# **UC San Diego**

# **UC San Diego Previously Published Works**

## **Title**

The Most Commonly Dispensed Prescription Medications Among Pregnant Women Enrolled in the U.S. Medicaid Program.

## **Permalink**

https://escholarship.org/uc/item/8hq239v9

## **Journal**

Obstetrics and gynecology, 126(3)

### **ISSN**

0029-7844

### **Authors**

Palmsten, Kristin Hernández-Díaz, Sonia Chambers, Christina D et al.

## **Publication Date**

2015-09-01

### DOI

10.1097/aog.0000000000000982

Peer reviewed



Author manuscript

Obstet Gynecol. Author manuscript; available in PMC 2016 September 01.

Published in final edited form as:

Obstet Gynecol. 2015 September; 126(3): 465–473. doi:10.1097/AOG.0000000000000982.

# The Most Commonly Dispensed Prescription Medications **Among Pregnant Women Enrolled in the United States Medicaid Program**

Kristin Palmsten, ScD<sup>1</sup>, Sonia Hernández-Díaz, MD, DrPH<sup>2</sup>, Christina D Chambers, PhD, MPH<sup>1,3</sup>, Helen Mogun, MS<sup>4</sup>, Sophia Lai, PharmD<sup>5</sup>, Todd P Gilmer, PhD<sup>3</sup>, and Krista F Huybrechts, MS, PhD<sup>4</sup>

<sup>1</sup>Department of Pediatrics, University of California, San Diego, La Jolla, CA

<sup>2</sup>Department of Epidemiology, Harvard School of Public Health, Boston, MA

<sup>3</sup>Department of Family Medicine and Public Health, University of California, San Diego, La Jolla, CA

<sup>4</sup>Division of Pharmacoepidemiology & Pharmacoeconomics, Department of Medicine, Brigham & Women's Hospital and Harvard Medical School, Boston, MA

<sup>5</sup>Skaggs School of Pharmacy and Pharmaceutical Sciences, University of California, San Diego, La Jolla, CA

### Abstract

**Objectives**—To characterize the 20 most common prescription medications and the 10 most common prescription medications classified in the former U.S. Food and Drug Administration categories D or X dispensed to pregnant women enrolled in the U.S. Medicaid program.

**Methods**—We conducted a cohort study of 1,106,757 pregnant women with live births using 2000-2007 Medicaid Analytic eXtract data. We used outpatient pharmacy records to identify medication dispensings and reported the proportion of pregnancies that were dispensed at least one prescription medication. Maternal age and race and ethnicity-stratified estimates were compared using prevalence ratios (PR) and 95% confidence intervals (CI).

Results—During pregnancy, 82.5% of the cohort had a dispensing for one or more prescription medication. The most commonly dispensed medications during pregnancy included nitrofurantoin (21.6%), metronidazole (19.4%), amoxicillin (18.0%), azithromycin (16.9%), and promethazine (13.5%). Proportions were highest among younger women for several medications; eg, nitrofurantoin (23.9% vs 15.4%; PR: 1.55, CI: 1.52-1.58), metronidazole (20.7% vs 12.0%; PR: 1.73, CI: 1.69-1.77), and azithromycin (21.1% vs 11.0%; PR: 1.93, CI: 1.89-1.97) were more common among women younger than 20 than among women aged 35 years or older. Proportions

Corresponding Author: Kristin Palmsten, 9500 Gilman Drive #0828, La Jolla, CA, 92093-0828, 858-246-1756, kpalmsten@ucsd.edu.

Financial Disclosure: In the past 12 months, Sonia Hernández-Díaz consulted for AstraZeneca and collaborated as an epidemiologist for the North American Antiepileptic Drug Pregnancy Registry and the National Pregnancy Registry for Atypical Antipsychotics, both funded by multiple companies.

Presented as a poster at the 50<sup>th</sup> Annual Meeting of the Drug Information Association (DIA), June 15-19, 2014, San Diego, CA.

were highest among white women with some exceptions; eg, compared with white women, metronidazole was more common among black women (29.8% vs 14.4%; PR: 2.07, CI: 2.05-2.09). Excluding fertility treatments, 42.0% had at least one dispensing for a D or X medication during pregnancy. Codeine (11.9%) and hydrocodone (10.2%) were the most common D medications.

**Conclusions**—Medications used to treat infections were the most commonly dispensed prescription medications. Dispensing of commonly used prescription medications during pregnancy varied by maternal age and race—ethnicity.

## Introduction

Data regarding the risks of most prescription medications during pregnancy are inadequate, posing serious public health concerns. Identifying medications commonly used in pregnancy is critical to inform research priorities regarding safety. This is particularly relevant considering the U.S. Food and Drug Administration's (FDA) December 2014 Pregnancy and Lactation Labeling Rule, which made historic changes to prescription medication labeling requirements regarding use during pregnancy and breastfeeding.

Several studies from the U.S. within the past two decades have reported on medication use during pregnancy within broad classes <sup>4-8</sup> Fewer have identified the most commonly used prescription medications during pregnancy. <sup>9-11</sup> These studies were based on maternal recall after delivery (National Birth Defects Prevention Study (NBDPS) and Slone Epidemiology Center Birth Defects Study (BDS)), <sup>10,11</sup> and on commercial health plan databases (HMO Research Network). <sup>9</sup> Furthermore, the use of medications with potential for fetal harm has been described using medical records and claims from commercial health plans and the Tennessee Medicaid program. <sup>12-14</sup>

Medicaid insures >40% of all US deliveries,<sup>15</sup> and pregnant women enrolled in Medicaid are low income, racially/ethnically diverse, and tend to be relatively young.<sup>16</sup> The Medicaid Analytic eXtract (MAX), which contains healthcare utilization data from Medicaid enrollees, provides an opportunity to study this large population of women whose demographics differ from previous descriptive studies.<sup>9-11</sup> We aimed to characterize the 20 most common prescription medications dispensed at least once (referred to hereafter as "most commonly dispensed"), the 10 most commonly dispensed prescription medications classified in the former FDA-categories D or X, and the 10 most commonly dispensed classes among pregnant women enrolled in Medicaid.

### **Materials and Methods**

MAX contains beneficiary enrollment information and claims from inpatient and outpatient procedures and diagnoses and outpatient pharmacy dispensings reimbursed by Medicaid. Medicaid data on medication type and dispensing dates are generally believed to be accurate <sup>17</sup> and have been used to study medication utilization during pregnancy. <sup>8,18-20</sup> We utilized MAX data from 2000-2007 because these years were available to our research group and overlapped with years from the previous studies. <sup>9-11</sup> As previously described, >7 million women ages 12-55 years old with delivery-related healthcare claims were identified

from 2000-2007 MAX data and were linked with newborns. <sup>16</sup> We estimated the date of the last menstrual period (LMP) to be 245 days before the newborn's birthdate for pregnancies with maternal or newborn International Classification of Diseases, Ninth Revision (ICD-9), codes indicative of preterm birth (644.0, 644.2, and 765.x), and 270 days before the newborn's birthdate for other pregnancies. <sup>21</sup> This method correctly classified gestational age at delivery within 2 weeks for 75% of preterm and nearly all term deliveries in a similar database. <sup>21</sup> We required that women have continuous enrollment in Medicaid, no private insurance, no restricted benefits, and appropriate enrollment type from three months before the LMP through delivery. The study cohort contained 1,106,757 pregnancies ending in live birth from 45 US states and Washington, DC. This project was approved by the Brigham and Women's Hospital, Harvard School of Public Health, and University of California, San Diego's Institutional Review Boards and a data use agreement was in place with the Centers for Medicare and Medicaid Services.

We used the MAX Prescription Drug file to identify medication dispensings excluding vitamins (including iron preparations), caloric agents, electrolytic replacement preparations, diagnostic agents, dental agents, and devices/medical supplies. The same woman could have multiple dispensings for the same medication. We defined medication prevalence as the proportion of pregnancies with at least one dispensing date for medications of interest during the pregnancy periods of interest including

- Pregnancy: LMP date until the day before the delivery date
- Pre-pregnancy: 90 days before LMP date until the day before the LMP date
- First trimester: LMP date until 89 days after the LMP date
- Second trimester: 90 days after the LMP date until 179 days after the LMP date
- Third trimester: 180 days after the LMP date until the day before the delivery date

There were 2,506 unique generic medication names dispensed during pregnancy. Generic medications that were identical except for the salt were merged. Medications with combination ingredients were not merged with single ingredient formulations. We identified the 20 medications most commonly dispensed during pregnancy and reported prevalence overall and by pregnancy period, maternal age, and race—ethnicity. Using prevalence ratios and Wald 95% confidence intervals, we compared proportions by age and race—ethnicity, two major demographic characteristics that differentiate Medicaid from other data sources. We stratified by birth year combining 2000 with 2001 because few pregnancies were available from 2000 as a result of the enrollment requirements. We plotted year-specific proportions for those with at least a 40% increase or decrease between any years.

We identified medications assigned to the former FDA D or X categories published in Briggs, Freeman, and Yaffe.<sup>22</sup> Although this classification system is limited for conveying teratogenic risk for clinical practice, in part because designations also depend on maternal benefits,<sup>11,23,24</sup> we used this method to classify medications with the potential to cause fetal harm. When the manufacturer's designated category differed from that assigned by Briggs et al or by trimester of use, we classified the medication in the least favorable category (e.g., medications with both C and D designations were classified as D). Clomiphene, follitropin,

and chorionic gonadotropin, identified as commonly used X medications in previous studies, \$^{10,11}\$ were excluded because fertility treatments are rarely covered by Medicaid.\$^{25}\$ After combining hormonal contraceptives, there were 180 different D or X medications dispensed during pregnancy. We reported the prevalence of all medications, D or X medications, and X medications overall and by pregnancy period, age, race—ethnicity, and year. Additionally, we reported proportions overall and by pregnancy period, age, and race—ethnicity for the 10 most commonly dispensed D and X medications during the entire pregnancy.

We grouped medications into classes according to the second tier of the American Hospital Formulary Service (AHFS) Pharmacologic-Therapeutic Classification system or the first tier for medications lacking a more granular classification. Medications may have multiple classes because of multiple indications, mechanisms of action, routes of administration, or ingredients. Because all AHFS classes for a medication are considered equally valid, and medications with multiple classes were included in more than one class. We identified the most commonly dispensed classes during the entire pregnancy. We reported the prevalence overall and stratified by pregnancy period, age, and race—ethnicity. We also stratified by year and plotted the year-specific proportions for those with at least a 20% increase or decrease between any years.

We identified medications used by >1.5% of women during the first trimester or by >3% of women during the entire pregnancy excluding fertility treatments and unspecified medications (e.g., not otherwise specified antibiotic) in at least one of the previous US studies with overlapping study years: BDS 1999-2003, NBDPS 2004-2007, BDS 2004-2008, or HMO Research Network 1996-2000. 9-11 We restricted to oral formulations as described in the publications. We identified the corresponding medication prevalence in the current study population.

## Results

In this cohort, the mean maternal age was 23.2 years (standard deviation: 5.8 years). Overall, 39.9% of women were white, 33.7% were black, 16.3% were Hispanic, 3.5% were Asian, 1.8% were American Indian, and 4.8% were classified as having other or unknown race—ethnicity. 11.2% of women had preterm delivery.

During pregnancy, 82.5% of the cohort was dispensed at least one prescription medication; the proportion was lowest among Asian women (69.7%) and did not differ meaningfully by age and year (Appendices 1–4, available online at <a href="http://links.lww.com/xxx">http://links.lww.com/xxx</a>). The proportion dispensed at least one prescription medication by trimester increased slightly from before pregnancy (52.3%) through the third trimester (57.3%) (Appendix 1, available online at <a href="http://links.lww.com/xxx">http://links.lww.com/xxx</a>).

The most commonly dispensed prescription medications during pregnancy were nitrofurantoin (21.6%), metronidazole (19.4%), amoxicillin (18.0%), azithromycin (16.9%), and promethazine (13.5%) (Table 1). Nitrofurantoin had the greatest relative increase from 1.4% before pregnancy to 9.8% in the third trimester. Compared with other pregnancy

periods, the prevalence of promethazine was highest in the first trimester (8.4%), as was metoclopramide (2.9%) and clindamycin (2.0%).

The prevalence of some of the most common medications differed by age and race–ethnicity (Tables 2-3). Women ages younger than 20 years had the highest proportions of several medications. Compared with women 35 years old, sulfamethoxazole and trimethoprim was 51% higher, nitrofurantoin was 55% higher, metronidazole was 73% higher, and azithromycin was 93% higher during pregnancy among women <20. White women had the highest proportions of common medications, with some exceptions. Notably, metronidazole was 107% higher among black women, miconazole was 126% higher among Hispanic women, and acetaminophen was >400% higher among Asian women than white women. Major changes in year-specific proportions are illustrated in Figure 1.

Excluding fertility treatments, 42.0% had at least one dispensing for a category D or X medication during pregnancy; the proportions were 39.6% for D and 5.3% for X medications. The proportion with D or X medications decreased from 39.8% before pregnancy to 18.2% in the third trimester (Appendices 1–4, available online at http://links.lww.com/xxx). When stratifying by age, women 25-29 years had the highest proportion of D or X medications (44.9%) and women <20 had the lowest proportion (36.2%). White women had the highest proportion of D or X medications (50.5%), and Asian women had the lowest proportion (30.6%). The proportion dispensed X medications increased between 2000-2001 (4.1%) and 2007 (5.4%).

During pregnancy, the most commonly dispensed D medications included: codeine (11.9%), hydrocodone (10.2%), ibuprofen (4.9%), sulfamethoxazole (4.0%), and hydrocortisone (4.0%), and the most prevalent X medications included hormonal contraceptives (4.9%), temazepam (0.11%), atorvastatin (0.07%), warfarin (0.04%), and simvastatin (0.04%) (Table 4). Age and race–ethnicity-stratified proportions of the most common D and X medications are listed in Appendices 5–6, available online at http://links.lww.com/xxx.

The most commonly dispensed classes during pregnancy included antibacterials (49.7%), analgesics and antipyretics (29.6%), skin and mucous membrane anti-infectives (28.7%), urinary anti-infectives (21.7%), and first generation antihistamines (18.6%) (Appendix 7, available online at <a href="http://links.lww.com/xxx">http://links.lww.com/xxx</a>). Respiratory antihistamines (18.1%) were frequently captured by other common classes including first generation antihistamines, sympathomimetic agents, and bronchodilators. Bronchodilators (14.3%), the tenth most commonly dispensed class, included sympathomimetic agents, antihistamines, and other agents. In terms of age, younger women had the highest proportions of several classes (Appendix 8, available online at <a href="http://links.lww.com/xxx">http://links.lww.com/xxx</a>). White women had the highest and Asian women had the lowest proportions of most of the common classes (Appendix 9, available online at <a href="http://links.lww.com/xxx">http://links.lww.com/xxx</a>). Major changes in year-specific class proportions are illustrated in Appendix 10, available online at <a href="http://links.lww.com/xxx">http://links.lww.com/xxx</a>).

Prevalence estimates of the most commonly used medications during the first trimester and during pregnancy from previous U.S. studies are reported in Appendices 11–12, available online at http://links.lww.com/xxx).<sup>9-11</sup>

## **Discussion**

Prescription medication use during pregnancy in this low-income cohort was common; 4 out of 5 pregnancies had at least one dispensing and 2 out of 5 had at least one dispensing for D or X medications. In agreement with previous U.S. studies using self-report, healthcare claims, and nationally representative survey data, medications used to treat infections and allergies or asthma were the most common prescription medications. <sup>9-11,27</sup> The prevalence of several medications varied by age and race–ethnicity. These differences could partially explain differences in use between this cohort, which was relatively young and racially–ethnically diverse, compared with women from previous studies.

Of the twenty most commonly dispensed medications, nine are rated by TERIS (Teratogen Information System) as having limited to fair data quality and quantity to inform human teratogenic risk assessments: azithromycin, cephalexin, terconazole, hydrocodoneacetaminophen, albuterol, clindamycin, miconazole, fluconazole, and sulfamethoxazole/ trimethoprim.<sup>28</sup> The other eleven received fair to good ratings. Lack of unambiguous safety information may lead to the use of medications with potential to cause adverse pregnancy outcomes, while beneficial medications may be avoided. <sup>29,30</sup> In this cohort, 82.5% were dispensed a prescription medication during pregnancy, which is higher than reports from the BDS (70.0%, 2006-2008), NBDPS (49.4%, 1997-2003), <sup>10</sup> and the HMO Research Network (64%, 1996-2000). A caveat for these comparisons is that the BDS and NBDPS included medications available only by prescription, whereas the database studies also included overthe-counter medications dispensed at pharmacies. Moreover, we identified differences in specific medication estimates in this study compared with the BDS, NBDPS, and HMO Research Network study. We relied on medication dispensing records, as did the HMO Research Network study, and may overestimate actual use. However, studies using maternal recall, including BDS and NBDPS, may underestimate use, especially for specific medications rather than classes, which may be difficult to remember months after delivery, e.g., amoxicillin vs. unspecified antibiotic. Potential contributions of population composition to the observed differences in medication utilization across studies are discussed in Appendix 13, available online at http://links.lww.com/xxx. Finally, other studies reported less D or X use but employed different classifications. 12-14 Each of the 10 most common D medications are also classified as B or C depending on circumstances of use.<sup>22</sup>

Besides overestimation of medication use from dispensing information, additional sources of exposure misclassification should be considered. First, no information was available for medications purchased over-the-counter or prescribed during hospitalizations. Dispensing information in healthcare databases underestimates use of medications also available over-the-counter including analgesics and antipyretics as a class, and acetaminophen, ibuprofen, and miconazole. The observed variability by age and race—ethnicity for these medications could be explained in part by demographic differences in over-the-counter versus prescription use. Second, gestational age at delivery was unavailable, and LMP and trimester dates had to be estimated. As such, misclassification of the dispensing timing by pregnancy period is possible but should be minor considering the long exposure windows (3-9 months long). Finally, the cohort was comprised of pregnancies ending in live births.

Consequently, medications that cause fetal harm may be underestimated because women with spontaneous abortions, terminations, and stillbirths are not included.<sup>9</sup>

Only women enrolled in Medicaid before pregnancy were included in this study, i.e., those who were Medicaid-eligible because they were classified as children, multiparae, or as having a disability. <sup>16</sup> We expect results to generalize well to pregnant women enrolled in Medicaid with live births, including those who became eligible because of pregnancy given similarities in eligibility classification, age, and race–ethnicity distributions. <sup>16</sup> However, if pre-pregnancy enrollees had greater medication utilization, then exposure may be overestimated for all Medicaid pregnancies.

This study is the first to describe the most commonly dispensed medications during pregnancy in a nationwide Medicaid cohort. Medication information was collected prospectively and avoided recall problems. Furthermore, information on generic names was available and vague classifications, e.g., unspecified antibiotic, were avoided.

The characterization of prescription medication use among pregnant women enrolled in Medicaid augments our knowledge of medication use during pregnancy by providing information from low-income women. Geographic variability in medication use and contributors to the identified age and racial/ethnic disparities should be investigated. Experts recommended frequency of medication use among pregnant women as one criterion to set priorities for the Centers for Disease Control and Prevention's 'Treating for Two: Safer Medication Use in Pregnancy' initiative. <sup>32</sup> Considering the differences observed between the current and previous studies, multiple data sources, including Medicaid, should be used to inform this criterion. The FDA's Pregnancy and Lactation Labeling Rule<sup>3</sup> is an impetus for research to inform labeling of newer medications. Our study indicates, however, that many older medications are commonly used and also lack safety evidence to inform treatment decisions. Class and medication rankings from this study and others could be used by the FDA to prioritize medications for pregnancy risk narrative label updates.

## **Supplementary Material**

Refer to Web version on PubMed Central for supplementary material.

## **Acknowledgments**

The Pharmacoepidemiology Program at the Harvard School of Public Health is partially supported by training grants from Pfizer, Takeda, Bayer and Phrma. The MAX pregnancy cohort development was funded by the Agency for Healthcare Research and Quality R01HS018533. Sonia Hernández-Díaz is partially funded by the National Institutes of Health R01MH100216. Krista F Huybrechts was supported by a career development grant K01MH099141 from the National Institute of Mental Health. The funders had no role in the collection, analysis and interpretation of data; in the writing of the report; and in the decision to submit the article for publication.

### References

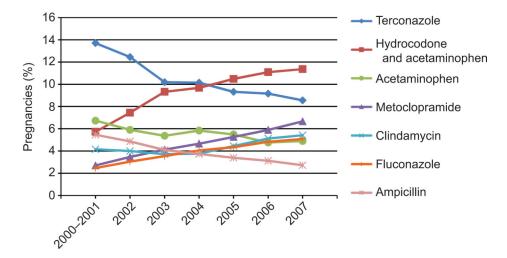
- Adam MP, Polifka JE, Friedman JM. Evolving knowledge of the teratogenicity of medications in human pregnancy. Am J Med Genet C Semin Med Genet. 2011; 157C:175–82. [PubMed: 21766440]
- Mitchell AA. Systematic identification of drugs that cause birth defects--a new opportunity. N Engl J Med. 2003; 349:2556–9. [PubMed: 14695418]

 U.S. Food and Drug Administration. [January 26, 2015] Pregnancy and lactation labeling final rule. Available at http://www.fda.gov/Drugs/DevelopmentApprovalProcess/DevelopmentResources/ Labeling/ucm093307.htm.

- 4. Toh S, Li Q, Cheetham TC, et al. 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. 2013; 16:149–57. [PubMed: 23389622]
- 5. Avalos LA, Chen H, Yang C, et al. The prevalence and trends of antiviral medication use during pregnancy in the US: a population-based study of 664,297 deliveries in 2001-2007. Matern Child Health J. 2014; 18:64–72. [PubMed: 23420306]
- Epstein RA, Bobo WV, Martin PR, et al. Increasing pregnancy-related use of prescribed opioid analgesics. Ann Epidemiol. 2013; 23:498–503. [PubMed: 23889859]
- Bateman BT, Hernandez-Diaz S, Rathmell JP, et al. Patterns of opioid utilization in pregnancy in a large cohort of commercial insurance beneficiaries in the United States. Anesthesiology. 2014; 120:1216–24. [PubMed: 24525628]
- 8. Desai RJ, Hernandez-Diaz S, Bateman BT, Huybrechts KF. Increase in prescription opioid use during pregnancy among Medicaid-enrolled women. Obstet Gynecol. 2014; 123:997–1002. [PubMed: 24785852]
- 9. Andrade SE, Gurwitz JH, Davis RL, et al. Prescription drug use in pregnancy. Am J Obstet Gynecol. 2004; 191:398–407. [PubMed: 15343213]
- Mitchell AA, Gilboa SM, Werler MM, Kelley KE, Louik C, Hernandez-Diaz S, National Birth Defects Prevention Study. Medication use during pregnancy, with particular focus on prescription drugs: 1976-2008. Am J Obstet Gynecol. 2011; 205:51 e1–8. [PubMed: 21514558]
- Thorpe PG, Gilboa SM, Hernandez-Diaz S, et al. Medications in the first trimester of pregnancy: most common exposures and critical gaps in understanding fetal risk. Pharmacoepidemiol Drug Saf. 2013; 22:1013–8. [PubMed: 23893932]
- 12. Riley EH, Fuentes-Afflick E, Jackson RA, et al. Correlates of prescription drug use during pregnancy. J Womens Health (Larchmt). 2005; 14:401–9. [PubMed: 15989412]
- 13. Andrade SE, Raebel MA, Morse AN, et al. Use of prescription medications with a potential for fetal harm among pregnant women. Pharmacoepidemiol Drug Saf. 2006; 15:546–54. [PubMed: 16586470]
- Cooper WO, Hickson GB, Ray WA. Prescriptions for contraindicated category X drugs in pregnancy among women enrolled in TennCare. Paediatr Perinat Epidemiol. 2004; 18:106–11. [PubMed: 14996249]
- [March 3, 2015] Maternal and child health (MCH) update: states increase eligibility for children's health in 2007. 2008. (Accessed, at http://www.nga.org/files/live/sites/NGA/files/pdf/ 0811MCHUPDATE.PDF.)
- Palmsten K, Huybrechts KF, Mogun H, et al. Harnessing the Medicaid Analytic eXtract (MAX) to Evaluate Medications in Pregnancy: Design Considerations. PLoS One. 2013; 8:e67405.
  [PubMed: 23840692]
- 17. Hennessy, S.; Palumbo Freeman, C.; Cunningham, F. US government claims databases.. In: Strom, BL.; Kimmel, SE.; Hennessy, S., editors. Pharmacoepidemiology. 5th Edition. Wiley-Blackwell; Chichester, West Sussex, UK: 2012. p. 209-223.
- 18. Huybrechts KF, Palmsten K, Mogun H, et al. National trends in antidepressant medication treatment among publicly insured pregnant women. Gen Hosp Psychiatry. 2013; 35:265–71. [PubMed: 23374897]
- 19. Bateman BT, Hernandez-Diaz S, Huybrechts KF, et al. Patterns of outpatient antihypertensive medication use during pregnancy in a Medicaid population. Hypertension. 2012; 60:913–20. [PubMed: 22966012]
- Phiri K, Fischer MA, Mogun H, et al. Trends in antiretroviral drug use during pregnancy among HIV-infected women on Medicaid: 2000-2007. AIDS Patient Care STDS. 2014; 28:56–65. [PubMed: 24517538]
- Margulis AV, Setoguchi S, Mittleman MA, Glynn RJ, Dormuth CR, Hernandez-Diaz S. Algorithms to estimate the beginning of pregnancy in administrative databases. Pharmacoepidemiol Drug Saf. 2013; 22:16–24. [PubMed: 22550030]

22. Briggs, GG.; Freeman, RK.; Yaffee, SJ., editors. Drugs in pregnancy and lactation: a reference guide to fetal and neonatal risk. 8 ed.. Lippincott Williams & Wilkins; Philadelphia: 2008.

- 23. Chambers CD, Polifka JE, Friedman JM. Drug safety in pregnant women and their babies: ignorance not bliss. Clin Pharmacol Ther. 2008; 83:181–3. [PubMed: 18073777]
- Ramoz LL, Patel-Shori NM. Recent changes in pregnancy and lactation labeling: retirement of risk categories. Pharmacotherapy. 2014; 34:389–95. [PubMed: 24390829]
- 25. Ranji, U.; Salganicoff, A.; Stewart, AM.; Cox, M.; Doamekpor, L. [January 20, 2015] State Medicaid Coverage of Family Planning Services: Summary of State Survey Findings. Nov. 2009 Available at:https://kaiserfamilyfoundation.files.wordpress.com/2013/01/8015.pdf.
- 26. [January 22, 2015] AHFS Pharmacologic-Therapeutic Classification. Available at: http://www.ahfsdruginformation.com/pt-classification-system.aspx.
- 27. Tinker SC, Broussard CS, Frey MT, Gilboa SM. Prevalence of prescription medication use among non-pregnant women of childbearing age and pregnant women in the United States: NHANES, 1999-2006. Matern Child Health J. 2015; 19:1097–106. [PubMed: 25287251]
- Friedman, JM.; Polifka, JE.; TERIS. Truven Health Analytics. Greenwood Village, Colorado, USA: Micromedex® 2.0, (electronic version).. Available at: http:// www.micromedexsolutions.com. [January 7, 2015]
- 29. Lagoy CT, Joshi N, Cragan JD, Rasmussen SA. Medication use during pregnancy and lactation: an urgent call for public health action. J Womens Health (Larchmt). 2005; 14:104–9. [PubMed: 15775727]
- 30. Parisi MA, Spong CY, Zajicek A, Guttmacher AE. We don't know what we don't study: the case for research on medication effects in pregnancy. Am J Med Genet C Semin Med Genet. 2011; 157C:247–50. [PubMed: 21766436]
- 31. Toh S, Mitchell AA, Werler MM, Hernandez-Diaz S. Sensitivity and specificity of computerized algorithms to classify gestational periods in the absence of information on date of conception. Am J Epidemiol. 2008; 167:633–40. [PubMed: 18194999]
- 32. Broussard CS, Frey MT, Hernandez-Diaz S, et al. Developing a systematic approach to safer medication use during pregnancy: summary of a Centers for Disease Control and Prevention-convened meeting. Am J Obstet Gynecol. 2014; 211:208–14 e1.. [PubMed: 24881821]



**Figure 1.** Medication prevalence by year of birth for the 7 medications with at least a 40% increase or decrease, between any years, among the 20 most commonly dispensed prescription medications during pregnancy.

**Author Manuscript** 

Table 1

**Author Manuscript** 

**Author Manuscript** 

06,757 for	
eriod. N=1,1	
pregnancy p	
stratified by	
valence, and	
, overall prev	
ng pregnancy	
lications duri	
scription med	
l pre	
The 20 most commonly dispensed	
The 20 most	each column.

Medication	During Pregnancy %	3 Months Prepregnancy %	1st Trimester %	2nd Trimester %	3rd Trimester %
Nitrofurantoin	21.6	1.4	7.0	9.1	8.6
Metronidazole	19.4	4.5	5.8	9.1	7.7
Amoxicillin	18.0	5.7	7.1	7.2	9.9
Azithromycin	16.9	4.5	6.0	7.1	9.9
Promethazine	13.5	2.0	8.4	4.9	3.4
Cephalexin	12.7	3.1	4.2	4.7	5.6
Codeine & Acetaminophen	10.7	3.9	3.4	4.5	4.7
Terconazole	10.2	6.0	2.2	4.3	5.5
Hydrocodone & Acetaminophen	9.6	T.T	5.0	3.7	3.5
Albuterol	8.1	3.8	3.8	4.1	3.8
Acetaminophen	5.5	1.2	2.2	2.4	2.0
Metoclopramide	4.8	0.3	2.9	1.6	1.0
Ibuprofen	4.8	8.3	3.5	1.1	9.0
Penicillin V	4.5	25	1.9	1.6	1.4
Clindamycin	4.4	1.4	2.0	1.6	1.3
Miconazole	4.4	0.4	1.1	1.7	2.0
Fluconazole	4.0	2.5	1.5	1.3	1.8
Sulfamethoxazole & Trimethoprim	4.0	3.4	1.9	1.3	1.0
Amoxicillin & Clavulanate	3.8	1.8	1.4	1.3	1.4
Ampicillin	3.8	0.3	1.0	1.3	1.7

Table 2

The 20 most commonly dispensed prescription medications during pregnancy by age group; prevalence, prevalence ratio (PR), and 95% confidence intervals (CI).

Medication	Age 35 N=68,716 Reference		e <20 N	Age <20 N=272,407	Age 2	.0-29	Age 20-29 * N=647,671	Age	30-34 N	Age 30-34 N=117,963
	%	%	PR	95% CI	%	PR	95% CI	%	PR	95% CI
Nitrofurantoin	15.4	23.9	1.55	1.52-1.58	22.0	1.43	1.40-1.45	18.0	1.17	1.14-1.19
Metronidazole	12.0	20.7	1.73	1.69-1.77	20.3	1.70	1.66-1.73	15.3	1.28	1.24-1.31
Amoxicillin	16.2	17.9	1.11	1.09-1.13	18.3	1.13	1.11-1.15	17.4	1.08	1.06-1.10
Azithromycin	11.0	21.1	1.93	1.89-1.97	16.5	1.50	1.47-1.54	13.0	1.18	1.15-1.22
Promethazine	8.1	14.1	1.74	1.69-1.79	14.3	1.77	1.73-1.82	11.1	1.37	1.33-1.41
Cephalexin	10.2	13.3	1.31	1.28-1.34	13.0	1.28	1.25-1.31	11.4	1.12	1.09-1.15
Codeine & Acetaminophen	8.8	7.9	0.89	0.87-0.92	12.2	1.38	1.34-1.41	10.4	1.18	1.15-1.22
Terconazole	8.9	10.4	1.17	1.14-1.20	10.4	1.17	1.15-1.20	8.6	1.11	1.08-1.15
Hydrocodone & Acetaminophen	8.2	6.5	0.79	0.77-0.82	11.0	1.34	1.30-1.37	6.6	1.20	1.16-1.24
Albuterol	8.9	7.9	0.88	0.86-0.90	8.0	0.89	0.87-0.91	9.0	1.00	0.97-1.03
Acetaminophen	9.3	5.0	0.53	0.52-0.55	5.0	0.54	0.52-0.55	7.1	0.76	0.74-0.78
Metoclopramide	4.0	4.1	1.04	0.99-1.08	5.2	1.31	1.26-1.36	5.1	1.28	1.23-1.34
Ibuprofen	0.9	4.3	0.71	0.69-0.73	4.8	0.79	0.77-0.82	5.5	0.92	96.0-68.0
Penicillin V	3.9	3.5	0.92	0.88-0.96	5.0	1.29	1.24-1.34	4.4	1.15	1.10-1.21
Clindamycin	3.1	4.2	1.38	1.32-1.45	4.7	1.53	1.47-1.60	4.0	1.31	1.25-1.38
Miconazole	5.1	3.9	0.76	0.73-0.79	4.5	0.87	0.84-0.90	8.4	0.93	0.89-0.97
Fluconazole	3.4	3.7	1.07	1.03-1.12	4.3	1.26	1.21-1.31	3.9	1.15	1.10-1.21
Sulfamethoxazole & Trimethoprim	3.0	4.5	1.51	1.44-1.58	4.0	1.36	1.30-1.42	3.4	1.13	1.08-1.20
Amoxicillin & Clavulanate	3.4	3.7	1.09	1.05-1.14	3.9	1.16	1.12-1.21	3.8	1.12	1.07-1.18
Ampicillin	3.4	3.9	1.17	1.11-1.22	3.8	1.11	1.07-1.16	3.7	1.10	1.04-1.15

 $<sup>^{\</sup>ast}$  Age groups 20-24 and 25-29 were combined because results were similar.

**Author Manuscript** 

**Author Manuscript** 

Table 3

The 20 most commonly dispensed prescription medications during pregnancy by race-ethnicity group; prevalence, prevalence ratio (PR), and 95% confidence intervals (CI).

Medication	White N=441,524 Reference	BIS	Black N=373,252	73,252	His	panic N=	Hispanic N=180,598	A	sian N	Asian N=38,557	Americ	an India	American Indian N=20,261	Ott	er or Unkr N=52,565	Other or Unknown N=52,565
	0%	%	PR	95% CI	%	PR	95% CI	%	PR	95% CI	%	PR	95% CI	%	PR	95% CI
Nitrofurantoin	22.3	22.2	66.0	0.98-1.00	21.6	0.97	86:0-96:0	12.7	0.57	0.55-0.59	17.6	0.79	0.77-0.81	19.8	0.89	0.87-0.90
Metronidazole	14.4	29.8	2.07	2.05-2.09	13.6	0.94	0.93-0.95	7.0	0.48	0.46-0.50	15.1	1.05	1.01-1.08	16.8	1.16	1.14-1.19
Amoxicillin	22.1	14.8	0.67	0.66-0.67	16.2	0.73	0.73-0.74	14.1	0.64	0.62-0.66	17.5	0.79	0.77-0.81	14.5	99.0	0.64-0.67
Azithromycin	19.7	18.7	0.95	0.94-0.96	6.6	0.50	0.49-0.51	6.2	0.31	0.30-0.32	14.4	0.73	0.71-0.76	14.0	0.71	0.69-0.72
Promethazine	17.3	13.7	0.79	0.78-0.80	7.8	0.45	0.44-0.46	5.8	0.34	0.32-0.35	6.6	0.57	0.55-0.59	6.9	0.40	0.38-0.41
. Cephalexin	14.9	11.4	0.77	0.76-0.78	12.2	0.82	0.81-0.83	7.4	0.50	0.48-0.52	13.2	0.89	0.86-0.92	10.0	0.67	0.66-0.69
Codeine & Acetaminophen	13.4	10.1	0.75	0.74-0.76	7.4	0.55	0.54-0.56	4.9	0.36	0.35-0.38	11.5	0.85	0.82-0.89	7.8	0.58	0.57-0.60
Terconazole	8.8	14.0	1.59	1.57-1.61	8.9	0.78	0.76-0.79	4.4	0.50	0.48-0.52	5.4	0.62	0.58-0.65	13.3	1.50	1.47-1.54
· Hydrocodone & Acetaminophen	14.0	7.4	0.53	0.52-0.54	5.3	0.38	0.37-0.39	3.1	0.22	0.21-0.23	11.4	0.81	0.78-0.84	6.5	0.46	0.45-0.48
Albuterol	10.1	7.0	69.0	0.68-0.71	6.1	0.61	0.60-0.62	5.0	0.50	0.47-0.52	7.3	0.72	92.0-69.0	8.8	0.88	0.85-0.90
Acetaminophen	2.5	5.2	2.08	2.03-2.13	11.2	4.51	4.41-4.61	13.6	5.49	5.32-5.66	6.3	2.55	2.41-2.70	7.4	2.99	2.88-3.10
· Metoclopramide	5.3	4.9	0.92	0.90-0.94	4.2	0.80	0.78-0.82	2.8	0.54	0.51-0.57	3.8	0.72	0.67-0.77	4.9	0.93	96.0-68.0
Ibuprofen	4.5	5.0	1.12	1.10-1.14	5.2	1.17	1.14-1.20	4.3	0.95	0.91-1.00	5.0	1.10	1.04-1.17	4.4	0.97	0.93-1.02
Penicillin V	5.1	4.6	0.89	0.88-0.91	3.3	0.64	0.63-0.66	2.5	0.48	0.45-0.51	4.3	0.84	0.78-0.89	4.0	0.78	0.75-0.82
Clindamycin	4.7	5.0	1.06	1.04-1.08	2.9	0.62	0.60-0.64	2.6	0.54	0.51-0.58	4.1	0.88	0.82-0.94	4.3	0.92	96.0-88.0
Miconazole	3.0	5.1	1.70	1.67-1.74	8.9	2.26	2.21-2.31	8.4	1.60	1.53-1.68	2.6	98.0	0.79-0.94	3.5	1.16	1.10-1.22
. Fluconazole	4.0	5.4	1.35	1.33-1.38	2.4	0.62	0.60-0.64	1.4	0.35	0.32-0.38	2.8	0.70	0.65-0.76	3.2	0.81	0.77-0.85
Sulfamethoxazole & Trimethoprim	4.5	4.3	0.95	0.93-0.97	2.9	0.65	0.63-0.67	1.8	0.40	0.37-0.43	3.5	0.77	0.71-0.83	3.1	69.0	0.66-0.72
Amoxicillin & Clavulanate	5.1	3.5	0.68	0.67-0.70	2.0	0.39	0.38-0.41	1.5	0.30	0.28-0.33	3.7	0.71	0.66-0.77	3.3	0.64	0.61-0.67
Ampicillin	3.4	4.1	1.21	1.18-1.24	4.6	1.36	0.32-1.39	2.8	0.83	0.78-0.88	1.4	0.42	0.38-0.47	3.0	0.88	0.84-0.93

Obstet Gynecol. Author manuscript; available in PMC 2016 September 01.

**Author Manuscript** 

Table 4

The 10 most commonly dispensed category D and X medications, excluding fertility treatments, during pregnancy, overall prevalence, and stratified by pregnancy period.

N=1,106,757 for each column.

Medication	During Pregnancy %	3 Months Prepregnancy %	1st Trimester %	2nd Trimester %	3rd Trimester %
Category D Medications					
* Codeine	11.9	4.5	3.9	5.0	5.3
* Hydrocodone	10.2	8.2	5.3	4.0	3.8
$\operatorname{Ibuprofen}^{ au}$	4.9	8.5	3.6	1.1	0.63
* Sulfamethoxazole	4.0	3.4	1.9	1.3	1.0
* Hydrocortisone	4.0	1.3	1.2	1.4	1.8
* Triamcinolone	3.3	1.3	1.2	1.2	1.4
* Propoxyphene	2.8	2.1	1.1	1.0	1.1
* Sertraline	2.2	1.4	1.1	1.1	1.1
$Oxycodone^{\dagger}$	2.2	1.9	1.0	0.79	0.90
* Prednisone	1.9	1.3	0.85	0.73	0.67
Category X Medications					
Hormonal Contraceptives	4.9	13.5	4.7	0.37	0.15
Temazepam	0.11	0.10	90.0	0.02	0.04
Atorvastatin	0.07	0.10	90.0	0.02	0.01
Warfarin <sup>‡</sup>	0.04	0.00	0.04	0.01	0.01
Simvastatin	0.04	0.05	0.04	0.01	0
Estrogens	0.02	90.0	0.02	0.01	0.01
Tazarotene	0.02	0.04	0.02	0.01	0
Misoprostol	0.02	90.0	0.02	0	0
Flurazepam	0.02	0.02	0.01	0	0.01
Lovastatin	0.02	0.02	0.02	0	0

 $<sup>^{\</sup>ast}$  Medications are also classified as Category C depending on circumstances of use.

 $\mathring{}^{\uparrow}$  Medications are also classified as Category B depending on circumstances of use.

Obstet Gynecol. Author manuscript; available in PMC 2016 September 01.