

MATERNAL SMOKING AND HOSPITAL TREATMENT DURING PREGNANCY

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Key words: Smoking, Health consequences, Pregnancy, Maternal health, Prenatal clinic, Specialized hospital care

Abbreviations: MSDP, Maternal smoking during pregnancy; ICD, International Classification of Diseases

Reference: Wallin HP, Gissler M, Korhonen PE, Ekblad M. Maternal Smoking and Hospital Treatment During Pregnancy. *Nicotine Tob Res.* 2019 Aug 16:ntz137. doi: 10.1093/ntr/ntz137.

ABSTRACT

Introduction Previous research suggests that young maternal age, smoking, hospitalization during a previous pregnancy and poor self-rated health could be risk factors for prenatal hospitalization.

Methods The objective of this retrospective observational register study was to investigate if maternal smoking during pregnancy is associated with mother's need for hospital treatment during pregnancy. The study population consists of all singleton pregnancies (n=961,127) in 1999–2015 in Finland. Information on maternal smoking was received from the Medical Birth Register in three classes: non-smoker, quit smoking in the first trimester and continued smoking throughout the pregnancy. These data were linked with the Hospital Discharge Register data and analyzed according to ICD-10 chapters.

Results 10.7% of women continued to smoke after the first trimester. After adjusting for confounding factors women in both smoking groups had more hospital treatment compared to non-smokers. Especially outpatient treatment was more frequent in several ICD-10 chapters if mother continued to smoke: due mental and behavioral disorders (F00-F99) aOR was 2.14 with 95% confidence interval 2.00 to 2.30 in the quit smoking group and 3.88(3.71–4.06) in the continued smoking group. Due respiratory diseases (J00-J99) aOR was 1.26(1.15-1.39) and 1.61(1.52-1.71) respectively and due genitourinary diseases (N00-N99) 1.10(1.03-1.17) and 1.29(1.23-1.35). Some similar findings were made also in inpatient care.

Conclusions Women who smoke during pregnancy seem to require more hospital care for various reasons. These findings emphasize the importance of actions for smoking cessation during pregnancy and women should be encouraged to quit as early as possible.

IMPLICATIONS

Maternal smoking during pregnancy is associated with greater rates of both outpatient and inpatient hospital care during pregnancy. Women who quit smoking had a similar risk for hospital care during pregnancy with non-smokers in certain diagnosis chapters, which is very motivational and could be used as an informational tool in prenatal clinics to encourage smoking cessation as it is never too late to quit smoking during pregnancy.

INTRODUCTION

Maternal smoking during pregnancy (MSDP) is a significant health risk, not only for the fetus but for the mother as well. The prevalence of smoking in general has decreased in Finland¹. However, the prevalence of MSPD during the first trimester has remained fairly static at 15% since the 1980s but a slightly decreasing trend in has been observed during the recent years. Women who have not been able to quit smoking before pregnancy are increasingly able to quit smoking as 50% of them quit during the first trimester in 2017.² The highest MSDP rates have been observed among teenagers, single women, and women with low socioeconomic status³.

The obstetric and fetal adverse outcomes of MSDP are well-reported, e.g. poor fetal growth and brain development⁴⁻⁸, miscarriage and preterm birth⁹, preterm rupture of membranes, chorioamnionitis and placental abruption¹⁰. Effects of MSDP on fetal intrauterine growth^{5,6} and fetal head growth⁷ seem to decrease when the mother stops smoking during early pregnancy. MSDP has been linked to greater health risks for the mother as well. Pregnant women

who smoke seem to have a higher risk for deep vein thrombosis, stroke, pulmonary embolus,

myocardial infarction, influenza or pneumonia, bronchitis, gastrointestinal ulcers, and suffer from a number of comorbidities, including asthma compared to non-smoking pregnant women¹¹. On the other hand, MSDP might have a potential protective effect on severe hyperemesis¹², pre-eclampsia^{11,13,14}, and gestational diabetes¹¹. The effects of MSDP on pregnancy-induced hypertension remains controversial^{10,14}, although maternal obesity combined with MSDP could be a risk factor for hypertension during pregnancy¹⁵.

Previous research has focused on the effects of MSDP on obstetric outcomes. Only few studies have investigated the association of MSDP and maternal hospital treatments during pregnancy. According to previous studies in North-America, the prevalence of hospitalization among pregnant women has declined, yet there are differences between social classes.¹⁶ Pregnant women were mostly hospitalized due to preterm labor.⁷ It seems that young pregnant women are more likely to be hospitalized compared to their older counterparts¹⁶⁻¹⁹. MSDP seems to be one of the risk factors for prenatal obstetric hospitalization²⁰ as well as hospitalization in previous pregnancies and poor self-rated health²¹. There is lack of information on the effects of MSDP on maternal general health during pregnancy, and especially, on the need for outpatient treatment. In order to address this gap in the literature, the current study utilizes comprehensive Finnish data registers to determine the association between MSDP and the necessity of maternal hospital treatment reflecting general maternal health during pregnancy.

Pregnancy, as well as time prior to the pregnancy, offers a favorable time period for beneficial changes in lifestyle e.g. quitting smoking and eating healthy food as well as following food restrictions to allow normal and healthy fetal development. Pregnancy can also be a stressful time for the body and mind, and it is essential that pregnant women look after of their own health in order to feel well during pregnancy. Thus, if there is difference in the general health of pregnant women between non-smokers and smokers as well as between pregnant women who quit

smoking in the first trimester and those who continued beyond the first trimester, this offers new information for cessation programs.

The aim of this study was to investigate the connection between MSDP and mother's hospital treatment during pregnancy. Our hypothesis was that MSDP, and especially continued MSDP beyond the first trimester, is associated with more hospital treatment during pregnancy compared to non-smokers.

METHODS

Our research is a population-based register study based on Finnish nationwide Medical Birth Register and Hospital Discharge Register. National Institute for Health and Welfare maintains the current register, and they allowed us the use of the confidential health register data, as required by national data-protection legislation. The statistical authority made the ethical evaluation and performed the data linkage, and only unidentifiable data was provided to the researchers.

Data sources

The Finnish Medical Birth Register includes all fetuses from gestational age 22 weeks onwards or with a birth weight over 500 grams. The data is received from the delivery hospitals and in the case of home births from the assisting health care personnel. The register contains mother's and child's identification numbers and information about maternal background, obstetric care and delivery. Maternal body mass index and infertility treatments have been collected from 2004 onwards. According to data quality studies, the Medical Birth Register data corresponds well or satisfactorily with hospital records^{22,23}.

The Hospital Discharge Register includes information on all episodes of inpatient care in public and private hospitals since 1969 and outpatient visits in public hospitals since 1998. The

register contains information on the patient's background, dates of admission and discharge, hospitalization period, procedures, and the main diagnosis (plus up to two other diagnoses by International Classification of Diseases (ICD) code; Tenth Revision [ICD-10] since 1996). Outpatient visits include mainly physician visits, but also nurse or midwife visits. A systematic review showed that the completeness and accuracy of the register range from satisfactory to very good²⁴.

Study sample

The study population consists of all pregnancies of newborns (n = 975 633) between 1999 and 2015 in Finland. This time period was chosen because, during this period, the register included all outpatient visits since 1999 (the ICD-10 classification was used during the whole study period). Multiple pregnancies (n=14 506, 1.5%) were excluded. The data on MSDP was derived from the Medical Birth Register. Midwives and public health nurses collect information about MSDP and it is categorized into three groups: "not smoking", "quit smoking in the first trimester" (i.e. quit smoking group), and "continued smoking beyond the first trimester" (later referred as "smoked throughout the pregnancy" (i.e. continued smoking group). The register does not separate between women who never smoked and women who recently quit. The data are sent from the delivery hospitals to the register keeper. The information on smoking status was missing from 25 014 singleton pregnancies (2.6%), which were excluded from the statistical analysis. The final study sample consisted of 936 113 pregnancies (95.9% of all births during the time period). The population was divided into three groups according to mother's smoking status: not smoking (82.3%), quit smoking (4.3%) and continued smoking (10.6%). See Table 1 for details.

Prenatal clinic records

The Medical Birth Register collects dichotomized information (yes/no) of maternal inpatient hospital care during pregnancy from the prenatal clinic records in following categories: hospital

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care due to bleeding, threatened premature birth, blood pressure and “other” (not further specified) reason. It gathers the number of prenatal clinic visits, hospital outpatient clinic control visits (e.g. fetal ultrasound screenings) and the total number of hospital control visits.

ICD-10 diagnoses from specialized hospital care

Diagnoses from specialized care were acquired from the Hospital Discharge Register, and this data were linked with the data from the Medical Birth Register by mothers’ unique encrypted personal identification numbers. The diagnoses were analyzed according to the ICD-10 diagnosis chapters, based on the different letter codes, and performed separately for the inpatient and outpatient hospital treatment in eighteen different ICD-10 chapters. We give an overview on all ICD-10 categories here since our data are too large for detailed analysis within more detailed ICD-10 categories. The following exclusions were made: environmental factors affecting accidents (codes U00-U99, V01-Y98), congenital anomalies for mothers (codes Q00–Q99) and certain conditions originating in the perinatal period (codes P00–P96) (Supplementary Table 1). One treatment episode could consist of up to three different diagnosis codes, and each of them were studied separately and not as a single episode. Mothers who suffer from psychiatric problems might have more substance use and be more prone to other illnesses during pregnancy²⁵. Therefore, we performed additional sensitivity analyses by inpatient and outpatient care diagnoses with pregnant women without psychiatric morbidity.

Statistics

The amount of inpatient and outpatient care was analyzed using logistic regression analyses. The registration on covariates is limited, but we had detailed information on sociodemographic background and obstetric history. The confounding factors we accounted for included the birth year (to eliminate the differences in diagnostics and any changes in the organization of maternal

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care), maternal age (continuous) and parity (0, 1 to 4, or 5 or more), BMI, marital status (single, married or cohabiting; i.e. not married but living together with the spouse), socioeconomic group based on maternal occupation and national classification (upper white-collar workers such as teachers, physicians and journalists, lower white-collar workers such as secretaries, nurses and shop assistants, blue-collar workers such as dressmakers, cooks and cleaners, and others including students, homemakers, unemployed and unclassified occupations), urbanity of living area (based on national classification) and infertility treatments. The data analysis was performed using commercially available software (*SAS, version 9.3*; SAS Institute Inc, Cary, NC). Non-overlapping confidence intervals were considered to be significant.

RESULTS

The prevalence of MSDP was 15.0% in the first trimester, further 10.7% of women continued to smoke throughout the pregnancy. The characteristics of the study population according to maternal smoking status are presented in Table 1.

Prenatal clinic records

According to prenatal clinic records, a total of 99.6% of the pregnant women attended the prenatal clinic at least once. Mothers who continued to smoke throughout the pregnancy were more likely to not attend the prenatal clinic at all, as well as smokers (regardless of length of MSDP) were more likely to not attend hospital control visits at all compared to non-smokers (Table 2). 90.1% of pregnant women had at least one control visit in the hospital. However, the mean number of control visits in the hospital was higher in smokers (quit smoking group: mean 3.38; SD \pm 2.92 and continued smoking group: 3.17; \pm 2.94) compared to non-smokers (2.93; \pm 2.68). 12.7% of pregnant women had at least one other hospital visit beyond the control hospital

visit. Table 2 depicts the adjusted Odds Ratios (aOR) and 95% Confidence Intervals (CI) for various reasons of maternal inpatient hospital care during pregnancy derived from the Medical Birth Register. Women who were admitted to the hospital for any reason, or due to threat of preterm labor were more likely to be smokers. A negative association was found for continued smoking and hospital treatment for elevated blood pressure.

Outpatient hospital care

MSDP was associated with increased outpatient care and the association was even stronger in the continued smoking group than in the quit smoking group in several ICD-10 chapters (Figure 1, Supplementary Table 2). The largest association of smoking was seen in mental and behavioral disorders (F00–F99) aOR = 2.14; CI = 2.00–2.30 in the quit smoking group and aOR = 3.88; CI = 3.71–4.06 in the continued smoking group. A similar association was found in infectious and parasitic diseases (A00–B99) aOR = 1.48; CI = 1.33–1.65 in the quit smoking group and aOR = 2.45; CI = 2.30–2.62 in the continued smoking group, the diseases of respiratory tract (J00–J99) (aOR = 1.26; CI = 1.15–1.39, aOR = 1.61; CI = 1.52–1.71) and in the diseases of the genitourinary tract (N00–N99) (aOR = 1.10; CI = 1.03–1.17 and aOR = 1.29; CI = 1.23–1.35) respectively. More outpatient care was found for diseases of the circulatory system (I00–I99) aOR = 1.21; CI = 1.12–1.32 in the continued smoking group only. MSDP was associated with an increased amount of outpatient care also in other ICD-10 chapters but no difference was seen between the smoking groups in these cases. The additional sensitivity analyses that excluded mothers who received psychiatric and behavioral diagnoses during pregnancy did not change the overall results (Supplementary Table 2).

Inpatient hospital care

MSDP was associated with an increased amount of inpatient care and the risk was similar in most ICD-10 chapters. Stronger association was found in the continued smoking group than in the quit smoking group in six ICD-10 chapters (Figure 2, Supplementary Table 3). MSDP was most robustly associated with the amount of inpatient care due to mental and behavioral disorders (F00–F99); aOR = 2.66; CI = 2.16–3.27 in the quit smoking group and aOR = 8.54; CI = 7.66–9.51 in the continued smoking group. The effect was also found for infectious and parasitic diseases (A00–B99) (aOR = 1.27; CI = 1.00–1.61 and aOR = 2.25; CI = 1.98–2.56 respectively) and for injury, poisoning and certain other consequences of external causes (S00–T98) (aOR = 1.39; CI = 1.07–1.81 and aOR = 2.70; CI = 2.33–3.12, respectively). Continued smoking throughout the pregnancy was associated with increased amount of inpatient care for diseases of the genitourinary system (N00–N99) (aOR = 1.47; CI = 1.32–1.64) and skin and subcutaneous tissue (L00–L99) (aOR = 2.82; CI = 2.16–3.69). Inpatient care diagnoses were also analyzed without mothers with mental or behavioral disorder during pregnancy. The changes in the results were minor (see Supplementary Table 3), but the number of women who had inpatient care episode due symptoms, signs and abnormal clinical and laboratory findings (R00–R99) were almost halved ($n = 6,825$ vs. $3,196$).

DISCUSSION

To our knowledge, this is the first large-scale epidemiological study to investigate association between MSDP and the use of hospital services during pregnancy. This study shows that MSDP is associated with a higher incidence of hospital treatment during pregnancy for multiple diagnosis groups. Women who continued smoking throughout pregnancy received significantly more hospital treatment, especially in outpatient care, compared to those who quit smoking in the first trimester. In addition, women who smoked were more likely to be admitted to the hospital for any reason from prenatal clinic.

Many women in Finland see prenatal clinic due to the heavily subsidized health care system, thus researchers are able to closely follow the health and progress of women and their pregnancies. All prenatal clinic visits are free-of-charge; medication and hospital care have small user charges. It is very rare that women do not attend the prenatal clinic visits. In this study, prenatal clinic records showed that pregnant women who continued to smoke throughout pregnancy were more likely to not attend the prenatal clinic visits. This may reflect other substance use²⁶ and other underlying issues (e.g. unfavorable lifestyle factors, denial of pregnancy, young age).

Pregnant women are admitted to specialized hospital care from prenatal clinic when necessary. According to data derived from prenatal clinic records both women who quit and continued smoking were more likely to be admitted to hospital inpatient care for any reason, threat of preterm labor, and other not specified reasons, compared to non-smokers. The continued smoking was associated with an increased risk amount of hospitalization due to bleeding. The previous findings are contradictory, as some studies found no association between MSDP and bleeding^{27,28}. However, bleeding might be associated with the risk of preterm labor, which has been shown to increase with MSDP²⁹. Contrary to our predictions, there were no differences in most of the parameters between women who quit and continued smoking in prenatal clinic records. The reason for this could be that we could not analyze the differences by type of care, number of visits or severity of the cause (e.g. threat of preterm labor) of admission between the groups due to dichotomized information in the Medical Birth Register. The original idea was to report hospital inpatient care only, but it remains unknown if the birth hospitals have interpreted the instructions similarly. Our study findings are in line with previous findings³⁰, specifically that continuous smoking throughout pregnancy is associated with a lower risk for elevated blood pressure according to the prenatal clinic records. However, there might be other underlying factors, such as quitting smoking, that are related to elevated weight gain³¹. This idea

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remains controversial since it has been shown that smoking is associated with lower risk for hypertensive disorders, regardless of BMI³².

Smoking in general is known to be a risk factor for several diseases and may affect the severity of infectious diseases such as influenza, sepsis, pneumonia and periodontitis³³. In our study of pregnant women, we showed that MSDP was associated with increased amount of care for infectious and parasitic diseases (A00–B99) and respiratory tract diseases (J00–J99), with the greatest association seen in the continued smoking group. The amount of outpatient care for genitourinary system diseases (N00–N99) was higher in both smoking groups and the amount of inpatient care in the continued smoking group. Continuous smoking throughout the pregnancy may increase the risk for more difficult diseases (infections for example) that require inpatient hospital admission. Importantly, there is also evidence that infections may increase the risk for preterm labor³⁴.

The higher amount of inpatient care in diagnoses related to pregnancy, childbirth and puerperium (O00–O99), is in agreement with previous studies, where effects of MSDP seemed to be dose-related to risk for preterm birth and low birth weight³⁵. The results of inpatient hospital treatment regarding this ICD-10 chapter were similar in Denmark²⁰, even though the study did not differentiate between continued or quit smoking.

The association between MSDP and mental and behavioral disorders in both smoking groups are more likely to be explained by comorbidities^{36,37} rather than a causal effect of MSDP. It is well known that women with psychiatric problems tend to smoke more often, also during pregnancy³⁸, and have unfavorable lifestyles when compared to other pregnant women³⁷. These women are often less educated and have lower socioeconomic statuses than others³⁹. Interventions should target this population of pregnant women (i.e., women with existing mental or behavioral condition) in prenatal clinic.

One particularly concerning finding is that women who smoke during pregnancy have more hospital outpatient and inpatient care due to injury, poisoning and other external causes. The association was strongest among women who continued to smoke and received inpatient hospital care. This finding might also reflect unfavorable lifestyle factors, like alcohol consumption and other substance use, which predisposes pregnant women to traumas^{25,40}. Additionally, pregnant women are more commonly victims of domestic violence in families with history of violence and depressive symptoms⁴¹.

The strengths of this study include the use of a large national study population covering all singleton pregnancies with information on smoking available (96%) from 1999 to 2015. The data covered information from the whole of Finland composed from national registers, which have been shown to be reliable for research purposes^{22,23}. Another strength of this study was that we obtained information on pregnant women who quit smoking during their first trimester as well as those who continued smoking throughout the pregnancy, which allows us to evaluate the effect of duration of MSDP.

The main limitation of this data is the accuracy of the smoking information, which is based on mother's self-reporting and collected by nurses in prenatal clinics. According to previous studies, people tend to underestimate their smoking⁴², which might further underestimate the effect of MSDP in our results. Birth Register has been found to be satisfactory for reliability of MSDP data⁴³. Details about smoking prior to the pregnancy (i.e. cessation point) are not collected and cannot be derived from any other current register. Therefore, "not smoking" group includes also women who are former smokers or quit while planning the pregnancy. Unfortunately, we did not have information on pre-existing medical conditions or other lifestyle factors than smoking (e.g. maternal alcohol or illicit drug use during pregnancy) nor could this data be reliably obtained from anywhere else.

When considering the results, we have to take into account that many diagnoses can be found in two ICD-10 diagnosis chapters for pregnant women (e.g. pyelonephritis N10 and pyelonephritis during pregnancy O23.0), therefore, cross group analyses as well as more detailed analysis of different diagnoses should be performed in the future. The question remains if our findings reflect readily impaired maternal health associated with MSDP and further research should be conducted to disentangle the effect of smoking from other underlying causes due to maternal overall health on maternal diagnoses during pregnancy.

Our study emphasizes that it is never too late to quit smoking during pregnancy. Pregnant women can obtain health benefits even during those few months in the second and third trimesters if they quit smoking during the first trimester. Our study also allowed us to evaluate the duration of smoking exposure, as many studies before have not differentiated between smoking in the early and late pregnancy. Especially, the need for outpatient treatment is reduced if mother quits smoking.

In conclusion, the results of this study show, that women, who smoke during pregnancy, utilize greater rates of hospital services during pregnancy compared to non-smoking women. As the health care system in Finland is largely publicly funded the use of health care services should reflect the actual need. This is economically significant and further attempts to reduce the MSDP rates should be made. As we discussed, it is likely that some of the observed associations we found is explained by unmeasured factors like maternal psychiatric problems and unfavorable lifestyle factors rather than causal effects of MSDP. However, this study emphasizes the importance of actions for smoking cessation during pregnancy and for supporting the health related behavior of smoking pregnant women.

FUNDING

This work was supported by the Foundation for Pediatric Research (Finland) (Wallin and Ekblad), Duodecim Research Foundation (Wallin), the Turku University Hospital Research Foundation (Wallin and Ekblad), the Orion Research Foundation sr (Ekblad), the Emil Aaltonen's Foundation (Ekblad), the Paulo Foundation (Ekblad), and the Maud Kuistila Memorial Foundation (Ekblad).

DECLARATION OF INTERESTS

None declared.

ACKNOWLEDGEMENTS

We want to thank Emily P. Rolan, M.S. from HDFS, Purdue University, West Lafayette, Indiana, USA for language editing.

REFERENCES

1. National Institute for Health and Welfare of Finland. Statistics on tobacco.
<http://urn.fi/URN:NBN:fi-fe2017111550709>. Accessed March 18, 2019.
2. National Institute for Health and Welfare of Finland. Perinatal statistics - parturients, delivers and newborns 2017 in Finland.
https://thl.fi/tilastoliite/tilastoraportit/2018/Perinataalitulasto_ennakot_2017.pdf. Accessed March 18, 2019.
3. Ekblad M, Gissler M, Korkeila J, Lehtonen L. Trends and risks groups for smoking during pregnancy in Finland and other Nordic countries. *Eur J Public Health*. 2014;24(4):544-551.
4. Jaddoe VW, Troe EJ, Hofman A, et al. Active and passive maternal smoking during pregnancy and the risks of low birthweight and preterm birth: the Generation R Study. *Paediatr Perinat Epidemiol*. 2008;22(2):162-171.
Wallin HP, Gissler M, Korhonen PE, Ekblad M. Maternal Smoking and Hospital Treatment During Pregnancy. *Nicotine Tob Res*. 2019 Aug 16:ntz137. doi: 10.1093/ntr/ntz137.

5. Ko T-J, Tsai L-Y, Chu L-C, et al. Parental Smoking During Pregnancy and Its Association with Low Birth Weight, Small for Gestational Age, and Preterm Birth Offspring: A Birth Cohort Study. *Pediatr Neonatol*. 2014;55(1):20-27.
6. Horta BL, Victora CG, Menezes AM, Halpern R, Barros FC. Low birthweight, preterm births and intrauterine growth retardation in relation to maternal smoking. *Paediatr Perinat Epidemiol*. 1997;11(2):140-151.
7. Roza SJ, Verburg BO, Jaddoe VW, et al. Effects of maternal smoking in pregnancy on prenatal brain development. The Generation R Study. *Eur J Neurosci*. 2007;25(3):611-617.
8. Ekblad M, Korkeila J, Lehtonen L. Smoking during pregnancy affects foetal brain development. *Acta Paediatr*. 2015;104(1):12-18.
9. Pineles BL, Park E, Samet JM. Systematic review and meta-analysis of Miscarriage and Maternal Exposure to Tobacco Smoke During Pregnancy. *Am J Epidemiol*. 2014;179(7):807-823.
10. Hayashi K, Matsuda Y, Kawamichi Y, Shiozaki A, Saito S. Smoking During Pregnancy Increases Risks of Various Obstetric Complications: A Case-Cohort Study of the Japan Perinatal Registry Network Database. *J Epidemiol*. 2011;21(1):61-66.
11. Roelands J, Jamison MG, Lyster AD, James AH. Consequences of Smoking during Pregnancy on Maternal Health. *J Womens Health (Larchmt)*. 2009;18(6):867-872.
12. Fell DB, Dodds L, Joseph KS, Allen VM, Butler B. Risk factors for hyperemesis gravidarum requiring hospital admission during pregnancy. *Obstet Gynecol*. 2006;107:277-284.
13. Wei J, Liu C-X, Gong T-T, Wu Q-J, Wu L. Cigarette smoking during pregnancy and preeclampsia risk: a systematic review and meta-analysis of prospective studies. *Oncotarget*. 2015;6(41):43667-43678.
14. Marcoux S, Brisson J, Fabia J. The effect of cigarette smoking on the risk of preeclampsia and gestational hypertension. *Am J Epidemiol*. 1989;130(5):950-957.

15. Gudnadóttir TA, Bateman BT, Hernández-Díaz S, Luque-Fernandez MA, Valdimarsdóttir U, Zoega H. Body Mass Index, Smoking and Hypertensive Disorders during Pregnancy: A Population Based Case-Control Study. *PLoS One*. 2016;11(3):e0152187. doi:10.1371/journal.pone.0152187.
16. Bennett TA, Kotelchuck M, Cox CE, Tucker MJ, Nadeau DA. Pregnancy associated hospitalizations in the United States in 1991 and 1992: a comprehensive view of maternal morbidity. *Am J Obstet Gynecol*. 1998;178(2):346–354.
17. Shrim A, Ates S, Mallozzi A, Brown R, Ponette V, Levin I, et al. Is young maternal age really a risk factor for adverse pregnancy outcome in a canadian tertiary referral hospital? *J Pediatr Adolesc Gynecol*. 2011;24(4):218-222.
18. Liu S, Heaman M, Sauve R, et al. An analysis of prenatal hospitalization in Canada, 1991–2003. *Matern Child Health J*. 2007;11(2):181-187.
19. de Vienne CM, Creveuil C, Dreyfus M. Does young maternal age increase the risk of adverse obstetric, fetal and neonatal outcomes: a cohort study? *Eur J Obstet Gynecol Reprod Biol*. 2009;147(2):151-156.
20. Bendix J, Hegaard HK, Langhoff-Roos J, Bergholt T. Changing prevalence and the risk factors for prenatal obstetric hospitalizations in Denmark 2003–2012 *Clin Epidemiol*. 2016;8:165-175.
21. Rostad B, Schei B. Factors predicting prenatal hospital admission in pregnancy. *Scand J Prim Health Care*. 1998;16(2):85–89.
22. Gissler M, Teperi J, Hemminki E, Meriläinen J. Data quality after restructuring a nationwide medical birth registry, *Scand J Soc Med*. 1995;23(1):75-80.
23. Teperi J. A multi-method approach to the assessment of data quality in the Finnish Medical Birth Registry. *J Epidemiol Commun H*. 1993;47(3):242-247.
24. Sund R. Quality of the Finnish Hospital Discharge Register: a systematic review. *Scand J Public Health*. 2012;40(6):505–515.

25. Havens JR, Simmons LA, Shannon LM, Hansen WF. Factors associated with substance use during pregnancy: results from a national sample. *Drug Alcohol Depend.* 2009;99(1-3):89-95.
 26. Aliyu MH, Wilson RE, Zoorob R, et al. Prenatal alcohol consumption and fetal growth restriction: potentiation effect by concomitant smoking. *Nicotine Tob Res.* 2009;11(1):36-43.
 27. Yang J, Savitz DA, Dole N, et al. Predictors of vaginal bleeding during the first two trimesters of pregnancy. *Paediatr Perinat Epidemiol.* 2005;19(4):276-283.
 28. Gargano JW, Holzman CB, Senagore PK, et al. Evidence of placental haemorrhage and preterm delivery. *BJOG.* 2010 Mar;117(4):445-455.
 29. Shah NR, Bracken MB. A systematic review and meta-analysis of prospective studies on the association between maternal cigarette smoking and preterm delivery. *Am J Obstet Gynecol.* 2000;182(2):465-472.
 30. Engel SM, Scher E, Wallenstein S, et al. Maternal active and passive smoking and hypertensive disorders of pregnancy: risk with trimester-specific exposures. *Epidemiology.* 2013;24(3):379-386.
 31. Levine MD, Cheng Y, Marcus MD, Emery RL. Psychiatric disorders and gestational weight gain among women who quit smoking during pregnancy. *J Psychosom Res.* 2015;78(5):504-508.
 32. Voigt M, Neudecker K, Schneider KT, et al. Effects of smoking specified as cigarettes per day and maternal body mass index on hypertensive disorders of pregnancy. *Z Geburtshilfe Neonatol.* 2013;217(1):24-27.
 33. Huttunen R, Heikkinen T, Syrjänen J. Smoking and the outcome of infection. *J Intern Med.* 2011;269(3):258-269.
 34. Goldenberg RL, Culhane JF, Johnson DC. Maternal Infection and Adverse Fetal and Neonatal Outcomes. *Clin Perinatol.* 2005;32:523-559.
 35. Grote NK, Bridge JA, Gavin AR, Melville JL, Iyengar S, Katon WJ. A Meta-analysis of Depression During Pregnancy and the Risk of Preterm Birth, Low Birth Weight, and Intrauterine Growth Restriction. *Arch Gen Psychiatry.* 2010;67(10):1012-1024.
- Wallin HP, Gissler M, Korhonen PE, Ekblad M. Maternal Smoking and Hospital Treatment During Pregnancy. *Nicotine Tob Res.* 2019 Aug 16:ntz137. doi: 10.1093/ntr/ntz137.

36. Dagklis T, Papazisis G, Tsakiridis I, Chouliara F, Mamopoulos A, Rousso D. Prevalence of prenatal depression and associated factors among pregnant women hospitalized in a high-risk pregnancy unit in Greece. *Soc Psychiatr Epidemiol*. 2016;51(7):1025-1031.
37. Whitaker RC, Orzol SM, Kahn RS. Maternal mental health, substance use, and domestic violence in the year after delivery and subsequent behavior problems in children at age 3 years. *Arch Gen Psychiatry*. 2006;63(5):551-560.
38. Tong VT, Farr SL, Bombard J, D'Angelo D, Ko JY, England LJ. Smoking Before and During Pregnancy Among Women Reporting Depression or Anxiety. *Obstet Gynecol*. 2016;128(3):562-570.
39. Smedberg J, Lupattelli A, Mårdbj A-C, Øverland S, Nordeng H. The relationship between maternal depression and smoking cessation during pregnancy—a cross-sectional study of pregnant women from 15 European countries. *Arch Wom Ment Health*. 2015;18(1):73-84.
40. Alvik A, Heyerdahl S, Haldorsen T, Lindemann R. Alcohol use before and during pregnancy: a population-based study. *Acta Obstet Gynecol Scand*. 2006;85(11):1292-1298.
41. Finnbogadóttir H, Dykes AK, Wann-Hansson C. Prevalence of domestic violence during pregnancy and related risk factors: a cross-sectional study in southern Sweden. *BMC Wom Health*. 2014;14:63.
42. George L, Granath F, Johansson AL, Cnattingius S. Self-reported nicotine exposure and plasma levels of cotinine in early and late pregnancy. *Acta Obstet Gynecol Scand*. 2006;85(11):1331–1337.
43. Gissler M, Teperi J, Hemminki E, Meriläinen J. Short Communication: Data Quality after Restructuring a National Medical Registry. *Scand J Soc Med*, 1995;23(1):75–80.

Table 1 Characteristics of the Subjects According to Smoking Status

	Total	Not smoking	Quit smoking	Continued smoking	No information about smoking
Age (years)					
Less than 20	24,306 (2.5%)	12,224 (50.3%)	2,535 (10.4%)	8,817 (36.3%)	730 (3.0%)
20-24	153,232 (15.9%)	106,754 (69.7%)	11,885 (7.8%)	30,504 (19.9%)	4,089 (2.7%)
25-29	301,551 (31.4%)	251,611 (83.4%)	13,748 (4.6%)	28,705 (9.5%)	7,487 (2.5%)
30-34	300 409 (31.3%)	262,622 (87.4%)	9,268 (3.1%)	20,857 (6.9%)	7,662 (2.6%)
35-39	147,488 (15.3%)	129,085 (87.5%)	3,579 (2.4%)	10,785 (7.3%)	4,039 (2.7%)
40 or more	34,140 (3.6%)	29,699 (87.0%)	707 (2.1%)	2,727 (8.0%)	1,007 (2.9%)
Marital status					
Married	561,008 (58.4%)	500,732 (89.3%)	14,367 (2.6%)	31,625 (5.6%)	14,284 (2.5%)
Cohabiting	292,850 (30.5%)	220,460 (75.3%)	20,450 (7.0%)	45,473 (15.5%)	6,467 (2.2%)
Single	95,189 (9.9%)	62,460 (65.6%)	6,462 (6.8%)	23,349 (24.5%)	2,918 (3.1%)
Parity					
0	398,525 (41.5%)	319,619 (80.2%)	24,958 (6.3%)	45,746 (11.5%)	8,202 (2.1%)
1	322,248 (33.5%)	273,392 (84.8%)	10,454 (3.2%)	29,753 (9.2%)	8,649 (2.7%)
2	144,432 15.0%	119,759 (82.9%)	4,304 (3.0%)	15,964 (11.1%)	4,405 (3.0%)
3	50,121 (5.2%)	40,430 (80.7%)	1,335 (2.7%)	6,668 (13.3%)	1,688 (3.4%)
4	19,044 (2.0%)	15,480 (81.3%)	412 (2.2%)	2,486 (13.1%)	666 (3.5%)
5 or more	25,913 (2.7%)	23,027 (88.9%)	254 (1.0%)	1,743 (6.7%)	889 (3.4%)
Socioeconomic status					
Upper white collar	158,423 (16.5%)	147,996 (93.4%)	2,933 (1.9%)	3,972 (2.5%)	3,522 (2.2%)
Lower white collar	318,657 (33.2%)	269,328 (84.5%)	13,272 (4.2%)	28,148 (8.8%)	7,909 (2.5%)
Blue collar worker	129,561 (13.5%)	93,247 (72.0%)	7,823 (6.0%)	24,858 (19.2%)	3,633 (2.8%)
Other	354,486 (36.9%)	281,424 (79.4%)	17,694 (5.0%)	45,418 (12.8%)	9,950 (2.8%)
Body-mass index (kg/m²)					
Less than 20.0	91,274 (9.5%)	73,949 (81.0%)	4,968 (5.4%)	10,557 (11.6%)	1,800 (2.0%)
20.0-24.9	340,547 (35.4%)	288,882 (84.8%)	16,808 (4.9%)	28,448 (8.4%)	6,409 (1.9%)
25.0-29.9	142,637 (14.8%)	116,612 (81.8%)	8,333 (5.8%)	14,839 (10.4%)	2,853 (2.0%)
30.0-34.9	52,949 (5.5%)	41,529 (78.4%)	3,404 (6.4%)	6,889 (13.0%)	1,127 (2.1%)
35.0 or more	25,636 (2.7%)	19,680 (76.8%)	1,702 (6.6%)	3,679 (14.4%)	575 (2.2%)
unknown	273,800 (28.5%)	225,535 (82.4%)	5,760 (2.1%)	34,613 (12.6%)	7,892 (2.9%)
Fertility treatment					
IVF ^a	16,316 (1.7%)	15,209 (93.2%)	368 (2.3%)	486 (3.0%)	253 (1.6%)

Other ART ^b	13,923 (1.4%)	12,801 (91.9%)	402 (2.9%)	539 (3.9%)	181 (1.3%)
Gestational age (weeks)					
Less than 28	2,760 (0.3%)	1,942 (70.4%)	89 (3.2%)	400 (14.5%)	329 (11.9%)
28-36	41,334 (4.3%)	32,498 (78.6%)	1,779 (4.3%)	5,487 (13.3%)	1,570 (3.8%)
37-41	868,950 (90.4%)	719,261 (82.8%)	37,470 (4.3%)	91,245 (10.5%)	20,974 (2.4%)

Table 1. Characteristics of the Subjects According to Smoking Status (continued)

42 or more	45,153 (4.7%)	37,032 (82.0%)	2,350 (5.2%)	4,908 (10.9%)	863 (1.9%)
Residential area					
Urban	647,719 (67.4%)	537,998 (83.1%)	27,637 (4.3%)	66,880 (10.3%)	15,204 (2.3%)
Semiurban	157,850 (16.4%)	127,980 (81.1%)	7,330 (4.6%)	17,740 (11.2%)	4,800 (3.0%)
Rural	152,702 (15.9%)	123,790 (81.1%)	6,710 (4.4%)	17,629 (11.5%)	4,573 (3.0%)
Abroad	2,856 (0.3%)	2,227 (78.0%)	45 (1.6%)	147 (5.1%)	437 (15.3%)
Birth weight (grams)					
Less than 1500	6,067 (0.6%)	4,410 (72.7%)	220 (3.6%)	886 (14.6%)	551 (9.1%)
1500-2499	24,946 (2.6%)	18,476 (74.1%)	1,044 (4.2%)	4,534 (18.2%)	892 (3.6%)
2500-3999	756,646 (78.7%)	619,375 (81.9%)	32,992 (4.4%)	85,614 (11.3%)	18,665 (2.5%)
4000 or more	172,474 (17.9%)	149,462 (86.7%)	7,461 (4.3%)	11,328 (6.6%)	4,223 (2.4%)
F00-F99 diagnosis during pregnancy					
No diagnosis	901,609 (96.3%)	770,711 (85.5%)	38,967 (4.3%)	91,931 (10.2%)	-
Mother has during pregnancy	34,504 (3.7%)	21,284 (61.7%)	2,755 (8.0%)	10,465 (30.3%)	-
^a IVF = in vitro fertilization ^b other ART = assisted reproductive technology i.e. ovulation induction, intrauterine insemination					

Table 2. Information from Birth Register (Prenatal Clinic) Records

	Adjusted odds ratios and 95% confidence intervals			
	No smoking	Quit smoking	Continued smoking	Total ^c
Did not attend prenatal clinic	1 [Reference]	0.94 (0.78-1.12)	1.83 (1.68-1.99)	3,554
No control visits in hospital	1 [Reference]	1.45 (1.40-1.51)	1.48 (1.44-1.51)	92,908
Hospital care for any reason	1 [Reference]	1.20 (1.16-1.23)	1.21 (1.19-1.24)	121,826
Hospital care due to bleeding	1 [Reference]	1.09 (0.98-1.23)	1.20 (1.13-1.27)	9,625
Hospital care due to elevated blood pressure	1 [Reference]	1.03 (0.97-1.10)	0.79 (0.76-0.83)	26,310
Hospital care due to threat of preterm labor	1 [Reference]	1.35 (1.26-1.45)	1.40 (1.34-1.45)	20,714
Hospital care for other reason	1 [Reference]	1.24 (1.19-1.28)	1.28 (1.26-1.31)	83,958
^c Total number presents the number of women with visits				

Figure 1. Adjusted odds ratios of maternal outpatient care according to ICD-10 chapters

Adjusted odds ratios and 95% confidence intervals presented in different ICD-10 chapters in both smoking groups. Non-smokers = 1 (reference).

Figure 1. Adjusted odds ratios of maternal outpatient care according to ICD-10 chapters

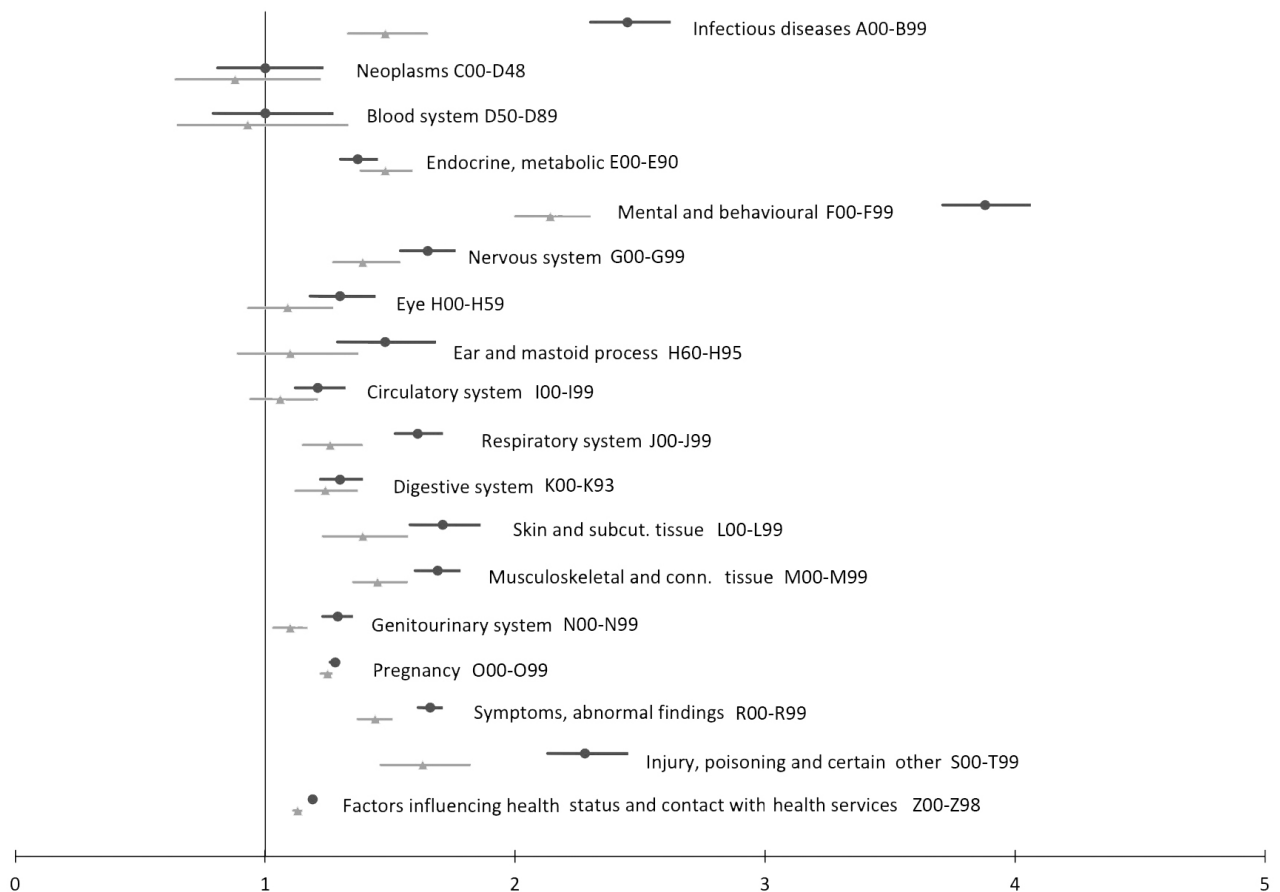


Figure 2. Adjusted odds ratios of maternal inpatient care according to ICD-10 chapters

Adjusted odds ratios and 95% confidence intervals presented in different ICD-10 chapters in both smoking groups. Non-smokers = 1 (reference).

