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Prescription and Other Medication Use in Pregnancy

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Abstract

Objective—To characterize prescription and other medication use in a geographically and ethnically diverse cohort of women in their first pregnancy.

Methods—In a prospective, longitudinal cohort study, nulliparous women followed through pregnancy from the first trimester, medication use was chronicled longitudinally throughout

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pregnancy. Structured questions and aids were utilized to capture all medications taken as well as reasons they were taken. Total counts of all medications taken including number in each category and class were captured. Additionally, reasons the medications were taken were recorded. Trends in medications taken across pregnancy and in the first trimester were determined.

Results—Of the 9,546 study participants, 9,272 (97.1%) women took at least one medication during pregnancy, with 9,139 (95.7%) taking a medication in the first trimester. Polypharmacy, defined as taking at least five medications, occurred in 2915 (30.5%) women. Excluding vitamins, supplements, and vaccines, 73.4% of women took a medication during pregnancy, with 55.1% taking one in the first trimester. The categories of drugs taken in pregnancy and in the first trimester include the following: gastrointestinal or antiemetic agents (34.3%, 19.5%), antibiotics (25.5%, 12.6%,), and analgesics (23.7%, 15.6%, which includes 3.6%; 1.4% taking an opioid pain medication).

Conclusions—In this geographically and ethnically diverse cohort of nulliparous pregnant women, medication use was nearly universal and polypharmacy was common.

Introduction

More adults in the U.S. are taking prescription medications over the last two decades.[1] Most pregnant women take prescription medications also, with rates as high as 95%.[2–4] In addition, in some populations the majority of women have been found to take more than three prescription medications during pregnancy.[5, 6] The use of over-the-counter medication is likewise increasing in the general population, as are the total dollars spent on over-the-counter medicines.[7, 8]

While several reports described prescription and other medication use in pregnancy, they have some limitations. Many prior studies reported on single-site cohorts of pregnant women, were case-control designs, or utilized larger databases of administrative or prescription data.[3, 4, 9–11] A prospectively evaluated study of nulliparous women beginning in the first trimester of pregnancy, the nuMoM2b cohort is ideally positioned to provide a snapshot of the use of both prescription and non-prescription medications in pregnancy. The objective of this study was to characterize medication use in a geographically and ethnically diverse cohort of women in their first pregnancy enrolled in the nuMoM2b study. A secondary objective was to chronicle trends in medication use over the course of pregnancy.

Materials and Methods

The nuMoM2b study was designed as a prospective, longitudinal cohort study whose aim was to determine maternal characteristics, including genetic, physiologic, and environmental factors that predict adverse pregnancy outcomes. A full description of the study methods and visits is described elsewhere.[12] Briefly, 10,038 nulliparous women were recruited in the first trimester of pregnancy between October 2010 and September 2013. Women had study visits between gestational weeks 6+0/7 and 13+6/7 (Study Visit 1), 16+0/7 and 21+6/7 (Study Visit 2), and between 22+0/7 and 29+6/7 (Study Visit 3). Study visits were not part of clinical care. At each study visit, a trained research team member administered several

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questionnaires and surveys and collected an array of biological samples. The study team also captured data and specimens from antepartum and delivery hospitalizations. At least 30 days after delivery, certified chart abstractors reviewed antenatal, intrapartum, and postpartum medical records to corroborate existing interview data and collect obstetric and infant outcome data.[12]

In the nuMoM2b study, women were recruited from 8 geographically diverse clinical centers in the United States to obtain a racial-ethnically diverse population of pregnant women. Sites were located in New York or Delaware (combined site), Pennsylvania (2), Ohio, Indiana, Illinois, Utah, and California. Women were recruited from both private practices and academic practices located near the main clinical site. Women could be recruited as young as age 13 into the cohort. Local governing IRBs approved the protocol at each clinical site and at the Data Coordinating Center and all participants gave written informed consent. The study was registered on clinicaltrials.gov (NCT01322529).

At each study visit, a log of medical conditions and prescription and other medication use was completed. At the time the study visit was scheduled, participants were encouraged to bring in all medications that they had taken since becoming pregnant or since the previous study visit, as applicable. At the study visit, participants were also asked to recall other medications, including any over-the-counter medications or supplements (including prenatal vitamins, micronutrients, herbals, etc.), they had taken or their provider had recommended in that same period. At the time of the delivery, women were asked to recall any medications taken up to the time of the delivery hospitalization. Research personnel recorded all answers on the data capture form, which were kept in the study file and added to or clarified at each subsequent study visit. Participants were asked the reason that the medications were taken and answers were coded from a list of conditions on the data capture form (Supplemental Material). At the time of final chart abstraction, additional prescribed medications that were used at any time during the pregnancy were recorded.

Medications were categorized based on typical use or medication classification. This was to allow for ease of grouping. An individual taking two different medications for a condition would have two different notations made for that medication category and reason. A key was provided with common examples of certain types of medications. For example, a number of calcium channel blockers (nifedipine, amlodipine, etc.) were listed for inclusion in the medication category of “Ca-Channel Blocker” in the Manual of Operations to facilitate data collection and abstraction.

Collected data underwent rigorous quality control review by a subset of investigators (DMH, DJM, DTD, CBP, AL, and UMR) to eliminate misspellings and miscategorizations. Questions about medication categorizations or indications for medication use were resolved through consensus discussion. For the purposes of this analysis, we did not include illicit or recreational drugs (such as marijuana, heroin, etc.) but included opioid prescription medications and medication-assisted treatment with opioids.

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Statistical analysis

We restricted this analysis to nulliparous women followed through pregnancy from the first trimester with medication use data forms completed. Descriptive statistics for individual medication category (during pregnancy and during the first trimester, including 95% confidence intervals) and indications for medication use are presented for both prescription and non-prescription medications and supplements taken at any time during the pregnancy. We excluded reports of vaccinations received during pregnancy for statistics pertaining to general medication use. Trends of medication use throughout the pregnancy and most common reasons for taking medications during pregnancy are also presented. Prevalence rates of medication use (overall, in the first trimester, and polypharmacy) were compared by ethnicity, geographic region, and other demographic characteristics. Polypharmacy was defined as use of at least five medications during the same epoch, a threshold commonly used in the literature.[1, 13] Trends by demographic characteristics were evaluated using chi-square tests. McNemar's test was used to evaluate differences in proportion of women using medications during the first trimester versus the second. There was no adjustment for multiple comparisons. Analyses were conducted using SAS version 9.4 (SAS Institute Inc).

Results

Of the 10,038 participants in nuMoM2b, medication data were available for 9,546 women followed through pregnancy from the first trimester with medication data. Restricting to women who were followed until the end of their pregnancy excluded 444 women. Restricting to women with medication data further excluded 48 women. Characteristics of this final cohort and comparison of rates of medication use are presented in Table 1. The mean age of the cohort was 27.0 (± 5.66) years.

In total, 9,262 (97.0%, 95% Confidence Interval (CI) 96.7%-97.4%) took at least one medication during pregnancy, 9,133 (95.7%, 95% CI 95.3%-96.1%) took a medication during the first trimester, and 2,195 (30.5%, 95% CI 29.6%-31.5%) met the definition for polypharmacy in taking 5 or more medications during pregnancy. The overall mean number of total medications taken during pregnancy was 3.74±2.71 (range 0-27; median 3; interquartile range [2, 5]). Women in the cohort took a mean of 2.54±1.96 (range 0-21; median 2; interquartile range [1, 3]) medications during the 1st trimester. 2,255 (23.6%) women only took prenatal vitamins during pregnancy. Additionally, 193 (2.0%) women took some type of herbal or probiotic supplement. The mean number of medications taken by women was 2.54±1.96 (range 0-21; median 2; interquartile range [1,3]) at the 1st study visit, 2.50±1.78 (range 0-18; median 2; interquartile range [1,3]) at the 2nd study visit, 2.59±1.93 (range 0-24; median 2; interquartile range [1,3]) at the 3rd study visit, and 2.71±2.00 (range 0-26; median 2; interquartile range [1,4]) at the time of delivery.

Excluding prenatal vitamins, multivitamins, additional iron and folic acid, 7,007 (73.4%, 95% CI 72.5%-74.3%) of women took a medication during pregnancy, with 5,263 (55.1%, 95% CI 54.1%-56.1%) taking at least one medication in the 1st trimester (Appendix 1, available online at http://links.lww.com/xxx). In this group, 1,240 (13.0%, 95% CI 12.3%-13.7%) of women met the definition of polypharmacy.

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The number of women taking medications anytime during pregnancy varied by maternal age, race-ethnicity, educational attainment at the time of pregnancy, method of payment for healthcare, and geographic region (Table 1). Women who were younger and non-Hispanic reported higher rates of taking medications in pregnancy. The number of women taking medications in the first trimester also varied by age, race-ethnicity, method of payment for health care, and region. The number of women reporting polypharmacy (≥ 5 medications) also varied by age, race-ethnicity, educational attainment, method of paying for health care, household income, and region. Women who were older, white, had commercial insurance, and more education tended to take more medication. Women in the northeast tended to take less medication.

The most commonly prescribed medications were gastrointestinal or anti-emetic agents (3,279 [34.3%]; 1,866 [19.5%] in the first trimester), followed by antibiotics (2,439 [25.5%]; 1,199 [12.6%] in the 1st trimester) and analgesics (2,265 [23.7%]; 1,485 [15.6%] in first trimester). Table 2 presents grouped medication code category data recorded. Appendix 2 (available online at http://links.lww.com/xxx) details all individual medication codes and prevalence of use. Regarding gastrointestinal (GI) & anti-emetic agents, 5-HT_3 antagonists were the most prescribed specific class of medications (1,167 [12.2%] women). The most common indication for this class of medication was nausea and vomiting. Penicillin-derivative antibiotics were the most commonly reported antibiotic group (715, [7.5%]) and were most commonly prescribed for urinary tract infection. However, they were not the most prevalently prescribed antibiotic group for such infections. Acetaminophen was reportedly taken during pregnancy by 1,903 (19.9%) of women, with 1,121 (11.7%) having taken it in the first trimester. Otherwise, non-steroidal anti-inflammatory drugs (NSAIDs) were the most commonly reported specific class of analgesics (6.6%), with opioids reported by 3.6% of women before delivery. Antihistamines (n=1,219 [12.8%]) were also commonly prescribed. Additional iron supplements were noted for 1,548 (16.2%) women.

Vitamin consumption early in pregnancy was nearly universal, with 8,800 women taking a prenatal vitamin in the first trimester of pregnancy (92.2%) (Table 2). Additionally, 543 (5.7%) and 1,859 (19.6%) women took another type of multivitamin or other vitamin, respectively, during the first trimester. In total, 9001 (94.3 %) women took some type of vitamin or additional folic acid during the first trimester of pregnancy.

Excluding medications taken which were marked as being taken for preventive reasons, “other” reasons, or from “provider recommendation”, the specific condition most often cited as the reason for taking a medication during pregnancy was nausea and vomiting (n= 1,599 [16.8%]). This was followed by urinary tract infections (1,132 [11.9%]), anemia (924 [9.7%]), respiratory infections (737 [7.7%]), yeast infections (717 [7.5%]), mental health conditions (706 [7.4%]), and asthma (653 [6.8%]). (Table 3)

Table 4 shows the classes of medications that demonstrated significant increase or decrease in use between the first trimester and the second trimester (when participants may have previously received counseling on appropriate medication use in pregnancy). The number of women who had taken NSAIDs, selective serotonin reuptake inhibitors (SSRIs), and progesterone (not for contraception) decreased between study visit 1 and 2 (Table 4). The

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greatest absolute increase in medication class reported occurred for other analgesics (category including acetaminophen) and gastrointestinal agents.

Discussion

Our results from a large, diverse, prospective cohort of nulliparous women in the U.S. detail that prescription or other medication use is nearly universal during pregnancy. The ubiquitous use of at least one medication during pregnancy and especially in the first trimester highlights the need for more attention to medication use in pregnancy. Even when vitamins, supplements and vaccines are excluded, 73.4% of women took at least one medication during pregnancy, with 55.1% taking a medication in the first trimester, a critical time in fetal development. Our findings support the need for more information on medications specific to pregnant women and counseling to limit exposure to medically unindicated medications in pregnancy.[14–17]

Our findings are consistent with other studies showing that >90% of women take at least one medication during pregnancy.[3–6] However, we noted a similar or higher rate of non-vitamin or supplement medication use than in other studies.[3, 4] This observation may have been because of our prospective, study visit interview-based methodology where all participants were encouraged to bring in all medications and supplements they were taking. Glover et al. utilized interviews but studied a relatively small rural population of 578 women and found that only 59.7% of women used a prescription medication excluding vitamins and iron supplements.[4] Our rate also may have been higher because we included prescription and non-prescription medications. We sought to obtain a more comprehensive picture of all medications being consumed in this national cohort. Glover et al. noted a very high rate of over the counter medication use (92.6%).[4] Utilizing a survey of 418 postpartum women, Refuerzo et al. found that 76.5% of women took a prescription medication after excluding vitamins and iron, a rate similar to ours.

Our finding of medications for nausea and vomiting being the most commonly utilized is not surprising given the high incidence of nausea and vomiting of pregnancy (NVP).[18] Interestingly, we found that 5-HT_3 antagonists were the most commonly used medication for this indication. Current recommendations do not support these medications as first line therapy for NVP.[18–20] In this way, these data can help shed light on current practice patterns in relationship to practice recommendations, highlighting areas of need for provider education. Taken as a whole medication class category, the high rate of use of GI medications (34.3%) is understandable as they treat common conditions such as NVP, acid reflux, and constipation. Our finding that anti-infective medications and analgesic medications were the next most commonly used medication classes is also consistent with other studies, nearly all of which have noted these classes as the three most commonly reported.[2, 4, 6, 9–11] Vaginal antifungals, penicillin-derivatives, and nitrofurantoin were the most common anti-infective medication classes utilized by women in our cohort. This finding is also consistent with other studies. Interestingly, other cohorts noted higher rates of antibiotic use, with Palmsten et al. reporting almost 50% of women filling prescriptions for such anti-infective agents, with nitrofurantoin at 21.6% of women and metronidazole at 19.4% of women.[11] We also found relatively high rates of pregnant women using URI

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agents (16.4%), asthma medications (9.1%), and antidepressants (6.1%). Other studies have noted increasing rates of use of various classes of medications over time, including these.[5] While differing data collection and categorization methodology prevent direct correlation, these relatively high rates are consistent with recently published rates from other studies.[3, 4, 11]

We found a relatively low rate of opioid use in our cohort (3.6%) compared to some other reports. This may have been due to our parsing out different types of analgesics methodically by reason codes. It also may be because we did not include medications taken during or after the delivery hospitalization, when many women are given opioids. With the current epidemic of opioid use disorder, it is important to monitor their use in pregnancy.[21] Our rate of opioid use in the 1st trimester is consistent with the 1.3% rate of hydrocodone use reported by Thorpe et al.[9] Other groups also found that opiates were commonly used by pregnant women, with rates from 8% to nearly 12%.[4, 11] These results do not include illicit drug use in this class. Rates of illicit drug use have varied but have been found to be as high as 13% in some general obstetrical populations.[22] These rates are increasing.[23] Our rates of reported NSAID use were higher than anticipated. However, other studies have reported rates of over-the-counter ibuprofen use in pregnancy of up to 18%.[10]

We found that medication use during pregnancy and in the first trimester varied by several demographic factors, consistent with other national data.[5] The regional difference in polypharmacy was interesting, with rates in the Midwest and West double that of the Northeast. As there were several centers in each region, this is unlikely to be due to practice patterns within individual centers. Other studies have also found regional variation in medication use in pregnancy.[2] Additionally, racial-ethnic differences are seen in polypharmacy rates. In our cohort, Hispanic and Asian women had a more than 10% lower rate of polypharmacy compared to White non-Hispanic women. These findings bear further exploration.

Our rate of polypharmacy of 13.0% after exclusion of vitamins and vaccines is consistent with the 15% rate found in a national survey of adults.[1] Other studies in pregnancy in which polypharmacy was defined as at least 4 medications, reported rates of 13.6-15.7%.[3, 5] However, vitamins or supplements often were included in this estimate. When including these medications in our cohort, the polypharmacy rate was 30.5%.

We did not classify our medication data by the FDA Pregnancy Category System. Since June 2015, this system has been replaced by the new Pregnancy and Lactation Rule.[24] As such, we did not determine rates of women taking medications in various Drug Categories per the old A,B,C,D,X system. Other reports consistently showed that pregnant women generally consume category D or X drugs with rates up to 4.5%.[2] One study of Medicaid prescription data noted that almost 40% of women received a prescription for a Category D drug.[11]

Our work is subject to the limitations of the study design. We attempted to enhance completeness of the data set by asking women to bring in prescriptions and any other medications taken since the prior study visit. Additionally, the study team had tables of

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common generic and brand name medications for different conditions to aid with recall. All study team members were trained in this interview process but we cannot know if all study aids were applied uniformly. We also did not separately categorize medications as being over the counter or prescription since we were more interested in ascertaining all medications that had been taken. This report does not include any medications taken during or after the delivery hospitalization. While there was geographic diversity to the clinical sites within nuMoM2b, there were no clinical sites in the South, potentially limiting generalizability for that region.

The nuMoM2b study comprises a large prospective cohort capturing prescription and over-the-counter medication intake longitudinally from the first trimester in a robust, interview-based manner. Thus, these data help to overcome limitations of other reports that were based on administrative prescription databases, retrospective questionnaires, and teratology databases. As the nuMoM2b cohort was geographically and ethnically diverse, these data should be generalizable to much of the U.S. population.

In conclusion, our findings indicate that medication use in pregnancy is ubiquitous and that most pregnant women take multiple medications, including during the first trimester. Gastrointestinal medications, antibiotics, and analgesics were the most commonly taken medication classes. Armed with data from this and other studies, research should focus on improving pregnancy-specific knowledge and guidance for prescribers and pregnant women.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1

Prevalence of Prescription and Other Medication Use in Pregnancy in the nuMoM2b Cohort

Baseline Characteristic	No. of Participants	Taking medication during pregnancy*	*P* Value†	Taking medication in the first trimester of pregnancy*	*P* Value†	Polypharmacy (taking ≥ 5 medications) in pregnancy	*P* Value†
Overall	9546	9262 [97.0 (96.7–97.4)]		9133 [95.7 (95.3–96.1)]		2915 [30.5 (29.6–31.5)]	
Maternal age, y							
<21	1518	1483 [97.7 (96.9–98.4)]	0.009	1440 [94.9 (93.8–96.0)]	0.02	388 [25.6 (23.4–27.8)]	<.001
21–34	7134	6925 [97.1 (96.7–97.5)]		6849 [96.0 (95.6–96.5)]		2188 [30.7 (29.6–31.7)]	
≥35	891	851 [95.5 (94.2–96.9)]		841 [94.4 (92.9–95.9)]		338 [37.9 (34.7–41.1)]	
Maternal race/ethnicity							
White non-Hispanic	5757	5645 [98.1 (97.7–98.4)]	<.0001	5600 [97.3 (96.9–97.7)]	<.001	1953 [33.9 (32.7–35.1)]	<.001
Black non-Hispanic	1328	1300 [97.9 (97.1–98.7)]		1265 [95.3 (94.1–96.4)]		365 [27.5 (25.1–29.9)]	
Hispanic	1598	1471 [92.1 (90.7–93.4)]		1430 [89.5 (88.0–91.0)]		357 [22.3 (20.3–24.4)]	
Asian	383	371 [96.9 (95.1–98.6)]		368 [96.1 (94.1–98.0)]		91 [23.8 (19.5–28.0)]	
Other	477	472 [99.0 (98.0–99.9)]		467 [97.9 (96.6–99.2)]		148 [31.0 (26.9–35.2)]	
Education status attained							
Less than high school	773	750 [97.0 (95.8–98.2)]	0.023	730 [94.4 (92.8–96.1)]	0.057	209 [27.0 (23.9–30.2)]	<.001
Completed high school or general education diploma	1107	1070 [96.7 (95.6–97.7)]		1045 [94.4 (93.0–95.8)]		268 [24.2 (21.7–26.7)]	
Some college	1829	1789 [97.8 (97.1–98.5)]		1753 [95.8 (94.9–96.8)]		573 [31.3 (29.2–33.5)]	
Associate or technical Degree	964	945 [98.0 (97.2–98.9)]		928 [96.3 (95.1–97.5)]		333 [34.5 (31.5–37.5)]	
Completed college	2652	2572 [97.0 (96.3–97.6)]		2554 [96.3 (95.6–97.0)]		838 [31.6 (29.8–33.4)]	
Degree work beyond college	2211	2127 [96.2 (95.4–97.0)]		2114 [95.6 (94.8–96.5)]		692 [31.3 (29.4–33.2)]	
Method of paying for health care‡							
Commercial	6485	6312 [97.3 (96.9–97.7)]	0.003	6263 [96.6 (96.1–97.0)]	<.001	2076 [32.0 (30.9–33.1)]	<.001
Government/military	2637	2535 [96.1 (95.4–96.9)]		2465 [93.5 (92.5–94.4)]		733 [27.8 (26.1–29.5)]	
Self-pay/other	358	352 [98.3 (97.0–99.7)]		346 [96.6 (94.8–98.5)]		93 [26.0 (21.4–30.5)]	
Income and size of household relative to federal poverty level							

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Baseline Characteristic	No. of Participants	Taking medication during pregnancy*	*P* Value†	Taking medication in the first trimester of pregnancy*	*P* Value†	Polypharmacy (taking ≥ 5 medications) in pregnancy	*P* Value†
>200%	5428	5273 [97.1 (96.7–97.6)]	0.301	5239 [96.5 (96.0–97.0)]	0.311	1771 [32.6 (31.4–33.9)]	0.001
100–200%	1108	1083 [97.7 (96.9–98.6)]		1060 [95.7 (94.5–96.9)]		332 [30.0 (27.3–32.7)]	
<100%	1217	1190 [97.8 (97.0–98.6)]		1168 [96.0 (94.9–97.1)]		334 [27.4 (24.9–30.0)]	
Region							
Northeast	2768	2522 [91.1 (90.1–92.2)]	<.001	2469 [89.2 (88.0–90.4)]	<.001	475 [17.2 (15.8–18.6)]	<.001
Midwest	3937	3910 [99.3 (99.1–99.6)]		3875 [98.4 (98.0–98.8)]		1413 [35.9 (34.4–37.4)]	
West	2841	2830 [99.6 (99.4–99.8)]		2789 [98.2 (97.7–98.7)]		1027 [36.1 (34.4–37.9)]	

Data are presented as n [% (95% Confidence Interval)]

*All women included in taking medication in the first trimester also by definition are included in the column as taking medication at any time in pregnancy.

†P values shown are from $\chi 2$ tests for medication use and the categorical baseline characteristics.

‡Women could have multiple sources of insurance. They were categorized as having “Commercial” insurance if they indicated having a commercial source of insurance. They were categorized as having “Government/Military” insurance if they indicated having insurance provided by the government or military while not indicating having a commercial source of insurance. They were categorized as having “Self-Pay/Other” insurance if they indicated having only having insurance that was not from a commercial, government, or military source.

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Table 2

Prevalence of Medication Classes Used During Pregnancy

Medication Class	Women taking medication	Women taking medication during pregnancy†	Women taking medication in the first trimester of pregnancy†
Analgesics	2470 (25.9)	2265 (23.7)	1485 (15.6)
Antibiotics	2701 (28.3)	2439 (25.5)	1199 (12.6)
Antifungals	814 (8.5)	749 (7.8)	304 (3.2)
Antivirals	461 (4.8)	428 (4.5)	133 (1.4)
Anticoagulants	79 (0.8)	72 (0.8)	49 (0.5)
Antipsychotics	55 (0.6)	44 (0.5)	38 (0.4)
Antidepressants	673 (7.1)	579 (6.1)	502 (5.3)
Anticonvulsants	373 (3.9)	301 (3.2)	238 (2.5)
Tocolytics	151 (1.6)	147 (1.5)	4 (0.0)
Antihypertensives	221 (2.3)	207 (2.2)	124 (1.3)
Diuretics	37 (0.4)	23 (0.2)	16 (0.2)
GI & Anti-emetic agents	3402 (35.6)	3279 (34.3)	1866 (19.5)
Chemotherapeutics	9 (0.1)	4 (0.0)	4 (0.0)
Steroids (systemic)	419 (4.4)	380 (4.0)	103 (1.1)
Hormonal contraceptives	347 (3.6)	90 (0.9)	90 (0.9)
Progesterone	377 (3.9)	319 (3.3)	242 (2.5)
Thyroid Agents	476 (5.0)	454 (4.8)	431 (4.5)
Asthma Medications	941 (9.9)	866 (9.1)	721 (7.6)
URI Agents	1675 (17.5)	1567 (16.4)	889 (9.3)
Other Mental Health Agents	26 (0.3)	22 (0.2)	13 (0.1)
Anti-diabetic medications	337 (3.5)	315 (3.3)	206 (2.2)
Other Medication	1052 (11.0)	797 (8.3)	464 (4.9)
Vitamins	9433 (98.8)	9165 (96.0)	9009 (94.4)
Overall	9479 (99.3)	9272 (97.1)	9139 (95.7)

Data are presented as n (%)

*Data presented as the count of the number of women who had indicated taking at least one medication in that overall class. GI= gastrointestinal, URI= upper respiratory infection

†All women included in taking prescription and other medications in the first trimester also by definition are included in the column as taking medications at any time in pregnancy. The “Women taking medication” includes women who took the medication during pregnancy or during the 3 months before pregnancy.

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Table 3

Counts of reason codes recorded for why a woman was taking a medication*

Reason Code	Count
Preventative, other	17858
Other, not elsewhere specified	5275
Provider recommendation	3419
Nausea and vomiting	2202
Urinary tract infection	1406
Respiratory infections, including influenza and other viral infections, bronchitis, etc.	1019
Mental health condition	975
Anemia	967
Asthma	965
Yeast infection	852
Migraine headaches	664
Hypothyroidism	455
Herpes	401
Bacterial vaginosis	357
Diabetes	350
Infertility	336
High blood pressure (hypertension)	258
Preterm contractions / labor	234
Chlamydia	172
Preterm birth prevention	110
Polycystic ovary disease (PCOS)	83
Trichomonas	75
Ulcerative colitis / Crohn’s disease	72
History of blood clots (thrombosis or thromboembolism) or stroke	63
Skin infection (cellulitis)	60
Seizure disorder	58
Kidney disease	54
Other collagen vascular or autoimmune disease	49
Congenital or inherited bleeding disorder, e.g., thrombophilia, hemophilia	30
Gonorrhea	30
Systemic lupus erythematosus (SLE)	27
Rheumatoid arthritis	25
Hyperthyroidism	22
Cholestasis of pregnancy	22
Liver/gall bladder disease	21
Prevention of cerebral palsy	18
Cardiac arrhythmias	16
Cancer/malignancy	14
Sickle cell disease	13

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Reason Code	Count
Fibroids	12
Antiphospholipid syndrome (APA) or other acquired thrombophilia	10
Other STD	10
Thrombocytopenia (platelet count too low)	7
Other structural heart disease (heart problem other than valves)	6
HIV/AIDS	6
Trauma	6
Hepatitis B	4
Cervical dysplasia	3
Syphilis	3
Valvular heart disease	2
PROM latency	2
Missing	1

* Does not prevent a reason code being counted multiple times if accompanying a medication listed multiple times for the same condition but with different time codes.

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Table 4

Medications where use differs significantly between first trimester and second

Direction	Medication	Taking medication before first study visit then stopping later in pregnancy	Began taking medication after first study visit	*P* Value*
Increase	Other Analgesics	70 (0.7)	358 (3.8)	<.001
	Motility Agents	13 (0.1)	46 (0.5)	<.001
	Anti-nausea	44 (0.5)	117 (1.2)	<.001
	5HT3 Antagonist	62 (0.6)	219 (2.3)	<.001
	H2 Receptor Agonists	17 (0.2)	99 (1.0)	<.001
	Other GI Agents	65 (0.7)	277 (2.9)	<.001
	Steroids (Systemic)	23 (0.2)	46 (0.5)	0.006
	Decongestants	58 (0.6)	100 (1.0)	0.001
	Antihistamines	107 (1.1)	192 (2.0)	<.001
	Prenatal Multivitamin	84 (0.9)	158 (1.7)	<.001
	Additional Iron	30 (0.3)	173 (1.8)	<.001
	Other Vitamin	169 (1.8)	237 (2.5)	0.001
	Pertussis	20 (0.2)	38 (0.4)	0.018
Decrease	NSAID	330 (3.5)	37 (0.4)	<.001
	Triptans	36 (0.4)	5 (0.1)	<.001
	Nitrofurantoin	176 (1.8)	138 (1.4)	0.032
	Other Antibiotic	92 (1.0)	51 (0.5)	0.001
	SSRI	144 (1.5)	32 (0.3)	<.001
	NDRI	33 (0.3)	6 (0.1)	<.001
	GABA Analogs	32 (0.3)	6 (0.1)	<.001
	Benzodiazepines	88 (0.9)	5 (0.1)	<.001
	Hormonal Contraceptives	81 (0.8)	0 (0.0)	<.001
	Progesterone (for Purpose Other than Contraception)	141 (1.5)	15 (0.2)	<.001
	Metformin	58 (0.6)	1 (0.0)	<.001
	Other Medication	265 (2.8)	63 (0.7)	<.001
	Other Multivitamin	277 (2.9)	46 (0.5)	<.001
	Additional Folate	89 (0.9)	47 (0.5)	<.001
	Influenza (Seasonal/Novel)	787 (8.2)	499 (5.2)	<.001

Data are presented as n (%)

*Medications must have had at least 25 mothers changing their use of the medication between the time periods to be considered. Counts are individual participants in the cohort. Comparisons made by McNemar's Test.