (95% CI, 15-21;  $P < .001$ ).

### **Does *H pylori* underlie ethnic differences in daily vomiting?**

Daily vomiting occurred more often in women of non-Western ethnicity (crude OR, 4.25; 95% CI, 3.55-5.10). After adjustment for *H pylori*, the OR diminished only slightly (model 2; adjusted OR, 3.47; 95% CI, 2.84-4.24). Across all ethnicities, the OR for daily vomiting according to the presence of *H pylori* was similar. After further adjustment for major confounders, non-Western ethnicity remained significantly associated with daily vomiting (model 3; adjusted OR, 2.49; 95% CI, 1.99-3.10). In fact, this was true for all non-Dutch ethnicities (Supplementary Table 1).

### **Are there *H pylori* strain specific effects?**

Subanalysis among women who were *H pylori*-positive ( $n=2363$ ) showed that women who were CagA-positive were more likely to experience daily vomiting compared with women who were *H pylori*-positive but CagA-negative (crude OR, 1.36; 95% CI, 1.09-1.70). After adjustment for ethnicity, this difference was rendered nonsignificant (adjusted OR, 1.17; 95% CI, 0.93-1.48).

### **Comment**

This study confirms the association between *H pylori* and daily vomiting and adds to the existing evidence that the presence of *H pylori* is associated with a reduction of total maternal weight gain. More importantly, we found evidence that *H pylori* contributes to reduced birth weight and SGA, which makes *H pylori* eradication in pregnancy in women with severe NVP an attractive target for future intervention studies.

Previous studies have established that *H pylori* infection is associated with severe NVP, although the strength and size of these associations varied between different populations and countries. 6, 25 Our findings confirm this association. Similarly, the prevalence of *H pylori* infection among Dutch (24%) and non-Dutch women (64%) in this cohort<sup>7</sup> is in line with the existing literature. We found that *H pylori* remained a risk factor for daily vomiting after

adjustment for ethnicity and socioeconomic status, which lends further support to the hypothesis that *H pylori* is implicated causally in the pathophysiologic condition of severe NVP.

Several studies that have evaluated birth outcome in pregnancies that are complicated by severe NVP have demonstrated modest negative effects on birthweight, SGA, and prematurity rates. 15 Both *H pylori* and severe NVP have been implicated in placental dysfunction disorders. 26, 27 Interestingly, we observed an increased risk for SGA only in women who were *H pylori*-positive with daily vomiting, which might explain why not all studies found adverse birth outcomes after pregnancies that were complicated by severe NVP. SGA may be a result of poor placentation, including failed remodeling of the spiral arteries. 25 Causes of impaired remodelling might include an excessive or atypical maternal immune response to trophoblasts. 26 Franceschi et al<sup>27</sup> have shown that anti-CagA antibodies in vitro were able to recognize b-actin on the surface of trophoblast cells in a dose-dependent binding activity. This binding resulted in impaired cytotrophoblast invasiveness, which is crucial for the development of the placental syndrome. This study may provide a biologic explanation for the epidemiologic association between *H pylori* and the placental syndrome. Taken together, it is possible that *H pylori* has a local gastrointestinal effect that leads to NVP symptoms and a systemic placental effect that results in an increased risk for SGA. A similar pathway might underlie the relationship between severe NVP and preeclampsia; however, this needs further study. Additionally, an interaction of *H pylori* and NVP might result in reduced maternal weight gain, which in turn negatively affects birth outcome.

Most likely *H pylori* is acquired at a young age and leads to lifelong colonization, unless specifically treated.<sup>28</sup> More pathogenic variants of *H pylori*, in particular CagA-positive strains, are associated with increased gastric inflammation.<sup>21</sup> Like Xia et al,<sup>14</sup> we found that women who were CagA positive were more likely to experience daily vomiting compared with women who were *H pylori*-positive but CagA negative, which might be partly explained by differences in geographic distribution of CagA-strains.

This study was embedded in a large prospective cohort study; data collection was performed by trained research assistants. Questionnaires that inquired about the presence of vomiting were collected prospectively, which made the risk of recall bias low. If misclassification of vomiting frequency had occurred, the presented effects could be underestimated. Furthermore, we were unable to confirm HG diagnosis based on hospital admission or other more commonly used criteria,<sup>29</sup> and numbers for persistent vomiting in late pregnancy were small. Because of the observational design, residual confounding might still be an issue. Based on the nature of the study, we did not adjust for multiple testing. Despite these limitations, characteristics of women who experienced daily vomiting largely resembled previous reported data on patient with severe NVP.<sup>30</sup> Additionally, we were informed about maternal weight gain and symptom persistence and were able to adjust for all previously described major confounders known to be associated with *H pylori* and severe NVP<sup>12</sup> with detailed information on ethnic background. Sensitivity analyses on the studied associations that included only Dutch women resulted in similar findings (data not shown). We were underpowered to show that the presence of *H pylori* was associated with daily vomiting

persistence or prematurity or to study potential effects of *H pylori* strains on vomiting severity and pregnancy outcome.

There is debate on the accuracy of various diagnostic strategies to establish *H pylori* infection. Many studies,<sup>6</sup> including this study, have investigated the presence of *H pylori* IgG antibodies in serum using ELISA. Other tests with greater accuracy have replaced serology in clinical practice; however, because of low costs, acceptability to patients, and practicability, serology is still indicated for epidemiologic studies.<sup>31</sup> The declining *H pylori* prevalence in The Netherlands might affect the positive predictive value of serology,<sup>32</sup> but it is unlikely that this has influenced our findings. Unlike most infectious diseases, *H pylori* infection does not result in acquired immunity. Therefore, IgG anti-*H pylori* and anti-CagA antibodies are indicative of active disease, unless eradication therapy has been prescribed in the previous months.<sup>33</sup> This would have been rare among pregnant women.

To date, no effective treatment options are available for severe NVP, nor do we know how to identify patients at risk for persistent symptoms during the course of pregnancy. Several case studies have reported that *H pylori* eradication effectively relieved symptoms in women with persistent vomiting that was unresponsive to conventional treatment.<sup>34–36</sup> *H pylori* eradication therapy in The Netherlands normally consists of triple therapy, including a proton pump inhibitor, amoxicillin, and clarithromycin or metronidazole.<sup>32</sup> A metaanalysis performed by Gill et al<sup>37</sup> showed no teratogenic effects of proton pump inhibitor use in early pregnancy. No teratogenic effects were described for amoxicillin, clarithromycin, and metronidazole.<sup>38–40</sup> Clarithromycin, but not amoxicillin and proton pump inhibitor, was associated with miscarriage when administered in the first trimester.<sup>40</sup> These studies indicate that triple therapy that consisted of proton pump inhibitor, amoxicillin, and metronidazole might be used safely in pregnancy. If remaining circulating anti-*H pylori* and CagA antibodies have the ability to affect placental function, *H pylori* eradication before pregnancy in women with a history of severe NVP should be considered. Further evidence to confirm the effectiveness of *H pylori* eradication on NVP symptom reduction and adverse birth outcome is needed from randomized controlled trials.

In conclusion, our study suggests that *H pylori* is an independent risk factor for vomiting in pregnancy, which leads to low maternal weight gain, reduced birthweight and increased risk of SGA. Because treatment options for severe NVP currently are lacking, the effect of *H pylori* eradication therapy on NVP severity and birth outcome should be target of future studies.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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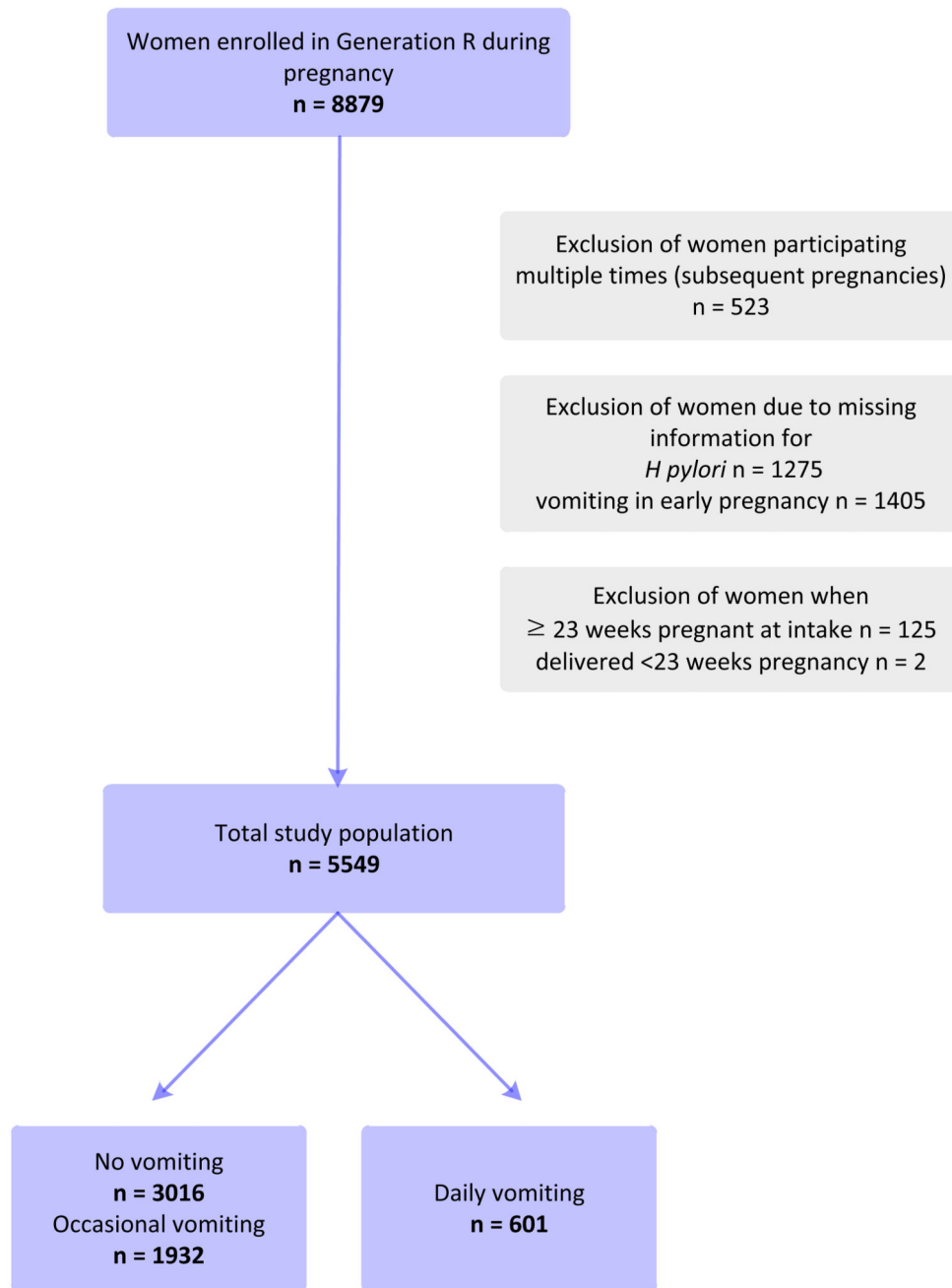
The general design of the Generation R Study is made possible by financial support from the Erasmus Medical Center, Rotterdam, Erasmus University Rotterdam, Netherlands Organization for Health Research and Development (ZonMw), Netherlands Organization for Scientific Research (NWO), Ministry of Health, Welfare and Sport and Ministry of Youth and Families; V.W.J. received grants from the Netherlands Organization for Health Research and Development (VIDI 016.136.361) and European Research Council (ERC-2014-CoG-648916). These funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

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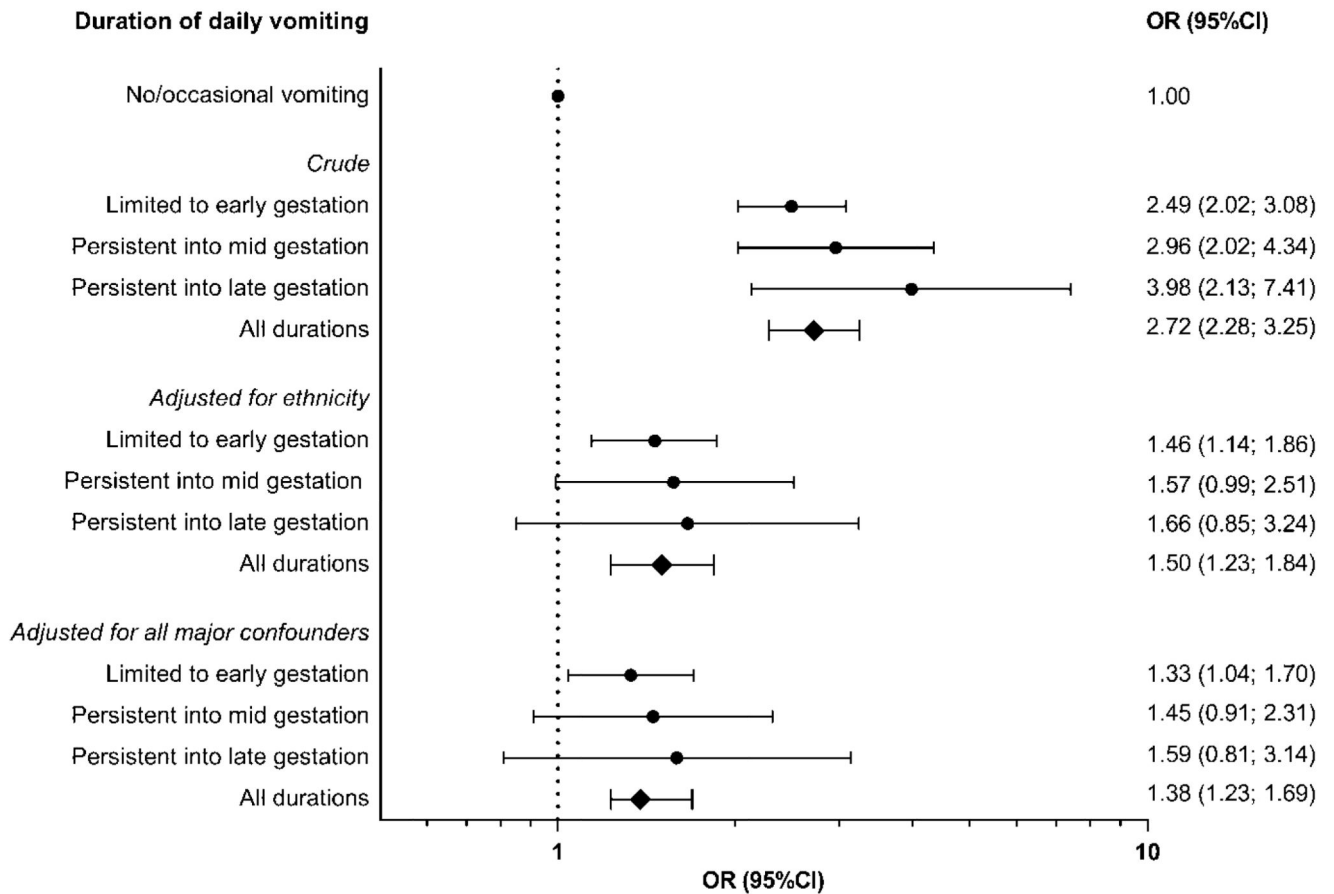
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**Figure 1. Flow diagram of participant selection**



'No/occasional vomiting' is reference group. Adjusted for all major confounders includes maternal age, parity, ethnicity, education level, smoking. OR: odds ratio; CI: confidence interval

**Figure 2. Logistic regression for *H pylori* and daily vomiting according to symptom duration**

**Table 1**  
**Demographics and clinical characteristics of women and neonates according to daily vomiting**

Characteristics n=	Total population 5549	No vomiting 3016	Occasional vomiting 1932	Daily vomiting 601	p Value
<b>Demographics</b>					
Age (y)	29.7±5.2	30.6±5.0	28.9±5.1	27.6±5.0	<0.001
Pre-pregnancy BMI (kg/m <sup>2</sup> )	22.6 (20.8-25.5)	22.4 (20.7-25.1)	22.7 (20.7-25.5)	23.7 (21.1-27.6)	<0.001
Ethnicity					<0.001
Western	62.7	71.6	58.5	31.8	
Non-Western	37.3	28.4	41.5	68.2	
Ethnic groups					<0.001
Dutch	50.8	58.9	46.7	23.5	
Other Western	11.9	12.8	11.7	8.3	
Moroccan	6.0	3.9	6.8	13.7	
Turkish	8.6	6.5	9.0	18.1	
Surinamese	9.2	7.4	10.5	14.6	
Cape Verdean/Dutch Antilles	7.6	5.7	9.0	12.4	
Other non-Western	5.9	5.0	6.3	9.5	
Education level					<0.001
Primary	10.6	8.2	11.2	20.0	
Secondary	47.3	42.5	50.7	59.9	
Higher	42.1	49.2	38.1	20.1	
Smoking	18.1	17.7	18.3	19.3	0.62
IgG anti- <i>H. pylori</i> positive *	42.6	36.5	45.2	64.4	<0.001
CagA +	14.6	11.9	15.4	41.1	<0.001
<b>Pregnancy characteristics</b>					
Nulliparous	61.8	63.1	62.0	54.9	<0.05
Twin pregnancy	1.1	0.9	1.4	1.0	0.23
Gestational age at enrollment (wk)	13.8 (12.4-16.2)	13.6 (12.2-16.1)	13.8 (12.5-16.4)	14.2 (12.5-16.6)	<0.05
Duration of daily vomiting					
Early gestation	7.2	-	-	66.6	
Mid gestation	2.4	-	-	22.1	
Late gestation	1.2	-	-	11.3	
Total weight gain (kg)**	10.5±5.1	10.9±4.9	10.6±5.2	8.5±5.9	<0.001
PE or HELLP-syndrome	2.7	2.4	3.0	3.5	0.31
<b>Neonatal characteristics</b>					
Gestational age at birth (d)	281 (273-287)	281 (274-287)	281 (274-287)	280 (273-286)	0.18
Prematurity (<37 wk)	5.6	5.3	5.7	6.5	0.51
Birth weight (g)	3402±569	3422±563	3387±572	3360±577	<0.05
SGA (<p10)	10.1	9.5	10.2	11.9	0.19

Data represent mean±SD, median (IQR) or %. Abbreviations: BMI: body mass index; IgG: immune globuline G; CagA: Cytotoxin-associated gene A protein; PE: preeclampsia; HELLP-syndrome: hemolysis, elevated liver enzymes, low platelets; SGA: small for gestational age.

\* CagA-negative or positive

\*\* Total weight gain based on pre-pregnancy weight and measured weight in late gestation

**Table 2**  
**Logistic regression for vomiting frequency and *H pylori***

	No vomiting		Occasional vomiting		Daily vomiting	
	OR		OR	95% CI	OR	95% CI
Crude						
<i>H pylori</i>	1.0		1.44**	1.28; 1.61	3.14**	2.62; 3.77
Adjusted						
<i>H pylori</i>	1.0		1.10	0.96; 1.26	1.44*	1.16; 1.78

'No vomiting' is reference group. Adjusted for maternal age, parity, ethnicity, education level, smoking. OR: odds ratio; CI: confidence interval.

\*  
 p<0.05

\*\*  
 p<0.001



**Table 3**  
**Linear and logistic regression for *H. pylori* and/or daily vomiting, maternal and neonatal outcome**

	<i>H. pylori</i>		Daily vomiting		<i>H. pylori</i> + daily vomiting	
	$\beta$ /OR	95% CI	$\beta$ /OR	95% CI	$\beta$ /OR	95% CI
Maternal outcome						
Total weight gain (kg)	-0.1	-0.4; 0.2	-1.2*	-1.9; -0.4	-2.1**	-2.7; -1.5
Neonatal outcome						
Birthweight (g)	-.31*	-58; -4	31	-30; 92	-.60*	-109; -12
SGA (<p10)	1.08	0.87; 1.34	0.77	0.45; 1.30	1.49*	1.04; 2.14
Prematurity (<37 wk)	1.13	0.85; 1.49	1.21	0.67; 2.18	1.35	0.83; 2.21

'No/occasional vomiting and no *H. pylori*' is reference group. Adjusted for neonatal sex, gestational age at birth, twin pregnancy, maternal age, parity, diabetes gravidarum, hypertensive disorders, ethnicity, education level, pre-pregnancy BMI, smoking.  $\beta$ : difference; OR: odds ratio; CI: confidence interval; SGA: small for gestational age.

\*  
p<0.05

\*\*  
p<0.001