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Using Insurance Claims Data to Identify and Estimate Critical Periods in Pregnancy: An Application to Antidepressants

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Abstract

Background—Health insurance claims are a rich data source to examine medication use in pregnancy. Our objective was to identify pregnant women, their pregnancy outcomes, and date of their last menstrual period (LMP), and to estimate antidepressant dispensations in pregnancy.

Methods—From a literature search, we identified diagnosis and procedure codes indicating the end of a pregnancy. Using Truven Health MarketScan® Commercial Claims and Encounters Databases, we identified all inpatient admissions and outpatient service claims with these codes. We developed an algorithm to assign: (1) pregnancy outcome (ectopic pregnancy, induced or spontaneous abortion, live birth, or stillbirth), and (2) estimated gestational age, to each inpatient or outpatient visit. For each pregnancy outcome, we estimated the LMP as the admission (for inpatient visits) or service (for outpatient visits) date minus the gestational age. To differentiate visits associated with separate pregnancies, we required ≥ 2 months between one pregnancy outcomes and the LMP of the next pregnancy. We used this algorithm to identify pregnancies in 2013 and to estimate the proportion of women who filled a prescription for an antidepressant from an outpatient pharmacy at various time points in pregnancy.

Results—We identified 488,887 pregnancies in 2013; 79% resulted in a live birth. A prescription for an antidepressant was filled in 6.2% of pregnancies. Dispensations varied throughout pregnancy and were lowest (3.1%) during the second trimester.

Conclusion—This work will inform future efforts to estimate medication dispensations during critical periods of preconception, interconception, and pregnancy using health insurance claims data.

Keywords

pregnancy; antidepressant; claims data; MarketScan; medication; SSRI

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Introduction

Estimates of the prevalence of medication use among pregnant women are limited. Most studies to date have relied on maternal self-reported medication use, either among mothers of live-born infants without congenital malformations (used as controls in case–control studies) or among representative samples of pregnant women (Mitchell et al., 2011; Thorpe et al., 2013; Tinker et al., 2015). However, maternal recall of medication use can be imprecise and subject to misclassification, particularly when mothers are interviewed months to years after early pregnancy exposures (Werler et al., 1989; Tinker et al., 2013). While some larger surveys, such as the National Health and Nutrition Examination Survey, have overcome some of these challenges by asking women about their medication use in the previous month and validating their responses by requesting to see a medication bottle, these do not allow for estimates of medication use across various time points in pregnancy (Tinker et al., 2015).

Access to health insurance claims data provides an opportunity to conduct studies of medication dispensations in pregnancy in large data sources without relying on self-report (Andrade et al., 2008; Huybrechts et al., 2013; Pasternak et al., 2013; Hanley and Mintzes, 2014). However, health insurance claims data tend to lack critical pieces of information (e.g., estimated due date, date of last menstrual period, date of delivery) that make it difficult to accurately identify pregnant women, pregnancy outcomes, or estimate the gestational length of pregnancies. Although some researchers have overcome these challenges by linking maternal and infant records within the same data source (Taylor et al., 2015) or linking administrative claims data to vital records, electronic medical records, or other healthcare data (Cooper et al., 2006; Pasternak et al., 2013), these types of linkages are not always possible. Thus, some researchers have attempted to identify and estimate gestational ages of pregnancy outcomes solely from information in administrative data; many of these methods are well-described by Margulis and colleagues (Margulis et al., 2015). Overall, most previous attempts to identify pregnancies in claims data have only assessed live birth outcomes, assumed the same gestation for all pregnancies, or used broad estimates of gestational age (Margulis et al., 2015).

Our objective was to identify pregnant women, their pregnancy outcomes, and date of their last menstrual period (LMP) to ultimately use in analyses of medication dispensations at critical periods in pregnancy. A secondary objective was to use our algorithm in an analysis of the prevalence of antidepres-sant dispensations to pregnant women during and immediately before and after pregnancy.

Materials and Methods

DATA SOURCE

We used the Truven Health MarketScan® Commercial Claims and Encounters Databases for our analysis, a large convenience sample of individuals with employer-sponsored private insurance (or their spouses or dependents) (Hansen and Chang, 2011). These databases include inpatient and outpatient services, outpatient pharmacy prescription claims, and healthcare plan annual enrollment information for each enrollee followed over their period

of enrollment. A major strength of this data source is the ability to track individuals longitudinally while they are employed through the same employer, even if they switch health insurance plans (Hansen and Chang, 2011).

PREGNANCY ALGORITHM

We did a focused search of the literature for studies that identified deliveries, as well as other pregnancy outcomes, using diagnosis and procedure codes in health claims data *and* provided estimates of gestational age at the time of pregnancy outcome. Based on these sources (Hornbrook et al., 2007; Korelitz et al., 2013; Li et al., 2013; Likis et al., 2013), we developed a list of diagnosis, procedure, and Diagnosis Related Group (DRG) codes that signified the end of a pregnancy (Supplementary Tables A1 and A2, which are available online). As preterm infant codes may be included on the maternal record during the birth hospitalization, we included both infant and maternal diagnosis, procedure and DRG codes in our list. Using these sources' gestational age assignments as a foundation, we developed an algorithm to assign: (1) a pregnancy outcome and (2) an estimated gestational age at the time when a diagnosis, procedure or DRG code was assigned. If a code did not have a gestational age assignment in one of the previous studies, we relied on the clinical (obstetrician-gynecology) expertise of one of our coauthors (E.E.P.).

Briefly, we identified all of the claims that mapped to one of the diagnosis, procedure, or DRG codes indicative of a pregnancy outcome, using data from inpatient and outpatient services files from women aged 15 to 44 years. We summarized all claims for a given visit and assigned a pregnancy outcome: stillbirth, live birth, induced abortion, spontaneous abortion, abortion of unknown type, or ectopic pregnancy. If more than one gestational age estimate was present, we used the minimum gestational age to avoid overestimating exposure during pregnancy. However, in the rare instance (less than 0.2% of all pregnancies included in the analysis) where a pregnant woman had multiple postterm codes (i.e., for 42 and 43 weeks gestations, see Supplementary Table A1), we assigned 43 weeks. If a visit indicated a full-term delivery without a code indicating a more specific gestational age, we estimated that to occur at 40 weeks gestation. For each pregnancy outcome visit, we estimated the LMP as the admission (for inpatient visits) or service (for outpatient visits) date minus the estimated/assigned gestational age.

To differentiate visits associated with separate pregnancies, we first grouped all the visits associated with the same pregnancy outcome (stillbirth, live birth, abortions of any type [including induced, spontaneous, and unknown type], and ectopic pregnancy) and then required there to be at least 2 months between the end of one pregnancy and the beginning (i.e., LMP) of a subsequent pregnancy, as has been done in other studies (Devine et al., 2010). Once this had been done for each pregnancy type, we then pooled the data from all pregnancy types and again required there to be at least 2 months between the end date of one pregnancy and the beginning (LMP) of a subsequent pregnancy.

ANALYTIC SAMPLE

We initially selected women 15 to 44 years of age at enrollment to a private health insurance plan in 2013. Then, using the 2013 annual enrollment file, we restricted our sample to

women with insurance plans that included prescription drug coverage in 2013. Using the aforementioned pregnancy algorithm, we identified women with end of pregnancy-related claims from 2013 or 2014 who were 15 to 44 years of age on their date of service and whose pregnancies (LMP through end of pregnancy) spanned at least 1 day in 2013. The 2012 to 2014 annual enrollment files were used to calculate a woman's enrollment during the 90 days before LMP to 90 days after the end of her pregnancy or through December 31, 2014, whichever was earliest (as 2015 data were not yet available). We then restricted the analytic sample to women enrolled from the 90 days before LMP to 90 days after the end of pregnancy or only missing one month of enrollment during that time period and considered all others to be "under enrolled." "Under enrolled" women were excluded from the analysis because we could not be certain that they did not fill a prescription during the study period.

ANALYSIS OF ANTIDEPRESSANT DISPENSATIONS DURING PREGNANCY

Using the RedBook™, we identified the national drug codes for antidepressant medications. We then identified antidepressant prescription claims from the outpatient pharmacy files for 2012 to 2014, and calculated the proportion of 2013 pregnancies with at least one filled prescription for an antidepressant during the first, second, or third trimester of pregnancy or during the 90 days before pregnancy or the 90 days after pregnancy. As women could have multiple pregnancies in this time period, the unit of analysis was a pregnancy. For calculations of dispensations of antidepressants during the second and third trimester of pregnancy, we only included pregnancies that were estimated to extend at least one day into each of those time periods. We examined antidepressant dispensations overall, as well as by medication class and type.

Results

Among the approximately 10.5 million women 15 to 44 years of age enrolled in a private health insurance plan captured in the 2013 MarketScan® Commercial Database, 643,872 had either at least one end of pregnancy claim in 2013 or at least one end of pregnancy claim in 2014 with an estimated LMP date in 2013, representing 744,630 pregnancies (Fig. 1). After excluding women with missing enrollment information during pregnancy or women "under-enrolled," there were 488,887 pregnancies to 472,341 women available for further analysis. The majority of these pregnancies (n = 386,127; 79.0%) were estimated to end in a live birth (Table 1). Among live births, 7.6% had a code for a preterm birth (<37 completed weeks gestation) and 13.1% had a code for a postterm (≥42 weeks completed gestation) birth.

Women filled a prescription for an antidepressant in 6.2% of pregnancies overall, though dispensations varied throughout pregnancy and were lowest (3.1%) during the second trimester (Table 2). Dispensations in the 90 days before LMP were less frequent (6.3%) than in the 90 days after pregnancy (8.0%). Selective serotonin reuptake inhibitors (SSRIs) were the most commonly dispensed class of antidepressants, with sertraline the most commonly dispensed medication in this class. Other commonly dispensed antidepressants (filled by approximately 0.9% of women during pregnancy) included other SSRIs such as citalopram, escitalopram, and fluoxetine, as well as an atypical antidepressant, bupropion.

Of the 57,440 pregnancies with antidepressant dispensations at any point from the 90 days before LMP through 90 days after the end of pregnancy, 16,264 (28.3%) filled only one prescription for an antidepressant during this time period and 22,754 (39.6%) filled four or more. The majority of prescriptions filled (85.7%) were for a 30-day supply of medications; 9.9% were filled for a 90-day supply. Among the 41,552 (72.4%) full- and postterm pregnancies (estimated as >37 weeks completed gestation) with at least one antidepressant dispensation, almost one-third only filled a prescription for an antidepressant in the 90 days after the end of their pregnancy, and 12.3% filled a prescription during each of the time periods assessed (Fig. 2).

Discussion

In summary, we developed an algorithm to identify pregnant women, their pregnancy outcomes, and estimate their gestational age and date of their LMP. We were able to implement this algorithm in a large (approximately 10.5 million women) dataset of reproductive-aged women with private health insurance. Furthermore, our algorithm allowed us to estimate antidepressant dispensations to pregnant women across various time points in pregnancy.

Overall, after restricting our sample to women with health plans including prescription drug coverage and sufficient enrollment before, during and after pregnancy, we identified 488,887 pregnancies occurring in 2013. Most (79.0%) were estimated to end in live birth, 14.5% in spontaneous abortion, 4.1% in induced abortion, and 0.6% in stillbirth. While the overall proportion of live births is higher than the 75% typically reported in previous studies of insured populations (Manson et al., 2001; Naleway et al., 2013), it falls within the range of estimates (61–82%) described across various geographic areas in a study of Vaccine Safety Datalink data by Naleway and colleagues (Naleway et al., 2013). Compared with these previous studies, our estimate of induced abortions seems to be lower. This could be due to an error in our algorithm or because women may have chosen to pay for elective terminations out-of-pocket and thus these procedures would not be recorded in these administrative data. Additionally, our estimate could be biased due to differences in the geographic distribution or other sociodemographic characteristics of the population of women captured in MarketScan® Commercial Database (Dawson et al., 2016), as abortion rates vary by socioeconomic status and geographic location in the United States (Jones et al., 2002; Pazol et al., 2015).

Among pregnancies estimated to end in a live birth, we found that 7.6% had a code for preterm birth and 13.1% had a code for postterm birth. Our preterm birth estimate is slightly lower, and postterm much higher, than those derived from obstetric estimates on birth certificates from the 2013 U.S. general population (9.6% and 0.41%, respectively). Postterm birth estimates of the 2013 general population based on birth certificate LMP estimates (5.5%) were much higher than the obstetric estimate and including “late term” infants (born at 41 weeks gestation) resulted in an estimate (14.0%) comparable to ours (Martin et al., 2015). Thus, it is unclear if these differences are due to variations in methods used to estimate gestational age, slight misclassification of some of the postterm infants in our study (as postterm rather than “late term”) or a broader reflection of differences in socioeconomic

characteristics. For instance, our estimates are strikingly similar to those derived from an analysis of Mini-Sentinel program data, a collaboration between the U.S. Food and Drug Administration and administrators of 18 health plans. In those data, Andrade and colleagues developed an algorithm to identify pregnancies ending in live birth from April 2001 to December 2013 (Andrade et al., 2016). Of the 1.7 million pregnancies to women aged 10 to 54 years in their cohort, 7.9% had a code for preterm birth and 13.3% had a code for postterm birth.

We estimated that women filled a prescription for an antidepressant in 6.2% of pregnancies overall, although dispensations varied throughout pregnancy. This estimate is similar to those from an analysis of the MarketScan® Commercial Database by Hanley and Mintzes, which was limited to the first live birth for each woman in the cohort (Hanley and Mintzes, 2014). Their analysis consisted of 343,299 deliveries from 2006 to 2011 meeting their enrollment criteria, and they estimated that 6.5% of women with pregnancies ending in a live birth filled a prescription for an antidepressant during pregnancy. Similarly, in an analysis of approximately 119,000 pregnant women from seven health maintenance plan organizations in 2001 to 2005, Andrade and colleagues found that 6.6% of pregnant women filled a prescription for an antidepressant during pregnancy (Andrade et al., 2008). Antidepressant dispensations during pregnancy were found to be somewhat higher (8.1%) in a cohort of 1.1 million pregnant women with Medicaid insurance (Huybrechts et al., 2013). Similar to our analysis, all of these studies also showed dispensations to be around 4% during the second and third trimesters of pregnancy. The increase in dispensations (8.0%) we observed during the 90 days postpartum may reflect resumption of medication use postpartum or identification of new postpartum depression, and the recognition of the important role of pharmacotherapy in its treatment (Siu et al., 2016).

Our analysis had several limitations. With respect to the development of our algorithm, the primary limitation is that we were unable to validate the pregnancy estimates derived from our pregnancy algorithm by using data from medical records or birth certificates. Thus, it is possible that we misclassified pregnancy outcomes, gestational length and LMP. However, Hornbrook et al. (2007) conducted a validation study of their algorithm compared with medical records abstraction using a stratified sample of approximately 500 pregnancies. That algorithm, which provided a basis for our algorithm, demonstrated good to excellent agreement on the designation and dating of pregnancy outcomes (Hornbrook et al., 2007). Yet the estimation of preterm birth using an algorithm based on diagnosis codes may be a bit more problematic.

Andrade et al. (2016) found that the positive predictive value of preterm birth diagnosis codes on infant records was higher (92%) than that of maternal records (76%) and that most maternal records do not contain infant diagnosis codes (Andrade et al., 2013). Furthermore, Li et al. (2013) compared gestational age estimates from their algorithm, which was a basis for some of the preterm codes used in our algorithm, to estimates from birth certificates and found that their algorithm had a 98% sensitivity for term births and 45% sensitivity for preterm births (Li et al., 2013). Thus, in our data, we may have underestimated the proportion of pregnancies ending in a preterm birth and, therefore, may have over-estimated

the gestational length (and opportunity for medication exposures) for some women in our cohort. Still, preterm births represent a small proportion of the total pregnancies in our study.

With respect to the application of the algorithm to our analysis of antidepressant dispensations in pregnancy, our algorithm may have misclassified the timing of medication dispensations, although this is less likely for chronic medications such as antidepressants as opposed to those used on an acute basis (Toh et al., 2008). Additionally, while our estimates of medication dispensations relied on pharmacy records, they did not account for inpatient medications or medications paid for out-of-pocket. Furthermore, while the records indicate that a medication prescription was filled, we cannot estimate adherence. Previous estimates of antidepressant adherence during pregnancy are conflicting; the proportion of pregnant women estimated to have low adherence ranges from 13 to 47% (Bosman et al., 2014; Lupattelli et al., 2015). In addition, our enrollment criteria may have further impacted the generalizabil-ity of our results. It is possible that women with chronic conditions are more likely to remain enrolled in their healthcare plan each month and thus more likely to be included in our study sample (Jensen et al., 2015).

Nevertheless, our analysis had multiple strengths, making it a valuable contribution to the literature. First, we expanded upon several previously used algorithms by including nonlive birth pregnancy outcomes, not requiring linkages to infant records, and using specific estimates of gestational age. Second, our use of this algorithm in the MarketScan® Commercial Database allowed for the analysis among a large cohort of pregnancies. Our sample size for pregnancies spanning 2013 was on par with or exceeded those derived in earlier studies encompassing deliveries that occurred over 5-year periods. Our large sample size will allow us to examine trends in medication dispensations across time and among rarer medication types. Lastly, our algorithm has potentially broad application and could be easily modified and applied to other similarly structured data sources.

In conclusion, we have developed an algorithm to identify pregnant women, their pregnancy outcomes, and estimate their gestational age and date of their last menstrual period. This work will inform future efforts to identify medication dispensations during critical periods of pregnancy, preconception, and the postpartum using health insurance claims data.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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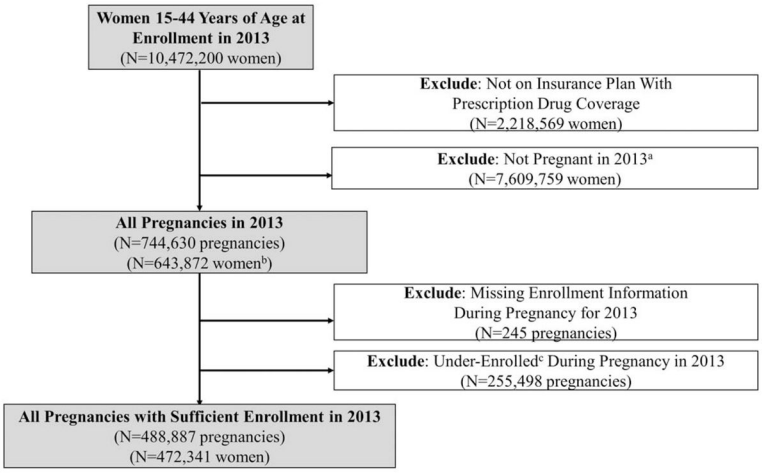

FIGURE 1.

Identification of Analytic Sample of Pregnancies, 2013 Truven Health MarketScan® Commercial Claims and Encounters Database. [a]No end of pregnancy related visit or estimated date of last menstrual period occurring in 2013. [b]Women 15 to 44 years of age at "end of pregnancy"-related visit. [c]Women enrolled from the 90 days before the estimated date of last menstrual period to 90 days after the end of pregnancy or only missing one month of enrollment during that time period were considered sufficiently enrolled; all others were considered to be "under-enrolled."

Timing of Antidepressant Prescription Dispensation(s)					
90 days before LMP to LMP	First Trimester	Second Trimester	Third Trimester	End of Pregnancy +90 days	N (%)
X	X	X	X	X	5,128 (12.3%)
X	X				3,571 (8.6%)
X					5,136 (12.4%)
X	X			X	2,168 (5.2%)
X				X	1,858 (4.5%)
				X	13,220 (31.8%)
			X	X	1,141 (2.8%)
-	-	*Other*[a]	-	-	9,330 (22.5%)

FIGURE 2.

Pattern of dispensation(s) of antide-pressant prescriptions from outpatient pharmacies, among pregnancies with at least 37 weeks estimated gestation (N = 41,552 pregnancies). Notes: X = filled a prescription for an antidepressant during this time period; LMP = Date of last menstrual period. [a]Includes all other possible exposure combinations, each of which accounted for less than 2.8% of pregnancies.

TABLE 1

Characteristics of Women and Pregnancies Included in Analysis, 2013 Truven Health MarketScan® Commercial Claims and Encounters Database

	***N* (%)**
Total women	472,341
Age, years (mean ± SD)	29.6 ± 5.6
Region of residence	
Northeast	80,940 (17.2%)
North Central	104,671 (22.2%)
South	165,536 (35.1%)
West	108,618 (23.0%)
Unknown	12,243 (2.6%)
Estimated to be pregnant in 2013	472,341 (100%)
Total pregnancies	488,887
Live birth	386,127 (79.0%)
Preterm code (<37 weeks)	29,520 (7.6%)[a]
Postterm code (≥ 42 weeks)	50,749 (13.1%)[a]
Spontaneous abortion	70,965 (14.5%)
Induced abortion	20,117 (4.1%)
Ectopic pregnancy	8,135 (1.7%)
Stillbirth[b]	2,749 (0.6%)
Abortion (unknown type)	794 (0.2%)

[a] Proportion out of live births only.

[b] Includes multiple gestations with one live birth and one stillbirth ($n = 117$).

TABLE 2

Estimated Number and Proportion of Women Who Filled at Least One Prescription for an Antidepressant from an Outpatient Pharmacy During, Before, or After Pregnancy, 2013 Truven Health Market-Scan® Commercial Claims and Encounters Database

	Timing of prescription dispensation(s) *N* (%)						
Antidepressant type	**Anytime during pregnancy (*N* = 488,887)**	**90 days before LMP to LMP (*N* = 488,887)**	**First trimester (*N* = 488,887)**	**Second trimester (*N* = 425,483)[a]**	**Third trimester (*N* = 388,541)[a]**	**End of pregnancy + 90 days (*N* = 488,887)**	**90 Days before LMP to 90 days after end of pregnancy (*N* = 488,887)**
Any	30,117 (6.2%)	30,864 (6.3%)	24,552 (5.0%)	13,104 (3.1%)	17,779 (4.6%)	39,221 (8.0%)	57,440 (11.8%)
SSRI[b]	23,242 (4.8%)	22,509 (4.6%)	18,128 (3.7%)	10,454 (2.5%)	14,181 (3.7%)	33,404 (6.8%)	47,068 (9.6%)
Citalopram	4,495 (0.9%)	5,011 (1.0%)	3,764 (0.8%)	1,715 (0.4%)	2,372 (0.6%)	4,957 (1.0%)	8,814 (1.8%)
Escitalopram	4,165 (0.9%)	4,515 (0.9%)	3,525 (0.7%)	1,620 (0.4%)	2,293 (0.6%)	5,845 (1.2%)	9,119 (1.9%)
Fluoxetine	4,451 (0.9%)	4,244 (0.9%)	3,506 (0.7%)	1,939 (0.5%)	2,596 (0.7%)	4,923 (1.0%)	8,157 (1.7%)
Paroxetine	705 (0.1%)	976 (0.2%)	653 (0.1%)	138 (0.0%)	327 (0.1%)	903 (0.2%)	1,781 (0.4%)
Sertraline	10,553 (2.2%)	8,140 (1.7%)	7,107 (1.5%)	5,156 (1.2%)	6,818 (1.8%)	17,920 (3.7%)	23,859 (4.9%)
SNRI[c]	3,125 (0.6%)	3,581 (0.7%)	2,865 (0.6%)	1,120 (0.3%)	1,537 (0.4%)	2,688 (0.6%)	5,289 (1.1%)
Desvenlafaxine	433 (0.1%)	538 (0.1%)	401 (0.1%)	128 (0.0%)	200 (0.1%)	317 (0.1%)	751 (0.2%)
Duloxetine	1,106 (0.2%)	1,247 (0.3%)	1,018 (0.2%)	363 (0.1%)	502 (0.1%)	938 (0.2%)	1,905 (0.4%)
Venlafaxine	1,583 (0.3%)	1,774 (0.4%)	1,435 (0.3%)	625 (0.2%)	832 (0.2%)	1,433 (0.3%)	2,698 (0.6%)
Tricyclics[d]	1,283 (0.3%)	1,725 (0.4%)	1,078 (0.2%)	304 (0.1%)	505 (0.1%)	874 (0.2%)	2,847 (0.6%)
Amitriptyline	795 (0.2%)	1,069 (0.2%)	662 (0.1%)	192 (0.1%)	301 (0.1%)	542 (0.1%)	1,749 (0.4%)
Nortriptyline	312 (0.1%)	430 (0.1%)	267 (0.1%)	71 (0.0%)	125 (0.0%)	215 (0.0%)	726 (0.2%)
Other[e]	5,684 (1.2%)	6,209 (1.3%)	4,796 (1.0%)	1,963 (0.5%)	2,915 (0.8%)	5,009 (1.0%)	10,532 (2.2%)
Bupropion	4,178 (0.9%)	4,352 (0.9%)	3,479 (0.7%)	1,585 (0.4%)	2,199 (0.6%)	3,766 (0.8%)	7,380 (1.5%)
Trazodone	1,309 (0.3%)	1,666 (0.3%)	1,133 (0.2%)	317 (0.1%)	628 (0.2%)	1,088 (0.2%)	2,922 (0.6%)

[a] Some pregnancies ended before the estimated beginning of the second or third trimester(s) so were not included in the denominator.

[b] Also includes fluvoxamine.

[c] Also includes levomilnacipran and milnacipran.

[d] Also includes amoxapine, clomipramine, desipramine, doxepin, imipramine, maprotiline, protriptyline, and trimipramine.

[e]Also includes mirtazapine, nefazodone, vilazodone, vortioxetine and monoamine oxidase inhibitors (isocarboxazid, phenelzine, selegiline, and tranylcypromine).

LMP, date of last menstrual period; SNRI, serotonin–norepinephrine reuptake inhibitor; SSRI, selective serotonin reuptake inhibitor.