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Recent epidemiologic studies have found that most patients with mental illness are seen exclusively in primary care medicine. These patients often present with medically unexplained somatic symptoms and utilize at least twice as many health care visits as controls. There has been an exponential growth in studies in this interface between primary care and psychiatry in the last 10 years. This special section, edited by Jürgen Unutzer, M.D., will publish informative research articles that address primary care-psychiatric issues.

National trends in antidepressant medication treatment among publicly insured pregnant women ☆,☆☆

Krista F. Huybrechts, M.S., Ph.D. [a,*], Kristin Palmsten, M.S. [b], Helen Mogun, M.S. [a], Mary Kowal, B.A. [a], Jerry Avorn, M.D. [a], Soko Setoguchi-Iwata, M.D., Dr.PH. [c], Sonia Hernández-Díaz, M.D., Dr.PH. [b]

[a] Division of Pharmacoepidemiology and Pharmacoeconomics, Department of Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, MA 02120, USA
[b] Department of Epidemiology, Harvard School of Public Health, Boston, MA 02115, USA
[c] Duke University School of Medicine, Durham, NC 27708, USA

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ABSTRACT

Objective: The risk of depression in women is greatest at childbearing age. We sought to examine and explain national trends in antidepressant use in pregnant women.
Methods: This was a cohort study including pregnant women aged 12–55 who were enrolled in Medicaid during 2000–2007. We examined the proportion of women taking antidepressants during pregnancy by patient characteristics (descriptive), by region (mixed-effects model) and over time (interrupted time series).
Results: We identified 1,106,757 pregnancies in 47 states; mean age was 23 years, and 60% were nonwhite. Nearly 1 in 12 used an antidepressant during pregnancy. Use was higher for older (11.2% for age ≥30 vs. 7.6% for <30) and white (14.4% vs. 4.0% for nonwhite) women. There was a four- to fivefold difference in rate of antidepressant use among states. Of the 5.3% of women taking antidepressants at conception, 33% and 17% were still on treatment 90 and 180 days, respectively, into pregnancy; an additional 4% began use during pregnancy. Labeled pregnancy-related health advisories did not appear to affect antidepressant use.
Conclusions: Antidepressant use during pregnancy remains high in this population; treatment patterns vary substantially by patient characteristics and region. Comparative safety and effectiveness data to help inform treatment choices are needed in this setting.

1. Introduction

The lifetime risk of depression in women is 10%–25%, twice that in men [1]. The risk is greatest at childbearing age, with 10%–15% of all pregnant women displaying some signs of depression [2]. The strongest risk factor for depression during pregnancy is a history of prior depression [3,4]. Young, low-income mothers are particularly vulnerable [5]. Use of antidepressant medications in pregnant women has grown steadily over time [6–9].

Although the evidence is less impressive for treatment of mild depression, in patients with moderate to severe depression, antidepressants often improve symptoms and can reduce the risk of serious consequences associated with untreated depression for both the mother and her offspring [10]. Untreated depression during pregnancy has been linked to increased risk of self-injurious or suicidal behavior; it has also been reported to be associated with inadequate self-care and poor compliance with prenatal care, miscarriage or preterm birth, poor fetal growth, and impaired fetal and postnatal development [11–15], although findings are not consistent and many studies are inconclusive [16].

However, in recent years, there has been increasing concern about the safety of antidepressant use during pregnancy. The risks of several maternal complications, including gestational diabetes, preeclampsia, placental problems, premature rupture of the membranes, bleeding, induced delivery and the requirement for a cesarean section, have been reported to be increased among women taking antidepressants during pregnancy [17]. First-trimester exposure to certain selective serotonin reuptake inhibitors (SSRIs) has been associated with some specific birth defects [18–22], while SSRI use late in pregnancy has been associated with pulmonary hypertension of the newborn (PPHN) [23],

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* Corresponding author. Tel.: +1 617 278 0933; fax: +1 617 232 8602.
E-mail address: khuybrechts@partners.org (K.F. Huybrechts).

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prematurity [24–27], low birth weight [26,27], small size for gestational age [28] and various neonatal complications [24–26,29]. For several of these outcomes, however, the evidence supporting an association is mixed [16]. Moreover, since most studies did not assess the potential independent effects of medications and depression severity, it remains unclear to what extent such associations are due to biologic or behavioral factors intrinsic to women with mood disorders (such as smoking, substance abuse or poor diet), to medications used to treat the disorder or to a combination of both. Based on the available evidence, the US Food and Drug Administration (FDA) issued a public health advisory in December 2005 noting an increased risk of congenital malformations associated with first-trimester exposure to paroxetine. In July 2006, it issued a health advisory warning regarding exposure to any SSRI after the 20th week of gestation and an increased risk of PPHN. In addition to these pregnancy-specific advisories, the labels of all antidepressants include a black box warning indicating that they are associated with an increased risk of suicidality in children and adolescents (since 2004) and in young adults ages 18–24 (since 2007). When making recommendations for the management of depression during pregnancy, clinicians must weigh the potential risk of untreated or suboptimally treated depression against the potential risks associated with antidepressant exposure, including medical and obstetric adverse events, teratogenesis, neonatal toxicity and long-term neurobehavioral problems in the offspring.

The objective of our study was to document patterns of antidepressant medication use during pregnancy in a national cohort of Medicaid-enrolled women in the United States. In addition to examining variations in use by patient characteristics and geographic region, we sought to evaluate changes in patterns of use throughout pregnancy, as well as temporal trends in light of the various health advisory warnings. Low-income women are at higher risk for depression than women in higher-income groups [5], as well as for perinatal complications and morbidity in offspring, making this an important population to study.

2. Methods

2.1. Data source and study cohort

The study cohort was drawn from the Medicaid Analytic eXtract (MAX) for all US states (except Arizona) and Washington, DC, for 2000–2007. Medicaid — the joint state and federal health insurance program in the United States for low-income people — is the largest health insurance program and covers the medical expenses for more than 40% of births in the United States [30]. The MAX data set is available from the Centers for Medicare and Medicaid Services, and it contains individual-level demographic and Medicaid enrollment information, as well as health care utilization data including physician services and hospitalizations and their accompanying diagnoses and procedures, and all filled medication prescriptions.

Our study population consisted of a cohort of completed pregnancies and linked mothers and their infants [31]. We identified all completed pregnancies in women aged 12–55 years using *Current Procedural Terminology* and *International Classification of Diseases*, *Ninth Revision*, procedure codes for in- and outpatient deliveries. We then linked these pregnancies to live-born infants using the date of birth and the state-specific Medicaid case identification number, which is typically shared by family members. We estimated the date of last menstrual period (LMP) based on the delivery date combined with diagnostic codes indicative of preterm delivery using a previously validated algorithm [32]. Finally, we required all women who were successfully linked to an infant to be Medicaid eligible from 3 months before the estimated LMP (to ascertain preconception medication use) through 1 month postdelivery. To ensure a complete, longitudinal stream of health care claims throughout pregnancy, we excluded women with supplementary private insurance, women with restricted benefits and women in selected capitated managed care plans (Fig. 1).

2.2. Use of antidepressant medications

Maternal exposure to antidepressant medications was derived from pharmacy dispensing records. Antidepressant medications considered include SSRIs, serotonin–norepinephrine reuptake inhibitors (SNRIs), tricyclic antidepressants (TCAs) and others (e.g., monoaminase oxidase inhibitors, tetracyclic antidepressants). Exposure status on any given day was based on the dispensing date and number of days supply. We accumulated days supply for consecutive dispensings of the same medication if overlap occurred.

2.3. Data analyses

We analyzed patterns of antidepressant medication use by patient characteristics, by pregnancy stage and by state. To estimate

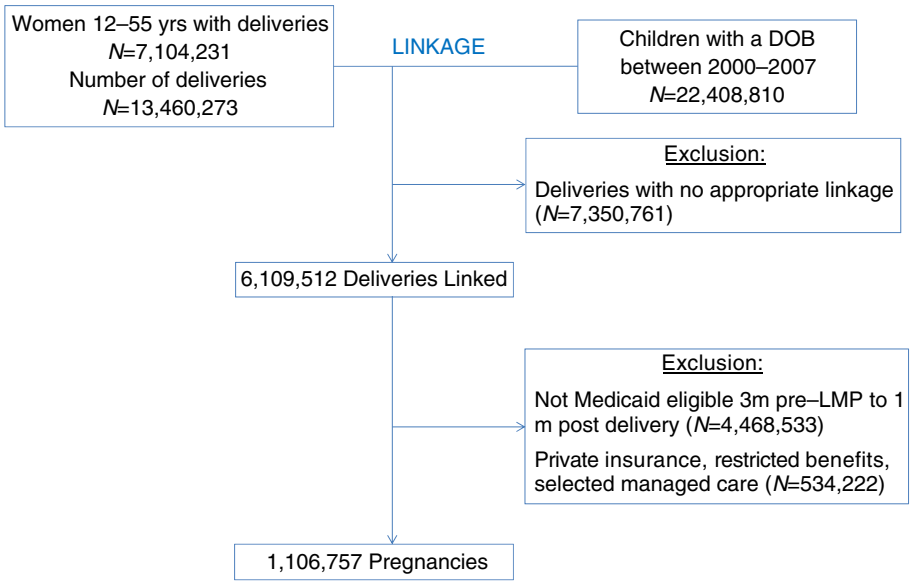

Fig. 1. Assembly of the study cohort. DOB: date of birth.