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Patterns and predictors for prescription of psychotropics and mood-stabilizing antiepileptics during pregnancy in Denmark 2000-2016.

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Abstract

Aims To analyze prescribing patterns during pregnancy for antipsychotics (AP), antidepressants (AD) and mood-stabilizing antiepileptics (AEDs) in Denmark from 2000-2016.

Methods Data were obtained from the Danish Medical Birth Register, the Register for Legally Induced Abortions, the Danish National Patient Register and the Register of Medicinal Product Statistics. Data were linked through a unique personal identifier (CPR) by Statistics Denmark.

Results The use of antipsychotics (AP) increased 2.5-fold from a prevalence of 1.5 per 1,000 pregnancies to 3.8 for pregnancies ending in a delivery. Use of mood-stabilizing AEDs increased from a prevalence of 0.1 to 2.1 during the study period. The prevalence for AP and mood-stabilizing AEDs was nearly twice as high for pregnancies ending in miscarriage or termination compared to pregnancies ending in delivery. A marked increase in the prevalence of AD use during pregnancy was seen from 2000-2011 (from 6 to 41 per 1000 pregnancies ending in a delivery) but appears slightly in decline. Age, smoking, obesity and social status were generally associated with increased use of psychotropic drugs.

Conclusions The use of AP, AD and mood-stabilizing AEDs during pregnancy has increased substantially in Denmark from 2000-2016. The use of AD appears slightly in decline from 2011.

Key Words antidepressants, antipsychotics, pregnancy, drug utilization
What is already known about this subject

- Treatment indications and choice of psychotropic drug treatment during pregnancy is complex and remain controversial
- Recent year patterns and predictors of psychotropic drug utilization during pregnancy are insufficiently studied

What this study adds

- A substantial 2 to 10-fold increase in the filled prescription of antidepressants, antipsychotics and mood-stabilizing antiepileptics were found from 2000-2016 in Denmark
- The filled prescription rate of second-generation antipsychotics, especially quetiapine, has increased sharply since 2005
- Age, smoking, obesity and social status were associated with increased rates of filled prescriptions for psychotropic drug
Introduction

The use of psychopharmacological drugs during pregnancy has been subject to considerable controversy for the last decade. While there is reasonably consensus that antidepressants (AD), specifically Selective Serotonin Re-uptake Inhibitors (SSRIs), are unlikely to pose a substantial risk to the unborn child (1–5), controversy remains on certain specific issues, not least the hypothesized impact on childhood neurodevelopment (6–11). For antipsychotic drugs (AP), the amount of data is less impressive, and the amount of safety data available has been lagging the transition from usage patterns from first-generation antipsychotics (FGAP) to second-generation antipsychotics (SGAP) (12–15). During the last 5 years, a substantial amount of safety data has emerged for the SGAP olanzapine and quetiapine especially (16–18), while data for other SGAP remain relatively scarce (15–17,19,20). Antiepileptic drugs (AED), used as mood stabilizers within psychiatry, is poorly evaluated for safety during pregnancy except for lamotrigine, which is considered safe, and valproate, which poses a significant risk of major congenital malformations (21–24).

Perception of teratogenicity of these drugs among treating physicians is an important factor to select the drug with the best level of safety evidence (25,26). National and international guidelines on the use of these drugs tend to be quite trivial (e.g. “should be used only if the expected beneficial effects outweigh the possible risks”) and rarely offer treating physicians meaningful decision support. These recommendations may change per emerging evidence and implementation thereof in various decision support systems as well as per regulatory designations and specific warnings. Both in the USA and in the UK, no updated specific decision support is offered for the choice of AP during pregnancy (26,27) and neither from the World Federation of Societies of Biological Psychiatry (28). In Denmark, national guidelines and treatment recommendations have emerged during the last 5 years suggesting sertraline, olanzapine, quetiapine and lamotrigine be first-line drugs during pregnancy for
antidepressive, antipsychotic and mood-stabilizing purposes, respectively (15). The extent to which actual prescription practices reflect guidelines and recommendations and the developing knowledge on safety during pregnancy is poorly documented.

Using complete and validated national filled prescription and health-care registers, we performed an up-to-date drug utilization study on the filled prescription pattern of ADs, APs and mood-stabilizing AEDs during pregnancy.

**Aims of the study**

We quantified the utilization pattern among pregnant women in treatment with APs, ADs and mood-stabilizing AEDs in Denmark from 2000-2016. For each group of drugs, and the most commonly prescribed individual drugs, we described the development in prevalence and, by regression analysis, the association to maternal demographic characteristics. We described the utilization patterns specifically for pregnancies resulting in live births or stillbirths, and pregnancies resulting in miscarriage or termination. We describe the utilization patterns according to clinical psychiatric diagnoses.

**Material and methods**

We included all pregnancies in Denmark from 2000-2016 and collected data on all filled prescriptions for APs, ADs and mood-stabilizing AEDs among pregnant women. The data were obtained from the following Danish national registries: the Danish Medical Birth Register (MBR) (29), the Danish National Patient Register (DNPR)(30), the Register of Legally Induced Abortions (ABR) a sub register of the DNPR, and the Register of Medical Products Statistics (RMPS)(31). Socioeconomic status, annual income, and level of education were obtained from Statistics Denmark. Data on income and socioeconomic status was only available until 2015.
Data sources

The MBR contains data on all live births and stillbirths in Denmark since 1968, comprising both hospital and home deliveries. Since 1997, the MBR has primarily been based on the DNPR but has been supplemented with data on home deliveries and stillbirths (32).

The MBR was supplemented with data from the DNPR and the ABR to include all pregnancies in Denmark from 2000-2016. ABR was established in 1974 and has since 1995 been a sub-registry of the DNPR. The DNPR holds information on all hospitalizations since 1977 and all outpatient visits, patients from emergency rooms and psychiatric wards since 1995 (30). It uses the 10th revision of the International Classification of Disease (ICD-10) by the World Health Organization (WHO).

The Danish National Prescription Registry, a subset of the RMPS of the Danish Medicines Agency, provides full coverage of individual-level prescription drugs filled at Danish pharmacies by Danish citizens since 1995 (31). The register includes detailed information on drug type, dispensing date, package size, identification number of the drug and prescription refills linked to an encrypted unique personal identification number. The register does, however, not include information on the indication of treatment, the daily dose prescribed, over-the-counter drugs and treatments during hospitalization (31). The drugs are classified according to the Anatomic Therapeutic Chemical (ATC) code established by WHO (33).

Data Linkage

In 1968, all Danish residents were assigned a unique identification number (CPR number) and registered in the Danish Civil Registration System (34). This unique identification number enables linkage across the different registers in this study. All linkage between these registers was performed by Statistics Denmark.
Analysis

We performed an individual-based analysis of data based on all pregnancies in Denmark from 2000 to 2016, both years included. Any individual with a previous diagnosis of epilepsy was excluded in the selection process. As we were only interested in exposure to AEDs, with a mood-stabilizing indication (and not e.g. neuropathic pain), we limited filled prescriptions for AEDs to those within 120 days before or after a filled prescription of either an antipsychotic or antidepressant drug.

Annual prevalence was defined as the number of women per 1,000 pregnant women in the population per calendar year who collected at least one filled prescription for one or more drugs overall and within each of the respective drug groups. The annual prevalence was calculated in total and for each of the three main drug groups: APs (ATC group: N05A), ADs (N06A), and AEDs (N03A).

Stratified analyses within each drug group were performed. APs were stratified as FGA, SGA and others. ADs were stratified as SSRI, Tricyclic Antidepressants (TCA) and others. The use of the five most common single substances within each of the three main drug groups was calculated and presented separately.

To demonstrate demographic differences between users and non-users of any of the considered psychotropic medications, we tabulated selected demographic subgroups for both overall drug use and use of each of the three main drug groups. Demographic variables for all included pregnancies included: maternal age at delivery, mother’s level of education, annual income, and socioeconomic status. Data on income and socioeconomic status was only available until 2015. For women with a pregnancy outcome in 2016, the income and socioeconomic data reflected their status in 2015. Demographic variables only tabulated for deliveries included: gestational age in weeks at delivery, pre-pregnancy body mass index (BMI) measured at the first antenatal visit, smoking status, and parity.
Timing of treatment before, during and after pregnancy was determined for all deliveries. We calculated the prevalence of the most common drugs within each of the three drug groups specified by five three-month periods: Three months prior to first day of pregnancy, 1\textsuperscript{st} (day 1-90) 2\textsuperscript{nd} (day 91-180) and 3\textsuperscript{rd} (day 181 to end of pregnancy) trimester of pregnancy, and three months after pregnancy. Exposure was defined as collection of one or more filled prescriptions for each main group and single drug within each period. Date of collection was used to define timing of filled prescription and did not take duration of treatment into account.

Diagnoses were assessed by linking pregnant women, who filled for psychotropic drugs prescriptions, with ICD-10 codes (F20-F48) DNPR database through the CPR identifier.

All analyses were performed using Stata Version 14.2 (Stata-Corp, College Station, TX, USA).

Ethics approval

Not applicable. Under Danish law, the use of anonymized healthcare data for pharmacoepidemiological research does not require subject consent or approval from Ethics Committee or

Results

We identified 1,442,196 pregnancies in Denmark from 1 January 2000 to 31 December 2016; the cohort selection process is illustrated in Figure 1.

Demographic characteristics and statistical inferences are listed in Table 1. The OR for filled prescriptions was higher among women who were older, obese or smokers and for women with low employment and in the second-lowest income status. While we are unable to link directly from diagnosis to filled prescriptions, patterns of utilization appear to compare reasonably well with the clinical diagnoses and approved indications (Supplementary Table
1). We observed a high filled prescription rate (13-31%) for AP among individuals assigned diagnoses for schizophrenia, schizotypal and delusional disorders or mood [affective] disorders including manic episode and bipolar affective disorder. (ICD-10 F20-F31).

We found prevalences among liveborn deliveries of 0.9, 24.0 and 3.4 per 1000 for filled prescriptions of an AP, AD or a mood-stabilizing AED. During the entire study period, 2.7% of women with a recorded delivery, 3.7% of women with a recorded miscarriage and 4.3% of women with a recorded termination of pregnancy had filled at least one AP, AD or mood-stabilizing AED prescription during pregnancy. The total use during pregnancy was highest in 2010-2011 with prevalence between 39.4 and 42.8 for deliveries, and prevalence between 42.4 and 44.4 for miscarriages and terminations (Supplementary Figure 1a-c), mainly reflecting ADs.

The prevalence for ADs increased 6-fold for deliveries and 4-fold for miscarriages and terminations from 2000-2011. A visible decline in 2012 is observed followed by a slight decrease since (Figure 2a-f).

The use of APs more than doubled during the study period with a prevalence of 3.8 for deliveries in 2016, mainly driven by SGAP, especially quetiapine (Figure 3a-f). The shift in use from FGAPs to SGAPs materializes clearly around 2011-2012.

The use of mood-stabilizing AEDs increased quite substantially for all pregnancies in the period of 2000-2016 (Figure 4a-c). Lamotrigine was the most used mood-stabilizing AED with a prevalence of 1.5 for deliveries and a prevalence of 2.7 for miscarriages and terminations in 2016. The rate of filled prescriptions for pregabalin appears to rise continuously since its introduction to the market.
Prevalence of antiepileptic, antipsychotic and antidepressant exposure among deliveries as related to preconception, specific trimesters and post-delivery are listed in Supplementary table 2. Detailed timing of specific drug exposure among deliveries is listed in Supplementary Table 3.

Discussion

In this up-to-date register-based population study of all pregnancies in Denmark between 2000 and 2016, we found prevalences among liveborn deliveries of 0.9, 24.0 and 3.4 per 1000 for filled prescriptions of an AP, AD or a mood-stabilizing AED. The OR for filling a prescription for an AP, AD or mood-stabilizing AED was higher among women, who smoked, were older, obese or had low socio-economic status. Inferential covariate analyses were only made for “any” psychotropic exposure and this this analysis is mainly driven by the use of antidepressants which account for about 85% of all psychotropic drugs used. Filled prescription rates according to clinical diagnosis, approved indications and clinical guidelines appeared reasonable (Supplementary Table 1). Generally, we found higher prevalences for the cohort comprising miscarriages and especially elective terminations. Elective terminations are more common among patients suffering from a psychiatric diagnosis (35,36), among young women and teenagers, and in women with low socio-economic status (37). The distribution of specific drug exposures appears similar among pregnancies ending in miscarriages and elective abortions (Figures 2b,c,e,f and 3b,c,e,f, and 4b,c) with the exception of perphenazine (Figure 3e).

The main strength of this study is the use of the up-to-date validated and complete Danish population-based registers (29–31) and the linkage on individual level between various health-care-related registers through Statistics Denmark. The use of these national registries ensures that data on drug use during pregnancy, whether it ended in live birth, stillbirth, miscarriage or termination, come from a well-defined, unselected population, hence reducing
selection bias. The Danish National Prescription Registry has a high coverage and quality of filled prescription data (31). All data are registered prospectively and do not rely on maternal involvement or self-report, which eliminates recall bias. If length of pregnancy or last date of menstruation were missing less than 1% of all deliveries), we did not estimate length of pregnancy to avoid drug exposure misclassification.

There are several limitations of our study as well. We used filled prescription data as a proxy for the pregnant women taking the drug. This assumption could lead to an overestimation of the drug use during pregnancy, and we did not have any data on changes in treatment upon pregnancy realization. The RMPS do not cover in-hospital use; however, this is unlikely to be relevant as study drugs are typically prescribed for prolonged use. We did not study specific intervals of filled drug prescriptions within pregnancy. Such is of interest but beyond the scope of this paper. We excluded all women diagnosed with epilepsy and for women purchasing an AED we only classified women who also filled a prescription for an AP or AD drug within 120 days before or after purchasing the AED as exposed. This latter approach was a proxy to exclude other indications for treatment with AED, as we could not account for the specific indication for filled prescriptions, and some patients may have received two different drug classes for different indications. We are not able to account for the utilization pattern of AP or AD for psychiatric disorders in women with a diagnosis of epilepsy, but this is unlikely to be of major influence our analysis and interpretation as the proportion of patients with epilepsy was low. Some covariate data are incomplete; notably 28% for BMI is missing. This compromises the inferences that can be made from the analysis of weight as a covariate.
Antidepressants

The use of AD during pregnancy increased in Denmark until 2011, upon which utilization stabilized with a slight decrease in most recent years. The former observation corresponds well with patterns elsewhere in Europe though data are only available until 2010 (38,39). The current Danish filled prescription rate of SSRIs of about 20 per 1000 pregnancies compares reasonably well to e.g. the latest data (2004-2010) for the Netherlands while below the rate described for the UK. European filled prescription rates are still considerably below estimates from USA that suggest pregnancy prevalence of about 80 per 1000 (40). Citalopram, sertraline and fluoxetine are the most popular ADs in Northern Europe, while in the Netherlands and Italy, paroxetine was more widely prescribed until about 2010. Various national and international guidelines have later been changed, as concerns on potential teratogenic effects of paroxetine and, to a lesser extent, fluoxetine emerged (1,4,15,38). Sertraline and citalopram were the most used ADs in Denmark, corresponding well to implementation of newer Danish guidelines (15) and changes to the recommendation in the primary Danish decision support system (www.pro.medicin.dk). Specifically, the status of sertraline as the first-line drug can be identified in our data.

Antipsychotics

From around 2014, the use of SGAP, especially olanzapine, in pregnancy has been recommended as first-line antipsychotic drugs during pregnancy in the most commonly used medical decision support system for health care professionals, www.pro.medicin.dk. A joint multidisciplinary guideline was issued in 2015, recommending either olanzapine or quetiapine (15). These recommendations and guidelines are well reflected in the observed utilization pattern. Quetiapine is now the predominantly prescribed AP during pregnancy in Denmark comprising more than 50% all filled AP prescriptions. In the USA, a 2.5-fold increase was observed for use of SGAP during pregnancy in their study period (2001-2007).
with much higher prevalence of SGAP, reaching 8.2 per 1000 in 2007, while 1.2 per 1000 in Denmark (13). Recent data from UK and Sweden report prevalences of 2.8 and 1.4 per 1000 for 2012 and 2009, respectively (41,42). The markedly higher prevalence, while still low in absolute terms, in the USA could be due to selection bias, clinical practice and differences in use of APs or methods used to identify medication exposure. While not recommended in Denmark, chlorprothixene has been one of the most commonly prescribed APs during pregnancy but utilization use has recently declined significantly. The relatively high use of chlorprothixene could reflect several indications outside schizophrenia and, perhaps especially, its widespread use in treating withdrawal symptoms from alcohol or drug abuse. Though still uncommon, perphenazine was among the 5 most filled prescriptions for miscarriages but not for elective terminations. Perphenazine was for many years the recommended first-line APs during pregnancy based on the available amount of safety data but largely phased out from 2013 as reflected in our data. (15).

Mood-stabilizing AEDs
In accordance with Danish guidelines and recommendations, lamotrigine is the most commonly prescribed mood-stabilizing drug during pregnancy (15). Following regulatory approval by FDA and EMA for the use of lamotrigine outside the strict domain of epilepsy, the use of lamotrigine as a mood-stabilizing drug during pregnancy increased noticeably until reaching a plateau in around 2011 (figure 4a). Other Danish data specifically pertaining to treatment for bipolar disorder in pregnancy confirm this pattern of use (43). Lamotrigine monotherapy may be used in prophylactic treatment of bipolar disorders. We did not include lamotrigine monotherapy in our dataset as it is likely more widely used as monotherapy within epilepsy. A total of 288 unique pregnancies were prescribed lamotrigine alone (data not shown). Pregabalin does not hold an indication as a mood-stabilizing agent, but in our findings, it is the second-most filled prescription AED during pregnancy. Until 2017, data on
malformations and other adverse pregnancy outcome is insufficient to provide a solid clinical risk estimate for pregabalin, which consequently was not recommended during pregnancy during the study period. Recent data do not suggest that in utero exposure to pregabalin confers a substantially increased overall risk of congenital malformations (44,45). The observed increased usage pattern among pregnant women may reflect the role of pregabalin in the treatment of anxiety disorders and neuropathic pain (46). No previous studies have specifically investigated patterns of antiepileptic drugs used as mood-stabilizers.

In conclusion, we demonstrate a substantial increase in the filled prescriptions of APs and mood-stabilizing AED in Denmark from 2010-2016. The filled prescriptions of AD peaked around 2011-12 and appears now slowly declining. The most commonly drugs with filled prescription are sertraline, quetiapine and lamotrigine, and the pattern largely follows national guidelines and recommendations.

Acknowledgements
Anton Pottegård, PharmD, PhD, and Morten Olesen are acknowledged for validation of the STATA code. This study was not funded.

Conflicts of interest
The authors declare no conflicts of interest.
References


33. WHOCC - ATC/DDD Index [Internet]. [cited 2017 Jul 12]. Available from: https://www.whocc.no/atc_ddd_index/


Figure 1: Flowchart of drug purchases during pregnancy, Denmark, 2000-2016. Antipsychotics (N05A), antidepressants (N06A) and mood stabilizing antiepileptics (N03A).
Figure 2A-F Prevalences of antidepressants during pregnancy in Denmark by calendar year from 2000-2016. Deliveries covers live births and stillbirths. (A): Antidepressants among deliveries. (B) Antidepressants among miscarriages. (C): Antidepressants among terminations. (D): The five most frequent antidepressants among deliveries. (E): The five most frequent antidepressants among miscarriages. (F): The five most frequent antidepressants among terminations.
Figure 3A-F Prevalences of filled prescriptions for antipsychotics during pregnancy in Denmark by calendar year from 2000-2016. Deliveries covers live births and stillbirths. (A): Antipsychotics among deliveries. (B) Antipsychotics among miscarriages. (C): Antipsychotics among terminations. (D): The five most frequent antipsychotics among deliveries. (E): The five most frequent antipsychotics among miscarriages. (F): The five most frequent antipsychotics among terminations.
Figure 4A-C Prevalences of the five most commonly filled prescriptions for mood stabilizing antiepileptics during pregnancy in Denmark by calendar year from 2000-2016. Deliveries covers live births and stillbirths. The use of antiepileptics are only shown for women, who purchased an antipsychotic and/or antidepressant 120 days before or after purchasing an antiepileptic while excluding women with a prior diagnosis of epilepsy. (A): Mood stabilizing antiepileptics among deliveries. (B): Mood stabilizing antiepileptics among miscarriages. (C): Mood stabilizing antiepileptics among terminations.
Table 1: Demographic and clinical characteristics of women exposed to mood stabilising antiepileptic drugs, antidepressants or antipsychotics at any point during pregnancy. P: Prevalence per 1000 pregnancies

<table>
<thead>
<tr>
<th>Demographic and clinical characteristics</th>
<th>Total number of pregnancies (P)</th>
<th>Any exposure (P)</th>
<th>OR (95% CI) (any exposure)</th>
<th>Exposure to antiepileptics</th>
<th>Exposure to antidepressants</th>
<th>Exposure to antipsychotics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>1,388,492</td>
<td>28.7</td>
<td>1.4</td>
<td>26.7</td>
<td>3.4</td>
<td></td>
</tr>
<tr>
<td>Outcome of pregnancy</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Liveborn</td>
<td>985,403 (71%)</td>
<td>25.4</td>
<td>(Reference)</td>
<td>0.9</td>
<td>24.0</td>
<td>2.5</td>
</tr>
<tr>
<td>Stillborn</td>
<td>3,717 (.3%)</td>
<td>33.4</td>
<td>1.19 (0.99-1.43)</td>
<td>2.4</td>
<td>30.9</td>
<td>6.2</td>
</tr>
<tr>
<td>Miscarriages</td>
<td>149,733 (10.8%)</td>
<td>25.3</td>
<td>0.91 (0.87-0.94)</td>
<td>1.5</td>
<td>23.2</td>
<td>3.3</td>
</tr>
<tr>
<td>Termination</td>
<td>249,639 (18%)</td>
<td>43.6</td>
<td>1.46 (1.43-1.50)</td>
<td>3.1</td>
<td>39.1</td>
<td>7.0</td>
</tr>
<tr>
<td>Maternal Age Group</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;20 years of age</td>
<td>54,518 (3.9%)</td>
<td>23.8</td>
<td>0.52 (0.49-0.55)</td>
<td>0.6</td>
<td>20.3</td>
<td>4.9</td>
</tr>
<tr>
<td>20-24 years of age</td>
<td>180,440 (13%)</td>
<td>32.3</td>
<td>0.94 (0.91-0.98)</td>
<td>1.5</td>
<td>29.4</td>
<td>4.8</td>
</tr>
<tr>
<td>25-29 years of age</td>
<td>413,145 (29.8%)</td>
<td>25</td>
<td>(Reference)</td>
<td>1.2</td>
<td>23.4</td>
<td>2.7</td>
</tr>
<tr>
<td>30-34 years of age</td>
<td>447,024 (32.2%)</td>
<td>26.8</td>
<td>1.22 (1.19-1.25)</td>
<td>1.2</td>
<td>25.4</td>
<td>2.7</td>
</tr>
<tr>
<td>35-39 years of age</td>
<td>232,308 (16.7%)</td>
<td>33.9</td>
<td>1.53 (1.48-1.58)</td>
<td>1.8</td>
<td>31.5</td>
<td>3.9</td>
</tr>
<tr>
<td>40+ years of age</td>
<td>61,057 (4.4%)</td>
<td>40.7</td>
<td>1.74 (1.66-1.82)</td>
<td>2.7</td>
<td>37.2</td>
<td>5.9</td>
</tr>
<tr>
<td>Mother's level of education</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low: 7-10 years</td>
<td>127,370 (9.2%)</td>
<td>50.3</td>
<td>1.36 (1.31-1.42)</td>
<td>3.1</td>
<td>44.2</td>
<td>9.7</td>
</tr>
<tr>
<td>Medium: 11-12 years</td>
<td>282,202 (20.3%)</td>
<td>26.7</td>
<td>(Reference)</td>
<td>1.3</td>
<td>25.1</td>
<td>2.7</td>
</tr>
<tr>
<td>High: 13+ years</td>
<td>465,065 (33.5%)</td>
<td>20.3</td>
<td>0.80 (0.77-0.82)</td>
<td>0.7</td>
<td>19.6</td>
<td>1.1</td>
</tr>
<tr>
<td>Vocational training</td>
<td>334,054 (24.1%)</td>
<td>36</td>
<td>1.18 (1.14-1.21)</td>
<td>1.8</td>
<td>33.8</td>
<td>4.0</td>
</tr>
<tr>
<td>No information</td>
<td>179,801 (12.9%)</td>
<td>24.3</td>
<td>0.66 (0.63-0.68)</td>
<td>1.2</td>
<td>21.8</td>
<td>4.8</td>
</tr>
<tr>
<td>Mother's socio status</td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Un-employed</td>
<td>245,622 (17.7%)</td>
<td>61.6</td>
<td>2.86 (2.79-2.94)</td>
<td>4.8</td>
<td>54.7</td>
<td>12.2</td>
</tr>
<tr>
<td>Students</td>
<td>93,781 (6.8%)</td>
<td>29.2</td>
<td>1.77 (1.68-1.86)</td>
<td>1.1</td>
<td>27.3</td>
<td>3.0</td>
</tr>
<tr>
<td>Employed</td>
<td>884,645 (63.7%)</td>
<td>21.6</td>
<td>(Reference)</td>
<td>0.6</td>
<td>20.9</td>
<td>1.2</td>
</tr>
<tr>
<td>Self-employed</td>
<td>24,523 (1.8%)</td>
<td>22.1</td>
<td>0.95 (0.87-1.04)</td>
<td>0.6</td>
<td>21.5</td>
<td>1.4</td>
</tr>
<tr>
<td>No information</td>
<td>139,921 (10.1%)</td>
<td>16.2</td>
<td>1.00 (1.00-1.00)</td>
<td>0.5</td>
<td>14.7</td>
<td>2.3</td>
</tr>
<tr>
<td>Income</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;100,000 annually</td>
<td>259,634 (18.7%)</td>
<td>32.3</td>
<td>0.96 (0.92-1.00)</td>
<td>1.5</td>
<td>29.2</td>
<td>5.1</td>
</tr>
<tr>
<td>100,000-200,000</td>
<td>652,965 (47%)</td>
<td>33.6</td>
<td>1.18 (1.14-1.22)</td>
<td>1.8</td>
<td>31.4</td>
<td>4.0</td>
</tr>
<tr>
<td>200,000-400,000</td>
<td>324,885 (23.4%)</td>
<td>21.6</td>
<td>(Reference)</td>
<td>0.9</td>
<td>20.8</td>
<td>1.4</td>
</tr>
<tr>
<td>400,000+</td>
<td>11,087 (.8%)</td>
<td>12.9</td>
<td>0.59 (0.50-0.70)</td>
<td>0.5</td>
<td>12.7</td>
<td>0.5</td>
</tr>
<tr>
<td>No information</td>
<td>139,921 (10.1%)</td>
<td>16.2</td>
<td>0.93 (0.89-0.98)</td>
<td>0.5</td>
<td>14.7</td>
<td>2.3</td>
</tr>
</tbody>
</table>

Below demographics are only presented for deliveries

<p>| Total number of deliveries | 989,120 (100%) | 25.4 | 0.9 | 24.1 | 2.5 |</p>
<table>
<thead>
<tr>
<th>Pre-pregnancy BMI</th>
<th>Cases</th>
<th>Mean BMI</th>
<th>Mean 95% CI</th>
<th>Weight</th>
<th>Mean 95% CI</th>
<th>Length</th>
<th>Mean 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;18 Underweight</td>
<td>10,548 (1.1%)</td>
<td>33.6</td>
<td>1.12 (1.00-1.25)</td>
<td>1.5</td>
<td>30.5</td>
<td>4.6</td>
<td></td>
</tr>
<tr>
<td>18-24 Normal weight</td>
<td>435,318 (44%)</td>
<td>25</td>
<td>(Reference)</td>
<td>0.8</td>
<td>24.0</td>
<td>2.0</td>
<td></td>
</tr>
<tr>
<td>25-29 Overweight</td>
<td>169,026 (17.1%)</td>
<td>32.9</td>
<td>1.30 (1.26-1.34)</td>
<td>1.4</td>
<td>31.4</td>
<td>3.3</td>
<td></td>
</tr>
<tr>
<td>30-34 Obese class I</td>
<td>60,835 (6.2%)</td>
<td>42.8</td>
<td>1.64 (1.57-1.71)</td>
<td>2.2</td>
<td>40.6</td>
<td>4.6</td>
<td></td>
</tr>
<tr>
<td>35+ Obese class II&amp;III</td>
<td>37,186 (3.8%)</td>
<td>53.4</td>
<td>2.02 (1.93-2.13)</td>
<td>2.6</td>
<td>50.8</td>
<td>6.1</td>
<td></td>
</tr>
<tr>
<td>No information</td>
<td>276,078 (27.9%)</td>
<td>13.4</td>
<td>0.47 (0.45-0.49)</td>
<td>0.3</td>
<td>12.3</td>
<td>1.8</td>
<td></td>
</tr>
<tr>
<td>Parity</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nullipara</td>
<td>443,640 (44.9%)</td>
<td>25.3</td>
<td>(Reference)</td>
<td>1.0</td>
<td>23.9</td>
<td>2.7</td>
<td></td>
</tr>
<tr>
<td>Multipara</td>
<td>545,351 (55.1%)</td>
<td>25.5</td>
<td>1.01 (0.99-1.04)</td>
<td>0.9</td>
<td>24.3</td>
<td>2.4</td>
<td></td>
</tr>
<tr>
<td>Smoking status</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-smoker</td>
<td>815,451 (82.4%)</td>
<td>21.1</td>
<td>(Reference)</td>
<td>0.6</td>
<td>20.2</td>
<td>1.7</td>
<td></td>
</tr>
<tr>
<td>Light smoker 1-10</td>
<td>110,354 (11.2%)</td>
<td>43.8</td>
<td>2.24 (2.17-2.31)</td>
<td>2.2</td>
<td>40.8</td>
<td>5.5</td>
<td></td>
</tr>
<tr>
<td>Heavy smoker 11+</td>
<td>35,030 (3.5%)</td>
<td>66.7</td>
<td>3.48 (3.32-3.64)</td>
<td>3.9</td>
<td>61.4</td>
<td>11.3</td>
<td></td>
</tr>
<tr>
<td>No information</td>
<td>28,156 (2.8%)</td>
<td>27.1</td>
<td>1.64 (1.52-1.76)</td>
<td>1.1</td>
<td>25</td>
<td>3.3</td>
<td></td>
</tr>
<tr>
<td>Gestation (weeks)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;30 weeks</td>
<td>6,761 (.7%)</td>
<td>33.4</td>
<td>1.26 (1.10-1.45)</td>
<td>2.4</td>
<td>30.8</td>
<td>4.3</td>
<td></td>
</tr>
<tr>
<td>30-36 weeks</td>
<td>53,737 (5.4%)</td>
<td>42.5</td>
<td>1.71 (1.63-1.78)</td>
<td>2.2</td>
<td>40.5</td>
<td>4.8</td>
<td></td>
</tr>
<tr>
<td>37+ weeks (term)</td>
<td>928,622 (93.9%)</td>
<td>24.3</td>
<td>(Reference)</td>
<td>0.9</td>
<td>23.1</td>
<td>2.4</td>
<td></td>
</tr>
</tbody>
</table>