Adequacy of prenatal care use among pregnant women with epilepsy: a population-based, cross-sectional study, Finland, 2000-2014

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ABSTRACT

Purpose: To examine the association between epilepsy and frequency and time of initiation of prenatal care use among pregnant women in Finland.

Methods: We conducted a nationally representative, population-based cross-sectional study including pregnant women with epilepsy in Finland between 2000-2014. Selected demographic and clinical data were obtained by linking multiple national health registers and census. Crude and adjusted odds ratios (aOR) and 95% confidence intervals (CI) were estimated using logistic regression analysis. Effect modification of the main association was examined by parity.

Results: We examined 10,798 and 921,873 women with and without epilepsy, respectively, and the two groups differed significantly on prenatal care constructs. Women with epilepsy were more likely to have 25 or more total prenatal visits (10.4 % vs. 5.8%) and earlier initiation of prenatal care (at <8 weeks of gestation) (30.8% vs. 24.7%) compared to women without epilepsy. Epilepsy was significantly associated with 25 or more prenatal care visits (aOR=1.84; 95% CI=1.71, 1.98). The association between epilepsy and early initiation of prenatal care (<8 weeks) was significantly modified by parity, where multiparous women had increased odds of early prenatal care initiation (aOR=1.32; 95% CI=1.24, 1.41) compared to nulliparous women (aOR=1.19; 95% CI=1.11, 1.28).

Conclusions: Finnish healthcare, which is publicly funded and freely accessible, provided pregnant women with epilepsy adequate and timely prenatal care. Parity modified the period when prenatal care was initiated as multiparous women were initiated early to receive prenatal care compared to nulliparous women.

Keywords: childbirth; epilepsy; Finland; pregnancy; pregnancy complications; prenatal care

1 | INTRODUCTION

Epilepsy is a common neurological condition characterized by abnormal brain activity leading to symptoms of varying degrees, including recurrent seizures. Globally, it is estimated that 15 million women with epilepsy are of reproductive age.[1] It is estimated that 0.3 to 0.8 percent of all pregnancies occur among women with epilepsy.[2] Epilepsy is associated with adverse maternal and neonatal outcomes in a small proportion of pregnancies.[3, 4] Successful prenatal care is often more difficult among women with epilepsy as it requires collaborative care from both obstetricians and neurologists.[5] Few studies have previously examined prenatal care utilization among women with epilepsy.[6-8]

The World Health Organization (WHO) recommends the first prenatal care visit at 12 weeks of gestation with increased frequency of visits as gestation progresses and additional visits for women with high-risk pregnancies.[9] WHO recommendations include a minimum of 8 visits to ensure adequate experience of care for women.[9] However, number of visits may range depending on risks associated with pregnancy. Despite benefits associated with pre-conception and prenatal care, various barriers prevent women from accessing services, including type of healthcare (private vs public), health insurance, financial incentives to utilize care and an overall understanding on accessing preconception and prenatal care.[10]

The prevalence of epilepsy varies by country throughout Europe. However, previous reports indicate active epilepsy occurring in 5.2 per 1000 adult women in Finland.[11] Approximately 0.7% of pregnant women in Finland are diagnosed with epilepsy, which is included within the recognized estimates.[12] Among all Finnish women, an average of 15 total prenatal care visits and first prenatal care visit occurring at 9.8 weeks of gestation has previously been reported.[13] As a result of a free, publicly funded prenatal care system in Finland, it is rare for women to forgo prenatal care or have insufficient use of prenatal care.[13, 14] Overall, studies in Finland on receipt of prenatal care among women with

epilepsy are limited. The objective of this study was to examine adequacy and timeliness of prenatal care utilization among mothers with epilepsy in Finland between 2000 and 2014.

2 | METHODS

2.1. Data sources

We linked multiple national data sources in Finland to generate our analytic dataset. Our first data source was the Finnish Hospital Discharge Register (FHDR), a nationwide dataset on all hospital discharges and identification codes. FHDR provides information on maternal inpatient care in hospitals and primary health care centers.[15] FHDR also provides information on the subject's area of residence, hospital identification code, admission and discharge days, patient diagnosis, and surgical procedures. Diagnoses are coded using the *International Statistical Classification of Diseases and Related Health Problems, 10th Edition* (ICD-10) coding scheme since 1996. Our second data source was the Finnish Medical Birth Register (MBR), which includes data on maternal demographic and health data.[16] The MBR, maintained by the Finnish Institute for Health and Welfare, provides information on live birth and stillbirths (from 22 weeks of gestation on 500 grams) from 1987. Our third data source was the Census data, based on administrative registers, from Statistics Finland providing information on income and educational attainment for each parturient.[17, 18] These three data sources were linked using unique identification codes for individuals who were characterized as citizens and permanent residents of Finland. Overall, 99.8% of women in Finland have valid identification code, and 99.9% of records were linked successfully between all data sources for our analysis.

The Finnish Institute for Health and Welfare Statistics Finland have approved the use of their register data in this study.

2.2. Subject selection

Our analysis included all women who were identified as pregnant in Finland from years 2000 through 2014.

2.3. Epilepsy (predictor variable)

The Finnish MBR provided detailed information including maternal diagnoses during pregnancy and delivery. Maternal epilepsy was defined using ICD-10 code G40. We categorized the response to this variable as 'yes' or 'no' depending on the presence of at least *ICD-10* code indicating epilepsy diagnosis during the study period among the study target population.

2.4. Prenatal care (dependent variable)

We examined both frequency and time of initiation of prenatal care as our dependent variable. Total number of prenatal visits were examined as a categorical variable (no visit / 1-4 visits / 5-9 visits / 10-14 visits / 15-19 visits / 20-24 visits / ≥25 visits). The time of initiation of prenatal care was examined was the recorded week when the first prenatal visit occurred (no visit / 0-7 weeks / 8-11 weeks / 12 – 15 weeks / ≥16 weeks or later).

2.5. Co-variables

Co-variables were selected based on the literature review of factors associated with epilepsy and prenatal care use among women of reproductive age. The following co-variables were identified, and were available in the linked dataset relevant to maternal index pregnancy: age at pregnancy (years; <20 / 20-34 / 35); highest attained education (basic or no education / upper secondary, pre-bachelors education / bachelors or greater); income level (percentile; <20 / 20–80 / >80); nativity (Finnish background, born in Finland / other); marital and cohabitation status (married and cohabiting / unmarried without cohabiting / other); cigarette smoking (never smoker / smoker during pregnancy); number of previous births or parity (none / 1 or more); number of previous pregnancies or gravidity (none / 1 or more);

previous miscarriages (none / 1 or more); previous induced abortions (none / 1 or more); previous ectopic pregnancies (none/1 or more); fertility treatment (no / yes); 1st trimester serum screening (no / yes); 2nd trimester serum screening (no/yes); 1st trimester ultrasound (no / yes); 2nd trimester ultrasound (no / yes); chorion villus biopsy (no / yes); and amniocentesis (no / yes).

2.6. Statistical analysis

The descriptive analysis was conducted to compare pregnant women with and without epilepsy on the prenatal care and other selected maternal variables using Pearson Chi square test. Crude and adjusted odds ratios ([cOR]s and [aOR]s, respectively) and their corresponding 95% confidence intervals (CIs) also were estimated to examine associations between epilepsy and prenatal care receipt using bivariate and multivariable logistic regression analysis, respectively. Covariables included in the multivariable model were selected if a statistically significant bivariable association ($p<.05$) was observed between epilepsy and the covariable; and retained if the covariable altered the main effect by more than 10% when the variable was entered into the model. The significance for all tests of associations was set at $p < 0.05$. We assessed effect modification of the association between total number of prenatal care visits and epilepsy, as well as the association between the week of first prenatal care visit and epilepsy, by parity, using the test for homogeneity, set at ($p < 0.05$); we presented stratified findings when interaction due to parity was significant. All analyses were performed using the SAS version 9.4 (SAS Institute Inc., 2013).

3 | RESULTS

A total of 10,798 and 921,873 women with and without epilepsy, respectively, between study years 2000-2014 were eligible for our analysis. Selected demographic, health behavior and reproductive characteristics were compared between the two groups (Table 1). There were significant differences between the two groups of women with respect to age, education, income level, nativity, marital and

cohabiting status, cigarette smoking behavior, and reproductive history including parity, miscarriages, induced abortions, and fertility treatment (p values < 0.05). Women with epilepsy had an increased odds, and 95% CI did not include a null effect, for being younger, more basic or no education, low income, unmarried or without cohabitation status, having a history of cigarette smoking, history of one or more miscarriages, and having a history of induced abortions (Table 2).

A total of 10-14 prenatal care visits was set as a reference level for the analysis. About 5% of women in both study groups (i.e., women with and without epilepsy) reported <10 prenatal care visits. Overall, 69.3% of women with epilepsy reported having more than 15 prenatal care visits for the index pregnancy compared to 60.5% of women without epilepsy. A higher proportion of women with epilepsy compared to those without had 20-24 visits (cOR=1.39; 95% 1.32, 1.47) and 25 or more visits (cOR=1.84; 95% CI=1.72, 1.96) (Table 2). The association persisted after controlling several potential confounders, where epilepsy was significantly associated with 20-24 visits (aOR=1.33; 95% CI=1.26, 1.42) and 25 or more prenatal care visits (aOR=1.84; 95% CI=1.71, 1.98) (Table 2). Effect estimates for the association were very similar in both full and reduced multivariable models (Table 2).

The time of prenatal care initiation analysis showed that 30.8% of women with epilepsy started prenatal care by 7th week of pregnancy while 24.7% of women without epilepsy initiated prenatal care during the same gestational age (Table 1). The association between epilepsy and time of initiation of prenatal care was significantly modified by parity (test of homogeneity: p value =0.0377). Multiparous women had increased odds of early prenatal care initiation (<8 weeks of gestation) (aOR=1.32; 95% CI=1.24, 1.41) while the association was slightly attenuated among nulliparous women (aOR=1.19; 95% CI=1.11, 1.28) (Table 3). Multiparous women also had an increased likelihood of a later prenatal care initiation, at 16 weeks of gestation or later (aOR=1.27; 95% CI=1.07, 1.51) (Table 3). Additionally, in both strata of parity, women with epilepsy were significantly more likely to have greater number of prenatal care visits at 20-24 visits (nullipara: aOR=1.49; 95% CI=1.36, 1.62 and multipara: aOR=1.21;

95% CI=1.11, 1.32) and 25 or more visits (nullipara: aOR=1.93; 95% CI=1.74, 2.15 and multipara: aOR=1.77; 95% CI=1.60, 1.95) (Table 3).

4 | DISCUSSION

4.1. Main Findings

Using nationally representative population-based multi-registry data, our study showed that women with epilepsy had a greater number of prenatal care visits and earlier initiation of prenatal care and were significantly more likely to achieve these compared with women without epilepsy. Women with epilepsy had a higher average of total prenatal care visits and earlier first visit compared with all Finnish women. To our knowledge, this is the first study to consider the association between epilepsy diagnosis among pregnant women and frequency and timing of prenatal care in Finland.

4.2. Strengths and Limitations

We utilized nationally representative, population-based datasets and linked multiple data sources. The study encompasses 15 years of most current data available with a high data linkage success rate. Registry quality control methods ensured high reliability and validity. Finnish registers systematically determine maternal diagnoses among others using ICD-10 codes. Finland, along with other Nordic countries, has an extensive population-based health care register with exhaustive information on patient information, allowing us to examine several characteristics.[15]

There are some limitations to our study. We lacked information on preconception care utilization. Our study did not evaluate distribution of visits over time or level of risk during pregnancy when assessing adequacy of prenatal care utilization. Overall, this study did not have sufficient data to study all factors associated with prenatal care use and diagnosis of epilepsy as these require secondary data from administrative registries.

4.3. Interpretation

The high rates of prenatal care utilization in Finland are most likely attributable to accessible, publicly funded and free prenatal care systems. In the present study, 69.3% of women with epilepsy attended ≥15-19 prenatal care visits and 89.5% attended the first visit within the first trimester. These rates are higher compared with the United States, which lacks universal access to prenatal care. In 2016, 40.9% of women in the United States received adequate prenatal care and 77.1% of women received care within the first trimester.[19] This study is comparable to a prior PRAMS study using the Kotelchuck index, which found that women with epilepsy were equally likely to receive adequate prenatal care (80%–110% of recommended visits) when compared with women without epilepsy.[7, 20] Additionally, the PRAMS study reported a positive association between epilepsy and >110% of prenatal care visits, although this association was not significant (OR=1.50, 95% CI=1.00, 2.27).[7] A study in Bhutan found that 95% of women with epilepsy attended prenatal care visits, although number and timing of visits were not specified.[6] Furthermore, a retrospective chart review found 78% of women with epilepsy at Stanford University Hospital during 1988-1995 to have least one prenatal care visit by the end of their first trimester.[8] A study on 151 pregnancies among women with epilepsy reported 93% of women having a prenatal visit to an obstetrician approximately every month with an average of 5.5 visits.[21] These studies did not consider timing of prenatal care among women with epilepsy.

Effect measure modification by parity was present for the association between epilepsy and time of prenatal care initiation, and our study was the first to examine this and find a significant interaction. Previous studies have demonstrated multiparous women being more likely to have inadequate prenatal care compared with nulliparous women.[22, 23] One nationwide study in Finland found that women with three or more previous births had fewer visits compared with other women and were more likely to have their first visit after 12 weeks of gestation.[24] Although previous studies did not include epilepsy diagnosis, one study considered interaction by parity regarding prenatal care and risk of pregnancy.[25]

This study found that nulliparous women with high risk pregnancies were more likely to initiate antenatal care later than nulliparous women with low risk (aOR=1.13, 95% CI 1.01, 1.27); this association was not evident when considering risk of pregnancy among multiparous women (aOR=0.92; 95% CI 0.82, 1.03).[25] Recommendations for prenatal care may not consider severity of pregnancy. Women with epilepsy may require a greater number of visits due to pregnancy concerns including intrauterine growth restriction, seizure control and other adverse outcomes.[7] A larger proportion of low risk women were reported to attend 80-109% of expected prenatal care visits compared with high risk women (93% vs. 7%).[26] However, among high risk women, the largest proportion attended ≥110% of prenatal care visits (33%).[26] A similar study found that more women with at least one risk factor (9.64%) attended ≥110% of prenatal care visits compared with those without risk factors (4.40%).[27] While these studies did not take into account diagnosis of epilepsy, this is consistent with our study which found that more women with epilepsy received 20-24 visits and 25+ visits compared with women without epilepsy (18.5% vs. 13.6% and 10.4% vs. 5.8%, respectively). This may be attributable to greater risk factors requiring more visits. The National Academy of Medicine suggest assessing risk of pregnancy to tailor levels of prenatal care needs for women, and that women with risk factors may be subject to more thorough and recurrent prenatal care visits.[28] In contrast, a systematic review conducted by the World Health Organization (WHO) suggest that adequate prenatal care can be accomplished within less visits than recommended for those not at risk for adverse pregnancy outcomes.[29] Recommendations on prenatal visits such as those instituted by the ACOG have not previously considered risk of pregnancy. Therefore, using measurements such as the Adequacy of Prenatal Care Utilization (APNCU) Index may not be indicative of proper prenatal care use for women with complicated pregnancies who may require more frequent prenatal care visits.[30]

5 | CONCLUSION

This study suggests that most pregnant women with epilepsy in Finland are accessing adequate prenatal care and are initiating this care early on in pregnancy. This may be unique to countries like Finland that emphasize and provide free prenatal care to women. Additionally, effect measure modification by parity was present among the association between initiation of first visit and diagnosis of epilepsy. Early initiation and adequate use of preconception and prenatal care should be emphasized among women of reproductive age to prevent unplanned pregnancies, inform them on interactions of AEDs on contraception and other risks associated with epilepsy. With adequate care and management during pregnancy, the incidence of adverse effects in women with epilepsy resemble that of the general population. Future studies in Finland should include data on preconception use among women with epilepsy to determine its effects on timely and adequate receipt of prenatal care. Additional studies stratifying level of risk during pregnancy and establishing whether women are receiving sufficient care would further elucidate this association.

Ethics Statement: Data for this study were determined to not require Institutional Review Board review by Emory University.

Author Contributions: VK and SM contributed to the concept and design of the study. Data analysis and interpretations was conducted by MG and SR. SM and VK drafted the manuscript and all authors performed revisions of the manuscript.

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Table 1. Selected characteristics of pregnant women with and without epilepsy in Finland, 2000-2014

	Epilepsy (n=10,798)	No Epilepsy (n=921,873)	P-value
Characteristics	**n (%)**	**n (%)**	
Total number of prenatal care visits			
No visit	27 (0.25)	2125 (0.23)	<0.01
1-4 visits	101 (0.94)	9724 (1.05)	
5-9 visits	368 (3.41)	32,469 (3.52)	
10-14 visits	2596 (24.04)	300,508 (32.60)	
15-19 visits	4364 (40.41)	379,661 (41.18)	
20-24 visits	1995 (18.48)	124,944 (13.55)	
25 or more visits	1127 (10.44)	53,437 (5.80)	
Week of first prenatal care visit			
No first visit	27 (0.25)	2125 (0.23)	<0.01
Visit at 0-7 weeks	3322 (30.77)	227,975 (24.73)	
Visit at 8-11 weeks	6343 (58.74)	594,445 (64.48)	
Visit at 12-15 weeks	509 (4.71)	47,343 (5.14)	
Visit at 16 weeks or later	390 (3.61)	32,596 (3.54)	
Age at pregnancy (years)			
<20	441 (4.08)	22,587 (2.45)	<0.01
20-34	9112 (84.39)	764,092 (82.88)	
≥35	1245 (11.53)	135,194 (14.67)	
Highest education			
Basic or no education	5893 (54.57)	415,798 (45.10)	<0.01
Upper secondary, Pre-bachelors	4153 (38.46)	410,826 (44.56)	
Bachelors or greater	752 (6.96)	95,249 (10.33)	
Income level			
<20th percentile	1159 (10.73)	75,965 (8.24)	<0.01
20-80th percentile	7107 (65.82)	599,709 (65.05)	
>80th percentile	665 (6.16)	76,205 (8.27)	
Nativity			
Finnish background, born in Finland	10,129 (93.80)	833,450 (90.41)	<0.01
Other	555 (5.14)	80,282 (8.71)	
Marital and Cohabiting Status			
Married and cohabiting	9380 (86.87)	826,551 (89.66)	<0.01
Unmarried without cohabiting	1381 (12.79)	92,509 (10.03)	
Unknown	25 (0.23)	1,622 (0.18)	
Cigarette smoking during pregnancy			
Non-smoker	8267 (76.56)	760,769 (82.52)	<0.01
Smoker	2226 (20.61)	137,441 (14.91)	
Parity			
Nulliparous	4677 (43.31)	383,858 (41.64)	<0.01
Multiparous	6115 (56.63)	537,275 (58.28)	
Gravidity			
None	3404 (31.52)	295,189 (32.02)	0.26
1 or more	7390 (68.44)	625,986 (67.90)	
Previous miscarriages			
None	8198 (75.92)	726,581 (78.82)	<0.01
1 or more	2588 (23.97)	194,159 (21.06)	
Previous induced abortions			
None	9078 (84.07)	804,340 (87.25)	<0.01
1 or more	1703 (15.77)	115,826 (12.56)	
Previous ectopic pregnancies			
None	10,578 (97.96)	905,035 (98.17)	0.08
1 or more	200 (1.85)	15,082 (1.64)	
Fertility treatment for index pregnancy			
No	10,667 (98.79)	905,102 (98.18)	<0.01
Yes	131 (1.21)	16,771 (1.82)	
1st trimester serum screening			
No	8112 (75.13)	696,241 (75.52)	0.33
Yes	2686 (24.87)	225,632 (24.48)	
2nd trimester serum screening			
No	10621 (98.36)	908,279 (98.53)	0.16
Yes	177 (1.64)	13,594 (1.47)	
1st trimester ultrasound			
No	5156 (47.75)	443,771 (48.14)	0.42
Yes	5642 (52.25)	478,102 (51.86)	
2nd trimester ultrasound			
No	4736 (43.86)	402,205 (43.63)	0.63
Yes	6062 (56.14)	519,668 (56.37)	
Chorionvillus biopsy			
No	10,706 (99.15)	913,584 (99.10)	0.61
Yes	92 (0.85)	8289 (0.90)	
Amniocentesis			
No	10,551 (97.71)	900,702 (97.70)	0.95
Yes	247 (2.29)	21,171 (2.30)	

n=Frequency

Table 2. Association between epilepsy and total number of prenatal care visits among pregnant women in Finland, 2000-2014

Characteristics	Crude ORs (95% CI)	Adjusted OR (95% CI) Full Model	Adjusted OR (95% CI) Reduced Model
Total number of prenatal care visits			
No visit	1.11 (0.76, 1.62)	0.31 (0.10, 0.96)	0.31 (0.10, 0.97)
1-4 visits	0.90 (0.74, 1.10)	0.64 (0.47, 0.87)	0.64 (0.47, 0.87)
5-9 visits	0.99 (0.89, 1.10)	0.98 (0.86, 1.12)	0.98 (0.86, 1.12)
10-14 visits	0.75 (0.72, 0.79)	0.77 (0.73, 0.81)	0.77 (0.73, 0.81)
15-19 visits	Ref	Ref	Ref
20-24 visits	1.39 (1.32, 1.47)	1.33 (1.26, 1.41)	1.33 (1.26, 1.42)
25 or more visits	1.84 (1.72, 1.96)	1.83 (1.70, 1.97)	1.84 (1.71, 1.98)
Week of first prenatal visit			
No first visit	1.19 (0.81, 1.74)	--	--
0-7 weeks	1.366 (1.31, 1.43)	1.26 (1.20, 1.32)	1.26 (1.20, 1.32)
8-11 weeks	Ref	Ref	Ref
12-15 weeks	1.01 (0.92, 1.10)	1.09 (0.98, 1.21)	1.09 (0.99, 1.21)
16 weeks or later	1.12 (1.01, 1.24)	1.20 (1.06, 1.36)	1.20 (1.06, 1.36)
Age at pregnancy (years)			
<20	1.64 (1.49, 1.80)	1.20 (1.07, 1.35)	1.20 (1.07, 1.35)
20-34	Ref	Ref	Ref
≥35	0.77 (0.73, 0.82)	0.84 (0.78, 0.90)	0.84 (0.78, 0.90)
Highest education			
Basic or no education	1.40 (1.35, 1.46)	1.46 (1.38, 1.53)	1.45 (1.38, 1.52)
Upper secondary, Pre-bachelors	Ref	Ref	Ref
Bachelors or greater	0.78 (0.72, 0.84)	0.86 (0.79, 0.93)	0.86 (0.79, 0.94)
Income level			
<20th percentile	1.29 (1.21, 1.37)	1.18 (1.10, 1.26)	1.18 (1.10, 1.26)
20-80th percentile	Ref	Ref	Ref
>80th percentile	0.74 (0.68, 0.80)	0.87 (0.80, 0.94)	0.87 (0.80, 0.94)
Nativity			
Finnish background, born in Finland	Ref	Ref	Ref
Other	0.57 (0.52, 0.62)	0.63 (0.57, 0.70)	0.63 (0.57, 0.71)
Marital and cohabiting status			
Married and cohabiting	Ref	Ref	Ref
Unmarried without cohabiting	1.32 (1.24, 1.39)	1.10 (1.03, 1.18)	1.11 (1.04, 1.19)
Unknown	1.36 (0.92, 2.01)	1.18 (0.63, 2.21)	1.19 (0.64, 2.23)
Cigarette smoking during pregnancy			
Non-smoker	Ref	Ref	Ref
Smoker	1.49 (1.42, 1.56)	1.16 (1.10, 1.23)	1.16 (1.10, 1.23)
Parity			
Nulliparous	Ref	Ref	Ref
Multiparous	0.93 (0.90, 0.97)	1.07 (0.99, 1.15)	1.07 (1.02, 1.12)
Gravidity			
None	Ref	Ref	Ref
1 or more	1.02 (0.98, 1.07)	1.01 (0.92, 1.10)	NA
Previous miscarriages			
None	Ref	Ref	Ref
1 or more	1.18 (1.13, 1.24)	1.21 (1.15, 1.28)	1.21 (1.15, 1.28)
Previous induced abortions			
None	Ref	Ref	Ref
1 or more	1.30 (1.24, 1.37)	1.14 (1.07, 1.22)	1.14 (1.08, 1.22)
Previous ectopic pregnancies			
None	Ref	Ref	Ref
1 or more	1.14 (0.99, 1.31)	1.14 (0.97, 1.33)	1.14 (0.98, 1.34)
Fertility treatment for index pregnancy			
No	Ref	Ref	Ref
Yes	0.66 (0.56, 0.79)	0.66 (0.53, 0.81)	0.65 (0.53, 0.81)
1st trimester serum screening			
No	Ref	Ref	Ref
Yes	1.02 (0.98, 1.07)	1.00 (0.94, 1.06)	NA
2nd trimester serum screening			
No	Ref	Ref	Ref
Yes	1.11 (0.96, 1.29)	1.07 (0.89, 1.28)	NA
1st trimester ultrasound			
No	Ref	Ref	Ref
Yes	1.02 (0.98, 1.06)	1.00 (0.94, 1.05)	NA
2nd trimester ultrasound			
No	Ref	Ref	Ref
Yes	0.99 (0.95, 1.03)	0.98 (0.93, 1.04)	NA
Chorionvillus biopsy			
No	Ref	Ref	Ref
Yes	0.95 (0.77, 1.17)	1.08 (0.86, 1.35)	NA
Amniocentesis			
No	Ref	Ref	Ref
Yes	1.00 (0.877, 1.131)	1.02 (0.89, 1.18)	NA

CI=Confidence Interval; NA=Not Applicable; OR=Odds Ratio; Ref=Reference
Adjusted models are controlled for all other variables in the columns.

Table 3. Association between week of initiation of first prenatal visit and epilepsy, stratified by parity, among pregnant women in Finland, 2000-2014

	Nulliparous			Multiparous		
Characteristics	**Crude OR (95% CI)**	**Adjusted OR (95% CI) Full Model**	**Adjusted OR (95% CI) Reduced Model**	**Crude OR (95% CI)**	**Adjusted OR (95% CI) Full Model**	**Adjusted OR (95% CI) Reduced Model**
Total number of prenatal care visits						
None	0.88 (0.46, 1.70)	--	--	1.27 (0.80, 2.02)	--	--
1-4 visits	1.02 (0.74, 1.39)	0.67 (0.41, 1.09)	0.67 (0.41, 1.10)	0.84 (0.65, 1.08)	0.62 (0.42, 0.91)	0.62 (0.42, 0.91)
5-9 visits	1.08 (0.91, 1.29)	1.13 (0.91, 1.40)	1.13 (0.91, 1.41)	0.94 (0.82, 1.07)	0.90 (0.76, 1.06)	0.90 (0.76, 1.06)
10-14 visits	0.80 (0.74, 0.86)	0.81 (0.75, 0.89)	0.81 (0.75, 0.89)	0.72 (0.68, 0.77)	0.74 (0.69, 0.80)	0.74 (0.69, 0.79)
15-19 visits	Ref	Ref	Ref	Ref	Ref	Ref
20-24 visits	1.50 (1.39, 1.63)	1.48 (1.36, 1.62)	1.49 (1.36, 1.62)	1.30 (1.20, 1.39)	1.21 (1.11, 1.31)	1.21 (1.11, 1.32)
25 or more visits	1.93 (1.75, 2.12)	1.92 (1.72, 2.14)	1.93 (1.74, 2.15)	1.77 (1.61, 1.93)	1.76 (1.59, 1.94)	1.77 (1.60, 1.95)
Week of first prenatal visit						
No first visit	0.89 (0.46, 1.71)	0.23 (0.03, 1.61)	0.23 (0.03, 1.64)	1.44 (0.90, 2.29)	0.37 (0.09, 1.50)	0.37 (0.09, 1.50)
0-7 weeks	1.28 (1.20, 1.36)	1.19 (1.11, 1.28)	1.19 (1.11, 1.28)	1.43 (1.35, 1.52)	1.32 (1.24, 1.41)	1.32 (1.24, 1.41)
8-11 weeks	Ref	Ref	Ref	Ref	Ref	Ref
12-15 weeks	1.09 (0.93, 1.28)	1.13 (0.95, 1.35)	1.14 (0.96, 1.35)	0.99 (0.88, 1.10)	1.07 (0.95, 1.22)	1.08 (0.95, 1.22)
16 weeks or later	1.10 (0.95, 1.29)	1.11 (0.92, 1.34)	1.11 (0.92, 1.35)	1.13 (0.99, 1.30)	1.27 (1.07, 1.51)	1.27 (1.07, 1.51)
Age at pregnancy (years)						
<20	1.59 (1.43, 1.76)	1.18 (1.05, 1.34)	1.19 (1.05, 1.34)	2.04 (1.53, 2.73)	1.33 (0.93, 1.89)	1.33 (0.93, 1.89)
20-34	Ref	Ref	Ref	Ref	Ref	Ref
≥35	0.76 (0.67, 0.86)	0.93 (0.80, 1.08)	0.93 (0.80, 1.07)	0.78 (0.73, 0.83)	0.81 (0.74, 0.88)	0.82 (0.75, 0.89)
Highest education						
Basic or no education	1.42 (1.33, 1.51)	1.45 (1.35, 1.57)	1.44 (1.34, 1.56)	1.38 (1.31, 1.46)	1.46 (1.36, 1.56)	1.45 (1.36, 1.55)
Upper secondary, Pre-bachelors	Ref	Ref	Ref	Ref	Ref	Ref
Bachelors or greater	0.73 (0.64, 0.83)	0.82 (0.71, 0.94)	0.82 (0.72, 0.94)	0.81 (0.74, 0.90)	0.89 (0.80, 0.98)	0.89 (0.80, 0.99)
Income level						
<20th percentile	1.31 (1.21, 1.42)	1.20 (1.10, 1.30)	1.20 (1.10, 1.30)	1.21 (1.09, 1.35)	1.13 (1.01, 1.27)	1.13 (1.01, 1.27)
20-80th percentile	Ref	Ref	Ref	Ref	Ref	Ref
>80th percentile	0.62 (0.53, 0.72)	0.76 (0.64, 0.89)	0.76 (0.64, 0.89)	0.80 (0.73, 0.87)	0.92 (0.83, 1.01)	0.92 (0.83, 1.01)
Nativity						
Finnish background, born in Finland	Ref	Ref	Ref	Ref	Ref	Ref
Other	0.54 (0.47, 0.62)	0.63 (0.53, 0.75)	0.63 (0.53, 0.75)	0.59 (0.53, 0.66)	0.63 (0.55, 0.73)	0.64 (0.55, 0.73)
Marital and cohabiting Status						
Married and cohabiting	Ref	Ref	Ref	Ref	Ref	Ref
Unmarried without cohabiting	1.29 (1.20, 1.40)	1.11 (1.01, 1.21)	1.11 (1.02, 1.21)	1.32 (1.21, 1.44)	1.10 (0.99, 1.22)	1.10 (0.99, 1.22)
Unknown	1.10 (0.62, 1.95)	0.96 (0.40, 2.31)	0.97 (0.40, 2.34)	1.71 (0.99, 2.96)	1.54 (0.63, 3.73)	1.54 (0.64, 3.74)
Cigarette smoking						
Never Smoker	Ref	Ref	Ref	Ref	Ref	Ref
Smoker during pregnancy	1.44 (1.34, 1.54)	1.15 (1.06, 1.24)	1.14 (1.06, 1.24)	1.53 (1.43, 1.63)	1.18 (1.09, 1.27)	1.18 (1.09, 1.28)
Gravidity						
None	Ref	Ref	Ref	Ref	Ref	Ref
1 or more	1.25 (1.17, 1.33)	1.10 (0.88, 1.38)	1.20 (1.11, 1.29)	--	--	--
Previous miscarriages						
None	Ref	Ref	Ref	Ref	Ref	Ref
1 or more	1.17 (1.08, 1.27)	1.10 (0.90, 1.36)	NA	1.22 (1.16, 1.29)	1.22 (1.15, 1.30)	1.23 (1.15, 1.31)
Previous induced abortions						
None	Ref	Ref	Ref	Ref	Ref	Ref
1 or more	1.28 (1.18, 1.40)	1.05 (0.85, 1.29)	NA	1.33 (1.24, 1.42)	1.15 (1.06, 1.24)	1.15 (1.06, 1.24)
Previous ectopic pregnancies						
None	Ref	Ref	Ref	Ref	Ref	Ref
1 or more	1.17 (0.90, 1.52)	1.13 (0.83, 1.56)	NA	1.14 (0.96, 1.35)	1.12 (0.93, 1.35)	NA
Fertility treatment for index pregnancy						
No	Ref	Ref	Ref	Ref	Ref	Ref
Yes	0.64 (0.51, 0.79)	0.67 (0.52, 0.87)	0.67 (0.52, 0.87)	0.68 (0.51, 0.91)	0.62 (0.43, 0.89)	0.62 (0.43, 0.90)
1st trimester serum screening						
No	Ref	Ref	Ref	Ref	Ref	Ref
Yes	1.05 (0.98, 1.12)	1.05 (0.95, 1.15)	NA	1.00 (0.94, 1.06)	0.96 (0.89, 1.05)	NA
2nd trimester serum screening						
No	Ref	Ref	Ref	Ref	Ref	Ref
Yes	1.24 (1.00, 1.53)	1.08 (0.83, 1.41)	NA	1.01 (0.81, 1.25)	1.06 (0.82, 1.35)	NA
1st trimester ultrasound						
No	Ref	Ref	Ref	Ref	Ref	Ref
Yes	1.01 (0.95, 1.07)	0.97 (0.89, 1.06)	NA	1.02 (0.97, 1.07)	1.02 (0.94, 1.10)	NA
2nd trimester ultrasound						
No	Ref	Ref	Ref	Ref	Ref	Ref
Yes	1.00 (0.95, 1.06)	0.97 (0.89, 1.06)	NA	0.98 (0.93, 1.03)	0.99 (0.92, 1.07)	NA
Chorionvillus biopsy						
No	Ref	Ref	Ref	Ref	Ref	Ref
Yes	0.85 (0.58, 1.23)	0.91 (0.59, 1.39)	NA	1.01 (0.79, 1.29)	1.16 (0.88, 1.52)	NA
Amniocentesis						
No	Ref	Ref	Ref	Ref	Ref	Ref
Yes	0.90 (0.71, 1.12)	0.97 (0.75, 1.24)	NA	1.06 (0.91, 1.23)	1.06 (0.89, 1.26)	NA

CI=Confidence Interval; NA=Not Applicable; OR=Odds Ratio; Ref=Reference
Adjusted models are controlled for all other variables in the columns.

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