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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

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Abstract

Purpose—To estimate the prevalence of and temporal trends in prenatal antipsychotic medication use within a cohort of pregnant women in the U.S.

Methods—We identified live born deliveries to women aged 15–45 years in 2001–2007 from 11 U.S. health plans participating in the Medication Exposure in Pregnancy Risk Evaluation Program

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(MEPREP). We ascertained prenatal exposure to antipsychotics from health plan pharmacy dispensing files, gestational age from linked infant birth certificate files, and ICD-9-CM diagnosis codes from health plan claims files. We calculated the prevalence of prenatal use of atypical and typical antipsychotics according to year of delivery, trimester of pregnancy, and mental health diagnosis.

Results—Among 585,615 qualifying deliveries, 4,223 (0.72%) were to women who received an atypical antipsychotic and 548 (0.09%) were to women receiving a typical antipsychotic any time from 60 days before pregnancy through delivery. There was a 2.5-fold increase in atypical antipsychotic use during the study period, from 0.33% (95% confidence interval: 0.29%, 0.37%) in 2001 to 0.82% (0.76%, 0.88%) in 2007, while the use of typical antipsychotics remained stable. Depression was the most common mental health diagnosis among deliveries to women with atypical antipsychotic use (63%), followed by bipolar disorder (43%) and schizophrenia (13%).

Conclusions—The number and proportion of pregnancies exposed to atypical antipsychotics has increased dramatically in recent years. Studies are needed to examine the comparative safety and effectiveness of these medications relative to other therapeutic options in pregnancy.

Keywords

Antipsychotics; database; pregnancy; prevalence

Introduction

Atypical (second-generation) antipsychotics have replaced typical (first-generation) antipsychotics as the first-line treatment for schizophrenia and related psychotic disorders since their introduction in the 1990s (Lehman et al. 2004; Stanniland and Taylor 2000; Bagnall et al. 2003). In recent years, the indications for atypical antipsychotics have been expanded to bipolar disorder and depression. There is also evidence of increasing off-label use of these medications (Alexander et al. 2011).

For conditions that are the major indications for antipsychotic use – schizophrenia and related psychotic disorders, bipolar disorder, and depression – onset in women is usually before or during the childbearing years (Kessler et al. 2005; Leung and Chue 2000; Kennedy et al. 2005). Decisions about antipsychotic treatment during pregnancy must balance the risks of leaving these conditions untreated against potential medication-associated risks to the mother and the infant (ACOG Committee on Practice Bulletins--Obstetrics 2008; Altshuler et al. 1996; Viguera et al. 2002; Yonkers et al. 2004; Yonkers et al. 2009). Existing studies of birth outcomes in women treated with antipsychotics during pregnancy have produced contradictory results (Newham et al. 2008; Reis and Kallen 2008; Boden et al. 2012b; Johnson et al. 2012; McKenna et al. 2005; Babu et al. 2010; Ernst and Goldberg 2002; Gentile 2010; Grover et al. 2006; Newport et al. 2007; Trixler et al. 2005; Wichman 2009). For example, some studies (Newham et al. 2008; Reis and Kallen 2008; Boden et al. 2012b; Johnson et al. 2012) have observed an association between prenatal atypical antipsychotic exposure and congenital malformations, gestational diabetes, preterm delivery, macrosomia, or lower neuromotor performance, but others (McKenna et al. 2005; Coppola et al. 2007) have not.

It is unclear how many women are exposed to these medications during pregnancy as little is known about the prevalence of and temporal trends in the use of antipsychotics during the prenatal period. In this study, we examined the use of atypical and typical antipsychotics during pregnancy according to year of delivery, trimester of pregnancy, and mental health diagnosis within a large U.S. cohort of pregnant women.

Materials and Methods

Data source

This study used data from the Medication Exposure in Pregnancy Risk Evaluation Program (MEPREP). MEPREP is a collaborative research program between the U.S. Food and Drug Administration and three contract sites: the HMO Research Network Center for Education and Research in Therapeutics, Kaiser Permanente of California, and Vanderbilt University School of Medicine/Tennessee State Medicaid (Andrade et al. 2012). Encompassed within these three contract sites are 11 health plan-affiliated research institutions, including Group Health Research Institute (Washington), Harvard Pilgrim Health Care Institute (Massachusetts), HealthPartners Research Foundation (Minnesota), Kaiser Permanente Colorado, Kaiser Permanente Georgia, Kaiser Permanente Northwest (Oregon), Meyers Primary Care Institute (Massachusetts), Lovelace Clinic Foundation (New Mexico), Kaiser Permanente Northern California, Kaiser Permanente Southern California, and Tennessee State Medicaid (through the auspices of Vanderbilt University School of Medicine). These health plans provide care to approximately 12 million current enrollees within nine states, covering geographically and ethnically diverse populations receiving care within a wide array of medical care delivery models.

To support multi-site studies of medication safety in pregnancy, the research institutions have extracted information on maternal and infant enrollment, demographics, outpatient pharmacy dispensings, and outpatient and inpatient health care encounters from their health plans' administrative and claims databases. They have also linked health plan data to infants' birth certificate files, which include information on sociodemographic, medical, and reproductive factors such as maternal race/ethnicity, parity and infants' gestational age at birth. All data have been transformed into standardized datasets. The study was approved by the Institutional Review Board of each participating organization and the state departments of public health, where applicable.

Study population

The source population for the current study included all live born deliveries between January 1, 2001 and December 31, 2007. To be eligible, the mothers had to be between 15 and 45 years of age at the time of delivery, and to have been continuously enrolled in the health plan with pharmacy benefits from 180 days before pregnancy through delivery. We used the 180-day pre-pregnancy period to ascertain maternal characteristics, and capture antipsychotic use and medical diagnoses before pregnancy.

Antipsychotics of interest

The atypical antipsychotics of interest included aripiprazole, clozapine, olanzapine, paliperidone, quetiapine, risperidone, and ziprasidone. The typical antipsychotics of interest were chlorpromazine, fluphenazine, haloperidol, loxapine, mesoridazine, molindone, perphenazine, pimozide, thioridazine, thiothixene, and trifluoperazine. In a secondary analysis, we further considered prochlorperazine and promethazine – two medications that are traditionally classified as typical antipsychotics but are more commonly used as anti-emetics in contemporary clinical practice.

We identified antipsychotic use from the outpatient pharmacy dispensing file using National Drug Codes and determined periods of drug exposure from the dispensing dates and days supplied. We incorporated a 14-day "grace period" after the calculated end of each prescription based on days supplied and considered women exposed during the grace period.

Definition and identification of trimesters of pregnancy

For deliveries for which the last menstrual period (LMP)-based gestational age was available in the birth certificate file (94% of the study population), we used the first day of the LMP as the beginning of the first trimester ("day zero"). We defined the first trimester as days 0–89, the second trimester as days 90–179, and the third trimester as day 180 through delivery. If the LMP was missing or had an improbable value (e.g., LMP-based gestational age <15 weeks), day zero was defined as delivery date minus the clinical or obstetric estimate-based gestational age. This method of assigning day zero is consistent with the approach used by the National Center for Health Statistics of the U.S. Centers for Disease Control and Prevention (Martin et al. 2010). The birth certificate LMP has been validated previously by one of the participating health plans, which found a concordance within two weeks between the birth certificate LMP and the hospital records in 94% of the records reviewed (Cooper et al. 2006).

For deliveries for which gestational age information was missing in the birth certificates (<1% of the study population), we applied a validated algorithm that used the delivery date and specific International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) codes recorded in the health plan claims data to estimate the trimesters (Li et al.). The algorithm assumed day zero as delivery date minus 270 days if there was no ICD-9-CM code for preterm birth; as delivery date minus 245 days if there was a code for preterm birth of unspecified gestational age; and as delivery date minus the upper limit of the gestational age range if there was a code for preterm birth with a specified range, e.g., delivery date minus 224 days for deliveries with an ICD-9-CM code 765.26 ("31 to 32 weeks of gestation").

Identification of maternal characteristics

We obtained information on maternal age at delivery, calendar year of delivery, and diagnoses for potential indications for antipsychotic use from the health plan administrative and claims data. Information on maternal race/ethnicity, educational level, marital status, smoking, and alcohol consumption was extracted from the birth certificate file.

Statistical analysis

We identified deliveries exposed to either atypical or typical antipsychotics from any time from 60 days before pregnancy through delivery, and compared their maternal characteristics with those without any exposure to antipsychotic medication during the same period. We described the temporal trend in prenatal antipsychotic use by calendar year of delivery. We also estimated the prevalence during different pregnancy periods, including the 60-day period before pregnancy, any time during pregnancy, and each trimester of pregnancy; these time periods were not mutually exclusive, e.g., deliveries with atypical antispsychotic exposure during the first and second trimester would appear in both periods. Antipsychotic exposure status was also not mutually exclusive, e.g., deliveries with both atypical and typical antipsychotic exposure would be included in both groups.

We calculated the proportion of antispsychotic-exposed deliveries with a diagnosis of schizophrenia (ICD-9-CM codes 295.xx), bipolar disorder (296.0x, 296.1x, 296.4x–296.8x), or depression (296.2x, 296.3x, 300.4x, 311) any time from 180 days before pregnancy through delivery. Multiple diagnoses per delivery were recorded if they occurred. All analyses were performed separately for atypical and typical antipsychotics.

Results

The study population was composed of 585,615 deliveries. For 4,223 deliveries (0.7%) the mothers had filled at least one prescription for an atypical antipsychotic any time during the period from 60 days before pregnancy through delivery. Only 548 deliveries (0.09%) were to women exposed to typical antipsychotics during the same period. Compared with deliveries without any exposure to antipsychotics, deliveries with exposure to atypical or typical antipsychotics (not including prochlorperazine and promethazine) were more likely to be to women who were younger, non-Hispanic White or Black (rather than Hispanic or Asian), or had a lower education level (Table 1).

Atypical antipsychotic use

The prevalence of atypical antipsychotic exposure increased 2.5-fold during the study period, from 0.33% of deliveries (95% confidence interval: 0.29%, 0.37%) in 2001 to 0.82% (0.76%, 0.88%) in 2007 (Figure 1). The prevalence was highest at 0.5% during the first trimester, and decreased to 0.3% in the second trimester and 0.2% in the third trimester (Table 2). Quetiapine was the most commonly used atypical antipsychotics (42% of atypical antipsychotic use), followed by olanzapine (32%) and risperidone (23%).

About 81% of the deliveries to women with atypical antipsychotic exposure any time from 60 days before pregnancy through delivery had a recorded diagnosis of depression, bipolar disorder, or schizophrenia. Depression was the most common diagnosis among these deliveries – with 63% having such diagnosis – followed by bipolar disorder (43%) and schizophrenia (13%) (Table 3).

During the study period, there appeared to be a modest shift in the diagnosis pattern among deliveries exposed to atypical antipsychotics, with more diagnosed with bipolar disorder and less with depression or schizophrenia over time (Table 4). In 2007, the proportion of deliveries with a diagnosis of bipolar disorder (53%) was similar to the proportion with a diagnosis of depression (58%), in contrast to 39% and 64%, respectively, in 2001.

Typical antipsychotics

The prevalence of typical antipsychotic use in each year was low and relatively stable at about 0.1% over the study period (Figure 1). Similar to what was observed for atypical antipsychotics, the prevalence was greatest during the first trimester, followed by a drop in the later two trimesters. Haloperidol and chlorpromazine had the highest use (Table 2). Approximately 73% of deliveries to women with typical antipsychotic exposure any time from 60 days before pregnancy through delivery had a diagnosis of bipolar disorder, schizophrenia, or depression (Table 3), with depression being the most common diagnosis (51%), followed by bipolar disorder (37%) and schizophrenia (27%). Compared with atypical antipsychotic-exposed deliveries, deliveries with typical antipsychotic use were more likely to have a diagnosis of schizophrenia (27% versus 13%).

Typical antipsychotics – Including prochlorperazine and promethazine

When we included prochlorperazine and promethazine, the number of deliveries with typical antipsychotic use became substantially higher (n=68,946, or 11.8% of all deliveries). Over the study years, prenatal use of typical antipsychotics including prochlorperazine and promethazine increased slightly from 10.6% in 2001 to 12.8% in 2007. The prevalence was highest at 7.3% during the first trimester, followed by 5.9% in the second trimester, 3.2% in the third trimester, and 1.5% in the 60-day pre-pregnancy period. Promethazine was prescribed far more commonly than prochlorperazine (10.9% vs. 1.1% of all deliveries). About 84% of deliveries were to women who were exposed to these two medications but did

not have a diagnosis of schizophrenia, bipolar disorder, or depression. This, along with the low prevalence of use during the pre-pregnancy period, strongly suggested that these two medications were used as anti-emetics.

Discussion

In this study, we observed a 2.5-fold increase in the prevalence of prenatal use of atypical antipsychotics, from 0.3% (95% confidence interval: 0.3%, 0.4%) in 2001 to 0.8% (0.8%, 0.9%) in 2007. The prevalence of typical antipsychotics during pregnancy remained low and relatively stable. To our knowledge, this is the largest U.S. study to date to examine the prevalence of atypical and typical antipsychotic use during pregnancy.

The prevalence of prenatal antipsychotic use in our cohort was higher than previous estimates. A single-site U.S study found that 16 of the 30,092 women (0.05%) who delivered at the Mayo Clinic between 1993 and 2007 had used atypical antipsychotics during pregnancy (Wichman 2009). A study of 958,729 women in the Swedish Medical Birth Register from 1995 to 2005 found that 2,830 (0.3%) of them were exposed to antipsychotics while pregnant (Reis and Kallen 2008). However, 2,260 of these women used dixyrazine (not marketed in the U.S.) or prochlorperazine, two antipsychotics that are commonly used to treat nausea and vomiting during pregnancy and rarely used for psychiatric disorders. Only about 150 women (0.02%) used atypical antipsychotics. A separate study using the same national Swedish data from 2005 to 2009 found that the prevalence of atypical antipsychotic use during pregnancy was about 0.1% (Boden et al. 2012a). In a study conducted within the Medical Birth Registry of Norway, the prevalence of prenatal use of antipsychotic medications – identified by Anatomical Therapeutic Chemical (ATC) code N05A, which includes prochlorperazine and lithium – was 1.6% (1,736 out of 106,329 deliveries) during the 2004–2006 period (Engeland et al. 2008).

The higher prevalence in our study might be due to differences in the study population, clinical practice or medication use between countries, secular trends, or the methods used to identify medication exposure. Specifically, we included a large Medicaid population from the Tennessee Medicaid, which might be enriched with users of antipsychotic medications. A smaller study that used data from the Tennessee Medicaid observed an increase in atypical antipsychotic use during pregnancy, from 0.2% in 1985–2000 to 1.7% in 2005 (Epstein et al. 2012).

Findings from our study are consistent with an increase in the use of atypical antipsychotics and a shift in the diagnosis pattern from schizophrenia to bipolar disorder among atypical antipsychotics users identified from the general population over the same period (Verdoux et al. 2010; Alexander et al. 2011). The increase in use may in part be due to the expanded indications for use of atypical antipsychotics in bipolar disorder (of which the prevalence has been increasing in recent years (Blader and Carlson 2007)) and treatment-resistant depression (Nelson and Papakostas 2009), an increase in off-label use (Alexander et al. 2011), or a combination of these.

Decisions about the use of antipsychotic medications during pregnancy have to take into account the risks of not treating the underlying disorders, the risks associated with antipsychotic medications, the availability and safety of alternative therapies. Treating psychiatric conditions during pregnancy is generally recommended (ACOG Committee on Practice Bulletins--Obstetrics 2008; Altshuler et al. 1996; Viguera et al. 2002; Yonkers et al. 2004; Yonkers et al. 2009) but evidence to guide treatment choice is limited and conflicting (Trixler et al. 2005; Gentile 2010). It is unlikely that this critically needed information will come from randomized trials because of ethical concerns. Large, well-designed

observational studies employing data from databases such as the MEPREP resources may help fill the knowledge gap about the comparative safety of antipsychotic medications in pregnancy.

Our study has several strengths. First, the large sample size and the demographic and geographic diversity of our population increase the generalizability of the study findings. Second, the use of electronic pharmacy dispensing data avoids the potential for recall bias that is common in studies that rely on patient self-report. Restricting the analysis to women with pharmacy benefits increases the likelihood that we captured most dispensings of the study medications. Third, linkage to birth certificate data allows us to define gestational age more accurately, reducing the potential for misclassification of prenatal exposure status (Toh et al. 2008; Li et al.).

On the other hand, our study is not without limitations. As with any study using pharmacy dispensing records to identify drug use, we could not ascertain whether antipsychotics dispensed were actually taken by the women. As we limited our study to live born deliveries, we were not able to assess the use of antipsychotics in pregnancies that did not result in a live birth. The prevalence is higher in the Medicaid population, but we did not stratify the analysis by insurance status. While not stratifying on insurance status would not affect the validity of the analysis, our overall findings may not be generalizable to other populations with different patient characteristics. We did not have data after 2007, so we could not examine the utilization pattern in recent years. The Tennessee Medicaid adopted a policy that capped the number of prescriptions per month at five for each patient in 2006. The cap may partially explain the apparent interruption in the temporal trend in atypical antipsychotic prevalence at the same time. However, we believe the impact of the cap was not likely to be major for two reasons: 1) the prescription limit did not apply to enrollees under the age of 21 years, and 2) antipsychotics are on the “Prescriber Attestation List”, meaning that a pregnant woman over 21 years of age can exceed the prescription limit and receive an antipsychotic medication so long as the prescriber preauthorizes the medicine. Finally, even though we were able to identify mental health diagnoses recorded during the prenatal period, we could not determine the accuracy of these diagnoses and whether the medications were actually being used for those indications. However, it is reassuring that the shift in the diagnosis pattern observed in our study was also seen in a large study of the U.S. general population (Alexander et al. 2011).

In conclusion, between 2001 and 2007, an increasing number and proportion of pregnancies were exposed to atypical antipsychotics. As the decision to initiate or continue antipsychotic medications during pregnancy must balance the risks of not treating the underlying psychiatric disorders against the risks associated with taking these medications, there is a need for large, well-designed studies to examine the comparative safety of antipsychotics and other treatment choices for each indication in pregnancy.

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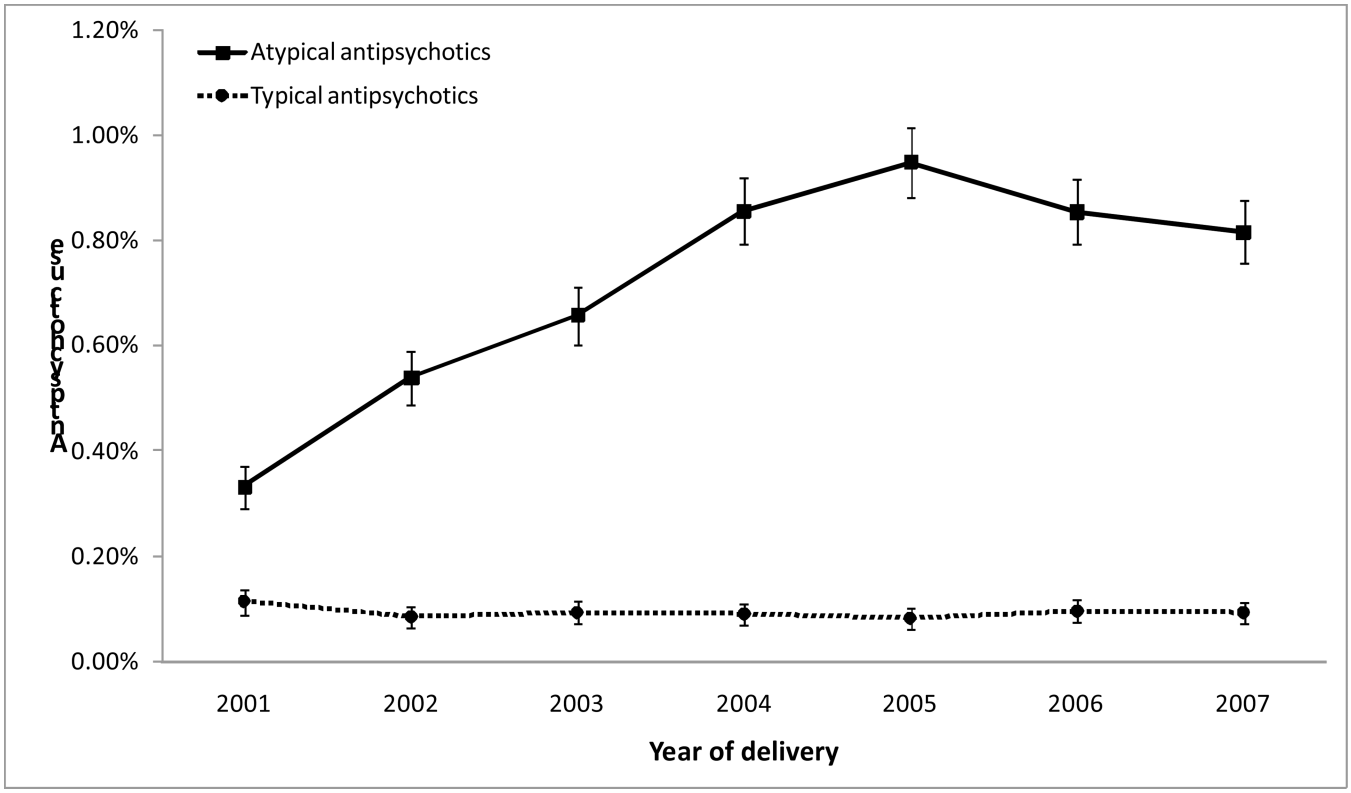

Figure 1.
The prevalence of antipsychotic use from 60 days before pregnancy through delivery by year of delivery, the Medication Exposure in Pregnancy Risk Evaluation Program, 2001–2007 The proportion in a given year was calculated using the number of deliveries exposed to atypical (or typical) antipsychotics in that year as the numerator and the total number of deliveries in that year as the denominator. Bars represent the 95% confidence intervals.

Table 1

Maternal characteristics by prenatal antipsychotic use status, the Medication Exposure in Pregnancy Risk Evaluation Program, 2001–2007[a]

Characteristics	Deliveries with atypical antipsychotic use	Deliveries with typical antipsychotic use	Deliveries with typical antipsychotic use including prochlorperazine and promethazine	Deliveries with no Antipsychotic use
	N (%)	N (%)	N (%)	N (%)
Total deliveries	4,223 (100)	548 (100)	68,946 (100)	514,782 (100)
Maternal age at delivery (years)				
<18	303 (7.2)	10 (1.8)	3,775 (5.5)	15,772 (3.1)
18–24	1,656 (39.2)	192 (35.0)	32,537 (47.2)	117,838(22.9)
25–34	1,756 (41.6)	244 (44.5)	27,051 (39.2)	279,629 (54.3)
35–45	508 (12.0)	102 (18.6)	5,583 (8.1)	101,543 (19.7)
Calendar year of delivery				
2001	264 (6.3)	90 (16.4)	8,432 (12.2)	70,954 (13.8)
2002	452 (10.7)	72 (13.1)	9,384 (13.6)	74,064 (14.4)
2003	555 (13.1)	79 (14.4)	9,345 (13.6)	74,441 (14.5)
2004	714 (16.9)	75 (13.7)	9,638 (14.0)	73,106 (14.2)
2005	794 (18.8)	69 (12.6)	10,335 (15.0)	72,596 (14.1)
2006	736 (17.4)	83 (15.1)	10,730 (15.6)	74,676 (14.5)
2007	708 (16.8)	80 (14.6)	11,082 (16.1)	74,945(14.6)
Maternal race/ethnicity				
Non-Hispanic White	2,967 (70.2)	292 (53.3)	39,991 (58.0)	241,717 (47.0)
Black/African American	911 (21.6)	185 (33.8)	18,536 (26.9)	75,282 (14.6)
Asian American	63 (1.5)	16 (2.9)	2,774 (4.0)	61,104 (11.9)
Hispanic	232 (5.5)	47 (8.6)	6,792 (9.9)	122,944 (23.9)
Native American	19 (0.4)	<5 (0.7)	213 (0.3)	1,532 (0.3)
Other	14 (0.3)	<5 (0.4)	187 (0.3)	3,080 (0.6)
Unknown	18 (0.4)	<5 (0.4)	453 (0.7)	9,123 (1.8)
Maternal education level (years)				
≤12	3,108 (73.6)	369 (67.3)	46,139 (66.9)	203,000 (39.4)
>12	1,036 (24.5)	169 (30.8)	21,301 (30.9)	287,110 (55.7)
Unknown	80 (1.9)	10 (1.8)	1,506 (2.2)	24,672 (4.8)
Maternal marital status				
Married	1,313 (31.1)	164 (29.9)	21,165 (30.7)	137,718 (26.8)
Not married	2,245 (53.1)	251 (45.8)	31,894 (46.3)	78,091 (15.2)
Unknown	666 (15.8)	133 (24.3)	15,887 (23.0)	298,973 (58.0)
Smoked during pregnancy				
Yes	1,533 (36.3)	141 (25.7)	14,630 (21.2)	29,651 (5.8)
No	1,313 (31.1)	211 (38.5)	28,947 (42.0)	223,154 (43.3)
Unknown	1,378 (32.6)	196 (35.8)	25,369 (36.8)	261,977 (50.9)
Alcohol intake during pregnancy				
Yes	46 (1.1)	13 (2.4)	386 (0.6)	4,192 (0.8)

Characteristics	Deliveries with atypical antipsychotic use	Deliveries with typical antipsychotic use	Deliveries with typical antipsychotic use including prochlorperazine and promethazine	Deliveries with no Antipsychotic use
	N (%)	N (%)	N (%)	N (%)
No	1,108 (26.2)	172 (31.4)	22,123 (32.1)	91,108 (17.7)
Unknown	3,070 (72.7)	363 (66.2)	46,437 (67.4)	419,482 (81.5)

[a]Antipsychotic exposure status was determined during the period from 60 days preceding pregnancy through delivery, it was not mutually exclusive (e.g., deliveries with both atypical and typical antipsychotic exposure would be included in both groups).

Table 2

Prenatal antipsychotic use by drug and gestational period, the Medication Exposure in Pregnancy Risk Evaluation Program, 2001–2007[a]

Drugs	Any time from 60 days before pregnancy through delivery		60-day pre pregnancy period		Any time during pregnancy		1st trimester		2nd trimester		3rd trimester	
	N	per 10,000 deliveries	N	per 10,000 deliveries	N	per 10,000 deliveries	N	per 10,000 deliveries	N	per 10,000 deliveries	N	per 10,000 deliveries
Atypical antipsychotics	4,223	72.0	3,169	54.0	3,476	59.3	3,030	51.7	1,565	26.7	1,144	19.5
Quetiapine	1,786	30.5	1,362	23.2	1,449	24.7	1,276	21.8	672	11.5	480	8.2
Olanzapine	1,342	22.9	884	15.1	1,077	18.4	867	14.8	465	7.9	358	6.1
Risperidone	970	16.5	676	11.5	750	12.8	628	10.7	303	5.2	211	3.6
Aripiprazole	443	7.6	331	5.6	351	6.0	310	5.3	140	2.4	87	1.5
Ziprasidone	314	5.4	229	3.9	249	4.2	223	3.8	92	1.6	60	1.0
Clozapine	12	0.2	8	0.1	12	0.2	10	0.2	5	0.1	7	0.1
Paliperidone	<5	0.02	<5	0.02	<5	0.02	<5	0.02	<5	0.02	<5	0.02
Typical antipsychotics	548	9.3	226	3.9	486	8.3	305	5.2	282	4.8	230	3.9
Haloperidol	225	3.8	76	1.3	206	3.5	112	1.9	126	2.1	119	2.0
Chlorpromazine	146	2.5	33	0.6	131	2.2	75	1.3	79	1.3	41	0.7
Perphenazine	95	1.6	59	1.0	81	1.4	64	1.1	44	0.8	32	0.5
Thiothixene	44	0.8	28	0.5	38	0.6	31	0.5	16	0.3	17	0.3
Trifluoperazine	27	0.5	10	0.2	24	0.4	13	0.2	14	0.2	11	0.2
Thioridazine	21	0.4	14	0.2	16	0.3	12	0.2	5	0.1	7	0.1
Fluphenazine	20	0.3	7	0.1	18	0.3	12	0.2	13	0.2	6	0.1
Loxapine	7	0.1	5	0.1	5	0.1	5	0.1	<5	0.02	<5	0.02
Pimozide	<5	0.03	<5	0.03	<5	0.03	<5	0.03	<5	0.02	<5	0.02
Mesoridazine	<5	0.02	<5	0.02	<5	0.02	<5	0.02	0	0	0	0
Molindone	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Other typical antipsychotics												
Prochlorperazine	6,266	106.8	841	14.3	5,659	96.5	3,643	62.1	2,856	48.7	946	16.1
Promethazine	64,037	1,091. 8	8,128	138.6	60,754	1,035.8	39,464	672.8	31,856	543.1	17,960	306.2

[a] Antipsychotic exposure status was not mutually exclusive (e.g., deliveries with both atypical and typical antipsychotic exposure would be included in both groups). Exposure time periods were not mutually exclusive (e.g., deliveries with atypical antispsychotic exposure during the first and second trimester would appear in both periods). Some deliveries might be exposed to more than one drug of the same drug class, so the sum of deliveries exposed to individual drugs within each class might be greater than the overall number of exposed deliveries of that class.

Table 3

Mental health diagnoses among deliveries exposed to antipsychotics, by drug class and gestational period, the Medication Exposure in Pregnancy Risk Evaluation Program, 2001–2007[a]

Drugs	Any time from 60 days before pregnancy through delivery		60-day pre pregnancy period		Any time during pregnancy		1st trimester		2nd trimester		3rd trimester	
	N	%[b]	N	%	N	%	N	%	N	%	N	%
Atypical antipsychotics												
Schizophrenia	528	12.5	415	13.1	475	13.7	412	13.6	275	17.6	222	19.4
Bipolar disorder	1,801	42.6	1,366	43.1	1,560	44.9	1,354	44.7	769	49.1	598	52.3
Depression	2,644	62.6	1,997	63.0	2,200	63.3	1,928	63.6	993	63.5	723	63.2
None of the above	785	18.6	500	15.8	600	17.3	493	16.3	244	15.6	147	12.8
Typical antipsychotics												
Schizophrenia	145	26.5	70	31.0	135	27.8	87	28.5	86	30.5	86	37.4
Bipolar disorder	204	37.2	77	34.1	188	38.7	117	38.4	112	39.7	107	46.5
Depression	281	51.3	116	51.3	253	52.1	152	49.8	140	49.6	131	57.0
None of the above	149	27.2	49	21.7	126	25.9	77	25.2	69	24.5	34	14.8

[a] Antipsychotic exposure status was not mutually exclusive (e.g., deliveries with both atypical and typical antipsychotic exposure would be included in both groups). Exposure time periods were not mutually exclusive (e.g., deliveries with atypical antispsychotic exposure during the first and second trimester would appear in both periods). Some deliveries might be exposed to more than one drug of the same drug class, so the sum of deliveries exposed to individual drugs within each class might be greater than the overall number of exposed deliveries of that class.

[b] Within each drug class, proportions were calculated using the number of each cell as the numerator and the total number of each column as the denominator. Some deliveries might have more than one diagnosis so the sum of proportions might be greater than 100%.

Table 4

Mental health diagnoses among deliveries exposed to antipsychotics, by drug class and year of delivery, the Medication Exposure in Pregnancy Risk Evaluation Program (MEPREP), 2001–2007[a]

Year of delivery	Schizophrenia		Bipolar disorder		Depression		None of the three	
	N	%[b]	N	%	N	%	N	%
Atypical antipsychotics								
2001 (n=264)	47	17.8	104	39.4	169	64.0	34	12.9
2002 (n=452)	69	15.3	168	37.2	305	67.5	68	15.0
2003 (n=555)	96	17.3	220	39.6	382	68.8	67	12.1
2004 (n=714)	84	11.8	287	40.2	494	69.2	110	15.4
2005 (n=794)	93	11.7	328	41.3	479	60.3	151	19.0
2006 (n=736)	68	9.2	316	42.9	408	55.4	162	22.0
2007 (n=708)	71	10.0	378	53.4	407	57.5	105	14.8
Typical antipsychotics								
2001 (n=90)	24	26.7	25	27.8	43	47.8	24	26.7
2002 (n=72)	26	36.1	19	26.4	39	54.2	18	25.0
2003 (n=79)	20	25.3	30	38.0	40	50.6	20	25.3
2004 (n=75)	20	26.7	38	50.7	43	57.3	20	26.7
2005 (n=69)	16	23.2	27	39.1	32	46.4	21	30.4
2006 (n=83)	19	22.9	34	41.0	40	48.2	23	27.7
2007 (n=80)	20	25.0	31	38.8	44	55.0	23	28.8

[a] Antipsychotic exposure status was not mutually exclusive (e.g., deliveries with both atypical and typical antipsychotic exposure would be included in both groups).

[b] Within each drug class, proportions were calculated using the number of each cell as the numerator and the total number of each row as the denominator. Some deliveries might have more than one diagnosis so the sum of proportions might be greater than 100%.