

Use of Antidepressant Medication in the United States During Pregnancy, 2002–2010

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Objective: The authors analyzed prescribing for antidepressant medications during 27,328 prenatal visits in ambulatory settings in the United States between 2002 and 2010. **Methods:** Data from the 2002–2010 National Ambulatory Medical Care Survey and National Hospital Ambulatory Medical Care Survey were used to compare prescribing for antidepressant medication during visits for outpatient prenatal care between 2002–2006 and 2007–2010. **Results:** Prenatal visits associated with a prescription for an antidepressant increased from .7% in 2002–2006 to 2.1% in 2007–2010 ($p<.01$). The proportion of prescriptions for selective serotonin reuptake inhibitors (SSRIs) declined (from 87% to 66%, $p=.04$), particularly for paroxetine (from 19% to <1%, $p<.01$). **Conclusions:** Despite controversy over possible negative effects, prescribing of antidepressants during pregnancy increased between 2002 and 2010. SSRIs represented a smaller proportion of all antidepressants prescribed, and prescribing of paroxetine, likely in response to

warnings by the U.S. Food and Drug Administration, dropped dramatically. (*Psychiatric Services* 64:1157–1160, 2013; doi: 10.1176/appi.ps.201200455)

The identification and treatment of depression during pregnancy have gained clinical attention over the past decade. Epidemiologic studies have shown that depression is common among pregnant women, with an estimated 18% experiencing a depressive disorder of some kind (1). Between 8% and 13% of women in the United States experience a major depressive episode during pregnancy (1–3).

When depression occurs in pregnancy, it is associated not only with high rates of maternal disability but also with adverse perinatal outcomes, including babies who have low birth weight or are small for gestational age, intrauterine growth restriction, and preterm delivery (4,5). Over the last decade, as the negative outcomes associated with perinatal depression have become apparent, prenatal care providers have become increasingly aware of the widespread nature and significance of depression among pregnant women. Responding to calls to improve identification and treatment of depression in the course of obstetric care, clinicians have shown increasing willingness to address this mental health concern (6,7).

The increased interest in the delivery of depression care in pregnancy has competed, however, with

concerns among clinicians and the public over fetal exposure to antidepressant medications. Although these medications are efficacious for pregnant women, some well-publicized studies suggested that the medications themselves might be associated with adverse neonatal outcomes (4,8). The total data available regarding the risk of using antidepressants during pregnancy are mixed, given that multiple high-quality studies have failed to identify an association of poor maternal or infant outcomes with use of antidepressant medication and could not rule out the effects of confounding factors, such as depression itself, concurrent use of other prescription medications, and associated poor health habits (4). On the basis of the totality of evidence, consensus guidelines have consistently supported the use of medication for treatment of depression in pregnancy, with the caveat that this approach should be individualized and should ensure patient understanding of the risks and benefits of the treatment (4,9).

Despite the interest in the use of antidepressant medication during pregnancy and the conflicting forces influencing its use, there has been relatively little description of the rates of use over the prenatal period and whether they have changed over time. The few existing studies were limited by the use of samples that were not representative of the United States as a whole (10–12). We wished to estimate national rates of antidepressant prescribing in pregnancy and determine if these rates have changed over the last decade.

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Methods

Data for this study were compiled from the 2002–2010 National Ambulatory Medical Care Survey (NAMCS) and National Hospital Ambulatory Medical Care Survey (NHAMCS) (13). These surveys are administered by the National Center for Health Statistics (NCHS) for the Centers for Disease Control and Prevention. The NCHS Institutional Review Board approved the protocol for its use of the NAMCS and the NHAMCS.

Women receiving prenatal care served as the study sample. Data from outpatient prenatal visits occurring between 2002 and 2010 were analyzed. Up to three diagnoses are recorded as free text for each visit surveyed and are coded by using the *International Classification of Diseases, Clinical Modification, Ninth Revision (ICD-9-CM)*. Visits with a diagnosis of normal pregnancy (code V22), supervision of high-risk pregnancy (V23), and obstetrical complications (640–673) were designated prenatal visits. Because three-digit *ICD-9-CM* codes can include diagnoses related to labor, postpartum care, or some unspecified aspect of care, we included only visits in which the five-digit *ICD-9-CM* code was used and the fifth digit was three, indicating an antepartum condition.

Only females were included. Patient age, race (white, black, or other), ethnicity (Latino), and insurance status (private, Medicaid, or self-pay or other) are recorded for each visit. Only visits by patients between the ages of 15 and 45 were included, and age was collapsed into three categories (≤ 20 , 21–30, and 31–45 years). Because Medicare patients comprised only 1.2% of our sample population, they were included in the “self-pay or other” insurance category. Whether each visit was for a new or established patient is recorded as well. Whether the visit setting was in a physician’s office or a hospital outpatient clinic is also recorded.

For each visit, the provider’s self-selected specialty (NAMCS) and clinic type (NHAMCS) are recorded. Visits that were attended by a family practitioner, an internist, or a pediatrician or that occurred in a general medical or pediatric clinic were coded as general

medical. Visits that were attended by an obstetrician or that occurred in an obstetric clinic were coded as obstetrics. Outcomes for this study included depression diagnosis and antidepressant prescription. Visits with the following diagnostic codes for depression were included: 296.2, 296.3, 298.0, 300.4, 309.1, and 311. After 2004, the surveys included the question: “Regardless of the diagnoses written (previously) does the patient now have depression?” A positive response was also considered to indicate a depression diagnosis.

Up to eight medications are recorded for each visit. From 2002 to 2005, the surveys identified the medications by using five-digit codes that had been assigned by the U.S. Pharmacopeia to each generic name of every drug entity (13). Beginning with the 2006 data release, the generic components and therapeutic classifications of drugs were coded by the NAMCS with Lexicon Plus, a proprietary database of Cerner Multum, Inc. (14). We identified antidepressant prescriptions by using the National Drug Code directory, generic names, drug names, and the Multum classification. The following medications were considered to be selective serotonin reuptake inhibitors (SSRIs): fluoxetine, sertraline, paroxetine, citalopram, escitalopram, and fluvoxamine.

For a more complete assessment of U.S. ambulatory settings, the NAMCS and NHAMCS data were combined. We used the weights, strata, and primary sampling unit design variables provided by the NCHS. All reported estimates were based on at least 30 unweighted observations and relative standard errors of less than 30%. We evaluated categorical variables with the chi square test. All analyses used survey weights and took into account the complex survey design by using the SVY command provided in Stata, version 11. All *p* values were two-tailed; $p < .05$ was considered significant.

Results

Data from 27,328 prenatal visits occurring between 2002 and 2010 were analyzed (Table 1). A majority of visits were by women 21 or older, with 52.9% by women between 21 and 30 years old and 33.3% by women over

30 years old. Most (76.5%) women were white, and 20.6% had Latino ethnicity. Women with both public and private insurance as well as those without insurance were represented in the study sample. Most visits took place with obstetricians in physicians’ offices. Over the full nine-year analysis, 4.2% of the visits were associated with a depression diagnosis and 1.4% was associated with an antidepressant prescription.

The proportion of visits by women who received a prescription for an antidepressant increased from .7% in 2002–2006 to 2.1% in 2007–2010 ($p < .01$). SSRIs constituted a majority of the antidepressants prescribed, but their proportion of the total decreased significantly from 2002–2006 (87%) to 2007–2010 (66%) ($p = .04$). The percentage of total antidepressant prescriptions for specific medications changed significantly between the two periods, including an increase in prescriptions for sertraline (16% to 35%, $p = .02$) and a decrease in prescriptions for fluoxetine and paroxetine (33% to 10%, $p = .01$, and 19% to $< 1\%$, $p < .01$, respectively). There were no significant changes in prescriptions for citalopram or escitalopram (18% to 22%, $p = .74$). The proportion of antidepressants that were not SSRIs or bupropion increased from 6% to 23% ($p = .01$).

Discussion

In this analysis of a nationally representative sample of women in prenatal care, we found that the rate of antidepressant use increased approximately threefold from 2002 to 2010. The increase occurred despite concerns among the public and clinicians regarding the safety of taking these medications during pregnancy.

Our finding that SSRIs made up a lower proportion of the antidepressant medications used for pregnant women in 2010 than in 2002 is of interest, given that the U.S. Food and Drug Administration (FDA) issued widely publicized warnings regarding specific antidepressants in 2005 and 2006. Although current guidelines allow for the use of all antidepressants in specific circumstances, an FDA warning recommended limiting the use of paroxetine in pregnancy (4). Consistent with the warning, we found that

use of paroxetine greatly decreased during the study period. As reported by previous studies, we found that sertraline was the most commonly prescribed SSRI agent during pregnancy (15). Bupropion, free of any reports of negative outcomes, was the most commonly prescribed non-SSRI medication and made up a greater share of prescriptions for antidepressants in 2007–2010 than in 2002–2006. It has also been promoted as a good choice for mothers who smoke, a health behavior associated with depression symptomatology (4).

This study had a number of limitations that should be considered. The NAMCS and NHAMCS do not examine actual medication use or compliance with prescriptions but rather assess the presence of a prescribed medication recorded by the medical provider. Although that could result in an overestimation of actual medication exposure by the patient and fetus, we believe that it is unlikely that any systematic bias would have changed the relative estimates over the course of the study period. This approach to assessing medication utilization is widely accepted, and the NAMCS is considered to be a gold standard for national estimates of prescribing.

Another limitation was that because only three diagnoses may be listed for each visit reported to NAMCS or NHAMCS, underreporting of depression could occur. However, the primary goal of the study was to identify antidepressant prescribing rather than depression diagnoses. Finally, the NAMCS and NHAMCS provide a repeat cross-sectional view of patient visits but not the ability to follow specific patients, their diagnoses, and treatments through time. However, this approach was appropriate for this study, which focused primarily on the change in rates of prescribing antidepressant medication for pregnant women across a significant period of time and not on changes in prescribing for individual women. Despite these limitations, this study adds valuable information, given that it provides the only national estimates currently available on the change in antidepressant use in the U.S. prenatal patient population over time.

Table 1

Patient characteristics and prescribing of antidepressants for prenatal visits in the United States in 2002–2006 and 2007–2010, in percentages

Characteristic	Total	2002–2006 (N=14,406)	2007–2010 (N=12,922)	p
Age (years)				
≤20	13.8	14.3	13.3	.26
21–30	52.9	53.7	52.1	
31–45	33.3	32.1	34.6	
Race				
White	76.5	78.3	74.5	.26
Black	16.3	15.6	17.1	
Other	7.2	6.2	8.4	
Latino	20.6	20.3	20.8	.81
Insurance				
Private	57.7	57.3	58.1	.37
Medicaid	33.4	32.7	34.1	
Self-pay or other	8.9	10.0	7.8	
Specialty				
General medical ^a	10.1	9.8	10.4	.70
Obstetrics	89.9	90.2	89.6	
Setting				
Physician's office	86.0	85.5	86.5	.55
Hospital outpatient	14.0	14.5	13.5	
New patient	7.5	7.0	8.1	.29
Depression diagnosis ^b	4.2	4.1	4.2	.95
Antidepressant prescription	1.4	.7	2.1	<.01
Antidepressant ^c				
Selective serotonin reuptake inhibitors	71	87	66	.04
Sertraline	30	16	35	.02
Fluoxetine	16	33	10	.01
Paroxetine ^d	5	19	<1	<.01
Citalopram or escitalopram	21	18	22	.74
Bupropion	12	7	14	.41
Other	19	6	23	.01

^a Specialties include family medicine (81%), internal medicine (4%), pediatrics (1%), general medical clinic (12%), and pediatric clinic (2%).

^b Only years 2005 and 2006 (N=5,220) were included in the 2002–2006 period because of an expansion of chronic diagnostic categories in the National Ambulatory Medical Care Survey and National Hospital Ambulatory Medical Care Survey data starting in 2005.

^c Percentages of each antidepressant were determined by dividing the number of visits associated with each type by total number of visits associated with antidepressants (N=267).

^d There were insufficient prescriptions in 2007–2010 to calculate a nationally representative percentage of antidepressants used.

Conclusions

Prenatal depression is a prevalent and serious disorder linked to negative outcomes. Current guidelines recommend individualized, multidisciplinary treatment strategies, including judicious use of antidepressant medications based on patients' symptoms and severity of those symptoms (1–4). Despite concern over potential negative effects of antidepressants, the use of these medications has substantially increased over the past decade, as clinicians have become increasingly aware of the significance of depression in pregnancy. Changes in antidepressant selection were consistent with warnings regarding risks of specific medications.

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The authors report no competing interests.

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