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HHS Public Access

Author manuscript

J Perinatol. Author manuscript; available in PMC 2015 October 01.

Published in final edited form as:

J Perinatol. 2015 April ; 35(4): 246–251. doi:10.1038/jp.2014.197.

Disparities in antidepressant use in pregnancy

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Abstract

Background—The American College of Obstetricians and Gynecologists and the American Psychiatric Association both recommend pharmacotherapy for perinatal depression when the benefits outweigh the risks. While minority adults are less likely to use antidepressant medications compared to Non-Hispanic Whites, whether this pattern occurs among pregnant women is unclear.

Objective—We sought to determine the frequency of antidepressant medication use reported during ambulatory care visits for pregnant women and whether these rates varied by race.

Methods—We combined the 2006–2010 National Ambulatory Medical Care Survey (NAMCS) and the National Hospital Ambulatory Medical Care Survey (NHAMCS) to obtain nationally representative estimates of outpatient preventive care visits for pregnant women. We then obtained estimates of the prevalence of reported depression and antidepressant use during outpatient visits for pregnant women. To determine whether these estimates varied by race, we used multivariable logistic regression analyses accounting for survey design using SAS 9.2 (PROC SURVEYLOGISTIC) to estimate odds ratios of reported antidepressant use after adjustment for age, insurance status and region of the country.

Results—Antidepressant use was reported during 2.2% of all outpatient visits for pregnant women. Providers indicated a depression diagnosis in 4.5% of visits. Among visits for depressed pregnant women, providers reported antidepressant use 25.4% of the time for all visits. Antidepressant use during pregnancy varied significantly by race/ethnicity. Among visits for Non-Hispanic White women, 3.1% included a code for antidepressant use vs. just 1.0% for Non-White women ($P<0.0001$). After adjustment for age, insurance status, and region of the country, this association persisted with Non-Hispanic White (vs. Non-White) pregnant women having higher odds of antidepressant use (adjusted OR 3.3, 95% CI 2.1, 5.3).

Conclusion—Non-Hispanic White women were more likely than Non-White women to be using antidepressants during pregnancy. Whether differences in antidepressant use by race/ethnicity indicates over-treatment of non-Hispanic White women or under-treatment of minorities remains

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Conflict of Interest

The authors declare no conflict of interest.

unclear. This disparity warrants investigation with the goal of optimizing maternal mental health while minimizing potential adverse sequelae of antidepressants on developing fetuses.

Keywords

pregnancy; perinatal depression; antidepressants; race; ethnicity; disparities; selective serotonin reuptake inhibitors; SSRI

Introduction

While depression affects approximately one in ten adults in the United States,[1] rates of depression among women while pregnant and post-partum are even higher, ranging from 14–23% during pregnancy,[2] and 8–19% post-partum.[3] It is also estimated that 15.4% of women experience depression during at least one pregnancy phase.[4] Given the social stigma associated with depression and antidepressant use,[5] these figures likely underrepresent the true prevalence of perinatal depression.[6] Recently, public health and clinical agencies have developed initiatives to screen women for depression during the course of pre- and peri-natal care to prevent the negative consequences of depression for both mothers and their infants. Perhaps because of increased awareness and depression diagnoses, more providers are prescribing antidepressants for pregnant women than in previous years.[7]

Antidepressant use during pregnancy, however, remains highly controversial. The American Psychiatric Association (APA) advise psychotherapy as the first line of treatment for mild to moderate depression and pharmacotherapy as the standard of care for severe perinatal depression.[8] The American College of Obstetricians and Gynecologist (ACOG) concurs.[8] Both bodies recommend balancing the benefits to the mother with potential risks to the fetus and newborn.[8] Potential risks of antidepressant use during pregnancy include miscarriage, birth defects, low birthweight, preterm birth, pre-eclampsia, cardiac abnormalities, including persistent pulmonary hypertension, neonatal withdrawal syndrome, and other long term neurodevelopmental abnormalities,[8, 9, 10, 11] although the absolute risks of such sequelae are relatively low.[12, 13, 14, 15] Other therapies such as psychotherapy would be equally effective in treating mild to moderate depression,[16] and, thus avoid risk of potential fetal harm,[17] but resources may not be available for such approaches[18]. In spite of concerns for fetal toxicity of antidepressants, in 2003, approximately 13% of women were taking antidepressants during pregnancy.[19] Additionally, antidepressant use during pregnancy is rising with a recent analysis of the Centers for Disease Control and Prevention's (CDC) National Ambulatory Medical Care Survey (NAMCS) and the National Hospital Medical Care Survey (NHAMCS) reporting threefold increase between 2002–2006 and 2007–2010.[7]

Whether rates of antidepressant use in pregnancy are uniform across the population has not been studied. While Black, Hispanic and Asian/Pacific Islander women have been reported to be less likely to have access to and seek care for depression,[20] these minority groups have a higher rate of maternal depression compared to non-Hispanic White women.[21, 22, 23] Black women are also more likely to experience stigma associated with depression compared to Non-Hispanic White women.[24] Given these barriers to depression diagnoses, our hypothesis

was that during the course of prenatal care, minority women were more likely to be taking antidepressants.

Methods

Survey Design

The NAMCS and the NHAMCS are national probability sample surveys administered by the CDC in outpatient ambulatory medical care settings.[25] NAMCS collects data on outpatient office-based clinics and community health centers whereas NHAMCS data is collected from hospital outpatient departments and emergency departments. These surveys are completed by non-federally employed physicians involved in direct patient care as described previously.[26] Each patient visit is assigned an inflation factor to allow for national estimates of outpatient visits when appropriate weights are applied. The primary units of analysis are health care visits. We used visits for pregnant women, and combined the two data sources because outpatient office settings as well as hospital-based clinics provide most of prenatal care visits in the United States. Visits to emergency departments (a subset of NHAMCS) were excluded from the analysis. To obtain a sample size with ample power we combined the data for 2006–2010. Starting in 2006, the CDC adopted a new drug coding scheme based on the drug's generic component and therapeutic class using Lexicon Plus®[27] instead of the NCHS-developed 5-digit code; therefore, data from 2006 to 2010 were selected for consistency.[28] Per the guidelines published by the National Center for Health Statistics, estimates were considered to be reliable when relative standard errors were 30 percent or less, and if they were based on no fewer than 30 observations.[29, 30] The Beth Israel Deaconess Medical Center Institutional Review Board (IRB) Committee deemed this study exempt from IRB review since it complied with federal policy as stated under Title 45 CFR 46.101(b)(4).

Variable Selection

We identified visits for pregnant women using methods described previously with the addition of visits for women with high risk (V23) or complications during pregnancy (ICD-9-CM codes 640.0–646.0, 671.0 and NCHS-generated reason for visit code[29, 30] 273.50).[26, 31] Depression diagnoses were identified using the International Classification of Diseases, Clinical Modification, 9th Revision (ICD-9-CM) codes (296.20–296.26, 296.30–296.36, 298.0, 296.82, 300.4, 309.0, 309.1, 311), reason for visit code for depression (111) and a checkbox indicator in the survey question, "Regardless of the diagnoses written (previously) does the patient now have depression?"

Visits where antidepressants were provided, prescribed or continued were identified using Lexicon Plus code for therapeutic drug category '249' which codes for 'Psychotherapeutic agents; antidepressants.' These codes did not distinguish between the types of antidepressants, so once the cohort was generated, antidepressant type was identified using prescription codes, '208', '209', '250', '306', '307', '308', under the category of 'Psychotherapeutic agents; antidepressants.' Among visits including prescribed antidepressants, a subset of visits indicated simultaneous antipsychotic use. We ensured that visits with antidepressant use included at least one of the antidepressant prescription codes

from above (‘208’, ‘209’, ‘250’, ‘306’, ‘307’, ‘308’) and not taking antipsychotics exclusively. Cognitive behavior therapy (CBT) was identified using a combination of reason for visit code ‘44100,’ diagnosis codes ‘V663-’, ‘V673-’ and “other procedure” codes (‘943-’, 9437’, ‘9438’, ‘9439’, ‘944-’, ‘9441’, ‘9442’, ‘9451’).

Race/ethnicity was the primary variable of interest. We classified race/ethnicity into four categories consisting of Non-Hispanic White, Non-Hispanic Black, Hispanic and Other. Asians and Pacific Islanders were included in the “Other” category due to small numbers. In the final analysis, we collapsed race/ethnicity into Non-Hispanic White (White) vs. Non-White (which includes Non-Hispanic Black, Hispanic, and Other) in order to meet the reliability criteria since some racial/ethnic groups had fewer than 30 observations per cell. Additionally, the direction of the associations supported dichotomization of race/ethnicity.

We analyzed several potential confounding variables including patients’ age at the time of the visit (>25, 25–29, 30–34, >34), type of insurance (Private, Medicaid, Other), the region in the US where the visit took place (Northeast, Midwest, South, and West), and type of survey (NAMCS vs. NHAMCS).

Inclusion Criteria

Our sample population was restricted to visits for pregnant women between the ages of 11–49 in order to exclude improbable ages for pregnancy (n=23).

Statistical Analyses

The average of the 2006–2010 combined patient weights were used in the PROC SURVEYFREQ/PROC SURVEYLOGISTIC procedures in SAS 9.2 (Cary, NC) to account for the complex study design and probability of sampling. Chi-square tests were performed to assess any bivariate relationships between each covariate and visits rates for depression, antidepressant use, and antidepressant use among depressed women. Multivariable logistic regression was performed to identify the relationship between race and depression among visits for all pregnant women, race and antidepressant use among visits for all pregnant women, and race and antidepressant use among visits for depressed pregnant women adjusting for covariates. P-values of <0.05 were considered to be significant.

Results

From 2006–2010 there were, on average, 37.8 million visits per year for pregnant women in outpatient settings. Among these visits, the prevalence of depression was 4.5% and 2.2% of all visits included a code for antidepressant use or prescription. Visits for White women had the highest rate of antidepressant use (3.1%) followed by non-Hispanic Black (1.6%) and Hispanic (0.8%) women (Table 1). Visits for White women also had the highest rates of depression (5.7% vs. 2.9% among Non-White women) (Figure 1). Of the visits for depressed White women, 28.3% included a code for antidepressant use, compared to just 18% among Non-White women. Reported antidepressant use during prenatal visits did not vary by maternal age or survey type (NAMCS vs. NHAMCS). Visits from the Western region were less likely to indicate antidepressant use during pregnancy. The majority (68%) of antidepressants used and prescribed were selective serotonin-reuptake inhibitors (SSRIs)

(Table 2). Providers reported the use of CBT very infrequently. Just 0.2% of all visits, 2.8% of the visits for depressed women, and 5.4% of the visits for women taking antidepressants included an indicator for CBT.

Differences by race/ethnicity for both depression and antidepressant use persisted after adjustment for potential confounding variables including maternal age, insurance type, region of the country, and survey type. Compared to visits for White women, prenatal visits for Non-White women had lower odds of reported depression (adjusted OR 0.5, 95% CI 0.4, 0.7), antidepressant use (adjusted OR 0.3, 95% CI 0.2, 0.5), and antidepressant use while depressed (adjusted OR 0.5, 95% CI 0.3, 0.9) (Table 3). Visits paid for by Medicaid had higher odds of depression compared to those with private or other insurance types even after adjusting for race and antidepressant use (adjusted OR 1.8 95% CI 1.3, 2.6).

Discussion

We found marked differences in rates of provider-reported maternal depression diagnoses and antidepressant use by race during prenatal care. White women were both more likely to be diagnosed with depression and to be receiving pharmacotherapy during pregnancy. These findings have several potential implications. Given that the true rates of depression are likely higher among Non-White women,[21, 22, 23, 24] it is likely that Non-White women are underdiagnosed with depression during pregnancy and potentially undertreated once diagnosed. Another possibility is that White women are being over-diagnosed and over-prescribed antidepressants during pregnancy. Either way, there could be negative consequences to both mothers and their infants by undertreating mothers suffering from depression or negative consequences to fetuses unnecessarily exposed to potentially harmful medications.

In addition to the potential harms of undertreating mothers with depression (poor nutrition, substance use, suicide, and distress on infant development[32, 33, 34, 35]), there are particular risks that may disproportionately affect minorities compared to White mothers. One study assessed data from the Pregnancy Risk Assessment Monitoring System that included 3732 women in New York City, found that having a diagnosis for prenatal depression not only increased the likelihood of a post-partum depression diagnosis across all racial groups but that Asian/Pacific Islander compared to Non-Hispanic White women were more likely to have post-partum depression after accounting for confounders.[36] Taveras et al[23] prospectively studied 1826 mother-child pairs and found high rates of maternal depression to be a significant risk factor for offspring childhood obesity among racial/ethnic minorities.

Increasing the detection of depression during pregnancy may not be without adverse sequelae if it leads to more pharmacotherapy for depression during pregnancy. In a study of 240 children between the ages of 3–6 years old, Nulman et al found that children exposed to SSRIs and SSNRIs during pregnancy had lower IQs and greater rates of problematic behaviors than children born to nondepressed mothers.[37] An analysis of the Swedish Medical Birth Register from 1997–2005 found a 2.4 fold increase in persistent pulmonary hypertension risk in neonates born to mothers with reported SSRI use during pregnancy.[38] A recent study by Clements et al found that prenatal antidepressant exposure was associated

with an 80% increased odds of ADHD even after controlling for maternal depression.[39] Domar et al reviewed studies pertaining to the effect of antidepressant use among depressed women experiencing infertility and found them to be associated with miscarriage, birth defects, preterm birth, newborn behavioral syndrome, persistent pulmonary hypertension of the newborn and long-term neurobehavioral effects.[40] These authors concluded that providers should have adequate understanding of the literature on the risks of pharmacotherapy and recommend safer alternatives when possible.

Policy statements[8] by ACOG and APA recommend balancing the risks and benefits to the mother and fetus before starting pharmacotherapy for depression. However, such a task remains exceedingly difficult, given the paucity of randomized controlled trials of antidepressant use in pregnancy as highlighted by a recent metanalysis on this issue.[41] However, one key aspect of these policy statements is that the recommendations include pharmacotherapy “for depression.” Our analysis suggests that women without depression are also receiving antidepressants. It is possible that women were well-controlled on their medications and thus the providers did not consider them “depressed” and omitted a code for depression. Alternatively, it is possible that women were receiving antidepressants for other diagnoses, such as anxiety, where the indication for treatment in pregnancy may be less clear. When the harm of not using medication and the benefits of medication are less certain, other therapies should be considered. While CBT has been shown to be effective for controlling depression,[42] we found little evidence of its widespread use in pregnancy with just 0.2% of women receiving CBT. CBT may be a safe, effective therapy in treating depression without the potential fetal toxicity antidepressants confer.

Our study is unique in its focus on racial/ethnic disparities in depression and antidepressant use among pregnant women on a national scale. Our findings are consistent with a recent study of pregnant women using the NAMCS and NHAMCS databases which found an antidepressant prescription rate of 2.1%, depression diagnosis rate of 4.2% and reported that the majority of the visits involving antidepressants were for White women.[7] Their rates are consistent with our analysis but are much lower than the reported prevalence of prenatal depression reported by other studies which range from 14 to 23%.[2, 4] This is likely due to two factors. First, studies designed to specifically evaluate the prevalence of a condition use screening tools to capture women at risk. Yonkers et al used multiple assessment tools, including the Edinburgh Postnatal Depression Scale, the Inventory of Depressive Symptomatology and the Structured Clinical Interview for DSM-IV (Diagnostic and Statistical Manual of Mental Disorders, 4th Edition, Text Revision) to detect a depression rate of 6.5–8.5% in women during the postpartum period.[43] NAMCS and NHAMCS rely on provider diagnostic codes which will miss women who might meet criteria based on a screening tool that a provider is not using in his or her office. Second, there may be underreporting of true diagnoses by missed codes on the data reporting form. In either case, we would not expect misclassification to vary by race or ethnicity and while the rates may not be generalizable to the population, the differences between groups remain important.

Contrary to studies based on screening or direct assessment,[21, 22, 23] however, we found that visits for White women had the higher reported or diagnosed depression rates compared to Non-White women. We also found that among all visits for pregnant and depressed pregnant

women, White women were more likely to be prescribed antidepressants compared to all other race/ethnicities. However, our study is consistent with Shen et al.'s findings from the 2006 National Inpatient Sample in which pregnant minority women had lower odds of depression at the time of their hospital delivery compared to White women.[44] Our data do elucidate whether this finding is explained by cultural differences in seeking help for mental health disorders, or variability in access to mental health professionals, but we speculate that both explanations are probable. We found that visits for Medicaid patients were more likely to include depression diagnosis after controlling for race but antidepressant use was not increased. We speculate that this might be a result of differences of prescription coverage by state,[45] but state-level data from NAMCS and NHAMCS are not available.

The primary strength of our study is the use of a large national database that enabled us to obtain national estimates by applying appropriate weights. There are several limitations inherent to observational studies including residual unmeasured confounding as well as measurement error and misclassification. While we speculate that cultural differences may contribute to variation in diagnostic and prescription practices by race/ethnicity or region, the datasets used does not permit further conclusions. The unit of analysis is the outpatient visit for NAMCS/NHAMCS so the national estimates represent frequencies of given diagnoses or treatment by visit and not by individual. Given the sampling design, the same individual is not likely to be sampled twice, but it is important to keep in mind that the denominator for this analysis is not pregnancies but pregnancy visits. Given the visit is the unit of analysis, this study only includes women who were pursuing prenatal care. Race/ethnicity was recorded by the provider and was not necessarily self-reported by the patient. This type of misclassification would likely be random and not a source of bias. A potential source of bias is the healthy user bias,[46] in which, White women could be more likely to utilize the healthcare system than other racial/ethnic groups due to socioeconomic status or cultural practices. However, because prenatal care is one period of time during which women almost uniformly pursue medical care, this is not likely a major source of bias in this study.

Conclusion

We found that during pregnancy, outpatient visits for White women had greater odds of reported depression and antidepressant use compared to non-White women. Whether this is a case of under-diagnosis and under-prescribing antidepressants for Non-White women or over-diagnosis and over-prescribing antidepressants for White women remains unknown. Regardless, variation in practice between groups may shed light on how to optimize screening for potentially depressed women as well as finding ways to promote antidepressant stewardship among pregnant women who might safely avoid antidepressants. Furthermore, providers might improve the mental health care of pregnant women by collecting data on the prevalence of depression and therapies offered to ensure equitable care.

Acknowledgments

The authors would like to thank the CDC and the participating patients and providers who contributed to NAMCS and NHAMCS. The last author is funded by the Klarman Scholars Program and by NIH/NIEHS K23-ES022242.

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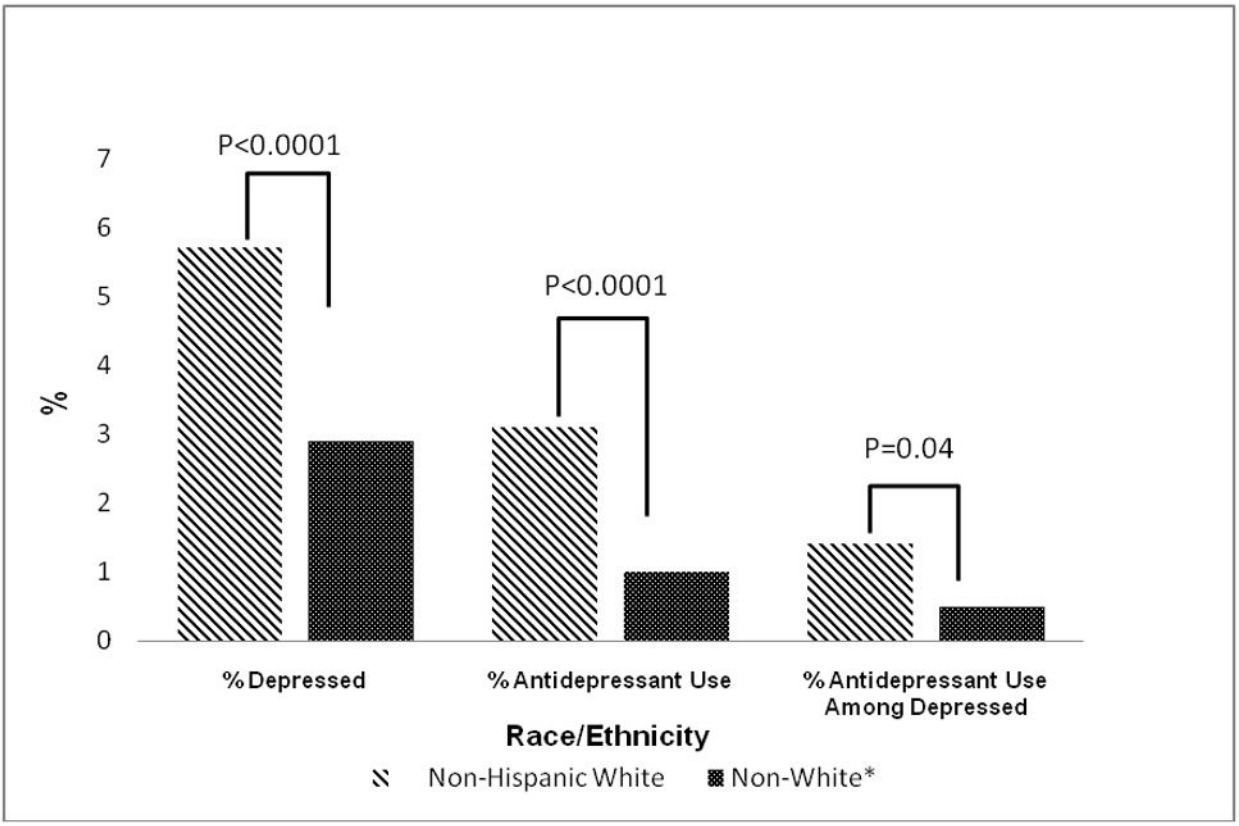

*Non-White includes Non-Hispanic Black, Hispanic and Other

Figure 1.
Proportion of provider-reported depression and antidepressant use during visits for pregnant women by race/ethnicity

Table 1

Annual visits n, in millions (%) for pregnant women in NAMCS and NHAMCS, associations with depression and antidepressant use by characteristics

	All Visits	Visits for depressed women		Visits with antidepressant use		Visits for depressed women taking antidepressants	
	Sample visits (n), Annual visits in millions	Sample visits (n)	Annual visits in millions (%)	Sample visits (n)	Annual visits in millions (%)	Sample visits (n)	Annual visits in millions (%)
All visits	18262, 37.8	1013	1.7 (4.5)	328	0.8 (2.2)	198	0.4 (25.4)
Race/Ethnicity							
NH White	7816, 21.6	578	1.2 (5.7)**	225	0.7 (3.1)**	127	0.3 (28.3)*
Non-White^	10446, 16.3	435	0.5 (2.9)**	103	0.2 (1.0)**	71	0.08 (18.0)*
NH Black	3729, 5.6	169	0.2 (3.4)**	49	0.09 (1.6)**	26	-
Hispanic	5559, 8.2	214	0.2 (3.0)**	42	0.06 (0.8)**	34	0.04 (18.7)*
Other	1158, 2.4	52	0.04 (1.7)**	12	-	11	-
Age categories (years)							
11–<25	7086, 12.4	378	0.5 (4.3)	95	0.2 (1.8)	59	0.1 (25.6)
25–29	4832, 10.7	279	0.5 (4.7)	105	0.3 (2.7)	66	0.1 (27.5)
30–34	3693, 8.9	203	0.4 (4.5)	73	0.2 (2.2)	40	0.09 (21.5)
35–<50	2651, 6.0	153	0.2 (4.1)	55	0.1 (2.0)	33	0.07 (27.0)
Insurance							
Other***	2453, 3.6	138	0.1 (3.6)	48	0.1 (2.7)	30	0.05 (35.8)
Private	5611, 20.8	254	0.8 (3.9)	124	0.5 (2.3)	66	0.2 (25.0)
Medicaid	9634, 12.4	598	0.7 (5.4)	146	0.2 (1.8)	99	0.2 (26.0)
Region							
Northeast	5050, 5.3	290	0.3 (6.2)	57	0.1 (2.2)*	36	0.1 (28.5)
Midwest	4675, 8.6	330	0.4 (5.0)	125	0.2 (2.8)*	79	0.1 (29.1)
South	4230, 14.3	174	0.5 (3.6)	83	0.4 (2.5)*	47	0.1 (28.7)
West	4307, 9.7	219	0.4 (4.3)	63	0.1 (1.0)*	36	0.06 (15.2)
Survey							
NAMCS	4660, 32.4	213	1.4 (4.3)	111	0.7 (2.2)	60	0.4 (26.2)

	All Visits	Visits for depressed women		Visits with antidepressant use		Visits for depressed women taking antidepressants	
	Sample visits (n), Annual visits in millions	Sample visits (n)	Annual visits in millions (%)	Sample visits (n)	Annual visits in millions (%)	Sample visits (n)	Annual visits in millions (%)
NHAMCS	13602, 5.4	800	0.3 (5.6)	217	0.1 (1.9)	138	0.06 (21.6)

* p<0.05

** p<0.0001

*** Other = Medicare, worker's compensation, self-pay, no charge and other

^ Non-White includes Non-Hispanic Black, Hispanic and Other. Categories were collapsed into 'Non-White' since several cells contained fewer than 30 observations and are considered unreliable and those cells are indicated by a dash.

NH=Non-Hispanic, *NAMCS*=National Ambulatory Medical Care Survey, *NHAMCS*=National Hospital Ambulatory Medical Care Survey

Table 2

Antidepressant use by class among pregnant women, NAMCS/NHAMCS 2006–2010.

Name	Weighted %
Selective serotonin reuptake inhibitors (SSRI)	68.3%
Selective serotonin-norepinephrine reuptake inhibitors (SSNRI)	10.6%
Phenylpiperazine	2.7%
Tricyclic	2.1%
Tetracyclic	0.7%
Miscellaneous	17.4%

* Note: percentages do not add up to 100% because some patients are taking multiple drugs simultaneously.

Table 3

Odds of antidepressant use among visits for pregnant women and depressed pregnant women

	Visits for pregnant women Adjusted* OR (95% CI)	Visits for depressed pregnant women Adjusted* OR (95% CI)
Race/Ethnicity		
White***	Ref	Ref
Non-White	0.3 (0.2, 0.5)	0.5 (0.3, 0.9)
Age categories		
< 25	0.7 (0.4, 1.2)	0.9 (0.4, 1.9)
25 – 29	Ref	Ref
30 – 34	0.9 (0.5, 1.6)	0.6 (0.3, 1.5)
> 34	0.7 (0.4, 1.4)	1.5 (0.7, 3.4)
Insurance status		
Other**	1.7 (0.9, 3.0)	2.1 (0.6, 7.1)
Private	Ref	Ref
Medicaid	1.0 (0.5, 2.0)	1.0 (0.6, 1.8)
Region		
Northeast	Ref	Ref
Midwest	1.2 (0.7, 2.3)	1.2 (0.6, 2.4)
South	1.2 (0.6, 2.5)	0.9 (0.4, 2.1)
West	0.5 (0.2, 1.1)	0.4 (0.2, 0.7)
Survey		
NAMCS	1.0 (0.7, 1.5)	1.6 (0.8, 3.0)
NHAMCS	Ref	Ref

* Models mutually adjusted for all listed variables.

** Other = Medicare, worker's compensation, self-pay, no charge and other

*** Race was collapsed to White vs. Non-White due to small sample sizes within Non-White groups (<30).

(White includes non-Hispanic White; Non-White includes Non-Hispanic Black, Hispanic, Other)

Ref=Reference, *OR*=Odds Ratio, *CI*=Confidence Interval, *NAMCS*=National Ambulatory Medical Care Survey, *NHAMCS*=National Hospital Ambulatory Medical Care Survey