Published in final edited form as:
Am J Obstet Gynecol. 2011 July ; 205(1): 51.e1–51.e8. doi:10.1016/j.ajog.2011.02.029.

Medication Use During Pregnancy, With Particular Focus On Prescription Drugs: 1976-2008

Allen A. Mitchell, M.D.[a], **Suzanne M. Gilboa, Ph.D**[b], **Martha M. Werler, Sc.D.**[a], **Katherine E. Kelley, MPH, RPh.**[a], **Carol Louik, Sc.D.**[a], **Sonia Hernández-Díaz, M.D., Dr.P.H.**[c], and **the National Birth Defects Prevention Study**

[a]Slone Epidemiology Center at Boston University, Boston, MA

[b]National Center on Birth Defects and Developmental Disabilities, Centers for Disease Control and Prevention, Atlanta, GA

[c]Department of Epidemiology, Harvard School of Public Health, Boston, MA

Abstract

Objective—To provide information on overall medication use throughout pregnancy, with particular focus on the first trimester and specific prescription medications.

Study Design—The Slone Epidemiology Center Birth Defects Study (BDS), 1976 to 2008, and the National Birth Defects Prevention Study (NBDPS), 1997 to 2003, which together interviewed over 30,000 women about their antenatal medication use.

Results—Over the last three decades, first trimester use of prescription medication increased by over 60%, and use of four or more medications more than tripled. By 2008, approximately 50% of women reported taking at least 1 medication. Use of some specific medications markedly decreased or increased. Prescription medication use increased with maternal age and education, was highest for non-Hispanic whites, and varied by state.

Conclusion—These data reflect the widespread and growing use of medications by pregnant women and reinforce the need to study their respective fetal risks and safety.

Keywords

Medications; OTC Medications; Pregnancy; Prescription Medications; Epidemiology

Introduction

Concern about medication use among pregnant women must focus not only on the intended subject, the pregnant woman, but also on the unintended subject, the fetus, who is placed at potential risk for a wide range of adverse effects. While a number of antenatal medication exposures are known to cause birth defects, there is insufficient information on the risks and safety for the vast majority of medications, whether they are obtained by prescription or over-the-counter (OTC). As a result, pregnant women may unknowingly take a medication that poses risk to their fetus; on the other hand, anxiety about the potential teratogenic effects of medications may discourage women from adhering to beneficial treatments.

Prior studies of medication use in pregnancy[1-4] have typically focused on drug classes (e.g., antibiotics); however, potential fetal effects may differ among medications within a given

Corresponding author: Allen A. Mitchell, M.D., Slone Epidemiology Center at Boston University, 1010 Commonwealth Avenue, Boston, MA 02215; office 617 734 6006; fax 617 738 5119; home 781 237 4485; allenmit@bu.edu.

class,[5] and analyses by class may fail to detect effects limited to one or a few class members. Studies based on electronic claims or medical records[6-7] are subject to considerable exposure misclassification since prescription records may not reflect actual use. To define research priorities, we need to understand patterns and factors associated with actual use of the wide range of specific medications that are taken during pregnancy, and particularly during the first trimester, which includes the period of organogenesis, when concerns about teratogenic effects are greatest. It is also critical to identify the prevalence of exposure to both prescription and OTC medications and how use of medications changes over time.

Despite the importance prescription and OTC medications, there are surprisingly little data available. We have previously described exposures exclusively to OTC medications[8] and to herbal products,[9-10] as identified through two U.S. multicenter case-control studies: the Centers for Disease Control and Prevention's (CDC) National Birth Defects Prevention Study (NBDPS) and the Slone Epidemiology Center Birth Defects Study (BDS). To provide additional critical information, we have used these same studies to identify total exposures to any medication (OTC or prescription), as well as focus particular attention on exposures to prescription medications, both overall and by specific agents. Taking advantage of the 33-year period covered by the BDS and the population-based nature of the NBDPS, we used the former to identify secular patterns and the latter to identify selected demographic characteristics.

Materials and Methods

BDS

Since 1976, the Boston University Slone Epidemiology Center BDS has interviewed mothers of infants with any major (i.e., medically-important) structural birth defects recruited from birth and tertiary care hospitals in a number of regional study centers (Boston, Philadelphia, Toronto, Iowa, and San Diego), as well as through birth defects registries in Massachusetts and New York State. Beginning in 1993, a sample of mothers of infants without birth defects has also been included from each center or registry. Subjects are identified within 5 months after delivery and mothers are interviewed within 6 months after delivery by trained nurses; interviews were conducted face-to-face (typically in the subject's home) until mid-1998 and by telephone thereafter. Spanish interviews were introduced in 2001. Pregnancy is defined as beginning with the last menstrual period (LMP), based on reported due date minus 280 days. Standardized questions are asked about various maternal factors, with emphasis on medication use for the period beginning 2 months before the LMP to the end of the pregnancy. Detailed information on medications is obtained via a series of questions.[11] Women are asked about illnesses they experienced and medications used in their treatment; medications taken for specified illnesses (e.g., infections, seizures, diabetes), categories of medications (e.g., antibiotics), and whether they took any agent from a list of specifically-named medications. Both brand-name and generic products are recorded. For medications reported to have been taken, women are asked to retrieve the bottle or package if available. In 1999, a booklet containing pictures of a wide range of OTC medications was introduced to assist in identification.[8] The BDS has been approved by the relevant institutional review boards.

To take advantage of the 33 years' data available in the BDS, and because the study did not always include control infants born without birth defects, this analysis included exposures independent of case-control status. Of note, though some increased risks associated with a particular drug and specific birth defect are included within these data, combining cases and controls does not have an appreciable impact on overall patterns of use—as reflected in the Results, below. Further, the analysis was limited to the Boston and Philadelphia centers, since only those centers participated throughout the study period. The study population thus

includes 25,313 mothers with LMP dates between 1976 and 2008; 19,297 subjects had infants born with birth defects and 6,016 had infants born without birth defects. Participation rates have varied over the 33-year study period, ranging from approximately 70 to 80%.

NBDPS

The NBDPS was initiated in 1997 and is an ongoing, population-based case-control study comprising data collected by 10 birth defects surveillance systems throughout the United States (Arkansas, California, Georgia/CDC, Iowa, Massachusetts, New Jersey (through 2002), New York, Texas, and beginning in 2003, North Carolina and Utah. The catchment areas for California, Massachusetts and New York do not overlap between the BDS and NBDPS. Case subjects in the study have at least one of over 30 eligible structural birth defects and include live births, stillbirths, and elective terminations. Control infants are live births without birth defects that are either randomly selected from birth certificates or selected from birth hospitals by using a stratified, random sampling scheme.[12] Each of the 10 study centers enrolls approximately 300 eligible case infants and approximately 100 control infants per year.[13]

Mothers are interviewed by telephone in English or Spanish using a computer-based questionnaire 6 weeks to 24 months after the estimated date of delivery. In addition to information on various maternal factors and behaviors, interviewers ask the women to report medications (prescribed or OTC), vitamins, or supplements taken for selected indications, read them a list of specific medications, and ask them to report other products used from three months before conception through the end of their pregnancy. Pregnancy is defined as beginning two weeks after the LMP. Estimated dates of use and the frequency and duration of use are recorded. The NBDPS has been approved by the institutional review boards of CDC and the participating study centers. Taking advantage of the population-based design in 10 study sites, the NBDPS analyses include only mothers of control subjects (n=5,008) with estimated delivery dates between October 1, 1997 and December 31, 2003.

Medication Exposures

In both data sets, a medication was defined as a single product containing one or more active ingredients (e.g., amoxicillin was considered as one medication, amoxicillin/clavulanate was considered as another). Different salts of the same active ingredient were considered to be the same medication (e.g., all salts of amoxicillin were considered as “amoxicillin”). We excluded vitamins/minerals, blood, oxygen, as well as medications administered topically (except vaginally) or intravenously. Where a respondent reported taking a medication within a class (e.g., an “antibiotic”) but could not identify the specific agent, the exposure was recorded as “NOS” (not otherwise specified) — e.g., “antibiotic NOS”. In such instances, we assigned prescription or OTC status based on the category into which most medications in that class fell (for example, “antibiotics NOS” were considered prescription medications, whereas “pain relievers NOS” were considered OTC). A number of medications were switched from prescription-only to OTC availability (primarily during BDS years). For those switched medications used commonly, we added 3 months to the switch approval date (to account for their distribution to patients) and considered the medications to be a prescription or OTC exposure according to whether the subject reported using the medication before or after that latter date, respectively.

Results

All Medications (OTC and Prescription Medications Combined)

For the 33-year BDS study, Figure 1 presents secular patterns of use of any medication at any time during pregnancy as well as any medication taken in the first trimester. Overall, the

average number used anytime in pregnancy increased by 68%, from 2.5 in 1976-1978 to 4.2 in 2006-2008 (range, 0-28); in the last years, 93.9% took at least one medication. During the first trimester, the average number of medications increased during those same years by 62.5%, from 1.6 to 2.6 (range, 0-25); 82.3% of women in the last years used at least one medication. Comparing study mothers who had malformed or non-malformed offspring, we found no appreciable differences in the average numbers of medications either over the entire period of study or by specific year (data not shown). Use of 4 or more medications also increased (Figure 1): For anytime in pregnancy, the proportion of women taking 4+ medications more than doubled, from 23.3% to 50.1%, between the earliest and latest years of the study. For use in the first trimester, proportions reporting 4+ medications almost tripled, from 9.9% to 27.6%.

In the NBDPS, between 1997 and 2003, the 5008 women took an average of 2.6 medications at anytime in pregnancy (range, 0-15). During the first trimester, they took an average of 1.5 medications (range, 0-14). The prevalence of women taking one or more medications anytime in pregnancy was 88.8%; during the first trimester, it was 70.0%. The average number of medications varied according to state of residence (Figure 2); use of one or more medications anytime in pregnancy and in the first trimester was highest in Arkansas (93.6% and 84.8% respectively), and lowest in California (82.5% and 57.6%, respectively). Use during both exposure periods increased with maternal age and education (Figure 3), and was highest for non-Hispanic whites and lowest for Hispanics.

Prescription Medications

In the BDS, secular patterns of prescription medication use at any time during pregnancy and use during the first trimester (Figure 4) reveal that for both periods, there was a slight decline in the average number of medications in the first 6 years; use then began to increase, such that by 2006-2008, the average number of medications used anytime in pregnancy was 1.8, with 70.0% of women using at least one medication; during the first trimester, the average number was 1.0, with 48.8% using at least one medication. For women using 4+ medications proportions increased 2.6-fold, from 6.1 to 15.7% for anytime in pregnancy (Figure 4), while first trimester use increased 3.3-fold, from 2.3 to 7.5%.

In the NBDPS, between 1997 and 2003, 49.4% of subjects reported use of at least one prescription medication during pregnancy; they took an average of 0.9 prescription medications at anytime in pregnancy (range, 0-14); 4.9% took 4+. During the first trimester, the women took an average of 0.5 medications (range, 0-12); 28.9% took at least one and 2.2% took 4+ medications.

The average number of prescription medications used varied according to state of residence (Figure 5). Use of 1+ medications, both for anytime in pregnancy and first trimester, was highest in Arkansas (59.3% and 39.3%, respectively). Utah had the lowest use for anytime in pregnancy (38.8%) and for the first trimester, three states --California, Utah, and Texas—had the lowest (24- 25%). The average numbers of medications increased steadily with age (Figure 6); for anytime in pregnancy, it increased from an average of 0.6 to 1.1 from the youngest to oldest women, and for the first trimester, the equivalent frequencies increased from 0.3 to 0.7. Similar trends were observed for education, with the highest rates observed among the most educated subjects. For race/ethnicity, use was highest among non-Hispanic whites, lowest among Hispanics, and intermediate among non-Hispanic blacks.

For BDS data, first trimester use of the 20 most common specific prescription medications is presented according to five time periods (Table 1). (“NOS” medications, such as “NOS antibiotic”, include exposures to specific, albeit unidentifiable, antibiotics, so the data presented for specifically-named antibiotics reflect minimal estimates of their actual use).

Some medications, such as levothyroxine, progesterone, and ampicillin/amoxicillin, have been used commonly throughout the 33-year study period. Others reflect secular decreases or increases that are often substantial. Besides changes in prescribing preferences, decreases may be due to withdrawal from the market (e.g, doxylamine/B6--Bendectin), or switches to OTC status (e.g., loratadine [Claritin]). Conversely, increases may be due to the introduction of new medications that came into widespread use (e.g. selected antinausea medications and antidepressants, detailed below). (The high rate of influenza vaccine in the BDS likely reflects the 2004 recommendation that pregnant women receive seasonal influenza vaccine and the addition to the questionnaire, in 2006, of detailed questions about exposure to vaccines).

Examples of secular changes in first trimester use of specific medications (Figures 7a, b) include the antinausea medication doxylamine/vitamin B6 (Bendectin) the most common prescription medication taken in the earliest study years; following its market withdrawal 1983, various alternatives were infrequently used More recently, antinauseant use has increased, with almost 3% using odansetron between 2003 and 2008. Antidepressant use has increased most dramatically, with <1% of women exposed to any antidepressant through 1988-90, followed by marked increases, reaching a peak of 7.5% in the most recent period. Further, use of specific antidepressants varied markedly over time, with fluoxetine and paroxetine increasing until 2000-2002 and 2003-2005, respectively, and then decreasing, whereas sertraline has become the most commonly used antidepressant, peaking in the last study years at over 2%.

The top 20 prescription medications reported between 1997 and 2003 in the NBDPS are presented in Table 2; despite the different regions covered by the two studies, the medications and rankings for NBDPS are roughly comparable to those identified for the contemporaneous period in the BDS.

Comment

The U.S. Collaborative Perinatal Project described specific prescription and OTC medication use in over 50,000 women drawn from 12 study centers.[15] However, those data, collected between 1957 and 1963, have limited relevance to current patterns. More recent data have been subject to important limitations. Two studies conducted in the 1980s were small and focused on geographically-limited populations over periods of only two[2] or six years.[3] Much larger data sets, drawn from electronic health maintenance organization or insurance claims data[6,7] have the strength of representing broader populations and time periods, but for prescription medications they are limited to medications ordered or filled and do not systematically capture OTC medications.

Concern about prescriptions written or filled but not taken is not trivial, and the large problem of non-adherence has been the subject of increasing attention. A recent review of electronic prescription records in Massachusetts among over 75,000 patients[15] found that, among the almost 196,000 prescriptions written, 28% were not filled. These findings, of course, do not take into account additional non-adherence among women who filled prescriptions but did not take them at all or did not follow the intended course. In these data sets, such misclassification would lead to substantial overestimates of actual exposures.

At the same time, claims data and medical records may substantially underestimate exposures. Recently researchers[16] found that about 25% of 700 adult subjects reported borrowing or sharing prescription medications. Earlier studies documented this same phenomenon among pregnant women or women of childbearing age. We[11, 17] reported that significant numbers of these women obtained prescription medications from friends, neighbors, and relatives (e.g., these sources accounted for 18% of exposures to Valium

(diazepam) and 22% of exposures to Darvon (propoxyphene). Others reported that 20.1% of teenage girls borrowed or shared prescription medications,[18] and in nationally-representative U.S. data, 36.5% of women of reproductive age acknowledged ever borrowing or sharing prescription medications.[19]

Recall of medications taken may be inaccurate or biased. For example, medications we reported as "NOS" (e.g., antibiotic NOS) reflects an exposure, but the study subject was unable to recall the specific medication taken. Thus, in studying the risks of a specific medication in that class (e.g., amoxicillin), one would have to consider that some exposures to amoxicillin are misclassified within "NOS antibiotic". To maximize recall accuracy and completeness, both the BDS and NBDPS use various prompts, trained interviewers, and increasing specificity of questioning; given its primary focus on medications, the BDS uses additional approaches (e.g., a booklet with photographs of various OTC medications). While we cannot claim to have captured every exposure for every subject, absent a gold standard for documenting exposure, we believe that carefully constructed and systematic questionnaires administered by trained interviewers elicit relatively accurate information on actual exposures and their duration, and that the "direct-to-consumer" approach used by both studies provides the most valid estimates of medication exposure during pregnancy.

These data demonstrate that overall (OTC and prescription) medication use during pregnancy has increased over the past three decades, and that the large majority of pregnant women take at least one medication; of particular note, the proportions of women taking 4+ medications has more than doubled for use anytime in pregnancy and nearly tripled for use in the first trimester. Though less common than OTC use, prescription medication use has also increased over the past three decades; the proportion taking at least one medication has increased, peaking in the last study years (despite that a number of commonly used prescription medications switched to OTC during the study period). As was the case for medication use overall, proportions of women using 4+ prescription medications anytime in pregnancy more than doubled and for the first trimester it more than tripled.

Using population-based data, we have also documented that patterns of medication use vary considerably by demographic variables such as socioeconomic status, maternal age, race/ethnicity, and state of residence. These variations likely explain the different proportions in the two studies who reported taking at least one medication.

These data identify prescription medications that are currently most commonly used, and therefore urgently require research on their risks and safety; they also reinforce the need for ongoing surveillance regarding medication use in pregnancy and its consequences. Such research will benefit women who are or might become pregnant, their health care providers who must know the relative risks and benefits of particular medications, and society at large, since common use of a medication that proves teratogenic has appreciable consequences.

Acknowledgments

The authors wish to thank Dr. Margaret Honein for her support and guidance.

Support: This work was supported by Cooperative Agreement no. U50/CCU113247 with the Centers for Disease Control and Prevention through the Massachusetts Department of Public Health, Cooperative agreements under program announcement No. 02081 from the Centers for Disease Control and Prevention to the centers participating in the National Birth Defects Prevention Study, and Grant RO1 HD 046595 from the Eunice Kennedy Shriver National Institute of Child Health and Human Development. The findings and conclusions of this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

References

1. Bluitendijk S, Bracken MB. Medication in early pregnancy: Prevalence of use and relationship to maternal characteristics. Am J Obstet Gynecol. 1991; 165:33–40. [PubMed: 1853911]
2. Rubin JD, Ferencz C, Loffredo C, the Baltimore-Washington Infant Study Group. Use of prescription and non-prescription drugs in pregnancy. Clin Epidemiol. 1993; 46:581–9.
3. Egen-Lappe V, Hasford J. Drug prescription in pregnancy: analysis of a large statutory sickness fund population. Eur J Clin Pharamacol. 2004; 60:659–66.
4. Henry A, Crowther C. Patterns of medication use during and prior to pregnancy: The MAP study. Aust NZ J Obstet Gynecol. 2000; 40:165–72.
5. Mitchell, AA. Studies of Drug-Induced Birth Defects. In: Strom, BL., editor. Pharmacoepidemiology. 4th. John Wiley & Sons; NY: 2005.
6. Andrade SE, Gurwitz JH, Davis RL, et al. Prescription drug use in pregnancy. Am J Obstet Gynecol. 2004; 191:398–407. [PubMed: 15343213]
7. Colvin L, Slack-Smith L, Stanley FJ, Bower C. Pharmacovigilance in pregnancy using population-based linked datasets. Pharamcoepi Drug Safety. 2009; 18:211–225.
8. Werler MM, Mitchell AA, Hernandez-Diaz S, Honein MA, the National Birth Defects Prevention Study. Use of over-the-counter medications in pregnancy. Am J Obstet Gynecol. 2005; 193:771–7. [PubMed: 16150273]
9. Broussard CS, Louik C, Honein MA, Mitchell AA, the National Birth Defects Prevention Study. Herbal use before and during pregnancy. Am J Obstet Gynecol. 2010; 202:443, e1–6. [PubMed: 20035911]
10. Louik C, Gardiner P, Kelley K, Mitchell AA. Use of herbal treatments in pregnancy. Am J Obstet Gynecol. 2010; 202:439, e1–10. [PubMed: 20452484]
11. Mitchell AA, Cottler LB, Shapiro S. Effect of questionnaire design on recall of drug exposure in pregnancy. Am J Epidemiol. 1986; 123:670–6. [PubMed: 3953545]
12. Cogswell ME, Bitsko RH, Anderka M, et al. Control selection and participation in an ongoing, population-based, case-control study of birth defects: the National Birth Defects Prevention Study. Am J Epidemiol. 2009; 170:975–85. [PubMed: 19736223]
13. Yoon PW, Rasmussen SA, Lynberg MC, Moore CA, Anderka M, Carmichael SL, et al. The National Birth Defects Prevention Study. Public Health Rep. 2001; 116(suppl):32–40. [PubMed: 11889273]
14. Heinonen, OP.; Slone, D.; Shapiro, S. Birth Defects and Drugs in Pregnancy. Publishing Sciences Group; Littleton, MA: 1977.
15. Fischer MA, Stedman MR, Lii J, et al. Primary medication non-adherence: Analysis of 195,930 electronic prescriptions. J Gen Intern Med. 2010; 25:284–90. [PubMed: 20131023]
16. Goldsworthy RC, Schwartz NC, Mayhorn CB. Beyond abuse and exposure: Framing the impact of prescription-medication sharing. Am J Publ Health. 2008; 98:1115–21.
17. Mitchell AA. Prescription medication sharing (letter-to-the-editor). Am J Publ Health. 2008; 98:1926.
18. Daniel KL, Honein MA, Moore CA. Sharing prescription medication among teenage girls: Potential danger to unplanned/undiagnosed pregnancies. Pediatrics. 2003; 111:1167–70. [PubMed: 12728132]
19. Petersen EE, Rasmussen SA, Daniel KL, Yazdy MM, Honein MA. Prescription medication borrowing and sharing among women of reproductive age. J Womens Health (Larchmt). 2008 Sep. 17:1073–80. [PubMed: 18774892]

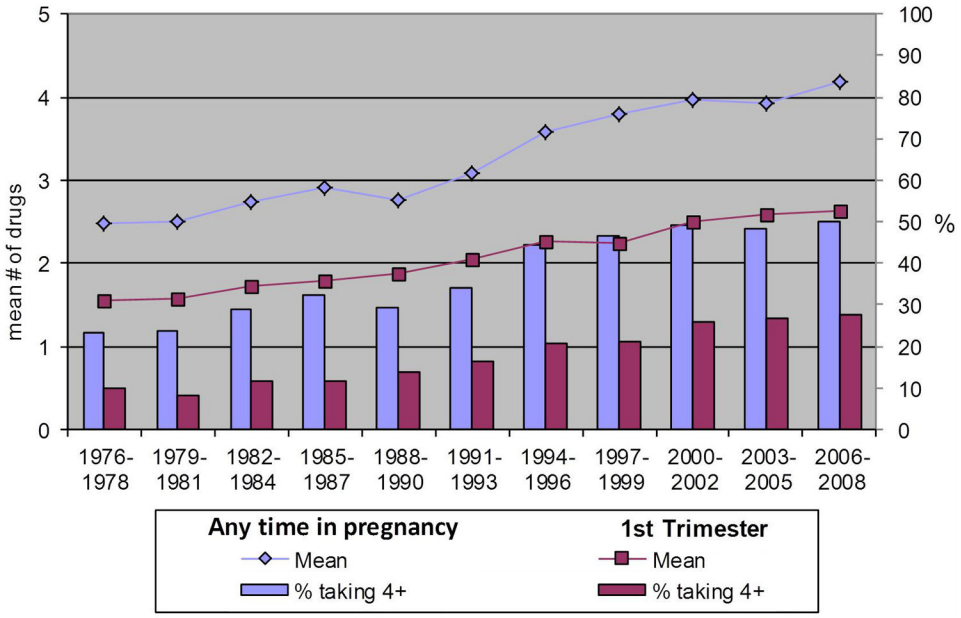

Figure 1.

BDS, 1976-2008, Boston and Philadelphia centers. Secular patterns of use of any medication at any time during pregnancy and restricted to the first trimester. Average number of medications and proportion of women taking 4 or more medications (n=25,313).

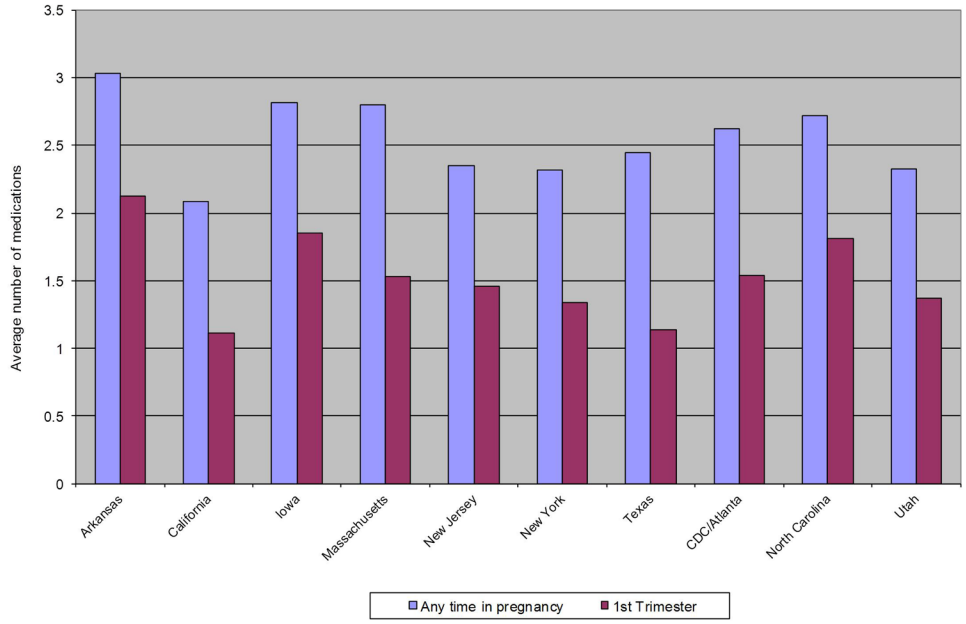

Figure 2.
NBDPS, 1997-2003. Average number of any medications taken during pregnancy and first trimester, by center (n=5008).

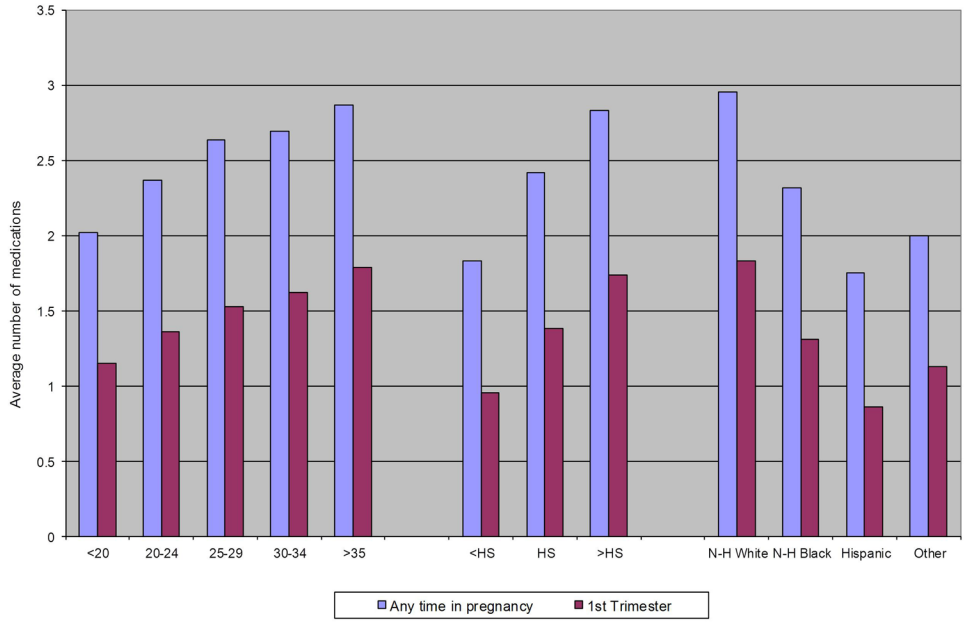

Figure 3.

NBDPS, 1997-2003. Average number of any medications taken during pregnancy and first trimester, by age, race-ethnicity, and education (n=5008).

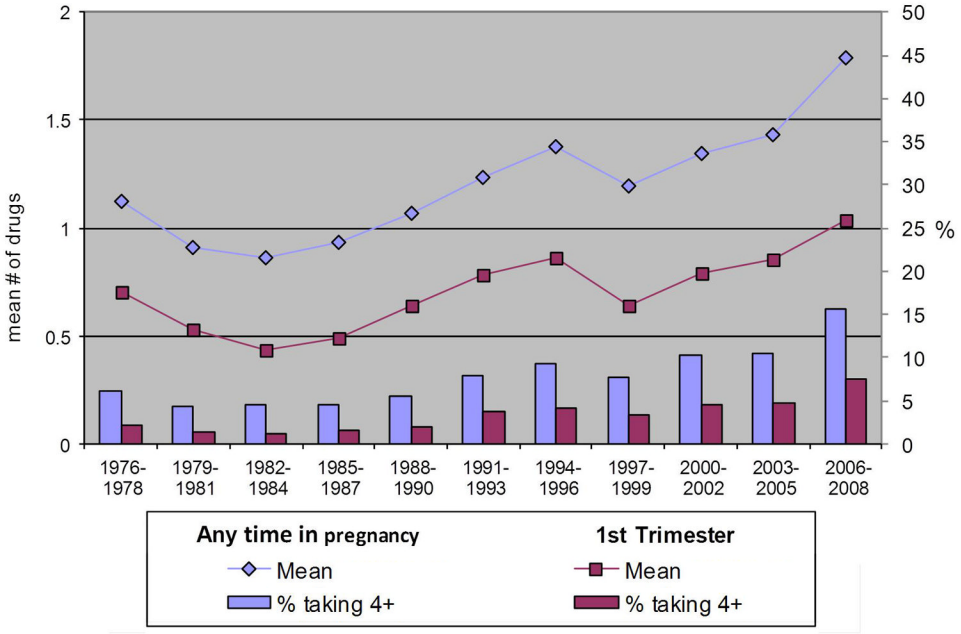

Figure 4.

BDS, 1976-2008, Boston and Philadelphia centers. Secular patterns of use of prescription medications at any time during pregnancy and restricted to the first trimester. Average number of medications and proportion of women taking 4 or more medications (n=25313).

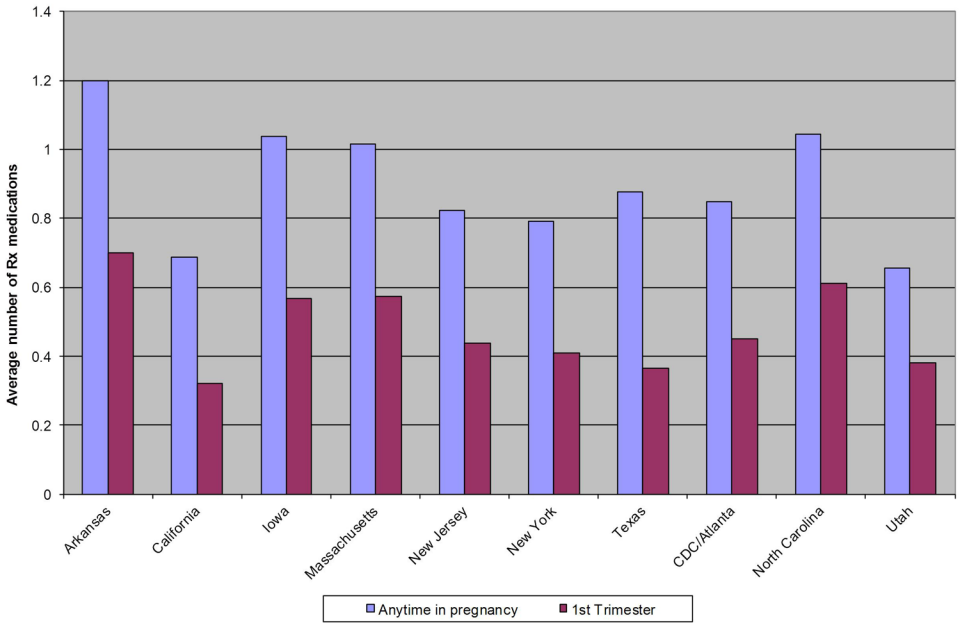

Figure 5.
NBDPS, 1997-2003, average number of prescription medications taken during pregnancy and first trimester by center (n=5008).

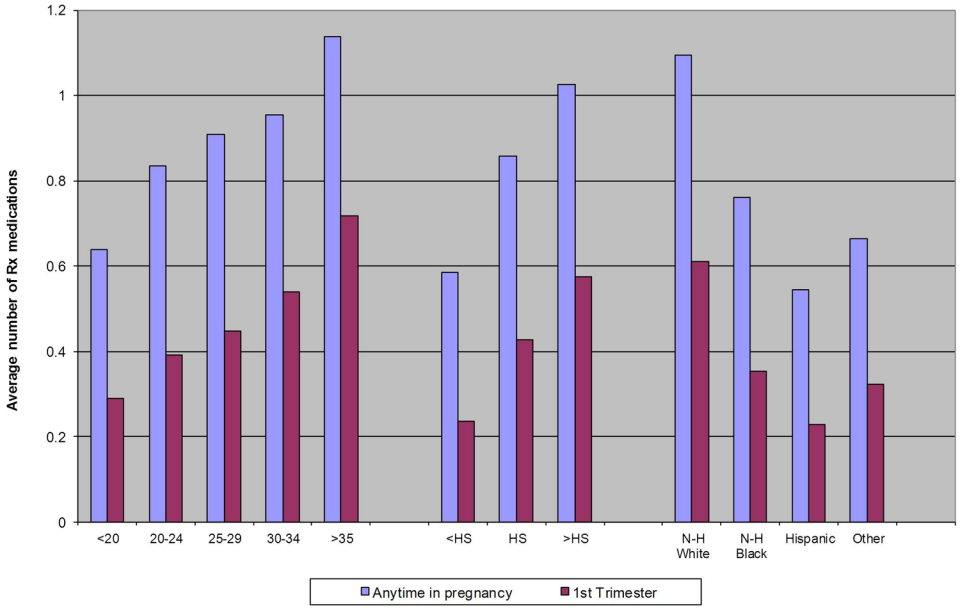

Figure 6.
NBDPS, 1997-2003. Average number of prescription medications taken during pregnancy and first trimester, by age, race-ethnicity, and education (n=5008).

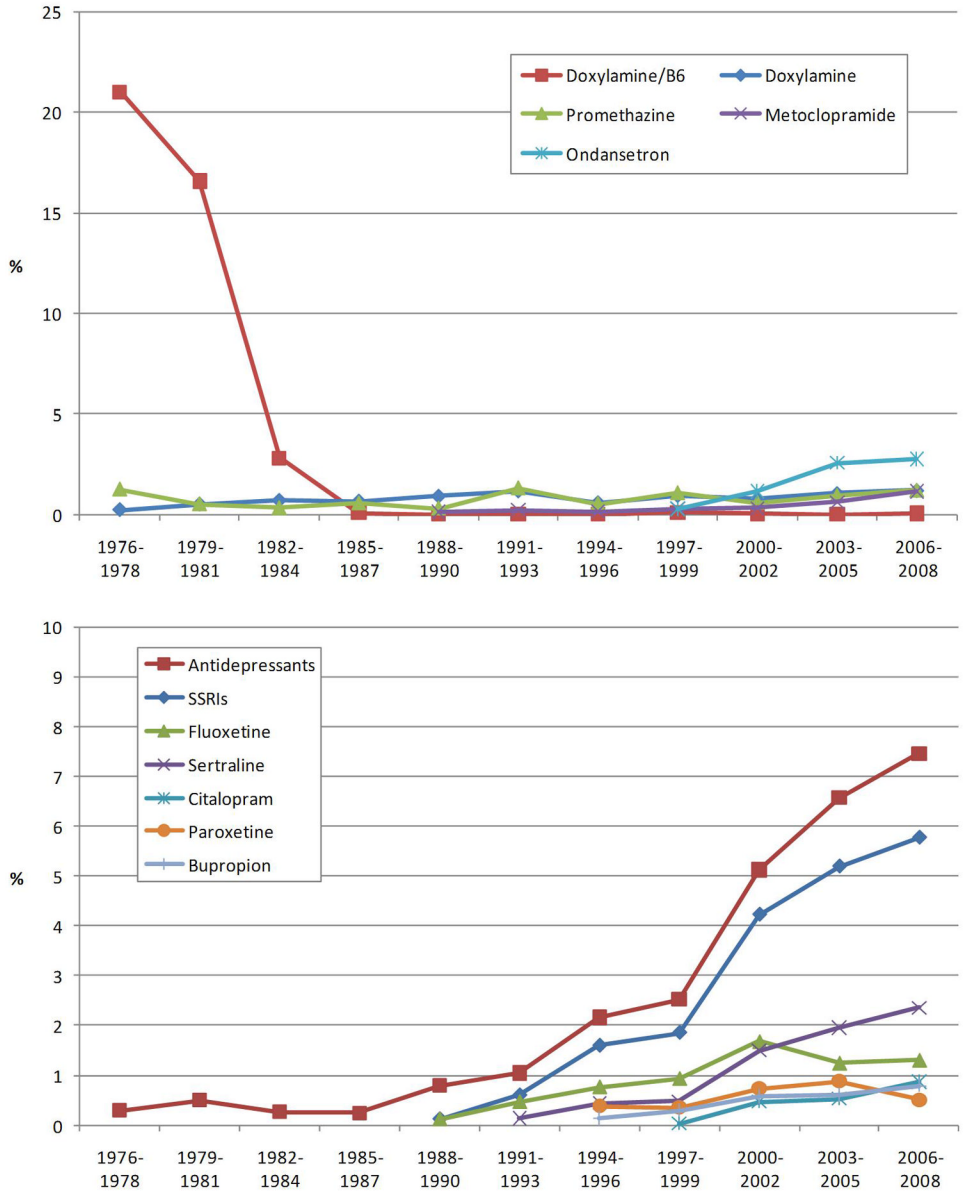

Figure 7.

BDS, 1976-2008, Boston and Philadelphia centers. Secular patterns of selected antinausea medications (A) and antidepressants (B) during the first trimester. Proportion of women exposed (n=25,313).

Table 1

Use of the 20 most common specific prescription medications in first trimester, the Slone Epidemiology Center Birth Defects Study (BDS), Boston and Philadelphia centers 1976-2008.

1976-1984		1985-1993		1994-1998		1999-2003		2004-2008	
N = 6,021	**%**	**N = 4,986**	**%**	**N = 3,289**	**%**	**N = 6,698**	**%**	**N = 4,319**	**%**
Doxylamine/vitamin B6	10.6	Progesterone	3.15	NOS- Antibiotic	5.38	NOS- Antibiotic	5.82	NOS- Influenza vaccine	6.07
Penicillin	1.91	NOS- Antibiotic	2.59	Progesterone	4.26	Albuterol	4.66	NOS- Antibiotic	5.35
NOS- Antibiotic	1.69	Clomiphene	1.89	Amoxicillin	3.98	Progesterone	3.51	Albuterol	4.86
Diazepam	1.53	Albuterol	1.85	Albuterol	3.62	Levothyroxine	3.33	Progesterone	4.51
Ampicillin	1.51	Erythromycin	1.81	Levothyroxine	2.49	Amoxicllin	2.87	Levothyroxine	3.75
Acetaminophen w/codeine	1.41	Levothyroxine	1.56	Procaine	1.82	Loratadine	1.91	Ondansetron	2.78
Clomiphene	1.41	Amoxicillin	1.52	Gonadotropin chorionic	1.55	Fluticasone	1.64	Amoxicillin	2.59
Erythromycin	1.08	Penicillin	1.42	Beclomethasone	1.34	Fexofenadine	1.43	Sertraline	2.22
Levothyroxine	1.00	Acetaminophen w/codeine	1.10	Clomiphene	1.28	Clomiphene	1.40	Azithromycin	1.97
Prochlorperazine	0.85	Ampicillin	1.06	Urofollitropin	1.25	Fluoxetine	1.39	Fluticasone	1.41
Tetracycline	0.76	Gonadotropin chorionic	1.04	Erythromycin	1.22	Sertraline	1.27	Fluoxetine	1.37
Progesterone	0.61	Terfenadine	1.02	NOS- Oral contraceptive	1.09	Ondansetron	1.10	Cetirizine	1.25
Phenytoin	0.58	Theophylline	0.92	Leuprolide	1.00	Cetirizine	1.02	Leuprolide	1.23
Theophylline	0.50	Follicle stimulating/leutinizing hormone	0.76	Loratadine	1.00	Azithromycin	0.99	Salmeterol/fluticasone	1.20
Trimthobenzamide	0.48	Prochlorperazine	0.64	Penicillin	0.94	Follitropin alpha	0.96	Follitropin alpha	1.18
Propoxyphene	0.48	Promethazine	0.62	Follicle stimulating/leutinizing hormone	0.88	Leuprolide	0.96	Metformin	1.11
Hydrochlorothiazide	0.45	Beclomethasone	0.60	Fluoxetine	0.85	Gonadotropin chorionic	0.94	Promethazine	1.09
Prednisone	0.45	Prednisone	0.60	Acetaminophen w/codeine	0.85	Loratadine/Pseudoephedrine	0.90	Nitrofurantoin	1.09

1976-1984		1985-1993		1994-1998		1999-2003		2004-2008	
N = 6,021	**%**	**N = 4,986**	**%**	**N = 3,289**	**%**	**N = 6,698**	**%**	**N = 4,319**	**%**
Phenobarbital	0.43	NOS- Oral contraceptive	0.58	Terfenadine	0.82	Ortho tricyclen	0.91	Escitalopram	1.04
Medroxyprogestrone	0.42	Cephalexin	0.54	Promethazine	0.79	Acetaminophen w/codeine	0.82	Follitropin beta	1.04

Table 2

Use of the 20 most common specific prescription medications in first trimester, National Birth Defects Prevention Study (NBDPS), 1997-2003.

N = 5,008	**%**
Amoxicillin	3.85
NOS- Antibiotic	2.74
Progesterone	2.44
Promethazine	2.26
Albuterol	2.24
Clomiphene	1.28
Loratadine	1.16
Levothryroxine	1.10
Gonadotropin chorionic	1.00
Azithromycin	0.90
Leuprolide	0.80
Nitrofurantoin	0.80
Sertraline	0.74
Sulfamethoxazole-trimethoprim	0.66
Fluoxetine	0.64
Penicillin	0.64
Fluticasone	0.60
Acetaminophen w/codeine	0.52
Cephalexin	0.52
Fexofenadine	0.52