Antidepressant Treatment Persistence in Low-Income, Insured Pregnant Women

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ABSTRACT

BACKGROUND: Pregnant women with depression face complicated treatment decisions, either because of the risk associated with not treating depression or because of the risks associated with antidepressant use. Approximately 1 in 5 women experience depressive symptoms during pregnancy. This information suggests that many women may take an antidepressant at some time during pregnancy. Once pregnant women initiate antidepressant prescription pharmacotherapy, medication treatment persistence plays an important role in managing depression, yet little is known regarding antidepressant use behavior in pregnant women.

OBJECTIVE: To determine antenatal antidepressant treatment nonpersistence and associated factors in low-income, insured pregnant women.

METHODS: We identified eligible pregnant women (≥18 years) diagnosed with major depression who initiated antidepressant medications during pregnancy from South Carolina Medicaid claims data (2004-2009). Our main outcome measure was treatment nonpersistence to antidepressant therapy during pregnancy. We defined treatment nonpersistence to antidepressant pharmacotherapy as having a gap between 2 consecutive prescriptions lasting at least 15 days during pregnancy. We applied a proportional hazards model to identify predictors associated with the risk for antidepressant nonpersistence during pregnancy.

RESULTS: Of 804 pregnant women meeting study criteria, nearly 45% of this cohort did not continue to use antidepressant pharmacotherapy, showing a gap ≥15 days between 2 prescriptions, after initiating antidepressant therapy during pregnancy. Women reporting nonwhite race were 36% more likely to show a gap in antidepressant medication use during pregnancy than white women. Women with a history of antidepressant use before pregnancy were 44% more likely to discontinue the antidepressant therapy during pregnancy.

CONCLUSIONS: Treatment persistence to antidepressant medications was poor during pregnancy in low-income, insured pregnant women. Individualized treatment might be considered to reduce the risks of untreated depression and antenatal antidepressant use in vulnerable women.

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What is already known about this subject

- The American Congress of Obstetricians and Gynecologists estimates that 14%-23% of pregnant women experience depressive symptoms during pregnancy. Although both untreated depressive symptoms and antidepressant exposure are associated with poor maternal and newborn outcomes, trends for antidepressant medication use during pregnancy have increased.
- Since antidepressant treatment guidelines recommend at least 6-9 months of antidepressant medication use for patients with major depression, medication adherence plays a key role to help patients achieve desired outcomes. However, more than 40% of patients discontinue treatment during the first 3-4 months, which may result in worse health and economic outcomes.
- Women with low socioeconomic status are at high risk to develop depression. Few studies report antenatal antidepressant medication use behavior in low-income pregnant women.

What this study adds

- Nearly 80% of depressed pregnant women were prescribed selective serotonin reuptake inhibitors, and 20% used more than 1 antidepressant during the antenatal period.
- The estimated median time to discontinuation of antidepressant medication use during pregnancy was 80 days.
- Of 804 pregnant women, 45% showed treatment nonpersistence to antidepressant medication therapy.
- Racial disparity in antidepressant treatment nonpersistence was identified in low-income pregnant women.

Depression is one of the most prevalent forms of mental illness, a major contributor to disability and disease burden and a major public health concern.[1,2] Depression affects approximately 9% of the adult U.S. population, with prevalence in women about twice that of men.[3] Over their lifetimes, women are 70% more likely than men to experience depression, with low-income, young, single, urban women significantly more likely to have atypical lifetime major depressive episodes.[4,5] Women of childbearing age are at high risk for major depression with an estimated 18.4%-20.0% experiencing depressive symptoms during pregnancy (termed antenatal),[6,7] with the first 2 months postpartum being a particularly vulnerable time for a depressive episode and new onset depression.[8] Risk of antenatal depression is influenced by lifestyle, nutrition, and socioeconomic factors, among others.[9] Of concern, antenatal depression is associated with poor maternal self-care,[10] contributing to increased risk for preterm birth, low birth weight, and intrauterine growth restriction.[11-13] Antidepressant medication exposure during pregnancy is significantly associated with an increased risk for postnatal adaptation syndrome, an inconclusive risk for persistent pulmonary

hypertension of the newborn, and shows equivocal findings for outcomes related to fetal growth and gestation.[6,14]

Although controversy exists regarding antidepressant use during pregnancy, trends for antidepressant medication use to treat antenatal depression continue to increase.[15-18] A recent meta-analysis found that antidepressant medication use during pregnancy significantly increases risks for low birth weight and preterm birth.[19] Yet, there is higher risk for depression recurrence when antidepressant medication maintenance therapy is not used during pregnancy,[20,21] with 1 study reporting recurrence 5 times more likely in women who discontinue antidepressant therapy during the antenatal period than in those who maintain antidepressant treatments.[22]

In adults with major depressive episodes, The American Psychiatric Association recommends continuous antidepressant pharmacotherapy lasting at least 6-9 months.[23] Antidepressant medication use persistence becomes an important factor when managing antenatal depression. Evidence shows that more than 40% of patients discontinue their medications during the first 3-4 months. Discontinuing antidepressant medication treatment shows an association with poor clinical outcomes.[24-28] Although antidepressant medication use for depressive episodes can positively affect behavioral, clinical, and health outcomes among various populations, few studies report antidepressant medication use in pregnancy, particularly in low-income populations. For instance, it is not clear whether pregnant women with depression actually receive appropriate pharmacotherapy, whether antidepressant medication use behavior changes during antepartum, or how frequently women discontinue antidepressant therapy when pregnant.

Moreover, low socioeconomic status is significantly associated with the occurrence of depression. Individuals with less than a high school education, work disability, unemployment, or without health insurance coverage tend to be more severely depressed.[3,29,30] Understanding antidepressant use behavior in low-income pregnant women could help identify barriers to managing antenatal depression and help develop effective and safe antidepressant treatment parameters for disadvantaged populations. Our objective was to examine antidepressant medication use behavior in low-income pregnant women by using South Carolina Medicaid administrative claims data. The purpose of this study was to assess antidepressant pharmacotherapy treatment persistence during pregnancy and identify patient characteristics predictive of antidepressant medication treatment persistence.

Methods

This retrospective cohort study used South Carolina Medicaid claims data (2004-2009). First, we identified pregnant women aged 18 years and older with single or multiparous live births during the study period. Then, we calculated the date of conception as 280 days prior to the maternal delivery date. Next, we restricted our analysis to pregnant women who had a primary diagnosis of major depression and who initiated antidepressant use during the 280 days preceding the delivery date. The major depression was identified by *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM) codes (296.2, 296.3, 300.4, or 311). The subject's index date was defined as the date of a patient's first pharmacy claim for an antidepressant medication after the estimated date of conception. Those who received antidepressants during 6 months prior to the index date were excluded. To measure persistence, we included women who had at least 2 antidepressant prescription claims during the pregnancy. Additionally, to be eligible for our study, the pregnant women needed to show continuous Medicaid enrollment for at least 1 year before and 1 year after the estimated date of conception. Women with a diagnosis for schizophrenia or bipolar disorders or those with any antipsychotic medication claim during the eligibility period were excluded from the study. Antidepressant medications were identified from pharmacy claims. If a woman had more than 1 maternal delivery during the study period, the first delivery meeting eligibility criteria was included for analysis.

Our main outcome measure was antidepressant medication treatment nonpersistence during pregnancy. Based on literature review and clinical perspectives, pharmacotherapy treatment discontinuation was defined as the presence of a 15-day gap in therapy.[25,31] Antidepressant medication treatment nonpersistence was defined as having a gap between 2 consecutive prescriptions of at least 15 days during the 180 days after the index date or from the index date to maternal delivery date, whichever occurred first.

Antidepressant medication use patterns during pregnancy among eligible pregnant women were measured, including type of antidepressant used, total number of antidepressants used, and trimester of antidepressant initiation. Potential predictors, including demographics (age, race); history of antidepressant use and depression diagnosis during the 1 year before pregnancy; comorbidity; and medical utilization, including all-cause physician office visits, hospitalization, and emergency department (ED) visits during 1 year before pregnancy were used to estimate the risk for antenatal antidepressant therapy nonpersistence. The Charlson Comorbidity Index, weighted score (ranging 1-6), was used as a proxy for severity of comorbidity. ICD-9-CM codes were used to identify comorbid conditions from Medicaid claims data.[32]

Descriptive statistics summarized the study population's characteristics and antidepressant use patterns. Antidepressant nonpersistence was reported by Kaplan-Meier plots for the time to discontinuation of antidepressant treatment during pregnancy. We employed a proportional hazards model to identify significant predictors associated with risk for antidepressant therapy nonpersistence during pregnancy. The level of statistical significance was set a priori at $P < 0.05$. All analyses were performed using SAS 9.2 (SAS Institute, Cary, NC).

FIGURE 1 Patient Selection

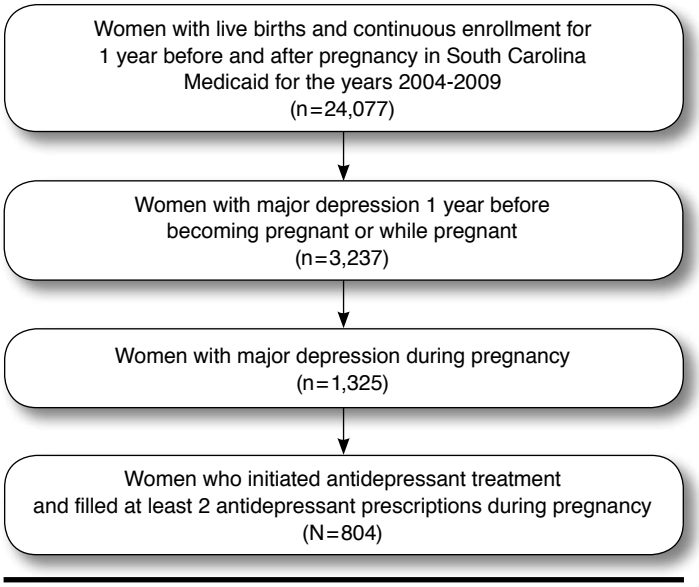


TABLE 1 Characteristics of a Cohort of Low-Income, Insured Pregnant Women Diagnosed with Depression

Variable	N = 804	
Age in years, mean (SD)	25.8	(6.2)
≤25, % (n)	56.1	(451)
>25, % (n)	43.9	(353)
Race, % (n)		
White	84.0	(675)
Black	13.4	(108)
Other	2.6	(21)
All-cause medical utilization during 1 year before pregnancy		
Total number of office visits, mean (SD)	3.8	(6.4)
Total number of outpatient visits, mean (SD)	1.3	(3.3)
Emergency department, % (n)	33.2	(268)
Hospitalization, % (n)	15.9	(128)
Comorbidity score, mean (SD)	0.12	(0.75)
0-2, % (n)	98.5	(792)
3-4, % (n)	0.9	(7)
≥5, % (n)	0.6	(5)
Antidepressant use during 1 year before pregnancy, % (n)	38.6	(310)
History of depression during 1 year before pregnancy, % (n)	17.9	(144)

SD = standard deviation.

Results

The final study sample consisted of 804 women aged 18 years and older with a diagnosis for major depression showing antidepressant medication use during the 280 days prior to their maternal delivery date for the years 2004 through 2009 (Figure 1). Table 1 presents the descriptive characteristics of the study population. More than 80% of the eligible women were white, with an average age of 26 years when giving birth. During the 1 year before pregnancy, nearly 40% of women used antidepressants; less than 20% had a diagnosis of depression; one-third showed at least 1 ED visit; and 15% experienced hospitalization. Comorbidities in this population were minor, with a mean Charlson Comorbidity Index score calculated as 0.12.

Table 2 summarizes the antidepressant use patterns and antidepressant therapy persistence during pregnancy. Nearly 80% of pregnant women were prescribed selective serotonin reuptake inhibitors, and 20% used more than 1 antidepressant during the antenatal period. Less than 40% initiated antidepressant treatment during the first trimester. Nearly 45% of the women showed treatment nonpersistence to antidepressant medication therapy with a gap ≥15 days between 2 consecutive prescriptions before 180 days or maternal delivery. The estimated median time to discontinuation of antidepressant use during pregnancy was 80 days (Figure 2).

Table 3 shows the associations between potential predictors and risk for antidepressant treatment nonpersistence during pregnancy. Race, a history of antidepressant use before pregnancy, hospitalization, and total number of physician office visits during the 1 year before becoming pregnant were associated with nonpersistence with antidepressants in pregnant women. The risk for antidepressant nonpersistence during pregnancy increased by 36% in nonwhite women (vs. whites) and by 44% in women who used antidepressants during the 1 year before becoming pregnant.

Discussion

Although psychological treatments with proven efficacy are available for the management of depression, antidepressant pharmacotherapy is the most common form of treatment.[33,34] Women with 4 or more prior depressive episodes or a depressive episode 6 months before pregnancy or women of black race or Hispanic ethnicity are at higher risk for depression relapse and potentially have poor outcomes associated with a major depressive episode.[14] Moreover, women from low socioeconomic backgrounds may have a higher risk for associated social risk factors, for instance, limited social support, exposure to domestic violence, or single parenthood, that add complicating factors when determining a treatment plan or may add to the risk for major depressive symptoms.[35]

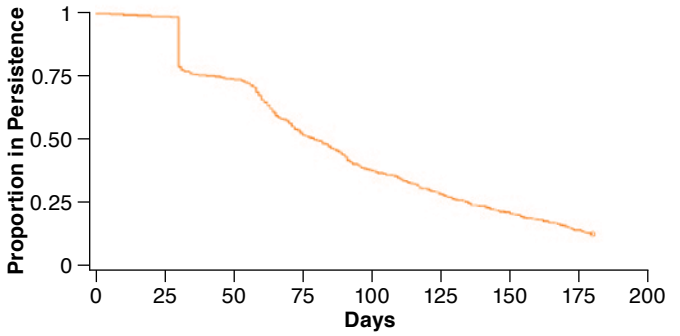
Antidepressant pharmacotherapy poses risks in pregnancy. The risks to the fetus, neonate, and mother must be weighed against the benefits to maternal well-being and effect of antenatal depression on obstetrical outcomes and increased risk for postpartum depression.[36] Some research shows evidence that discontinuation of antidepressant treatment during pregnancy is associated with relapse of major depression.[22,37] Thus, gaining a better understanding of the magnitude and predictors of

TABLE 2 Antidepressant Medication Use and Nonpersistence in Low-Income, Insured Women During Pregnancy

Variable	N = 804	
Type of antidepressant, % (n)		
SSRI	78.4	(633)
SNRI	9.5	(76)
TCA	7.2	(58)
Miscellaneous	24.5	(197)
Total number of antidepressant use, % (n)		
1	80.3	(646)
2	17.9	(144)
>2	1.7	(14)
Trimester of antidepressant initiation, % (n)		
First trimester	37.3	(300)
Second trimester	47.6	(384)
Third trimester	14.9	(120)
Antidepressant nonpersistence, % (n)	45.0	(362)

SNRI = serotonin-norepinephrine reuptake inhibitor; SSRI = selective serotonin reuptake inhibitor; TCA = tricyclic antidepressant.

FIGURE 2 Time to Discontinuation of Antidepressant Therapy During Pregnancy



antidepressant nonpersistence may provide additional insights for effectively managing depression in low-income pregnant women. To our knowledge, this research is one of the first explorations examining the association between patient predisposing characteristics and antidepressant use behavior in low-income pregnant women.

We found actual antidepressant treatment persistence during pregnancy was poor and similar to the general overall nonpregnant male/female population, where 40%-50% of patients discontinue antidepressant therapy within 6 months.[26-28,38] For instance, in the United Kingdom and Spain, 40% and 56% of patients abandon antidepressant treatment during the first 3 and 4 months after initiating the treatment.[27,39] A U.S. study of a large sample of health maintenance organization patients found that 32%-42% had not filled antidepressant medication prescriptions 6-8 weeks after starting treatment.[38] Although improving antidepressant treatment persistence and outcomes are important goals across various adult populations, pregnancy adds special circumstances that may require additional individualized attention. We cannot rule out the possibility of adverse effects on maternal and newborn outcomes as a contributing factor leading to the discontinuation of antidepressant therapy during pregnancy. Some women may switch to psychological or other alternative therapy after discontinuing pharmacological treatment in an effort to continue some form of antidepressant therapy while avoiding untoward effects on the fetus. Further studies examining clinical outcomes and persistence are needed to understand antenatal antidepressant medication use behavior. Research identifying differences between pregnant versus nonpregnant women's access to and persistence with antidepressant medications is needed.

Our study found that less than 40% of pregnant women initiated antidepressant therapy during the first trimester. However, this does not mean overall antenatal antidepressant use decreased during pregnancy. Notably, nearly half of our study cohort initiated therapy during the second trimester. Possibly, women engage in evaluating the risks and benefits of treatment versus nontreatment for depression and weigh the pros and cons of initiating antidepressant medication use during pregnancy. Risk benefit conversations with clinicians may play an important role in medical prescriber decision making.

For the predictors of treatment nonpersistence, we observed lower persistence among nonwhite women, as well as those with a history of depression during 1 year before pregnancy. Our analysis showed racial disparities for antidepressant medication use as defined by persistence among white and nonwhite races. The inadequate antidepressant medication treatment levels among all pregnant women in our study, as well as the racial disparities in medication use patterns when viewed in context with overall depression prevalence in minority populations, suggest areas of concern needing future research. Racial differences about treatment preferences for depression and collateral health beliefs may influence medication use behavior during pregnancy. Women with a history of antidepressant use before pregnancy were also less likely to persist in antidepressant use, suggesting that past antidepressant use behavior may impact antidepressant medication use during pregnancy. When a pregnant woman shows recurrent or severe depression, pharmacological therapy is usually recommended. To address all the challenges associated with antidepressant pharmacotherapy use during the gestational period, additional research is needed to develop optimal medication treatment guidelines for pregnant women experiencing severe or recurrent depression.

TABLE 3 Association Between Potential Predictors and Risk for Nonpersistence with Antidepressant Therapy in Women During Pregnancy (N = 804)

Independent Variable	Dependent Variable: Hazard Ratio of Antidepressant Nonpersistence (95% CI)	*P* Value
Age in years	1.01 (0.99-1.03)	0.368
Race		
White	1.00	
Nonwhite	1.36 (1.10-1.57)	0.025
Previous diagnosis of depression in 1 year before pregnancy		
No	1.00	
Yes	0.94 (0.34-1.32)	0.625
Previous antidepressant use in 1 year before pregnancy		
No	1.00	
Yes	1.44 (1.17-1.62)	0.004
Charlson Comorbidity Index score	0.99 (0.77-1.17)	0.920
All-cause medical utilization in 1 year before pregnancy		
Hospitalization		
No	1.00	
Yes	0.41 (0.05-0.97)	0.028
Emergency department		
No	1.00	
Yes	0.91 (0.42-1.25)	0.658
Total number of office visits	1.04 (1.01-1.07)	0.029

CI = confidence interval.

Limitations

This study represents a preliminary exploration of antidepressant medication use behavior in women during pregnancy. The results should be interpreted in light of some limitations. We did not assess alternative antidepression therapy use. Our 280-day gestation from date of maternal delivery assumes full-term births and may affect our estimates for the antenatal period and time frame for trimesters. The measure for persistence depends on pharmacy claims data that do not necessarily reflect actual antidepressant medication use in pregnant women. We also assumed that a prescription filled was a prescription taken. Antidepressant therapy may have been discontinued by the prescriber for clinically appropriate reasons, such as potential adverse effects on maternal or newborn outcomes, lack of efficacy, or conversion to nonpharmacological treatments. The severity of each patient's depressive conditions could not be obtained from claims data, thus medication use behavior cannot be linked to clinical outcomes. In addition, we found 40% of the women used antidepressants in the year prior to pregnancy, but less than 20% had a diagnosis of depression. One possible reason for this finding may be because we identified our cohort with major depression by using the primary diagnoses and did not include secondary or tertiary diagnoses. This absence may have prevented us from capturing all the diagnoses for depression. Moreover, we did not identify off-label indications for antidepressant medication use. Finally, the study cohort consisted of pregnant women enrolled in South Carolina Medicaid, predominantly with moderate to low incomes. Although this population may represent many low income and insured women in the United States, different results may be found for other states or in a more affluent cohort.

Conclusions

Despite limitations, our findings suggest implications deserving further investigation for clinicians and other policymakers responsible for appropriate antidepressant medication use in pregnant women. Our study suggests that antidepressant medication persistence is as poor as that found in other populations and that racial disparities exist in low-income pregnant women. Previous research shows medication adherence as being associated with lower medical costs.[25,31,40] Thus, further studies are needed to assess the relationship between antidepressant medication persistence and health care utilization and costs in pregnant women. Such studies would provide evidence for policymakers and health care providers to optimize mental health benefits for pregnant women and further the development of effective interventions to achieve improved treatment outcomes and cost savings. Additional research is needed in larger populations, particularly with appropriate adherence-enhancing interventions, to fully explore associations between antidepressant pharmacotherapy persistence during pregnancy and the benefits and risks related to maternal and newborn outcomes. Selectively targeting high-risk pregnant women with depression, using known predisposing characteristics and a review of the woman's past medication use behaviors as a guide, may serve to identify women more prone to antidepressant medication treatment nonpersistence for gestational depression. Having a strategy to identify those at risk for subpar antidepressant medication use may help clinicians more effectively manage depression in low-income, insured pregnant women in practice settings.

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DISCLOSURES

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Study concept and data collection came mostly from Wu, with assistance from Davis-Ajami. Both authors contributed equally to interpretation, manuscript writing, and revision.

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