Selective Serotonin Reuptake Inhibitors During Pregnancy and Risk of Stillbirth and Infant Mortality

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Depression during pregnancy is common with prevalences ranging between 7% and 19% in economically developed countries. Maternal depression is associated with poorer pregnancy outcomes, including increased risk of preterm delivery, which in turn may cause neonatal morbidity and mortality. However, it is difficult to disentangle whether such reproductive hazards are caused by the underlying depression, the medical treatment, or possible confounding by lifestyle factors such as stress, alcohol use, and smoking status.

Management of depression during pregnancy is a clinical challenge. The Nordic countries generally recommend a careful risk-benefit analysis of each patient for treatment decisions. Nonpharmaceutical interventions are generally recommended for milder conditions while major depression is frequently treated with antidepressant medication. Selective serotonin reuptake inhibitors (SSRIs) are now the most commonly prescribed drugs for depression during pregnancy. Although somewhat equivocal, the evidence suggests that use of SSRIs during pregnancy must take into account other perinatal outcomes and risk of stillbirth, neonatal mortality, or postneonatal mortality. However, decisions about use of SSRIs during pregnancy taking into account maternal characteristics and previous psychiatric hospitalization.

Results Among 1,633,877 singleton births in the study, 6,054 were stillbirths; 3,609, neonatal deaths; and 1,578, postneonatal deaths. A total of 29,228 (1.79%) of mothers had filled a prescription for an SSRI during pregnancy. Women exposed to an SSRI presented with higher rates of stillbirth (4.62 vs 3.69 per 1000, P = .01) and postneonatal death (1.38 vs 0.96 per 1000, P = .03) than those who did not. The rate of neonatal death was similar between groups (2.54 vs 2.21 per 1000, P = .24). Yet in multivariable models, SSRI use was not associated with stillbirth (adjusted odds ratio [OR], 1.17; 95% CI, 0.96-1.41; P = .12), neonatal death (adjusted OR, 1.23; 95% CI, 0.96-1.57; P = .11), or postneonatal death (adjusted OR, 1.34; 95% CI, 0.97-1.86; P = .08). Estimates were further attenuated when stratified by previous hospitalization for psychiatric disease. The adjusted OR for stillbirth in women with a previous hospitalization for psychiatric disease was 0.92 (95% CI, 0.66-1.28; P = .62) and was 1.07 (95% CI, 0.84-1.36; P = .59) for those who had not been previously hospitalized. The corresponding ORs for neonatal death were 0.89 (95% CI, 0.58-1.39; P = .62) for women who were hospitalized and 1.14 (95% CI, 0.84-1.56; P = .39) for women who were not. For postneonatal death, the ORs were 1.02 (95% CI, 0.96-1.08; P = .24) for women who were hospitalized and 1.10 (95% CI, 0.71-1.72; P = .66) for women who were not.

Conclusions and Relevance Among women with singleton births in Nordic countries, no significant association was found between use of SSRIs during pregnancy and risk of stillbirth, neonatal mortality, or postneonatal mortality. However, decisions about use of SSRIs during pregnancy must take into account other perinatal outcomes and the risks associated with maternal mental illness.

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JAMA. 2013;309(1):48-54

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suggests that SSRI use during pregnancy may be associated with poor birth outcomes, such as congenital anomalies, spontaneous abortion, neonatal withdrawal syndrome, and persistent pulmonary hypertension of the newborn.10,11 The influence of SSRI use on risk of stillbirth, neonatal death, and infant death has been less studied.12

Conversely, discontinuing antidepressant treatment has been associated with increased risk that pregnant women will experience a relapse of major depression.13 According to a recent study on women delivering in Sweden in 2007, 3% of women filled a prescription for antidepressants in the 3-month period before conception while only 1% filled a prescription during the third trimester.14 Maternal mental illness has consistently been associated with risks of infant mortality15 and in particular sudden infant death syndrome.16

Because the Nordic countries have similar nationwide registries of births and dispensed drugs, studies on the effect of medications on birth outcomes are possible. By using these data sources and taking into account previous psychiatric disease and maternal characteristics, we aimed to elucidate whether SSRI exposure during pregnancy was associated with increased risks of stillbirth, neonatal death, and postneonatal death.

METHODS

We conducted a registry-based cohort study that included women and their infants born in the Nordic countries (Denmark, Finland, Iceland, Norway, and Sweden) between 1996 and 2007. Each Nordic country has national registries, which include prospectively collected health and social information on all inhabitants. All registries include the Civil Personal Registration (CPR) numbers, a unique number assigned to each resident at birth or immigration. Reporting to the registries is mandatory and regulated by national laws. The national parliaments in the Nordic countries have on behalf of their populations given informed consent to be included in the registries.17

The start of follow-up was defined from the initiation of the nationwide prescription registry in each participating country and end of follow-up by availability of registry data. We therefore identified all singletons born after 154 gestational days between January 1, 1996, and December 31, 2007, in Denmark; January 1, 1996, and December 31, 2006, in Finland; January 1, 2003, and December 31, 2007, in Iceland; January 1, 2005, and December 31, 2007, in Norway; and January 1, 2006, and December 31, 2007, in Sweden.

Ascertainment of Exposure

Exposure was defined as 1 or more filled prescriptions for an SSRI from 3 months before the start of pregnancy until birth. Eligible pregnancies were identified through the Nordic medical birth registries along with data on maternal demographics, the pregnancy, delivery, and neonatal period.18 Determination of start of pregnancy and gestational age were based on prenatal ultrasound estimation or on last menstrual period.10,19 The prescription registries in the Nordic countries include data on the dispensed item, substance, brand name, and formulation together with date of dispensing for more than 95% of the total outpatient population. All drugs are classified according to the World Health Organization Anatomical Therapeutic Chemical (ATC) classification. The SSRIs used during the study period and included in the analyses were fluoxetine, citalopram, paroxetine, sertraline, fluvoxamine, and escitalopram (eTable 1 available at http://www.jama.com). In general, prescriptions are filled for a maximum of 3 months.20 We excluded pregnancies and births (n=5396) of mothers who had used other antidepressants with an effect on serotonin or norepinephrine activity (imipramine, amitriptyline, duloxetine, dosulepine, melnacipran, trazodone, nefazodone, and moklobemide).

Ascertainment of Outcome

We assessed 3 outcomes: stillbirth (intrauterine death after 22 weeks of gestation in Finland, Norway, Iceland, and Denmark from 2004 onward, and after 28 weeks in Sweden and Denmark from 1997 through 2003), neonatal death (death within 0-27 days among live born infants), and postneonatal death (death between 28-364 days among neonatal survivors). Information on stillbirth was obtained from the medical birth registries in each country and on neonatal and postneonatal deaths from the Nordic causes of death registries, which contain information on the date and causes of death for all individuals who were residents at the time of death. All diagnoses and causes of death are classified according to the national version of International Statistical Classification of Diseases, 10th Revision (ICD-10) codes.

Potential Confounders or Effect-Modifiers

As possible confounders, we included information from the birth registries on maternal age, parity, birth year, country of birth, and maternal smoking status (not available in Iceland), and information on maternal diseases from birth registries and patient registries (except for Norway), although only hypertension and diabetes were retained in the final models. Women with diabetes were identified by filled prescriptions of antidiabetic medications from 3 months before pregnancy through delivery using prescription registries. Complications and maternal diseases are recorded according to the ICD-10 codes.

Because psychiatric disease has been associated with the outcomes under study25 and SSRI use, we obtained available information from each country on the previous psychiatric hospitalizations of the mothers. The patient registries in Denmark, Finland, Iceland, and Sweden record information on all hospitalizations (including treatment of psychiatric disorders), with date of admission and discharge, and primary and secondary diagnoses. Additionally, the Danish Psychiatric Central Register includes information on psychiatric treatments at specialized psychiatric clin-
ics and emergency care units. During the study period, the Norwegian patient registry did not contain CPR numbers, which are needed for linkages to other registries. Thus, we included data on the mother's previous psychiatric hospitalizations from patient registries in Denmark, Iceland, Sweden, and Finland and from the Danish Psychiatric Central Register during a 10-year period before giving birth. For Norway, previous psychiatric treatments were obtained from the medical birth registry; information on past medical history, including treatment for psychiatric disease, is reviewed with the general practitioner, midwife, or an obstetrician and then later recorded in the medical birth registry.

Statistical Analyses
We used logistic regression analysis to estimate the association of SSRI use during pregnancy with 3 outcomes: stillbirth, neonatal death, and postneonatal death. Women with missing data on any of the covariates were excluded from the multivariable analysis. Because information on cigarette smoking was missing in 9.5% of exposed and 6.2% of unexposed women, we performed a sensitivity analysis that included women whose smoking status was missing by adding smoking as a separate category in the multivariable analysis.

Analyses were performed using crude and adjusted odds ratios (ORs) with 95% CIs. In stratiﬁed analyses, we further explored whether history of maternal psychiatric hospitalization modiﬁed the association between SSRI use during pregnancy and risk of stillbirth, neonatal death, and postneonatal death. We also analyzed ORs for SSRIs by time of exposure during pregnancy divided into (1) only within 3 months before first trimester, (2) only before and during first trimester, (3) before and during first and second trimester, and (4) before and during the entire pregnancy. Because observations are not independent in women who delivered more than once during the study period, we calculated estimates using clustered data in the generalized estimation equation method. We ﬁnally present rates of speciﬁc causes of death for neonatal and postneonatal mortality.

All analyses were conducted using SAS software, version 9.2 (SAS Institute Inc). We used a signiﬁcance level of .05 (2-sided testing). The study was approved by the Regional Ethical Review Board at Karolinska Institute in Stockholm, Sweden; the National Board of Health, Denmark; the Danish Data Protection Agency; the National Institute for Health and Welfare of Finland; Statistics Finland; the Data Protection Authority and the National Bioethics Committee in Iceland; and the Norwegian Data Inspectorate.

RESULTS
Descriptive Data
In total 1 633 877 singleton births occurred during the study periods and were included in the analysis. Of these, in 29 228 births (1.79%), the mother had ﬁlled a prescription for an SSRI during pregnancy. Of those women, 91.21% used a single SSRI. Filling of SSRI prescriptions was more common in the later years of the study period (Table 1). The mothers who had ﬁlled a prescription with an SSRI were generally older, more often smokers, previously hospitalized for psychiatric disease, and more likely to have diabetes and hypertension than mothers not using SSRIs. The most frequently ﬁlled SSRI prescription was for citalopram (6.49 per 1000) followed by ﬂuoxetine (4.66 per 1000) and sertraline (3.93 per 1000). The distribution of the different SSRI use is presented in eTable 1 (available at http://www.jama.com).

The 6054 stillbirths corresponded to a rate of 3.71 per 1000 births. The 3609 neonatal deaths corresponded to a rate of 2.22 per 1000 live births, and 1578 postneonatal deaths corresponded to a rate of 0.97 per 1000 live births. A cause of death was reported in 96.92% of neonatal and 96.96% of postneonatal deaths. Of the neonatal deaths, 55.77% were due to perinatal conditions; 28.10%, congenital anomalies; 7.83%, chromosomal abnormalities; 1.57%, sudden infant death syndrome; 0.29%, external causes; and 6.43%, other causes (eTable 2). Of the postneonatal deaths, 29.54% were due to congenital anomalies; 20.33%, sudden infant death syndrome; 11.57%, perinatal conditions; 6.47%, chromosomal abnormalities; 5.10%, external causes; and 26.99%, other causes (eTable 2).

SSRIs and Risks of Stillbirth, Neonatal Death, and Postneonatal Death
In total, 135 stillbirths, 74 neonatal deaths, and 40 postneonatal deaths occurred among mothers exposed to SSRIs during pregnancy. Compared with women who were unexposed, those who were exposed to SSRIs presented with higher rates of stillbirth (4.62 vs 3.69 per 1000 births) with a crude OR of 1.25 (95% CI, 1.06–1.49; P = .01) and postneonatal death (1.38 vs 0.96 per 1000) with a crude OR of 1.43 (95% CI, 1.04–1.96; P = .03; Table 2). Selective serotonin reuptake inhibitor use was not associated with increased risk of neonatal death (2.54 vs 2.21 per 1000) with a crude OR of 1.15 (95% CI, 0.91–1.45; P = .24). After adjusting for maternal characteristics, country, and year of birth, SSRI exposure was no longer signiﬁcantly associated with stillbirth (adjusted OR, 1.17; 95% CI, 0.96–1.41; P = .12) or postneonatal death (adjusted OR, 1.34; 95% CI, 0.97–1.86; P = .08). The adjusted OR for neonatal death was 1.23 (95% CI, 0.96–1.57; P = .11). In the sensitivity analysis including women with missing data on smoking in early pregnancy, the estimates were only marginally altered.

When we stratiﬁed by previous psychiatric hospitalization, estimates for stillbirth, neonatal death, and postneonatal death were attenuated (Table 2). The adjusted OR for stillbirth in women who were previously hospitalized for a psychiatric disease was 0.92 (95% CI, 0.66–1.28; P = .62) and was 1.07 (95%
CI, 0.84-1.36; P = .59) for women who were not. For neonatal death, the adjusted ORs were 0.89 (95% CI, 0.58-1.39; P = .62) for women previously hospitalized and 1.14 (95% CI, 0.84-1.56; P = .39) for women who were not. For postneonatal death, the adjusted OR was 1.02 (95% CI, 0.61-1.69; P = .95) for women who were hospitalized and 1.10 (95% CI, 0.71-1.72; P = .66) for women who were not. Because information on previous hospitalization could not be obtained from Norway, we performed a sensitivity analysis excluding Norwegian data, which demonstrated only marginal changes in the point estimates (eTable 3, available at http://www.jama.com). When restricting the analysis for stillbirths to include gestational age 22 weeks or longer, the adjusted OR was 1.16 (95% CI, 0.92-1.47; P = .21) and for 28 weeks or longer, 1.07 (95% CI, 0.86-1.34; P = .55).

Table 3 presents associated risks with SSRI use by trimester of exposure. Among women exposed from 3 months before pregnancy and during the first trimester, there was an increase in the OR for stillbirth compared with unexposed (adjusted OR, 1.56; CI, 1.06-2.30; P = .03), whereas this was not observed when the exposure window included from 3 months before pregnancy to the first and second trimester or entire pregnancy. For women exposed to an SSRI from before pregnancy through the first trimester, the adjusted OR for stillbirth among women hospitalized for a psychiatric disease was 1.04 (95% CI, 0.54-2.02; P = .90) and was 1.64 (95% CI, 1.08-2.50; P = .02) for women who were not hospitalized. For neonatal and postneonatal deaths, no significant associations were observed by trimester of exposure. We then estimated risks of neonatal and postneonatal mortality by cause of death. However, no significant associations between maternal SSRI and specific causes of death were found (eTable 2).

Finally, absolute rates of stillbirth, neonatal death, and postneonatal death varied by specific SSRI type during pregnancy (eTable 4).

**COMMENT**

The present study of more than 1.6 million births suggests that SSRI use during pregnancy was not associated with increased risks of stillbirth, neonatal death, or postneonatal death. The increased rates of stillbirth and postneonatal mortality among infants exposed to an SSRI during pregnancy were explained by the severity of the underlying maternal psychiatric disease and unfavorable distribution of maternal characteristics such as cigarette smoking and advanced maternal age.

Data on potential risks of stillbirth and infant mortality by SSRI use are scarce. Recently the Danish Medicines Agency reported 2 cases of neonatal death following use of fluoxetine in pregnancy.22 To our knowledge, only 2 studies have specifically addressed the risk of stillbirth or infant death after prenatal SSRI exposure. Kulin et al23 did not find any increased risk of stillbirth among 267 women exposed to SSRIs. Colvin et al24 recently reported no increased risk of stillbirth but found an increased risk of infant...
mortality among 3703 Australian women exposed to SSRIs. Whether the risk of infant mortality was due to prenatal exposure to SSRIs or underlying maternal psychiatric disease could not be determined from these studies. The few studies exploring potential risks of miscarriages by SSRIs use have mostly been small (<250 exposed women) and some have reported increased risks, while others have not. The small size of the studies along with other methodological problems has hampered solid conclusions. Finally, I study found increased infant mortality among women with previous psychiatric disease. In our study, when taking disease severity and maternal characteristics into consideration, women taking SSRIs did not have an increased risk of stillbirth or infant death.

We were able to study risk of stillbirth and infant mortality among SSRI users by trimester of pregnancy. Although the risk of stillbirth appeared to be increased among women exposed before pregnancy through the first trimester, these results should be interpreted with caution due to the few observations for each category of exposure. Yet, a possible explanation for this finding may be the increased risk of congenital anomalies reported to be associated with SSRI use including fluoxetine and sertraline. Risk estimates for neonatal death appeared not to differ by trimester exposure. However, the number of exposed women in this analysis was restricted and estimates should be interpreted with caution.

Strengths and Limitations
This cohort study was population based, using information on almost all singleton births in the 5 Nordic countries during the study period. The large size enabled us to study rare pregnancy outcomes such as stillbirth, neonatal death, and postneonatal death. The minimal clinically detectable differences for an assumed power of 86% (given 1.6 million pregnancies, 2% of

### Table 2. Exposure to Selective Serotonin Reuptake Inhibitors From 3 Months Before Pregnancy Until Birth and Risk of Stillbirth and Infant Mortality

<table>
<thead>
<tr>
<th>Exposure</th>
<th>SSRI</th>
<th>No SSRI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
<td>Per 1000</td>
</tr>
<tr>
<td>Stillbirth</td>
<td>135</td>
<td>4.62</td>
</tr>
<tr>
<td>No previous psychiatric hospitalization</td>
<td>84</td>
<td>3.97</td>
</tr>
<tr>
<td>Previous psychiatric hospitalization</td>
<td>51</td>
<td>6.33</td>
</tr>
<tr>
<td>Neonatal death</td>
<td>74</td>
<td>2.54</td>
</tr>
<tr>
<td>No previous psychiatric hospitalization</td>
<td>45</td>
<td>2.13</td>
</tr>
<tr>
<td>Previous psychiatric hospitalization</td>
<td>29</td>
<td>3.62</td>
</tr>
<tr>
<td>Postneonatal death</td>
<td>40</td>
<td>1.38</td>
</tr>
<tr>
<td>No previous psychiatric hospitalization</td>
<td>23</td>
<td>1.09</td>
</tr>
<tr>
<td>Previous psychiatric hospitalization</td>
<td>17</td>
<td>2.13</td>
</tr>
</tbody>
</table>

**Abbreviation:** OR, odds ratio; SSRI, serotonin reuptake inhibitor.

### Table 3. Exposure to Selective Serotonin Reuptake Inhibitor per Trimester and Risk of Stillbirth and Infant Mortality

<table>
<thead>
<tr>
<th>Outcome, Trimester of SSRI Exposure</th>
<th>No. of Women Exposed</th>
<th>Per 1000</th>
<th>Adjusted OR (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stillbirth T0</td>
<td>49</td>
<td>4.92</td>
<td>1.19 (0.87-1.65)</td>
<td>.28</td>
</tr>
<tr>
<td>T0-T1</td>
<td>31</td>
<td>6.17</td>
<td>1.56 (1.06-2.30)</td>
<td>.03</td>
</tr>
<tr>
<td>T0-T2</td>
<td>8</td>
<td>4.94</td>
<td>1.11 (0.50-2.48)</td>
<td>.80</td>
</tr>
<tr>
<td>T0-T3</td>
<td>14</td>
<td>3.71</td>
<td>0.94 (0.53-1.65)</td>
<td>.83</td>
</tr>
<tr>
<td>Other</td>
<td>33</td>
<td>3.73</td>
<td>1.01 (0.70-1.46)</td>
<td>.94</td>
</tr>
<tr>
<td>Unexposed</td>
<td>5919</td>
<td>3.69</td>
<td>1 [Reference]</td>
<td></td>
</tr>
<tr>
<td>Neonatal death T0</td>
<td>22</td>
<td>2.22</td>
<td>1.04 (0.66-1.64)</td>
<td>.86</td>
</tr>
<tr>
<td>T0-T1</td>
<td>12</td>
<td>2.40</td>
<td>1.16 (0.61-2.21)</td>
<td>.65</td>
</tr>
<tr>
<td>T0-T2</td>
<td>4</td>
<td>2.48</td>
<td>1.35 (0.51-3.62)</td>
<td>.55</td>
</tr>
<tr>
<td>T0-T3</td>
<td>13</td>
<td>3.45</td>
<td>1.56 (0.86-2.83)</td>
<td>.14</td>
</tr>
<tr>
<td>Other</td>
<td>23</td>
<td>2.61</td>
<td>1.31 (0.85-2.02)</td>
<td>.22</td>
</tr>
<tr>
<td>Unexposed</td>
<td>3535</td>
<td>2.21</td>
<td>1 [Reference]</td>
<td></td>
</tr>
<tr>
<td>Postneonatal death T0</td>
<td>14</td>
<td>1.42</td>
<td>1.28 (0.72-2.26)</td>
<td>.40</td>
</tr>
<tr>
<td>T0-T1</td>
<td>5</td>
<td>1.00</td>
<td>1.02 (0.42-2.46)</td>
<td>.96</td>
</tr>
<tr>
<td>T0-T2</td>
<td>3</td>
<td>1.87</td>
<td>2.06 (0.66-6.39)</td>
<td>.21</td>
</tr>
<tr>
<td>T0-T3</td>
<td>6</td>
<td>1.60</td>
<td>1.76 (0.79-3.93)</td>
<td>.17</td>
</tr>
<tr>
<td>Other</td>
<td>12</td>
<td>1.36</td>
<td>1.31 (0.72-2.37)</td>
<td>.38</td>
</tr>
<tr>
<td>Unexposed</td>
<td>1538</td>
<td>0.96</td>
<td>1 [Reference]</td>
<td></td>
</tr>
</tbody>
</table>

**Abbreviations:** OR, odds ratio, SSRI, selective serotonin reuptake inhibitor.

**Note:**
- T0 denotes from 3 months before until last menstrual period before pregnancy; T1, first trimester; T2, second trimester; and T3, third trimester.
- Adjusted for country and year of birth, maternal age, birth order, smoking in early pregnancy, and maternal diabetes and hypertension.

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mothers exposed to SSRIs, and the anticipated rates of outcomes) were ORs of 1.3 for stillbirth, 1.4 for neonatal death, and 1.6 for postneonatal death. Because these are small, the study is unlikely to be underpowered.

In addition, information on SSRI exposure and maternal characteristics was prospectively collected, excluding the possibility of recall bias. The study included information on maternal smoking, which was more common among women with SSRI use and has been associated with stillbirth and neonatal mortality. Furthermore, in sensitivity analyses, we evaluated women with missing data on smoking in early pregnancy. We did not have information on alcohol intake during pregnancy or use of illegitimate drugs, and the use of these could be related to SSRI use as well as stillbirth and infant death. However, since we did not observe any association between SSRIs and stillbirth or infant death, the absence of this information may be of limited concern.

Our study considered previous psychiatric disease. For Denmark, Finland, Iceland, and Sweden, this information was obtained from recorded hospitalizations. In Norway, information on previous psychiatric disease was obtained from the birth registry, which may be a concern because it differs from the data from the other countries. However, excluding Norwegian data did not alter the results.

Apart from previous psychiatric hospitalization, we did not have detailed information on the severity of the disease or any information on mild depression treated in outpatient psychiatric clinics or by general practitioners. Relative risk estimates for adverse outcomes by SSRI use during pregnancy were generally higher among women without previous hospitalization for psychiatric disease than women with previous hospitalization. Hence it is possible that residual confounding due to unmeasured mild psychiatric disorders treated in outpatient clinics or among general practitioners affects our estimates in the population of women without previous psychiatric hospitalization.

We also do not know what psychiatric disease was responsible for hospitalizations. Although SSRIs are used for depression, they also may be used for women with a history of bipolar disorder or schizophrenia. Because the outcome under study is rare, we may have reduced power in stratified analyses by previous psychiatric hospitalization and for specific trimester use during pregnancy, as seen by the wide CIs. Consequently, despite being the largest study investigating this question, the lack of power in the subanalyses has to be considered a limitation and these results should be interpreted with caution.

In the present study, we did not have information on spontaneous and induced abortions. It is therefore possible that we have underestimated an association between SSRI use and adverse pregnancy outcome if women exposed to SSRIs were more likely to have a spontaneous or induced abortion because of a severe congenital abnormality. Because inclusion of stillbirths by gestational age differed between countries for the study period, we presented estimates for stillbirths from the gestational age of 22 weeks and longer and for the gestational age of 28 weeks and longer. However, choice of gestational week for defining stillbirth did not influence the results because we found no association between SSRI exposure and stillbirth for either gestational age cutoff.

Information on dispensed drugs is not the same as intake of drugs. A recent Swedish study showed close to 60% agreement of maternal antidepressant use, when comparing information on dispensed drugs and reported drug intake at the first antenatal care visit. Whether this moderate agreement reflects a lower drug intake compared with dispensing or unwillingness to report intake of antidepressants at antenatal care is unknown. We also did not have information on dosage levels. In addition, it is possible that women lower their dose of antidepressants when planning pregnancy. Consequently, we may have underestimated the proportion of women using SSRIs during pregnancy. The start of the study period varied by country because it was set by the year prescription data were available. This should not introduce bias because we have complete follow-up data for all pregnancies and end points for each country during the periods they provided data. Furthermore, we included both country of origin and calendar year in our models.

In conclusion, we found that after taking maternal characteristics and psychiatric disease hospitalizations into account, there was no significant association between use of SSRIs during pregnancy and risk of stillbirth, neonatal mortality, or postneonatal mortality. However, decisions regarding use of SSRIs during pregnancy must take into account other perinatal outcomes and the risks associated with maternal mental illness.

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Acquisition of data: Kieler, Haglund, Engeland, Furu, Gissler, Nørgaard, Nielsen, Zoega, Valdimarsdóttir.

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Obtained funding: Kieler.

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Conflict of Interest Disclosures: All authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest and none were reported.

Funding/Support: This study was funded by the Swedish Pharmacy Company and by the authors’ affiliations. Olof Stephansson was supported by a postdoctoral scholarship from the Swedish Society of Medicine.

Disclaimer: The Swedish Pharmacy Company was not involved in the design and conduct of the study, collection, management, analysis, or interpretation of the data; and preparation, review, or approval of the manuscript.


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