

## Pregnancy as a Major Determinant for Discontinuation of Antidepressants: An Analysis of Data From The Health Improvement Network

Irene Petersen, PhD; Ruth E. Gilbert, MD; Stephen J. W. Evans, MSc; Shuk-Li Man, BSc; and Irwin Nazareth, PhD

**Background:** Potential adverse effects of antidepressants during pregnancy have caused concern about their use. There are, however, very limited detailed data on patterns of antidepressant prescribing in pregnancy.

**Objective:** To examine secular trends in prescribing during pregnancy, to assess whether pregnancy is a major determinant for stopping antidepressants, and to identify characteristics of those who stopped antidepressants during pregnancy.

**Method:** In this cohort study, we obtained data on 114,999 pregnant women (median age at delivery, 30.5 years [interquartile range, 26–34 years]) who had a live birth between 1992 and 2006 and 22,677 nonpregnant women from The Health Improvement Network primary care database, one of the largest sources of continuous anonymized primary care data in the United Kingdom and broadly representative of UK general practice. This database includes information on age, sex, medical diagnosis and symptoms, health promotion activities, referrals to secondary care, and prescriptions for each registered individual. The database also holds information about social deprivation as measured using quintiles of the Townsend score. We used Cox regression analysis to compare time to last prescription in pregnant versus nonpregnant women and to identify characteristics of those women who stopped antidepressants during pregnancy.

**Results:** Antidepressant prescribing in pregnancy increased nearly 4-fold from 1992 to 2006 (relative risk = 3.87; 95% CI, 1.73–8.66;  $P < .001$ ). Since 2001, approximately 3% of the cohort received antidepressants at some stage during pregnancy. Selective serotonin reuptake inhibitors accounted for approximately 80% of the prescribed antidepressants. Antidepressants were more likely to be stopped in pregnant than in nonpregnant women, in particular during the first 6 weeks of pregnancy (hazard ratio = 5.19; 95% CI, 4.85–5.56;  $P < .001$ ). Only 10% of women treated before pregnancy still received antidepressants at the start of the third trimester. In contrast, 35% of nonpregnant women were still treated after a similar time period.

**Conclusions:** Although antidepressant prescribing in pregnancy increased nearly 4-fold from 1992 to 2006, pregnancy was a major determinant of cessation of antidepressant medication, and most women did not receive further antidepressant prescriptions beyond 6 weeks of gestation. This finding may be explained by concerns about potential adverse effects of the medications, even though these concerns need to be balanced against the potential harm of inadequate treatment of depression during pregnancy.

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*Corresponding author:* Irene Petersen, PhD, Department of Primary Care & Population Health, University College London, Rowland Hill St, London NW3 2PF, United Kingdom (i.petersen@ucl.ac.uk).

Depression is common among women of childbearing age<sup>1</sup>; up to 13% of women may suffer an episode of major depression during pregnancy,<sup>2</sup> and some may be treated with antidepressants. However, the results of studies examining the safety of antidepressants are inconclusive,<sup>3–10</sup> and the decision on whether to stop or continue antidepressant treatment in pregnancy remains a dilemma for both the women and the health care providers. The British National Formulary<sup>11</sup> recommends against prescribing any medication during the first trimester, if possible. It states that “drugs should be prescribed in pregnancy only if the expected benefit to the mother is thought to be greater than the risk to the fetus, and all drugs should be avoided if possible during the first trimester.”<sup>11(p817)</sup> In many instances, however, it is impossible to assess this trade-off between benefit and harm.<sup>8</sup> Data from insurance and health sources in Europe, Canada, and the United States suggest that antidepressants are prescribed more commonly during pregnancy,<sup>12–15</sup> but that many women are known to stop at early stages of their pregnancy.<sup>12,15–19</sup> Yet, no studies have made a direct comparison of discontinuation of antidepressant prescriptions between pregnant and nonpregnant women.

The focus of this study was to assess whether pregnancy is a major determinant for discontinuation of antidepressants. Further, we examined trends in antidepressant prescribing during pregnancy, and, lastly, we identified characteristics of those women who stopped receiving antidepressant prescriptions during pregnancy. We used data from The Health Improvement Network primary care database in the United Kingdom.

### METHOD

#### Study Design: Cohort Study

**Settings and participants.** We identified 145,532 pregnancies for 114,999 women who had a live birth between 1992 and 2006 using The Health Improvement Network primary care database. (For information on accessing The Health Improvement Network data, see <http://www.epic-uk.org/our-data/accessing-the-data.html>.) This database is one of the largest UK sources of continuous anonymized primary

care data. Nearly 400 general practices volunteer to contribute data to the scheme, which is broadly representative of UK general practices in terms of patients' age and sex, practice size, and geographical distribution.<sup>20</sup> Over 98% of the UK population is registered with a general practitioner. While antenatal care, in most cases, is shared between general practitioners and midwives, the general practitioner is still responsible for patients' general care during pregnancy, including prescribing of medicine. Patients who are registered with a practice contributing data to The Health Improvement Network have the opportunity to opt out. However, less than 200 of more than 3.6 million individuals have done so.

General practitioners enter data from consultations using Read codes, a hierarchical recording system used to record clinical summary information.<sup>21</sup> Some Read codes can be cross-referenced to ICD-10 diagnostic categories. The age, sex, medical diagnosis, symptom records, health promotion activity, referrals to secondary care, and prescriptions are recorded for each registered individual. In addition, the database holds information about social deprivation measured for each individual using quintiles of the Townsend score<sup>22</sup> from 1 (least deprived) to 5 (most deprived). The Townsend score is based on a patient's postal code and linkage to population census data for 2001 (Office for National Statistics, <http://www.ons.gov.uk/census/get-data/index.html>) for approximately 150 households in a postal area. The score is a combined measure of owner occupation, car ownership, overcrowding, and unemployment.<sup>22</sup>

Women were included in the study if they were registered with a general practice for at least 6 months before they became pregnant and were still registered with the practice when the child was delivered. We randomly selected a pregnancy in instances in which women had more than 1 pregnancy. The duration of pregnancy was determined from information on the gestational age of the baby at birth, the Read code entries for the last menstrual period, and associated free text. If this information was not available and if there was no information in the notes of a preterm birth, the length of the pregnancy was imputed as 280 days. This method was used for 31% of the pregnancies. Pregnancy trimesters were defined as the first day of the last menstrual period to 14 weeks and 6 days (first trimester); 15 weeks to 27 weeks and 6 days (second trimester); and 28 weeks to delivery (third trimester).

For our study on time trends, we identified all pregnant women who received at least 2 antidepressant prescriptions within 3 months. As primary care databases do not have information on dispensing or compliance, we used a repeat prescription as a marker of women likely to have used some of the prescribed drug. We also extracted information on women who received a single antidepressant prescription in order to compare prescribing trends over time with other published studies in which a single prescription has been used (eg, reference 12). We included only women who received antidepressants at or above the standard recommended British National Formulary<sup>11</sup> level for the treatment

of depression and excluded women prescribed antidepressants at weaker strengths (eg, amitriptyline 10 mg), which are used for other indications.

We then identified women who received at least 1 antidepressant prescription at any time in the 3 months before the pregnancy. For comparative purposes, we identified up to 6 nonpregnant women who received antidepressants within the same general practices as the pregnant women and within the same 5-year age band. For the nonpregnant cohort, we randomly selected 1 time period for each of these women when they were not pregnant for at least 15 months and selected a random index date within this time period. Women who received at least 1 antidepressant prescription at any time in the 3 months before the index date were eligible for the comparison cohort. The comparison cohort included 22,677 individuals.

### Statistical Analyses

**Secular trends.** Antidepressant prescribing before and during pregnancy was estimated for each calendar year between 1992 and 2006, and individual drug classes were tabulated for each trimester of pregnancy. Rate ratios of antidepressant prescribing over time (with 1992 as baseline) before and during pregnancy were estimated using Poisson regression, adjusted for maternal age and social deprivation.

**Comparison of time to last antidepressant prescription in pregnant and nonpregnant women.** We followed pregnant and nonpregnant women from 3 months before the pregnancy (or index date) and identified when they had their last consecutive prescription. Thus, a prescription was regarded as the last prescription if no further prescriptions were made within 92 days. We censored the follow-up after 341 days (equivalent to 1 month before delivery). In the case of a premature delivery, follow-up was terminated at delivery. Although we defined stopping of antidepressants as the time of issue of the last prescription, we are aware that some women would continue taking the drug beyond this point (a prescription would usually be for 28 days).

First, we compared the pregnant and nonpregnant cohort using Kaplan-Meier survival estimates to examine whether the timing of the last consecutive antidepressant prescription was associated with the onset of pregnancy. Then we estimated hazard ratios (HRs) for the time to last prescription between pregnant and nonpregnant cohorts using Cox regression for 3 time periods: The first period covered 0 to 91 days ( $\approx$  3 months before pregnancy to start of pregnancy), the second period covered 92 to 134 days ( $\approx$  start of pregnancy up to 6 weeks of pregnancy), and the third period covered 135 to 341 days ( $\approx$  6 weeks of gestation up to 1 month before delivery).

**Factors determining cessation of antidepressant prescriptions in pregnant women.** For pregnant women, we further examined whether stopping antidepressant prescriptions was associated with age of the mother, social deprivation, or number of previous antidepressant prescriptions received

between 6 and 3 months before pregnancy using Cox regression.

These variables were included in the analysis as we sought to examine the following hypotheses:

1. Younger women taking antidepressants are more likely than older women to stop being prescribed antidepressants once they became pregnant. Our reasoning for this hypothesis was that younger women may be less likely to have been through a pregnancy before and are also less likely to have had depression for a long period of time and are therefore more likely to be uncertain about the value of antidepressants in pregnancy.
2. Women from the least deprived areas are more likely to give up being prescribed antidepressants than women from the most deprived areas. Our reasoning for this hypothesis was that women from the least deprived areas may be more likely to seek alternative treatment options.
3. Women with few previous prescriptions are more likely to stop being prescribed antidepressants than are women with many prior prescriptions. Our reasoning for this hypothesis was that women with few previous prescriptions may have less experience with the drug and therefore may be more uncertain about the value of antidepressants. Furthermore, previous prescriptions were used as a proxy measurement for severity as UK primary care databases do not offer a direct measurement of severity of disease/illness.

Data were managed and analyzed using Stata, version 10.1 (StataCorp LP, College Station, Texas).

The study was given a favorable opinion by the Cambridgeshire 4 Research Ethics Committee (08/H0305/33). The study was also reviewed by the primary care database steering committee within the University College London Department of Primary Care & Population Health.

## RESULTS

### General Description

Overall, 114,999 pregnant women were included in the study. The median age at delivery was 30.5 years (interquartile range, 26–34 years). A total of 5,577 women (4.8%) received antidepressant prescriptions at some point in the 6 months before pregnancy, and 2,654 women (2.3%) continued their prescriptions during pregnancy. A total of 437 women were prescribed antidepressants only during pregnancy, accounting for 14% of all those who received antidepressants during pregnancy.

While 2,792 women (2.4%) received antidepressants in the first trimester, only 1% received prescriptions in each of the second and third trimesters (Table 1). The

**Table 1. Type of Antidepressants Prescribed During Pregnancy (N = 114,999)<sup>a</sup>**

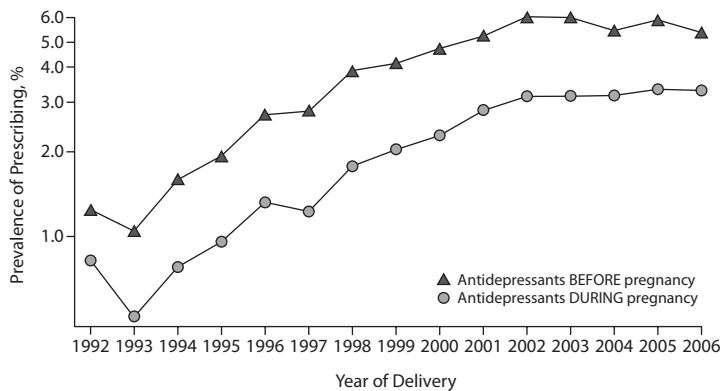
Prescribed Antidepressant	Any Time During Pregnancy, n (%)	First Trimester, n (%)	Second Trimester, n (%)	Third Trimester, n (%)
Any antidepressant	3,091 (2.7)	2,792 (2.4)	1,197 (1.04)	1,142 (0.99)
Selective serotonin reuptake inhibitor	2,427 (2.1)	2,141 (1.9)	881 (0.77)	866 (0.75)
Citalopram	571 (0.5)	508 (0.4)	186 (0.16)	174 (0.15)
Escitalopram	110 (0.1)	103 (0.1)	15 (0.01)	16 (0.01)
Fluoxetine	1,054 (0.9)	871 (0.8)	374 (0.33)	380 (0.33)
Fluvoxamine	8 (<0.1)	8 (<0.1)	3 (0.00)	3 (0.00)
Paroxetine	510 (0.4)	460 (0.4)	215 (0.2)	198 (0.17)
Sertraline	288 (0.3)	235 (0.2)	99 (0.1)	105 (0.09)
Tricyclic antidepressant	554 (0.5)	436 (0.4)	252 (0.22)	221 (0.19)
Amitriptyline	126 (0.1)	95 (0.1)	60 (0.1)	56 (0.05)
Clomipramine	61 (<0.1)	54 (0.1)	31 (<0.1)	19 (0.02)
Dosulepin	191 (0.2)	156 (0.1)	83 (0.1)	75 (0.07)
Doxepin	6 (<0.1)	5 (<0.1)	4 (<0.1)	4 (0.00)
Imipramine	9 (<0.1)	3 (<0.1)	8 (<0.1)	8 (0.01)
Lofepramine	141 (0.1)	98 (0.1)	52 (0.1)	52 (0.05)
Mianserin	1 (<0.1)	0 (0.0)	1 (<0.1)	1 (0.00)
Nortriptyline	3 (<0.1)	2 (<0.1)	0 (0.0)	1 (0.00)
Trazodone	36 (<0.1)	29 (<0.1)	16 (<0.1)	8 (0.01)
Trimipramine	3 (<0.1)	3 (<0.1)	1 (<0.1)	1 (0.00)
Tetracyclic antidepressant	63 (0.1)	62 (0.1)	14 (<0.1)	12 (0.01)
Maprotiline	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.00)
Mirtazapine	63 (0.1)	62 (0.1)	14 (<0.1)	12 (0.01)
Monoamine oxidase inhibitor	5 (0.0)	5 (<0.1)	1 (<0.1)	0 (0.00)
Moclobemide	3 (0.0)	3 (<0.1)	0 (0.0)	0 (0.00)
Phenelzine	2 (0.0)	2 (<0.1)	1 (<0.1)	0 (0.00)
Other	313 (0.3)	304 (0.3)	85 (0.1)	73 (0.06)
Bupropion	8 (<0.1)	8 (<0.1)	0 (0.0)	0 (0.00)
Flupentixol	19 (<0.1)	17 (<0.1)	4 (<0.1)	3 (0.00)
Nefazodone	6 (<0.1)	6 (<0.1)	0 (0.0)	0 (0.00)
Reboxetine	8 (<0.1)	7 (<0.1)	2 (<0.1)	1 (0.00)
Tryptophan	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.00)
Venlafaxine	273 (0.2)	267 (0.2)	79 (<0.1)	69 (0.06)

<sup>a</sup>Some women received more than 1 antidepressant; hence, the sums of drug categories and individual drugs may be higher than the number of women receiving those antidepressants.

proportion of women prescribed antidepressants in the 6 months before pregnancy increased 4-fold from 1.2% in 1992 to 5.3% in 2006 (relative risk [RR] = 4.15; 95% CI, 2.15–8.01;  $P < .001$  [adjusted for age and deprivation]) (Figure 1). Similar increases were found in the proportion prescribed antidepressants during pregnancy—from 0.8% in 1992 to 3.3% in 2006 (RR = 3.87; 95% CI, 1.73–8.66;  $P < .001$  [adjusted for age and deprivation]) (Figure 1). The increase was largely prior to 2001. Since then, the proportion receiving antidepressants at some point during pregnancy has remained stable at around 3% (Figure 1).

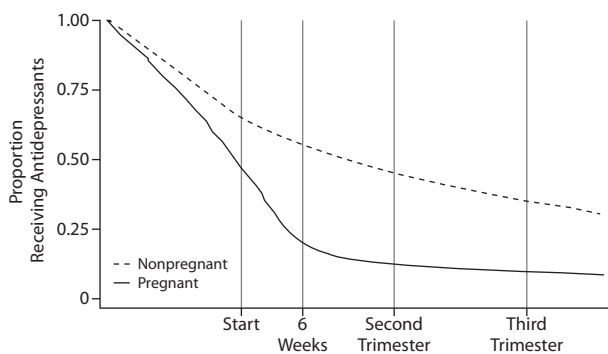
Older women were more likely than younger women to be prescribed antidepressants before they became pregnant (RR = 1.01; 95% CI, 1.01–1.02 per 5-year increase in age;  $P < .001$ ) and were also more likely to continue treatment during pregnancy (RR = 1.03; 95% CI, 1.02–1.04 per 5-year increase in age;  $P < .001$ ). There was no association between age and the proportion of women who were first prescribed antidepressants during pregnancy (RR = 0.99; 95% CI, 0.97–1.00 per 5-year increase in age;  $P = .125$ ).

Figure 1. Time Trends of the Prevalence of Antidepressant Prescribing<sup>a</sup>



<sup>a</sup>For individuals at 0–6 months before pregnancy and during pregnancy. Includes individuals who received at least 2 prescriptions within 3 months (logarithmic scale shows consistent proportionate differences between time periods).

Figure 2. Time to Last Prescription of Antidepressants in Pregnant and Nonpregnant Women<sup>a</sup>



<sup>a</sup>Women were followed from 3 months before the start of pregnancy (or 3 months before the index date for nonpregnant women); 3 months before pregnancy = 0 days, start of pregnancy = 92 days, 6 weeks = 134 days, second trimester = 197 days, and third trimester = 288 days.

The number of women receiving one or more antidepressant prescriptions was 7,338 (6.4%) in the 6 months before pregnancy, and 2,946 women (2.6%) continued receiving prescriptions during pregnancy. A total of 965 women were prescribed the drug only during pregnancy; this number accounted for 25% of the women prescribed antidepressants during pregnancy.

### Time Trends and Types of Drugs Prescribed

Selective serotonin reuptake inhibitors accounted for nearly 80% of the antidepressants prescribed during pregnancy (Table 1). Fluoxetine and paroxetine were most frequently prescribed until 2002, but prescriptions for paroxetine declined steeply between 2002 and 2005 and in 2006 dropped to the same level as in 1996. Fluoxetine was the most commonly prescribed selective serotonin reuptake inhibitor in 2006, followed by citalopram and sertraline. Over the years, venlafaxine prescriptions have been

on the increase during pregnancy, and in 2006 venlafaxine was prescribed at the same level as sertraline. Tetracyclics (ie, mirtazapine and maprotiline) were rarely prescribed and accounted for only 2% of all antidepressants prescribed during pregnancy, while tricyclic antidepressants accounted for 20% of all antidepressants used, with dosulepin and lofepramine being the most commonly prescribed tricyclic antidepressants (Table 1).

### Comparison of Time to Last Prescription in Pregnant and Nonpregnant Women

Pregnancy was a key determinant for discontinuation of antidepressants (Figure 2). While there was a steady decline in prescribing among nonpregnant women throughout the observation period, the decline was noticeable in the pregnant cohort even before the pregnancy started.

In the 3 months before the start of pregnancy, a total of 5,229 women received at least 1 antidepressant prescription. Of these women, 2,455 (47%) were still prescribed antidepressants at the beginning of their first trimester. In the following 6 weeks, the proportion of women receiving further prescriptions fell noticeably, and only 1,060 women (20%) received additional prescriptions after 6 weeks. At the beginning of the second trimester, 652 women (12%) received further prescriptions, and, at the beginning of the third trimester, this figure was down to 512 (10%). In comparison, of 22,677 nonpregnant women, a total of 14,774 (65%) were still prescribed antidepressants after 92 days (≈ start of pregnancy), and, after 288 days (≈ start of third trimester), a total of 8,007 (35%) still received further prescriptions.

The HR for stopping prescriptions in the time period before pregnancy (0–91 days) was 1.70 (95% CI, 1.62–1.77) when comparing pregnant with nonpregnant. In the first 6 weeks of pregnancy, the HR for stopping prescriptions increased to 5.19 (95% CI, 4.85–5.56). Thereafter, the HR was slightly lower than for the time period before the start of the pregnancy (1.57 [95% CI, 1.45–1.71]).

### Factors Influencing Continued Prescriptions

For pregnant women, prior experience with antidepressant prescribing was a major factor influencing continued prescriptions. Women who had received no prescriptions or 1 prescription in the time period 6 to 3 months before pregnancy were nearly twice as likely to stop their prescriptions compared to women who had received at least 2 prescriptions in that time period (HR = 1.73; 95% CI, 1.63–1.84) (Table 2). Antidepressant prescriptions were also stopped more often in women aged 15–24 years (HR = 1.31; 95% CI, 1.19–1.43) and women aged 25–34 years (HR = 1.15; 95% CI, 1.06–1.24) compared to women aged 35 years and above (Table 2). No association was found between continuation of prescriptions and social deprivation (Table 2).

**Table 2. Factors Associated With Discontinuation of Antidepressant Prescriptions During Pregnancy: Results From Cox Regression Analysis**

Factor	Number of Women (N = 5,229)	Hazard Ratio <sup>a</sup> (95% CI), Unadjusted	P Value <sup>b</sup>	Hazard Ratio <sup>a</sup> (95% CI), Adjusted <sup>c</sup>	P Value <sup>b</sup>
Age, y			< .001		< .001
15–24	1,428	1.39 (1.27–1.52)		1.31 (1.19–1.43)	
25–34	2,912	1.15 (1.06–1.25)		1.15 (1.06–1.24)	
35+	889	1		1	
No. of prescriptions during 6 months to 3 months before pregnancy					
0–1	2,880	1.76 (1.66–1.86)	< .001	1.73 (1.63–1.84)	< .001
2+	2,349	1		1	
Deprivation score (quintiles) <sup>d</sup>			.49		.39
1	785	1		1	
2	745	0.99 (0.89–1.10)		0.99 (0.89–1.10)	
3	1,045	1.05 (0.95–1.16)		1.03 (0.93–1.14)	
4	1,208	1.06 (0.97–1.17)		1.05 (0.95–1.16)	
5	1,058	1.01 (0.92–1.11)		0.97 (0.88–1.07)	
Missing score	388	1.10 (0.96–1.24)		1.08 (0.96–1.23)	

<sup>a</sup>Value of 1 for hazard ratio indicates reference category.

<sup>b</sup>P value is from Wald test.

<sup>c</sup>Mutually adjusted for age, previous prescriptions, and deprivation scores.

<sup>d</sup>Townsend score: 1 = least deprived and 5 = most deprived.

## DISCUSSION

There was a 4-fold increase in antidepressant prescriptions both before and during pregnancy between 1992 and 2006. Selective serotonin reuptake inhibitors were the most commonly prescribed antidepressants in pregnancy. However, prescriptions were stopped in the majority of women in the first 6 weeks of gestation. Only 1 in 10 women treated before pregnancy still received consecutive prescriptions of antidepressants at the beginning of the third trimester. Pregnancy is a major determinant for stopping antidepressant prescriptions. Young age and having no prescriptions or 1 prescription in the time period 6 to 3 months before pregnancy were associated with discontinuation.

Similar increases over time in prescribing of antidepressants during pregnancy have been reported in other countries. In the United States, a 4-fold increase was observed between 1996 and 2004, when nearly 8% of pregnant women received antidepressants.<sup>12,13</sup> In the Netherlands, the number of women receiving selective serotonin reuptake inhibitors during pregnancy has also increased in the last decade.<sup>23</sup> About 2% of pregnant Dutch women were prescribed antidepressants between 2000 and 2003.<sup>15</sup> However, almost 60% of the women who used antidepressants in the Netherlands before pregnancy discontinued during the first trimester.<sup>15</sup> A decline in antidepressant prescribing during pregnancy was also reported in Canada, where 3.7% of women were prescribed antidepressants during the first trimester compared with 1.6% in the last 2 trimesters.<sup>14</sup> In Norway, 1.8% of women were prescribed antidepressants in the 3 months before conception. This number fell to 1.1% in first trimester and more than halved in the second and third trimesters.<sup>16</sup> Similar patterns have been reported in Finland<sup>18</sup> and Germany.<sup>17</sup> The steep decline in prescribing of paroxetine among pregnant women after 2002 mirrors the pattern in the general UK population following the warning

from the US Food and Drug Administration of severe withdrawal symptoms and possible links between paroxetine and suicidal behavior.<sup>24</sup>

Point prevalence estimates of depression reveal that between 7% and 13% of women suffer from depression at some point during pregnancy.<sup>2,25</sup> Yet, our results imply that only around 1% of women receive antidepressant treatment in the second and third trimesters. This finding may suggest that many women are not adequately treated for depression and other indications for antidepressant medication (eg, anxiety disorders) during pregnancy. While the time around the beginning of pregnancy may be an obvious point at which to reconsider or withdraw drug treatment for some women, and it is possible that a number of pregnant women receive other treatment (counseling and psychotherapy), it is known that many depressed women do not seek any treatment during pregnancy.<sup>26</sup>

We found that “new” antidepressants such as venlafaxine, escitalopram, and citalopram are increasingly prescribed, particularly in the first trimester of pregnancy, despite the British National Formulary’s recommendation that “drugs which have been extensively used in pregnancy and appear to be usually safe should be prescribed in preference to new or untried drugs.”<sup>11(p817)</sup> It is quite likely that many of these drugs were prescribed before the women were aware of their pregnancies. Most drugs are not licensed for use in pregnancy. Yet, many of the newer drugs are effective in managing psychiatric disorders and may have a better side effect profile and overall tolerance than some of the older drugs given to women in the reproductive age group.<sup>27</sup> Therefore, it is important that the safety of these newer drugs in pregnancy is assessed.

It appears that knowledge of pregnancy was a major reason for stopping antidepressant prescriptions. A large proportion of the women who received their last prescription within the first 6 weeks of gestation may not have been

aware of their pregnancy. However, by the time the prescription was due for renewal (usually within 28 days), many women would then know they were pregnant, and either the woman or her general practitioner would decide to stop the prescription.

While previous studies have compared the level of prescribing before and during pregnancy, this study is the first, to our knowledge, that directly compares discontinuation of antidepressant prescriptions between pregnant and nonpregnant women. This comparison demonstrates that pregnancy was a key determinant for stopping prescriptions but that awareness of the pregnancy may not have been the sole reason for stopping antidepressant prescriptions. Other factors such as experience of adverse effects, stigmatization associated with antidepressants, and reluctance to consider long-term treatment may influence continuous prescribing in pregnant as well as nonpregnant women.<sup>28,29</sup>

The general practitioner plays a pivotal role in guiding pregnant women on continuation of prescribed medicine in pregnancy. The general practitioner's guidance may be informed by the recommendations made in national formularies. However, since the recommendations are often not specific enough, both the general practitioner and the women are left with a very difficult decision. More research is urgently needed to establish both the potential harm and benefit to both mother and fetus of continuation of antidepressant prescribing during pregnancy.<sup>8</sup> There is limited research that has examined the potential effects of discontinued antidepressant treatment during pregnancy.<sup>30,31</sup> The study by Einarson et al<sup>31</sup> emphasizes that abrupt discontinuation may have serious consequences for the mother's mental health. It is possible that the effects of undertreatment of depression in pregnancy might be at least as damaging as the potential adverse effects of treatment on the fetus.<sup>32</sup>

## CONCLUSIONS

Despite a 4-fold rise in antidepressants prescribed before and during pregnancy from 1992 to 2006, few women continued prescriptions beyond 6 weeks of gestation. Pregnancy was a key determinant for stopping antidepressants; the decline in prescribing was most profound in the first 6 weeks of pregnancy when compared with nonpregnant women. Fewer than 1 in 10 of the women who received antidepressants in the 3 months before pregnancy continued their medication throughout pregnancy, leaving many women untreated. Although this finding might be explained by concern about adverse effects of the drugs, this concern needs to be balanced against the potential harm of inadequate treatment of depression during pregnancy.

**Drug names:** bupropion (Wellbutrin, Aplenzin, and others), citalopram (Celexa and others), clomipramine (Anafranil and others), doxepin (Zonalon, Silenor, and others), escitalopram (Lexapro and others), fluoxetine (Prozac and others), fluvoxamine (Luvox and others), imipramine (Tofranil and others), mirtazapine (Remeron and others), nortriptyline (Pamelor, Aventyl, and others), paroxetine (Paxil, Pexeva, and others), phenelzine (Nardil), sertraline (Zoloft and others),

trazodone (Oleptro and others), trimipramine (Surmontil and others), venlafaxine (Effexor and others).

**Author affiliations:** Department of Primary Care & Population Health (Drs Petersen and Nazareth and Ms Man) and Medical Research Council Centre of Epidemiology for Child Health, UCL Institute of Child Health (Dr Gilbert), University College London; Department of Medical Statistics, London School of Hygiene and Tropical Medicine (Mr Evans); and Medical Research Council General Practice Research Framework (Ms Man and Dr Nazareth), London, United Kingdom.

**Author contributions:** Dr Petersen had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis, which was performed by Dr Petersen and Ms Man. Dr Petersen designed the study, with contributions from Dr Nazareth, Dr Gilbert, Mr Evans, and Ms Man. All authors were involved in the interpretation of the data. Dr Petersen drafted the article, and all other authors participated in revision of the article and approved the final version.

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*Editor's Note:* We encourage authors to submit papers for consideration as a part of our Focus on Women's Mental Health section. Please contact Marlene P. Freeman, MD, at [mfreeman@psychiatrist.com](mailto:mfreeman@psychiatrist.com).