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Discontinuation of antipsychotic medication in pregnancy: A cohort study

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ABSTRACT

Background: Women prescribed antipsychotics face the dilemma on whether to continue medication in pregnancy in terms of balancing risks and benefits. Previous research on other psychotropic medications suggests that many women discontinue treatment in early pregnancy. However, very limited evidence exists on discontinuation of antipsychotic medication.

Methods: We identified 495,953 pregnant women from THIN primary care database. Kaplan–Meier plots were used to examine time to last antipsychotic prescription. Poisson regression was used to examine characteristics of those who stopped treatment during pregnancy.

Results: There has been an overall increase in prevalence of antipsychotic prescribing since 2007. However, antipsychotics were more likely to be stopped in pregnant than non-pregnant women. Only 107/279 (38%) of women on atypical antipsychotics and 39/207 (19%) of women on typical antipsychotics before pregnancy still received treatment at the start of third trimester. Older women were more likely to continue typical antipsychotic treatment in pregnancy (35+ versus <25 years risk ratio: 3.09 [95% CI 1.76, 5.44]). Likewise, those who received typical antipsychotics for longer periods before were most likely to continue treatment in pregnancy (12+ versus <6 months: RR: 3.12 [95% CI 1.97, 4.95]). For atypical antipsychotics length and dose of prior prescribing were also associated with continuation in pregnancy.

Conclusions: Pregnancy was a major determinant of cessation of antipsychotics. Only 38% of women on atypical and 19% on typical antipsychotics were still prescribed the drug in the third trimester. Duration of prior treatment, maternal age as well as dose was significantly associated with continued treatment of antipsychotics in pregnancy.

1. Introduction

The onset of schizophrenia and bipolar disorder in women usually occurs within childbearing age (Yonkers et al., 2004; Einarson and Boskovic, 2009; Hardoon et al., 2013) and many women with these illnesses are prescribed psychotropic medication including antipsychotics (Einarson and Boskovic, 2009; Hayes et al., 2011; Prah et al., 2012). Some women are prescribed antipsychotics either before they get a diagnosis of refractory mood and anxiety disorders. Women prescribed antipsychotics face the dilemma at the time of pregnancy or when planning a pregnancy on whether to continue psychotropic medication in terms of balancing the potential teratogenic effects and other adverse effects of the medication against the consequences of a relapse of their illness (Galbally et al., 2011). However, limited information is available on the risks and benefits of antipsychotic treatment in pregnancy (Einarson and Boskovic, 2009).

Webb et al. conducted a systematic review in 2004 (updated in 2009) to establish whether the benefits of taking antipsychotic drugs outweigh the risks for pregnant or postpartum women and found no randomised controlled trials (Webb et al., 2004). A Swedish population registry study identified 570 women being prescribed antipsychotics in pregnancy and found that this was associated with increased risk of gestational diabetes (OR 1.78 95% CI 1.04–3.01) (Reis and Källén, 2008) and congenital malformations (OR 1.52 (95% CI 1.05–2.19)) in comparison

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to women not prescribed antipsychotics. This association was not specific to certain drugs suggesting that the underlying pathology or unidentified confounding could explain the excess risk of congenital malformations (Reis and Källén, 2008). A recent Canadian study assessed 133 pregnant women exposed to second generation antipsychotics against healthy women (Sadowski et al., 2013). Exposed neonates were more likely to be born prematurely and had higher rates of congenital malformations and this was particularly the case for those subject to poly-therapy (atypical antipsychotics as well as other psychotropic medication). In this study a relatively high proportion (72%) of women were on poly-therapy and 101/133 (76%) continued treatment throughout pregnancy (Sadowski et al., 2013).

Advice on treatment varies across countries and in some places standard psychiatric advice is that women maintain pharmacological treatment across the perinatal period (Galbally et al., 2011). The National Institute for Health and Clinical Excellence (NICE) guideline on antenatal and postnatal mental health raises specific issues with certain antipsychotics, but does not provide general recommendations on whether to stop or continue antipsychotic treatment in this period (National Institute for Health and Clinical Excellence, 2007). Previous research on other psychotropic medications including antidepressants and antiepileptic drugs suggests that many women discontinue treatment in early pregnancy (Petersen et al., 2011; Man et al., 2012). However, very limited evidence exists on extent of antipsychotic prescribing in pregnancy and whether pregnancy is associated with discontinuation of antipsychotic medication.

We investigated prescribing of antipsychotic medication in the United Kingdom primary care before and during pregnancy using data from The Health Improvement Network (THIN), a large primary care database. The aim of our study was to examine whether pregnancy was a determinant for discontinuation of antipsychotics and if so, to identify factors associated with discontinuation.

2. Methods

2.1. Data source

We used data from The Health Improvement Network (THIN) primary care database (http://csdmruk.cegedim.com/), one of the largest primary care databases that provide longitudinal health records. The database currently holds data from 578 practices and is approximately representative of the United Kingdom population (Blak et al., 2011). Over 98% of the UK population are registered with a general practitioner (family doctor) (Lis and Mann, 1995). Diagnoses and symptoms are recorded by practice staff using Read codes, a hierarchical coding system (Chisholm, 1990). In addition, THIN holds individual patient level information about year of birth, date of registration, and death or transfer out of the practice. Social deprivation is recorded for each individual by quintiles of Townsend scores, which is based on information from the 2001 census.

While antenatal care is often shared between general practice staff and midwives, the general practitioner remains responsible for women's general medical care during pregnancy including prescribing of medicines. Some women with psychosis also receive care from local National Health Service (NHS) mental health trusts, but most mental health trusts have limited prescribing budgets and for most women the continuing prescription of psychotropic medication will still remain with the general practitioners.

2.2. Participants

We identified women who were permanently registered with one of the general practices that contributed data to THIN for the period between 1 January 1995 and 31 December 2012 for at least six months before the pregnancy and throughout their pregnancy. We included women who received continuous antipsychotic medication before they became pregnant i.e. women were selected if they received prescriptions between 6 and 4 months (inclusive) before they became pregnant and received at least one further prescription in the three months before the start of pregnancy. Thus, we focused on women who received two or more prescriptions of antipsychotics in the six months leading up to pregnancy. In accordance with clinical practice in the United Kingdom, the first day of the last menstrual period was considered as the start of pregnancy. The duration of the pregnancy was estimated from information on the date of the last menstrual period, antenatal records, delivery information, dates of postnatal examinations and gestational age at birth. Pregnancies that ended in miscarriage or termination were not included in the study. We conducted separate analyses for women in receipt of typical and atypical antipsychotics prior to pregnancy and for each of these groups we identified comparison groups of twice as many women also in receipt of antipsychotic prescriptions, but not being pregnant for at least 12 months before and 24 months after a randomly selected index date. We stratified this group such that the age distribution was similar in the pregnant and non-pregnant sample.

A few women treated with antipsychotics ($n = 19$) had records of more than one eligible pregnancy; in these situations we randomly selected one of the pregnancies.

Antipsychotic prescribing was most commonly prescribed at monthly intervals, although there was substantial variation. Therefore, we considered women to have discontinued antipsychotic medication if they had received no further prescriptions after three months.

We also calculated the average daily dose of antipsychotic medication during the period from six to four months before the start of pregnancy by dividing the total mass of drug prescribed over the period by the expected total duration of the relevant prescriptions. Durations were estimated with the help of the Enhanced Dosage Determination method developed by the University of Nottingham Division of Epidemiology and Public Health (Gibson, 2012). The mass of each antipsychotic drug was standardised into units of the Defined Daily Dose (DDD) for maintenance treatment of psychosis (WHO Collaborating Centre for Drug Statistics Methodology, 2013).

2.3. Data analysis

2.3.1. Secular trends

We estimated annual prevalence of antipsychotic prescribing before and during pregnancy for every two calendar years between 1995 and 2012, stratified by typical and atypical antipsychotics. Subsequently, we followed pregnant and non-pregnant women who were prescribed antipsychotics from 3 months before the pregnancy (or the index date for the non-pregnant women) and identified when they had their last consecutive prescription. We ended the follow-up after 220 days (two months before delivery). In the case of a premature delivery earlier than 220 days, follow-up was terminated at delivery. Although we defined stopping of antipsychotics as the date of issue of the last prescription, some women would continue taking the drug beyond this point.

2.3.2. Factors determining continuation of antipsychotic prescribing in pregnant women

For pregnant women we further examined whether continuation of antipsychotic prescribing beyond six weeks of pregnancy was associated with age, the average daily dosage, length of time the antipsychotic had been prescribed prior to pregnancy, prescription of antidepressants and/or mood stabilisers, records of illicit drug or alcohol problems, obesity, parity, social deprivation and ethnicity using a Poisson regression model with robust variance estimates to account for clustering within general practice. We estimated the univariate relative risk ratios for each of the variables as well as relative risk ratios adjusted for age and average daily dose.

Many factors may impact the decisions to continue or discontinue antipsychotic medication in pregnancy. However, we chose to examine the variables described above as they were available from primary care electronic health records. While there is no direct measurement of

severity of illness the average daily dosage and length of time the antipsychotic had been prescribed prior to pregnancy may be indicative of the severity of illness.

2.4. Ethics

The scheme for THIN to obtain and provide anonymous patient data to researchers was approved by the National Health Service South-East Multicenter Research Ethics Committee (MREC) in 2002 and scientific approval for this study was obtained from CSD Medical Research's Scientific Review Committee.

3. Results

Overall, we identified 495,953 pregnancies in 365,138 women. Of these pregnancies, we identified 1442 (0.29%) in which women were prescribed antipsychotics in the six months before they became pregnant and 945 (0.19%) in which women were prescribed antipsychotics after the pregnancy was likely to be known (after six weeks). The overall annual prevalence of prescribing of antipsychotics before and in pregnancy was relatively constant between 1995 and 2007 (Fig. 1). Prescribing of typical antipsychotics has been declining since 1998, while prescribing of atypical antipsychotics has been increasing, resulting in an overall increase since 2007 in prescribing of antipsychotics both before and during pregnancy (Fig. 1).

3.1. Discontinuation of antipsychotic prescription in pregnancy

We identified 207 women receiving typical antipsychotics and 279 receiving atypical antipsychotics in the six to four months before they became pregnant and at least one further prescription within the following three months.

Pregnant and non-pregnant women prescribed atypical antipsychotics discontinued at similar rates up to the start of pregnancy (or index date) (Fig. 2). However, after six weeks of pregnancy (when the woman is likely to become aware of the pregnancy) only 150/279 (54%) of the women received further prescriptions and by the start of the third trimester this figure was reduced to 107/279 (38%) (Fig. 2). For women on typical antipsychotics there was a substantial difference in the rates of discontinuation between pregnant and non-pregnant women even before the pregnancy (Fig. 2). By six weeks of pregnancy only 73/207 (35%) received further prescriptions thereafter and by the start of the third trimester it was down to 39/207 (19%) (Fig. 2).

The rates of discontinuation differed by dose and type of antipsychotics (Fig. 3). Women prescribed lower doses were least likely to continue treatment in pregnancy. Among women receiving prescriptions of less than 0.25 of the defined daily dose (DDD) of typical antipsychotics, only 29/118 (25%) continued prescriptions after six weeks. For women on atypical antipsychotics the figure was 24/52 (46%) after six weeks (Fig. 2). The comparisons with non-pregnant women, however, suggest that awareness of the pregnancy may not be the only reason for

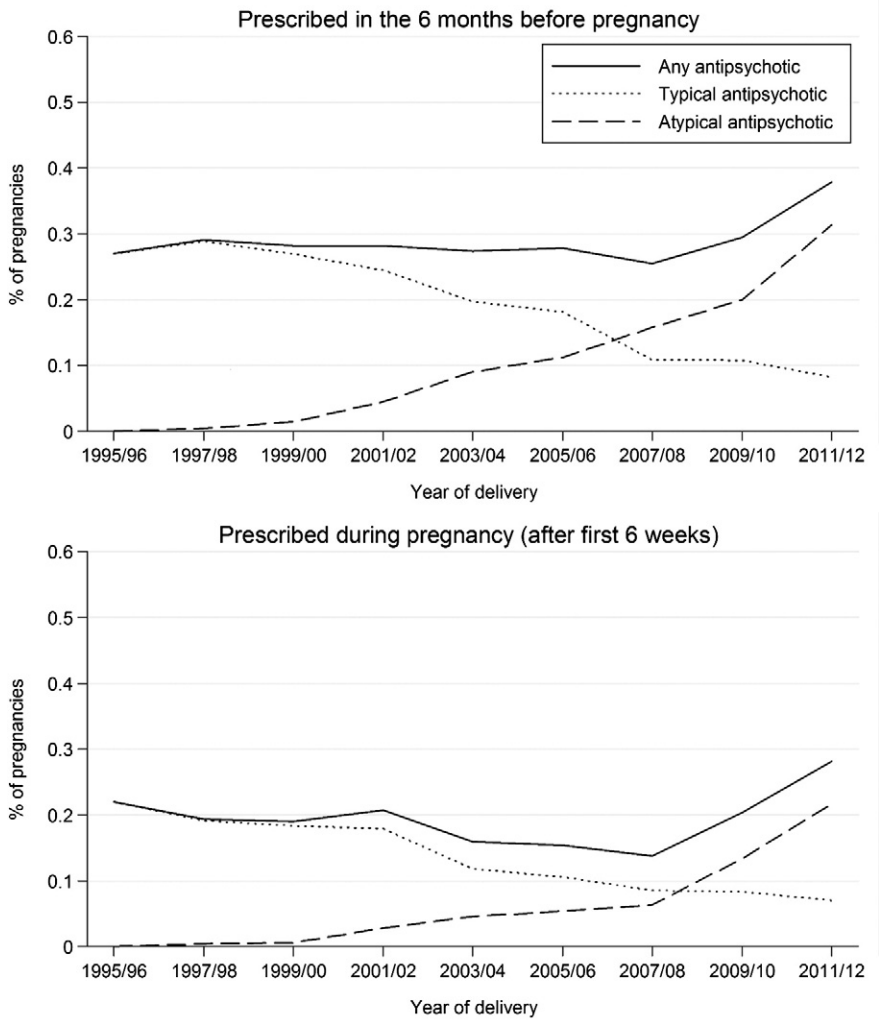

Fig. 1. Trends in prevalence of prescribing of antipsychotics before (upper graph) and during pregnancy (lower graph).

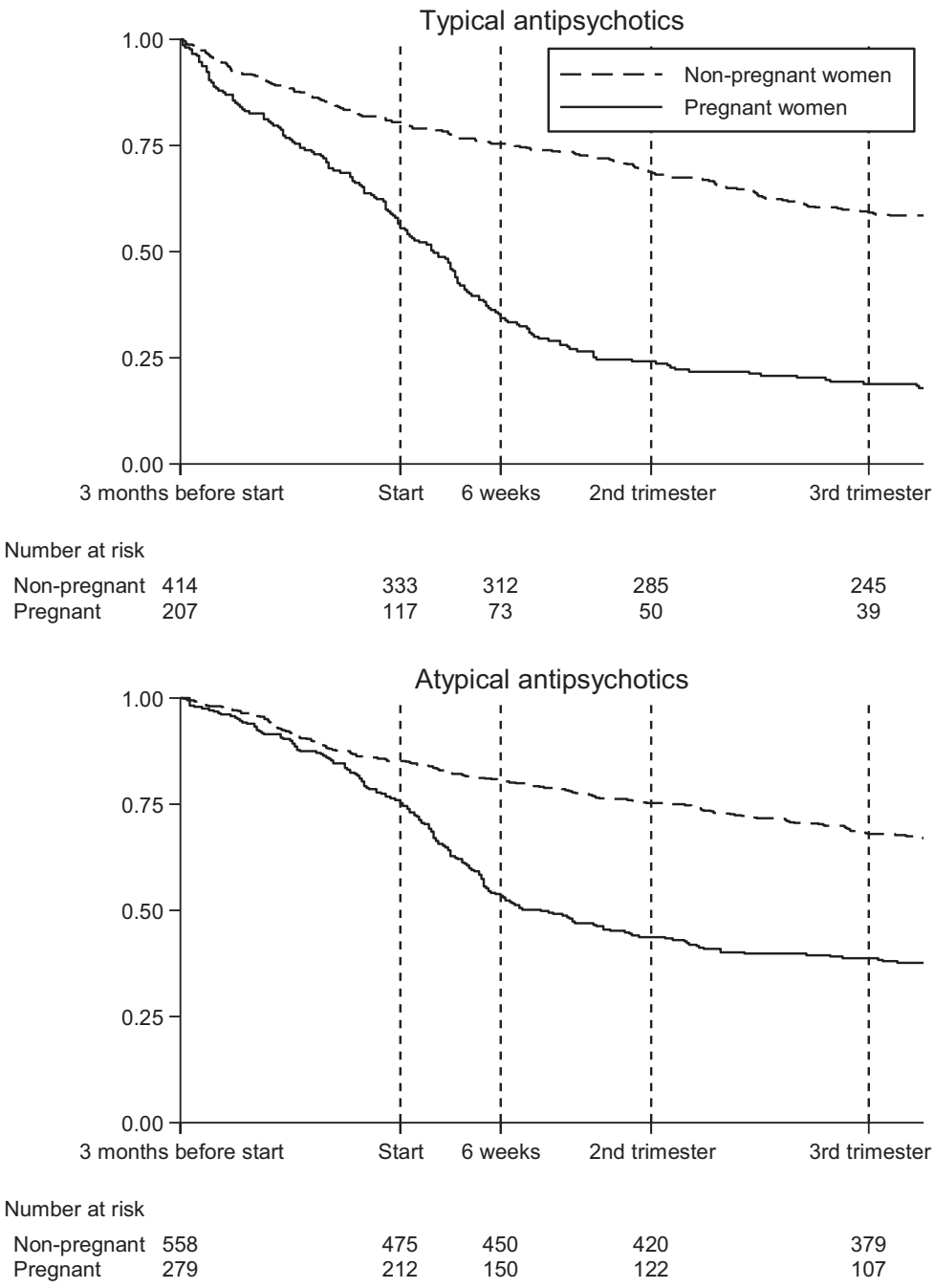

Fig. 2. Discontinuation of antipsychotic drugs in pregnant and non-pregnant women, by a) typical and b) atypical antipsychotics.

stopping antipsychotics. About 25% of non-pregnant women stopped both typical and atypical antipsychotics over the same time period as the pregnant women. Women on a high dose (DDD > 1) of typical antipsychotics were highly likely to *discontinue* prescriptions prior to pregnancy in contrast to women on a high dose (DDD > 1) of atypical antipsychotics (Fig. 3). Three out of fifteen women on high dose typical antipsychotics were on depots.

Factors associated with continuation of receiving antipsychotic prescriptions beyond six weeks of pregnancy for typical antipsychotics included age and durations of treatment prior to pregnancy (Table 1). Those aged 35 years or above were more than three times as likely to continue treatment compared to those below 25 years (RR: 3.09 [95% CI 1.76,5.44] (Table 1)). The effect of age attenuated slightly after adjustment for dose (Table 1). Likewise, those who had received continuous treatment for more than 12 months prior to pregnancy were also more likely to continue treatment in pregnancy compared to those who had received less than 6 months of continuous treatment prior to pregnancy (RR: 3.12 [95% CI 1.97, 4.95] (Table 1)). This was still the case after adjustment for age and dose (RR: 2.48 [95% CI 1.54, 3.99] (Table 1)). For atypical antipsychotics length and dose of prior prescribing were also associated with continuation in pregnancy (Table 2). However, those aged 30–34 years were the most likely to continue prescriptions in pregnancy (Table 2). For other factors examined (diagnosis of severe mental illnesses, also taking antidepressants and mood stabilisers, social deprivation, estimated parity, obesity, smoking, records of alcohol problems, illicit drug use and ethnicity) none of the adjusted effect sizes were larger than 1.65 or lower than 0.64 (Tables 1 and 2).

In general, few women switched between typical and atypical antipsychotic treatment just before or in pregnancy. Only 5/207 (2.4%)

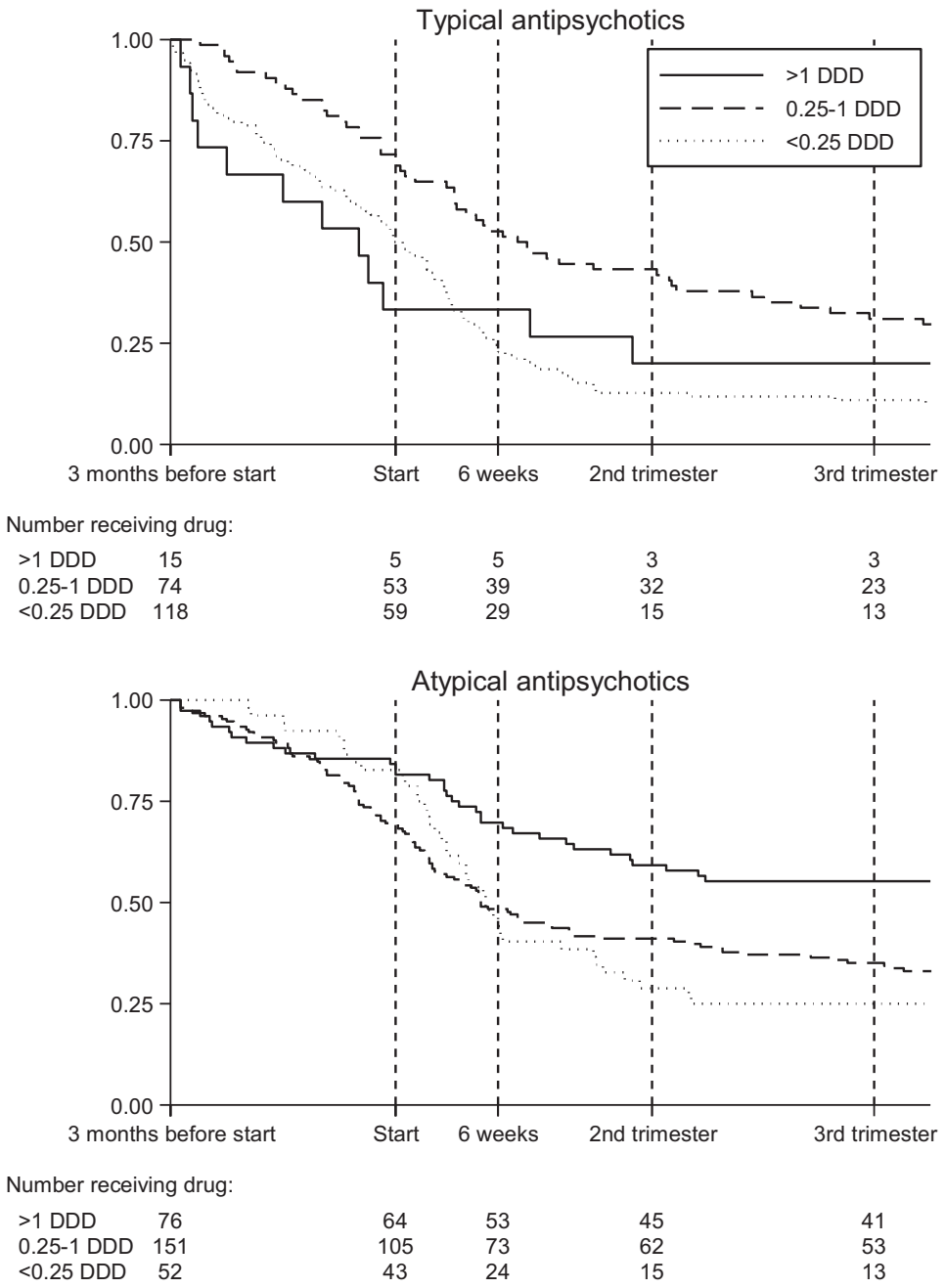

Fig. 3. Discontinuation of antipsychotic drugs in pregnant women, by dose in women who were prescribed a) typical and b) atypical antipsychotics.

women switched from typical to atypical antipsychotics and 9/279 (3.2%) switched from atypical to typical antipsychotics. However, among the more frequently used antipsychotics, switching levels were high for a couple of drugs: 12/50 women (24.0%) switched from risperidone to another antipsychotic, while 9/48 (18.8%) switched from trifluoperazine to another antipsychotic.

4. Discussion

The overall prescribing of antipsychotics in pregnancy has been relatively constant up to 2007 although there seems to be an increase in the last few years due to more women being prescribed atypical antipsychotics. Many women were not prescribed further antipsychotics after six weeks of pregnancy suggesting that pregnancy is a major determinant for stopping antipsychotic prescribing. Those most likely to continue treatment were those who had received continuous treatment for more than 12 months prior to pregnancy. Other determinants for continuation of antipsychotic prescribing in pregnancy included women's age and being on higher pre-pregnancy treatment doses.

As primary care databases do not have information on dispensing or compliance, we cannot be sure that women actually took the prescribed antipsychotics and we won't have the exact date women may have stopped their medication. However, by including women who received repeat prescriptions prior to pregnancy it is more likely that they were using the medication compared to those who just received a single prescription. As outlined in the Methods section, the primary prescribing budget is with the NHS primary care trusts and hence it is likely that we have captured most antipsychotic prescriptions issued during pregnancy. However, inpatient prescriptions and some specialist medications prescribed in secondary care, such as clozapine, will not have been captured by primary care databases. Although, we expect this would have been the case for a very small minority of the women. The

Table 1
Factors associated with receiving typical antipsychotics prescriptions beyond 6 weeks after the estimated pregnancy start date. Results of Poisson regression (using robust variance estimation).

	n	Typical antipsychotics (n = 207)					
		Unadjusted			Adjusted		
		RR	95% CI	p value	RR	95% CI	p value
Average daily dose (in units of DDD)				<0.001			0.011
<0.25 DDD	118	1			1		
0.25–1 DDD	74	2.14	[1.46,3.15]		1.78	[1.22,2.60]	
>1 DDD	15	1.36	[0.62,2.97]		1.25	[0.58,2.68]	
Age band				<0.001			<0.001
<25	53	1			1		
25–29	42	1.49	[0.74,2.99]		1.34	[0.68,2.62]	
30–34	59	1.22	[0.62,2.43]		1.15	[0.58,2.29]	
35+	53	3.09	[1.76,5.44]		2.60	[1.47,4.59]	
Continuous prior time on antipsychotics				<0.001			0.001
<6 months	98	1			1		
6–12 months	34	1.92	[1.03,3.57]		1.78	[0.97,3.26]	
>12 months	75	3.12	[1.97,4.95]		2.48	[1.54,3.99]	
SMI diagnosis code				0.018			0.404
No	160	1			1		
SMI diagnosis code	47	1.57	[1.08,2.27]		1.17	[0.81,1.71]	
Also taking an antidepressant				0.238			0.566
No	66	1			1		
Taking an antidepressant	141	0.80	[0.55,1.16]		0.90	[0.64,1.28]	
Also taking a mood stabiliser				0.033			0.281
No	191	1			1		
Taking a mood stabiliser	16	1.68	[1.04,2.71]		1.31	[0.80,2.12]	
Townsend quintile				0.562			0.440
1	16	1			1		
2	22	0.85	[0.35,2.05]		0.72	[0.32,1.61]	
3	36	0.67	[0.28,1.56]		0.64	[0.29,1.43]	
4	61	1.14	[0.57,2.28]		1.07	[0.57,1.99]	
5	68	0.98	[0.48,1.99]		0.89	[0.47,1.68]	
Unrecorded	4						
Estimated parity				0.103			0.159
0	84	1			1		
1	57	1.47	[0.91,2.40]		1.34	[0.87,2.08]	
2	44	1.82	[1.13,2.93]		1.65	[1.06,2.57]	
3 or more	22	1.39	[0.72,2.69]		1.52	[0.80,2.90]	
Obesity status				0.771			0.759
Not obese	186	1			1		
Obese	21	1.09	[0.61,1.95]		1.09	[0.63,1.90]	
Smoking status				0.912			0.602
Non-smoker	106	1			1		
Smoker	101	1.02	[0.71,1.48]		1.09	[0.78,1.53]	
Alcohol problems				0.154			0.094
No	191	1			1		
Yes	16	1.47	[0.87,2.50]		1.59	[0.92,2.75]	
Illicit drug use				0.941			0.866
No	181	1			1		
Yes	26	0.98	[0.56,1.72]		1.05	[0.60,1.84]	
Ethnicity							
Other	204	1			1		
Black or minority ethnic	3	Could not be estimated—all 3 continue receiving prescriptions					

Adjustment variables: dose and age band.

strength of our study is that the database covers real time clinical practice and the prospective nature of study would make it not subject to recall biases.

Other studies have found an increase in atypical antipsychotic prescription in pregnancy over the last decades (Epstein et al., 2013; Toh et al., 2013). However, to our knowledge, this is the first study to examine in detail the patterns of antipsychotic prescribing in pregnancy and the level of discontinuation during gestation. It appears that knowledge of pregnancy was a major reason for stopping antipsychotics. A large proportion of the women who received their last prescription within the first six weeks of gestation may not be aware of the pregnancy. By the time the prescription would be due for renewal many women would have been aware of their pregnancy and have decided to stop the medication. The general practitioner as well as the pregnant woman's mental health team/consultant may play a pivotal role in advising an individual woman on continuation of prescribed medicines in pregnancy. This would be in keeping with the recommendations made by national formularies and the NICE guidelines (National Institute for Health and Clinical Excellence, 2006, 2007). Since the recommendations are often non-specific, both health care professionals and the women are left with a very difficult and complex decision. In each individual case they have to weigh up risks to the mother and child of continuation versus discontinuation of medication in the absence of clear evidence. This is the first study to examine discontinuation of antipsychotic prescribing in pregnancy based on the UK primary care data. However, further research is needed in other settings to examine whether the background and training of the health care professionals may impact the decision process.

The greatest risk of discontinuation of the antipsychotic medication is the possibility of relapse of the mental illness in pregnancy and postpartum. An observational study of mood disorders in 2252 pregnancies and postpartum periods demonstrated that women with bipolar

Table 2
Factors associated with receiving atypical antipsychotic prescriptions beyond 6 weeks after the estimated pregnancy start date. Results of Poisson regression (using robust variance estimation).

	n	Atypical antipsychotics (n = 279)					
		Unadjusted			Adjusted		
		RR	95% CI	p value	RR	95% CI	p value
Average daily dose (in units of DDD)				0.002			0.003
<0.25 DDD	52	1			1		
0.25–1 DDD	151	1.05	[0.75,1.47]		1.04	[0.74,1.47]	
>1 DDD	76	1.51	[1.09,2.10]		1.48	[1.06,2.07]	
Age band				0.147			0.201
<25	53	1			1		
25–29	74	1.24	[0.84,1.83]		1.23	[0.84,1.80]	
30–34	82	1.50	[1.04,2.15]		1.45	[1.02,2.08]	
35+	70	1.34	[0.92,1.97]		1.31	[0.90,1.92]	
Continuous prior time on antipsychotics				<0.001			0.001
<6 months	100	1			1		
6–12 months	53	1.34	[0.93,1.93]		1.34	[0.93,1.94]	
>12 months	126	1.78	[1.34,2.35]		1.67	[1.27,2.21]	
SMI diagnosis code				0.005			0.073
No	136	1			1		
SMI diagnosis code	143	1.39	[1.11,1.74]		1.25	[0.98,1.59]	
Also taking an antidepressant				0.097			0.402
No	96	1			1		
Taking an antidepressant	183	0.83	[0.67,1.03]		0.91	[0.73,1.13]	
Also taking a mood stabiliser				0.098			0.574
No	232	1			1		
Taking a mood stabiliser	47	1.23	[0.96,1.58]		1.08	[0.83,1.40]	
Townsend quintile				0.880			0.805
1	26	1			1		
2	32	1.10	[0.70,1.74]		1.07	[0.68,1.67]	
3	52	0.93	[0.59,1.45]		0.87	[0.56,1.35]	
4	72	0.93	[0.61,1.42]		0.87	[0.57,1.33]	
5	85	1.03	[0.69,1.54]		0.94	[0.63,1.41]	
Unrecorded	12						
Estimated parity				0.474			0.511
0	110	1			1		
1	89	0.89	[0.70,1.15]		0.92	[0.72,1.18]	
2	49	0.79	[0.57,1.11]		0.82	[0.58,1.14]	
3 or more	31	0.82	[0.55,1.22]		0.80	[0.54,1.18]	
Obesity status				0.055			0.119
Not obese	223	1			1		
Obese	56	1.26	[1.00,1.59]		1.21	[0.95,1.53]	
Smoking status				0.875			0.935
Non-smoker	142	1			1		
Smoker	137	0.98	[0.79,1.22]		0.99	[0.80,1.23]	
Alcohol problems				0.595			0.385
No	264	1			1		
Yes	15	1.12	[0.73,1.73]		1.22	[0.78,1.90]	
Illicit drug use				0.370			0.340
No	246	1			1		
Yes	33	1.15	[0.85,1.55]		1.16	[0.85,1.58]	
Ethnicity				0.087			0.214
Other	249	1			1		
Black or minority ethnic	30	1.28	[0.97,1.69]		1.20	[0.90,1.59]	

Adjustment variables: dose and age band.

disorders were at particularly high risk of developing major depression in the postpartum period (prevalence: 19% and 29% in women with bipolar I disorder and bipolar II disorder, respectively) (Viguera et al., 2011). Likewise, it has been shown that women with a history of psychotic disorder were at higher risk of postpartum psychiatric illness, in particular non-psychotic anxiety and depressive disorders (Howard et al., 2004). Case-reports of suicide among these women highlight the severity of these illnesses (Jones, 2005). Aside from the direct effects of discontinuation of psychotropic medication on the mother, the indirect impact on the foetus and child of severe depression and puerperal psychosis also need to be taken into consideration. Yet we observed a large proportion of women discontinuing antipsychotics in pregnancy —similar to the trends observed for pregnant women on antidepressants and women treated with antiepileptic drugs for bipolar disorder (Petersen et al., 2011; Man et al., 2012). Women may have different reasons to discontinue, some may discontinue as they fear the antipsychotic medication will harm the unborn child and weigh that uncertainty of risk higher than the potential risk of relapse. Other women may discontinue antipsychotics in this period because they may no longer need the medication. We also observed that a number of women on high dose typical antipsychotics ceased prescribing before they became pregnant, including three women on depots. This may be a part of pregnancy planning, but could also be explained by the fact that typical antipsychotics are known to reduce fertility by inducing hyperprolactinaemia. Finally, the comparison of discontinuation between non-pregnant and pregnant women revealed that pregnancy is not the only reason for women to discontinue antipsychotic medication. Other factors such as experience of adverse effects and stigmatisation associated with antipsychotics may influence continuous prescribing in pregnant as well as non-pregnant women.

5. Conclusion

Overall, prescription rates for antipsychotics in pregnancy have been relatively stable over the last two decades. Prescribing of atypical antipsychotics has been increasing both before and during pregnancy, resulting in a slight increase in overall prevalence of prescribing since 2007. However, pregnancy is strongly associated with women discontinuing antipsychotic medication. Less than 40% of women who received atypical antipsychotics prior to pregnancy were still in receipt of them at the start of their third trimester. For typical antipsychotics the figure was down to 19% by the start of third trimester. Duration of prior treatment, maternal age as well as dose was significantly associated with continued treatment of antipsychotics in pregnancy.

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Contributors

The funder had no involvement in the design or conduct of the study.

Conflict of interest

None of the authors have any conflicts of interest to report.

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References

Blak, B.T., Thompson, M., Dattani, H., Bourke, A., 2011. Generalisability of The Health Improvement Network (THIN) database: demographics, chronic disease prevalence and mortality rates. Inform. Prim. Care 19 (4), 251–255.

Chisholm, J., 1990. The Read clinical classification. Br. Med. J. 300 (6732), 1092 (Apr 28).

Einarson, A., Boskovic, R., 2009. Use and safety of antipsychotic drugs during pregnancy. J. Psychiatr. Pract. 15 (3), 183–192 (May).

Epstein, R.A., Bobo, W.V., Shelton, R.C., Arbogast, P.G., Morrow, J.A., Wang, W., et al., 2013. Increasing use of atypical antipsychotics and anticonvulsants during pregnancy. Pharmacoepidemiol. Drug Saf. 22 (7), 794–801 (Jul).

Galbally, M., Snellen, M., Lewis, A.J., 2011. A review of the use of psychotropic medication in pregnancy. Curr. Opin. Obstet. Gynecol. 23 (6), 408–414 (Dec).

Gibson, J., 2012. Enhanced Dosage Determinations. CSD Medical Research UK.

Hardoon, S., Hayes, J.F., Blackburn, R., Petersen, I., Walters, K., Nazareth, I., et al., 2013. Recording of severe mental illness in United Kingdom primary care, 2000–2010. PLoS ONE 8 (12), e82365 (Dec 12).

Hayes, J., Prah, P., Nazareth, I., King, M., Walters, K., Petersen, I., et al., 2011. Prescribing trends in bipolar disorder: cohort study in the United Kingdom THIN primary care database 1995–2009. PLoS ONE 6 (12), e28725 (Dec 7).

Howard, L.M., Goss, C., Leese, M., Appleby, L., Thornicroft, G., 2004. The psychosocial outcome of pregnancy in women with psychotic disorders. Schizophr. Res. 71 (1), 49–60 (Nov 1).

Jones, I., 2005. Bipolar disorder and childbirth: the importance of recognising risk. Br. J. Psychiatry 186 (6), 453–454 (Jun 1).

Lis, Y., Mann, R.D., 1995. The VAMP research multi-purpose database in the UK. J. Clin. Epidemiol. 48 (3), 431–443 (Mar).

Man, S.-L., Petersen, I., Thompson, M., Nazareth, I., 2012. Antiepileptic drugs during pregnancy in primary care: a UK population based study. PLoS ONE 7 (12), e52339 (Dec 18).

National Institute for Health and Clinical Excellence, 2006. Bipolar disorder: the management of bipolar disorder in adults, children and adolescents, in primary and secondary care [Internet]. Available from: http://www.nice.org.uk/CG38.

National Institute for Health and Clinical Excellence, 2007. Antenatal and postnatal mental health: clinical management and service guidance [Internet]. Available from: http://www.nice.org.uk/CG45.

Petersen, I., Gilbert, R.E., Evans, S.J.W., Man, S.-L., Nazareth, I., 2011. Pregnancy as a major determinant for discontinuation of antidepressants. J. Clin. Psychiatry 72 (07), 979–985 (Jul 15).

Prah, P., Petersen, I., Nazareth, I., Walters, K., Osborn, D., 2012. National changes in oral antipsychotic treatment for people with schizophrenia in primary care between 1998 and 2007 in the United Kingdom. Pharmacoepidemiol. Drug Saf. 21 (2), 161–169.

Reis, M., Källén, B., 2008. Maternal use of antipsychotics in early pregnancy and delivery outcome. J. Clin. Psychopharmacol. 28 (3), 279–288 (Jun).

Sadowski, A., Todorow, M., Yazdani Brojeni, P., Koren, G., Nulman, I., 2013. Pregnancy outcomes following maternal exposure to second-generation antipsychotics given with other psychotropic drugs: a cohort study. BMJ Open 3 (7).

Toh, S., Li, Q., Cheetham, T.C., Cooper, W.O., Davis, R.L., Dublin, S., et al., 2013. Prevalence and trends in the use of antipsychotic medications during pregnancy in the U.S., 2001–2007: a population-based study of 585,615 deliveries. Arch. Womens Ment. Health 16 (2), 149–157 (Apr 1).

Viguera, A.C., Tondo, L., Koukopoulos, A.E., Reginaldi, D., Lepri, B., Baldessarini, R.J., 2011. Episodes of mood disorders in 2,252 pregnancies and postpartum periods. Am. J. Psychiatry 168 (11), 1179–1185 (Nov 1).

Webb, R.T., Howard, L., Abel, K.M., 2004. Antipsychotic drugs for non-affective psychosis during pregnancy and postpartum. Cochrane Database Syst. Rev. 2, CD00441.

WHO Collaborating Centre for Drug Statistics Methodology, 2013. WHOCC—ATC/DDD Index [Internet]. [cited 2013 Dec 2]. Available from: http://www.whocc.no/atc_ddd_index/.

Yonkers, K.A., Wisner, K.L., Stowe, Z., Leibenluft, E., Cohen, L., Miller, L., et al., 2004. Management of bipolar disorder during pregnancy and the postpartum period. Am. J. Psychiatry 161 (4), 608–620 (Apr).