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 Evaluate patients' psychiatric history to identify women at increased risk for postpartum depression

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# as Risk Factors for **Postpartum Depression:**

A Nationwide Cohort Study

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#### **ABSTRACT**

**Objective:** To compare risk for postpartum depression across prior psychiatric diagnoses.

Methods: The deidentified Optum© Clinformatics Data Mart of national commercial insurance claims was used to identify 1,166,577 women of reproductive age with first-observed incidence of pregnancy across all 50 United States from 2003 to 2016. Women with insurance coverage for at least 6 months prior to conception and following delivery were eligible (n = 336,522). Psychiatric diagnoses prior to pregnancy were identified by ICD-9-CM and ICD-10-CM codes, including depression, anxiety and panic disorders, bipolar disorder, obsessive-compulsive disorder, posttraumatic stress disorder, and eating disorders. Primary outcomes included postpartum depression diagnosis at 2 months and 1 year after delivery. Multiple variable logistic regression analysis assessed for independent associations between predictors and outcomes.

Results: Among 336,522 pregnancies, 9.4% of women were diagnosed with postpartum depression (n = 31,610). Five percent of women with no depression history developed postpartum depression, compared to 65% of women with depression prior to and during pregnancy. Among women with history of depression who were euthymic during pregnancy, 20% were diagnosed with postpartum depression. A major risk factor was a history of depression (OR = 2.7; 95% CI, 2.6–2.8; P < .001), and depression in pregnancy was a risk factor for continued depression in the postpartum period (OR = 13.1; 95% CI, 12.6–13.6; P < .001). All other psychiatric conditions, including anxiety and panic disorders, bipolar disorder, obsessive-compulsive disorder, posttraumatic stress disorder, and eating disorders, conferred risk for postpartum depression, independent of a comorbid depression history.

Conclusions: We report that all psychiatric diagnoses investigated independently increase risk for postpartum depression and suggest that care providers inquire about psychiatric history to identify and closely monitor women at increased risk for postpartum depression.

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## It is illegal to post this copyrighted PDF on any website. Clinical Points

#### **Clinical Points**

- It is widely known that specific preexisting psychiatric diagnoses increase risk for postpartum depression, but the risks of past psychiatric diagnoses on postpartum depression risk have rarely been compared in large samples across diagnoses.
- In one of the largest nationwide US cohort analyses, we report that all psychiatric diagnoses investigated increase risk for postpartum depression independent of a comorbid depression history.
- Care providers should inquire into psychiatric history in early pregnancy in order to identify women at increased risk for postpartum depression who would benefit from careful observation in the perinatal period.

Perinatal depression is among the most common morbidities of the perinatal period, affecting 12%-13% of women. 1,2 Perinatal depression is defined as a major depressive episode occurring during pregnancy or up to 4 weeks postpartum<sup>3</sup>; however, in both research and clinical practice this definition variably extends to 3 months, 6 months, and 1 year postpartum. 4 The US Preventive Services Task Force, American College of Obstetricians and Gynecologists,<sup>5</sup> and American Academy of Pediatrics<sup>6</sup> recommend screening with a validated tool such as the Edinburgh Postnatal Depression Scale<sup>7</sup> during pregnancy and postpartum. Compared to usual care, universal depression screening leads to higher rates of diagnosis and treatment.8 High-risk women should be followed more closely than a simple one-time screen during the perinatal period permits, and defining pertinent risk factors is critical.

A recent study including over 5 million individuals showed that all mental disorders increase risk for all future mental disorders in the general population, but research on how this risk manifests in perinatal populations is lacking. Research shows that lifetime histories of depression, 10-13 postpartum depression, 14-16 anxiety, 17 bipolar disorder, 18 premenstrual dysphoric disorder, 16,19 and eating disorders 20,21 increase postpartum depression risk, but research to compare risk across multiple past psychiatric conditions in large samples is limited. One study compared relative contributions of past psychiatric conditions to postpartum depression risk in a majority black community in North Carolina. 17 In nationwide population-based studies that compare risk for postpartum depression across psychiatric conditions, reported results are inconsistent and limited by sample size. 22,23 A recently published study used a large Danish cohort to compare postpartum depression risk across psychiatric diagnoses in the maternal family psychiatric history but did not address the psychiatric history of the mothers themselves.<sup>24</sup> Another study examined the recurrence risk of postpartum depression but selected for women with no prior psychiatric history. 15 Thus, the existing evidence is inconclusive regarding the relative effect of past psychiatric conditions on postpartum depression risk.

multiple psychiatric diagnoses using one of the largest US cohorts, representing all 50 states in a dataset of over 300,000 pregnancies. Our primary outcomes are postpartum depression diagnosis at 2 months and 1 year after delivery. We identify prior psychiatric conditions that are risk factors for postpartum depression. This research suggests that providers should inquire about psychiatric history to support close monitoring of women at high risk for postpartum depression.

#### **METHODS**

This retrospective cohort study used commercial insurance claims data to identify predictors of postpartum depression. We identified 1,166,577 women of reproductive age (14 to 50 years) with a first-observed incidence of pregnancy ending in 1 or more live births between January 2003 and December 2016. "First-observed" refers to the first pregnancy with an insurance claim. From this cohort, 336,522 women with continuous insurance coverage for at least 6 months prior to conception and 6 months following delivery were eligible. Some period of continuous insurance was required, and although this method selects against women who lose insurance, 73% (n = 244,514) of the total cohort were still enrolled at 1 year postpartum. Multiple gestations in a single pregnancy were included. A total of 261,811 women with multiple separate pregnancies were excluded because this dataset cannot distinguish between postpartum depression and antepartum depression for women with another pregnancy in the first postpartum year. Sensitivity analysis indicated that results were not significantly different when multiple separate pregnancies were excluded from the cohort. Select individuals with insurance claims for delivery were excluded; 2,535 subjects were excluded due to male gender (n = 2,421) and unknown gender (n = 114), and 1,484 subjects were excluded due to maternal age outside the chosen period of reproductive potential (480 subjects ages 0 to 13 years; 1,004 subjects ages 51 to 88 years).

Institutional Review Board approval was obtained at Stanford University. All data were obtained from Optum© Clinformatics Data Mart, a deidentified database from a national insurance provider. We defined the pregnancy period by estimating conception at 39 weeks prior to delivery. Procedure codes corresponding to vaginal and cesarean delivery were selected using the International Classification of Disease, Clinical Modification, Ninth Revision (ICD-9-CM) and Tenth Revision (ICD-10-CM, effective October 1, 2015), as noted in Table 1.

The primary outcomes were depression diagnosis at 2 months and 1 year postpartum (Table 1). The 2-month time point was chosen to maximize specificity for early postpartum onset, while leaving sufficient time for a depression diagnosis to be recorded, since most postpartum women do not receive medical attention until the 6-week postpartum visit. The 1-year time point was chosen to maximize sensitivity for

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#### Table 1. ICD-9-CM and ICD-10-CM Codes Used to Define Diagnoses in Insurance Claims Data

Diagnosis	ICD-9-CM Codes	ICD-10-CM Codes
Vaginal delivery	72.0–72.9, 73.22, 73.5	10E0
Cesarean delivery	74.0–74.2, 74.4, 74.99	10D0
Depression	296.20–296.25, 296.30–296.35, 296.82, 300.4, 309.0, 309.1, 309.28, 311, 648.4	F32.0-F32.4, F32.9, F33.0-F33.41, F33.9, F32.89, F34.1, F43.21, F43.23, F53
Hyperemesis gravidarum	643.0-643.2	021.0-021.2
Gestational diabetes	648.8	024.41, 024.42
Gestational hypertension	642.3	013.1-013.4, 013.9
Preeclampsia	642.4, 642.5	014.00-014.04, 014.10-014.14, 014.20-014.24, 014.90-014.94
Eclampsia	642.6	O15.0, O15.1, O15.9
Postpartum hemorrhage	666.0–666.2	072.0-072.2
Anxiety disorders	300.00, 300.02, 300.20, 300.22, 300.23, 300.29, 309.21, 309.24	F40.0–F40.9, F41.1–F41.9, F43.22
Panic disorders	300.01, 300.21	F40.01, F41.0
Bipolar disorder	296.00–296.06, 296.10–296.16, 296.40–296.46, 296.50–296.56, 296.60–296.66, 296.7, 296.80, 296.89	F31.0, F31.10–F31.13, F31.2, F31.30–F31.32, F31.4, F31.5, F31.60–F31.64, F31.70–F31.78, F31.81, F31.89, F31.9, F30.10–F30.13, F30.2–F30.4, F30.8, F30.9
OCD	300.3	F42.2-F42.9
PTSD	309.81	F43.1
Eating disorders	300.7, 307.1, 307.50, 307.51	F45.22, F50.0-F50.9

Abbreviations: ICD-9-CM and ICD-10-CM = International Classification of Diseases, Clinical Modification, Ninth Revision and Tenth Revision (effective October 1, 2015), OCD = obsessive-compulsive disorder, PTSD = posttraumatic stress disorder.

detection of individuals who do not present until later in the postpartum course, as is often the case in postpartum depression.<sup>25,26</sup>

Using previously established methods,<sup>27</sup> for diagnoses billed under "Mental Disorders Specific to Pregnancy," which encompasses multiple disorders, the diagnosis qualified as depression if an antidepressant medication was filled within 30 days of diagnosis. Recognizing the limitation that antidepressant medications can have multiple indications, we did not use medications to define depression for billing codes that specifically refer to a depression diagnosis.

We assessed postpartum antidepressant treatment, defined by at least 1 medication dispensed in pharmacy claims data. Antidepressant medications included selective serotonin reuptake inhibitors (SSRIs; citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, sertraline), tricyclics (amitriptyline, clomipramine, desipramine, doxepin, imipramine, and nortriptyline), monoamine oxidase inhibitors (isocarboxazid, phenelzine, selegiline, tranylcypromine), and others (bupropion, mirtazapine, nefazodone, trazodone, venlafaxine).

Predictors were analyzed for associations with outcomes, including demographic and socioeconomic variables, obstetric complications, and psychiatric diagnoses prior to pregnancy, including depression, anxiety disorders, panic disorders, bipolar disorder, obsessive-compulsive disorder (OCD), posttraumatic stress disorder (PTSD), and eating disorders (Table 1). Psychiatric diagnoses were identified over a 10-year period prior to estimated conception, selected based on analyses indicating that 10 years captured the entirety of an individual's coverage period through Optum for the majority of individuals.

The total sample size in all statistical analyses was consistent (n = 336,522). In the cohort of 335,522 unique pregnancies, no imputation was required for the primary outcomes of postpartum depression diagnosis at 2 months and 1 year postpartum. Select individuals had missing

data in socioeconomic predictors and were included with "response unknown" in analysis; therefore, counts and percentages for socioeconomic predictors may not sum to the total N and 100% (Table 2).

We used multiple variable logistic regression analysis to assess for independent associations between predictors and primary outcomes. Due to extensive comorbidity among variables in psychiatric history and tested outcomes, in which of the 31,610 individuals diagnosed with postpartum depression, 60.2% had a history of at least 1 additional psychiatric diagnosis, we did not correct for multiple hypotheses. Sensitivity analysis was used to evaluate the effect of variables for cohort selection on outcomes. Reference groups were chosen based on the group at lowest risk for postpartum depression, considering adequate sample size. Results of logistic regression analysis were reported as odds ratios with 95% confidence intervals (CI) and level of significance at  $\alpha$  = .05.

#### **RESULTS**

## Prevalence of Postpartum Depression and Past Psychiatric Conditions

The majority of women in the study were white (62.5%), were between the ages of 31–40 years (51.2%), and had obtained some college education (51.0%; Table 2). Among the 336,522 pregnancies, 9.4% of women received a depression diagnosis in the first postpartum year (n = 31,610; Table 3). This prevalence was stable throughout the study period from 2003 to 2016. The first 2 months postpartum represented the period of highest risk. Of the 31,610 women diagnosed with postpartum depression, 41.7% (n = 13,178) presented within the first 2 months (Table 3).

Among women with depression, 47.2% were diagnosed with "mental disorders specific to pregnancy" (n = 14,927), 46.8% with "depressive disorder NOS" (n = 14,806), 21.1% with "major depression" (n = 6,685), 11.3% with "dysthymic

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Table 2. Prevalence and Odds Ratios of Demographics, Socioeconomic Variables, and Obstetric Complications as Predictors of Postpartum Depression Diagnosis Among the Total Sample (n = 336,522)<sup>a</sup>

	No PPD	PPD	PPD Diagnosis 1 Year Postpartum		
	(n=304,912),	(n=31,610),	UOR	AOR <sup>d</sup>	
Characteristic	% (n)	% (n)	(95% CI)	(95% CI)	
Maternal age at birth					
14–20 y	88.5 (13,232)	11.5 (1,715)	1.32*** (1.25-1.39)	1.08** (1.01-1.15)	
21–30 y	91.0 (124,437)	9.0 (12,241)	Reference	Reference	
31–40 y	90.5 (156,032)	9.5 (16,347)	1.07*** (1.04-1.09)	0.97 (0.94-1.00)	
41–50 y	89.6 (11,211)	10.4 (1,307)	1.19*** (1.12-1.26)	0.95 (0.88-1.01)	
Race					
White	89.0 (187,046)	11.0 (23,181)	3.39*** (3.17-3.63)	2.26*** (2.10-2.43)	
Asian	96.5 (25,146)	3.5 (918)	Reference	Reference	
Black	92.4 (31,398)	7.6 (2,592)	2.26*** (2.09-2.44)	1.70*** (1.56-1.85)	
Hispanic	93.0 (39,550)	7.0 (2,965)	2.05*** (1.90-2.22)	1.61*** (1.48-1.75)	
Education					
Less than 12th grade	95.0 (2,050)	5.0 (107)	0.56*** (0.46-0.68)	0.76** (0.61-0.94)	
High school diploma	90.8 (70,941)	9.2 (7,193)	1.08*** (1.05-1.12)	1.05 (1.00-1.10)	
Less than bachelor degree	90.0 (154,397)	10.0 (17,169)	1.19*** (1.15-1.23)	1.09*** (1.05-1.13)	
Bachelor degree plus	91.4 (68,208)	8.6 (6,378)	Reference	Reference	
Occupation					
White collar <sup>e</sup>	89.6 (12,718)	10.4 (1,478)	1.11* (1.01-1.21)	1.10 (0.99-1.22)	
Blue collar	89.4 (4,471)	10.6 (532)	1.13* (1.01–1.27)	1.08 (0.94–1.23)	
Not in labor force <sup>f</sup>	88.2 (7,364)	11.8 (989)	1.28*** (1.16-1.41)	1.17*** (1.04-1.31)	
Manager/owner/professional	90.5 (7,492)	9.5 (786)	Reference	Reference	
Income	. , ,	, ,			
<\$40,000	89.9 (30,348)	10.1 (3,425)	1.11*** (1.06-1.16)	1.12*** (1.05-1.19)	
\$40,000-\$49,000	89.7 (14,476)	10.3 (1,664)	1.13*** (1.07–1.19)	1.07 (1.00–1.15)	
\$50,000-\$59,000	89.8 (15,504)	10.2 (1,752)	1.11*** (1.05–1.17)	1.04 (0.97–1.11)	
\$60,000-\$74,000	89.9 (23,002)	10.1 (2,596)	1.11*** (1.06–1.16)	1.06 (1.00–1.12)	
\$75,000-\$99,000	90.2 (34,326)	9.8 (3,750)	1.07*** (1.03-1.12)	1.01 (0.97–1.07)	
\$100,000+	90.8 (83,328)	9.2 (8,487)	Reference	Reference	
Hyperemesis gravidarum					
Yes	85.5 (15,534)	14.5 (2,627)	1.69*** (1.62-1.76)	1.32*** (1.25-1.38)	
No	90.9 (289,378)	9.1 (28,983)			
Gestational diabetes					
Yes	89.9 (47,222)	10.1 (5,330)	1.11*** (1.07-1.14)	1.07*** (1.03-1.11)	
No	90.7 (257,690)	9.3 (26,280)			
Gestational hypertension					
Yes	88.0 (26,444)	12.0 (3,591)	1.35*** (1.30-1.40)	1.14*** (1.09-1.19)	
No	90.9 (278,468)	9.1 (28,019)			
Preeclampsia					
Yes	88.3 (20,061)	11.7 (2,664)	1.31*** (1.25-1.36)	1.06** (1.01-1.12)	
No	90.8 (284,851)	9.2 (28,946)			
Eclampsia					
Yes	88.6 (621)	11.4 (80)	1.24 (0.98-1.57)	1.06 (0.81-1.38)	
No	90.6 (304,291)	9.4 (31,530)			
Cesarean delivery					
Yes	89.9 (127,441)	10.1 (14,239)	1.14*** (1.12-1.17)	1.12*** (1.09-1.15)	
No	91.1 (177,471)	8.9 (17,371)			
Postpartum hemorrhage					
Yes	89.0 (7,908)	11.0 (977)	1.20*** (1.12-1.28)	1.11** (1.02-1.20)	
No	90.7 (297,004)	9.3 (30,633)			

<sup>&</sup>lt;sup>a</sup>Counts and percentages may not sum to the total N and 100% due to unknown records in select socioeconomic variables, including race, region, education, occupation, and income.

disorder" (n = 3,565), 11.1% with "adjustment disorder with mixed anxiety and depressed mood" (n = 3,511), and 5.3% with "adjustment disorder with depressed mood or prolonged depressive reaction" (n = 1,686).

Postpartum depression prevalence varied depending on depression history (Table 4). Women with any previous history of depression accounted for 53.6% of cases of postpartum depression. Of the 31,610 women with postpartum depression, 60.2% had a history of at least 1 additional psychiatric diagnosis. Among the total cohort, 11.7% (39,235) had a prior diagnosis of depression, 9.4% (31,624) with an anxiety disorder, 1.4% (4,632) with panic

<sup>&</sup>lt;sup>b</sup>P values: \*P<.05, \*\*P<.01, \*\*\*P<.001; level of significance, α=0.05.

<sup>&</sup>lt;sup>c</sup>Reference groups were selected based on lowest prevalence of postpartum depression, taking into account adequate sample size.

<sup>&</sup>lt;sup>d</sup>Odds ratios were adjusted for variables: depression during pregnancy and any 10-year history of psychiatric diagnosis including depression, anxiety, panic, bipolar disorder, obsessive-compulsive disorder, posttraumatic stress disorder, and eating disorders.

elncludes occupations in health, civil service, and the military.

fincludes women who self-reported either "homemaker" or "retired" for their occupation.

Abbreviations: AOR = adjusted odds ratio, PPD = postpartum depression, UOR = unadjusted odds ratio.

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Table 3. Prevalence and Adjusted Odds Ratios of Prior Psychiatric Diagnoses as Predictors of Postpartum Depression Diagnosis Among the Total Sample (N = 366,522), Comparing Outcomes in the Early and Late Postpartum Periods

	2 Months Postpartum			1 Year Postpartum				
	No PPD PPD F		PPD Dia	PD Diagnosis <sup>a</sup> No		No PPD PPD	PPD Diagnosis <sup>a</sup>	
	(n=323,344), % (n)	(n=13,178), % (n)	UOR (95% CI)	AOR <sup>b</sup> (95% CI)	(n=304,912), % (n)	(n=31,610), % (n)	UOR (95% CI)	AOR <sup>b</sup> (95% CI)
<u> </u>	70 (11)	70 (11)	(93% CI)	(93% CI)	70 (11)	70 (11)	(93% CI)	(93% CI)
Prior depression	00 = (00 111)	4=0 (4=04)	0 = 4 1/1 1/1 1/1	4 = 0 11 11 11	(0	224 (42.224)	- a a shahah	0 = 0 1/4 1/4 1/4
Yes	82.7 (32,441)	17.3 (6,794)	9.54***	1.70***	66.9 (26,241)	33.1 (12,994)	7.41***	2.70***
No	97.8 (290,903)	2.2 (6,384)	(9.21–9.89)	(1.61–1.79)	93.7 (278,671)	6.3 (18,616)	(7.22-7.61)	(2.61-2.79)
Depression in pregnancy								
Yes	54.1 (9,858)	45.9 (8,350)	55.0***	34.64***	37.9 (6,903)	62.1 (11,305)	24.0***	13.1***
No	98.5 (313,486)	1.5 (4,828)	(52.8-57.3)	(33.0-36.3)	93.6 (298,009)	6.4 (20,305)	(23.3-24.8)	(12.6-13.6)
Anxiety disorder								
Yes	86.9 (27,472)	13.1 (4,152)	4.95***	1.59***	74.0 (23,416)	26.0 (8,208)	4.22***	1.76***
No	97.0 (295,872)	3.0 (9,026)	(4.77 - 5.15)	(1.51-1.68)	92.3 (281,496)	7.7 (23,402)	(4.10 - 4.34)	(1.70 - 1.83)
Panic disorder								
Yes	82.6 (3,828)	17.4 (804)	5.42***	1.27***	68.6 (3,177)	31.4 (1,455)	4.58***	1.28***
No	96.3 (319,516)	3.7 (12,374)	(5.02-5.86)	(1.14 - 1.41)	90.9 (301,735)	9.1 (30,155)	(4.30 - 4.88)	(1.18 - 1.39)
Bipolar disorder								
Yes	80.2 (2,693)	19.8 (666)	6.34***	1.46***	66.9 (2,247)	33.1 (1,112)	4.91***	1.23***
No	96.2 (320,651)	3.8 (12,512)	(5.81-6.91)	(1.30-1.65)	90.8 (302,665)	9. 2 (30,498)	(4.57 - 5.28)	(1.12 - 1.34)
OCD	, , ,	. , ,	,	,	, , ,	, , ,	,	,
Yes	76.4 (923)	23.6 (285)	7.72***	1.76***	64.1 (774)	35.9 (434)	5.47***	1.36***
No	96.2 (322,421)	3.8 (12,893)	(6.75-8.83)	(1.46-2.12)	90.7 (304,138)	9.3 (31,176)	(4.86-6.16)	(1.17-1.58)
PTSD		(:=,:::)	(=====	(,	( , ,	712 (21)112)	( ,	(
Yes	77.9 (1,362)	22.1 (386)	7.13***	1.18**	63.4 (1,109)	36.6 (639)	5.65***	1.17**
No	96.2 (321,982)	3.8 (12,792)	(6.36–8.00)	(1.01–1.38)	90.7 (303,803)	9.3 (30,971)	(5.12–6.23)	(1.03–1.32)
Eating disorder	2 3.2 (32 . /202)	(,, )-)	(2.50 0.50)	(	(555,565)	2.0 (00,271)	(=::2 3:23)	(1.00 1.02)
Yes	79.2 (805)	20.8 (212)	6.55***	1.25**	64.5 (656)	35.5 (361)	5.36***	1.27***
No	96.1 (322,539)	3.9 (12,966)	(5.63–7.63)	(1.02–1.54)	90.7 (304,256)	9.3 (31,249)	(4.71–6.10)	(1.08–1.50)

 $<sup>^{</sup>a}$ P values: \*P<.05, \*\*P<.01, \*\*\*P<.001; level of significance α = 0.05.

Table 4. Prevalence of Postpartum Depression Given Depression History Prior to and During Pregnancy

Prior Depression	Depression in Pregnancy	Proportion of Total, % (n) <sup>a</sup>	PPD Diagnosis, % (n) <sup>b</sup>
+	+	3.4 (11,312)	65.0 (7,355)
+	_	8.3 (27,923)	20.2 (5,639)
_	+	2.0 (6,896)	57.3 (3,950)
_	_	86.3 (290,391)	5.1 (14,666)

<sup>&</sup>lt;sup>a</sup>Proportion of women among the total sample (n=336,522) with the depression history prior to and during pregnancy as defined in columns 1 and 2.

Abbreviation: PPD = postpartum depression.

Symbols: += depression, -= no depression.

disorder, 1.0% (3,359) with bipolar disorder, 0.4% (1,208) with OCD, 0.5% (1,748) with PTSD, and 0.3% (1,017) with an eating disorder.

#### **Prevalence of Antepartum and Postpartum Treatment**

Sixty-seven percent of women with postpartum depression received antidepressant medication in the first postpartum year (n=21,176). The majority received SSRIs (82.7%, n=17,518), most commonly sertraline (n=8,614) and escitalopram (n=3,206). Of the 18,208 women with depression during pregnancy, 46.7% received antidepressant treatment during pregnancy (n=8,509). Seventy-four percent (n=6,297) received treatment with SSRIs, most commonly sertraline (n=2,679) and fluoxetine (n=1,327).

#### **Risk Factors for Postpartum Depression**

History of depression conferred the greatest increase in postpartum depression risk in the first postpartum year (OR = 2.7; 95% CI, 2.61-2.79; P < .001; Table 3). Depression during pregnancy was a risk factor for continued depression postpartum (OR = 13.1; 95% CI, 12.6-13.6; P<.001). All other psychiatric diagnoses increased postpartum depression risk at both 2 months and 1 year postpartum, although adjustment for comorbid depression reduced all odds ratios for nondepressive psychiatric illnesses to 1.7 or less (Table 5; crude odds ratios are presented in Table 3). Among nondepressive psychiatric illnesses, anxiety carried the greatest risk for postpartum depression at 1 year postpartum (adjusted odds ratio [AOR] = 1.8; 95% CI, 1.70–1.83; P<.001; Table 5), and PTSD, the least risk (AOR = 1.2; 95% CI, 1.03–1.32; *P*<.01; Table 5). Changing the definition of the postpartum period (2 months versus 1 year) did not have any systematic effect on AORs for the various psychiatric disorders, with the exception of depression during pregnancy, which was associated with greater risk of continuation of the antenatal depression episode in early postpartum (AOR = 34.6; 95% CI, 33.0–36.3; *P*<.001; Table 5).

Our results affirm previous findings that younger women, women not in the labor force, and women in the lowest income bracket are at increased risk for postpartum depression. Additionally, all obstetric disorders except eclampsia were associated with small but measurable

bOdds ratios were adjusted for variables: age, race, region, education, occupation, income, and obstetric complications.

Abbreviations: AOR = adjusted odds ratio, OCD = obsessive-compulsive disorder, PPD = postpartum depression, PTSD = posttraumatic stress disorder, UOR = unadjusted odds ratio.

<sup>&</sup>lt;sup>b</sup>Proportion of women with the depression history defined in column 3 diagnosed with postpartum depression.

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Table 5. Impact of Depression History on the Adjusted Odds Ratios of Nondepression Psychiatric Diagnoses in the Early and Late Postpartum Periods

	2 Months Postpartum PPD Diagnosis		1 Year Postpartum PPD Diagnosis		
	Unadjusted	Adjusted	Unadjusted	Adjusted	
	for Depression	for Depression	for Depression	for Depression	
	AOR <sup>a</sup> (95% CI)	AOR (95% CI)	AOR (95% CI)	AOR (95% CI)	
Prior depression	•••	1.70*** (1.61-1.79)	•••	2.70*** (2.61-2.79)	
Depression in pregnancy	•••	34.6*** (33.0-36.3)	•••	13.1*** (12.63-13.59)	
Anxiety disorders	3.63*** (3.48-3.79)	1.59*** (1.51-1.68)	3.34*** (3.23-3.44)	1.76*** (1.70-1.83)	
Panic disorders	1.76*** (1.61-1.92)	1.27*** (1.14-1.41)	1.73*** (1.62-1.86)	1.28*** (1.18-1.39)	
Bipolar disorder	2.57*** (2.33-2.83)	1.46*** (1.30-1.65)	2.25*** (2.07-2.44)	1.23*** (1.12-1.34)	
OCD	2.61*** (2.25-3.03)	1.76*** (1.46-2.12)	2.12*** (1.87-2.42)	1.36*** (1.17-1.58)	
PTSD	2.41*** (2.12-2.74)	1.18** (1.01-1.38)	2.33*** (2.09-2.60)	1.17** (1.03-1.32)	
Eating disorders	2.33*** (1.97-2.76)	1.25** (1.02-1.54)	2.35*** (2.04-2.71)	1.27*** (1.08-1.50)	

<sup>&</sup>lt;sup>a</sup>Odds ratios were adjusted for variables: age, race, region, education, occupation, income, and obstetric complications.

increases in risk for postpartum depression, with adjusted ORs typically around 1.1 (Table 2).

#### **DISCUSSION**

Four major results highlight the importance of inquiring about past psychiatric history to support careful observation of high-risk women during pregnancy: (1) prevalence of postpartum depression varies significantly depending on depression history; (2) history of depression confers the greatest risk for postpartum depression, and prior psychiatric conditions including anxiety disorders, panic disorders, bipolar disorder, OCD, PTSD, and eating disorders are all significantly positively associated with postpartum depression even after controlling for comorbid depression; (3) postpartum depression diagnoses are concentrated in the first 2 months after delivery compared to later in the postpartum year, particularly among women with prior psychiatric conditions; and (4) a high proportion of women with depression during pregnancy and postpartum do not receive pharmacotherapy.

The overall mean prevalence of 9.4% that we report is consistent with literature on postpartum depression prevalence<sup>1,2,28</sup>; however, our data indicate that this prevalence varies depending on depression history. Only 5% of women with no depression before or during pregnancy developed postpartum depression, compared to 65% of women with depression prior to and during pregnancy. Even among women with a history of depression who were euthymic during pregnancy, 20% developed postpartum depression. These data emphasize that prior depression is a major risk factor for postpartum depression, and women with depression during pregnancy are at high risk for continued depression in the postpartum period.

While prior depression is a known risk factor for postpartum depression, <sup>11</sup> population-based studies that examine risk across multiple psychiatric diagnoses are limited by sample size and conflicting evidence. <sup>22,23</sup> In this study, all psychiatric conditions investigated, including anxiety

disorders, panic disorders, bipolar disorder, OCD, PTSD, and eating disorders, increased postpartum depression risk. While much of their effect is explained by comorbid depression, all of these conditions conferred a significant increase in postpartum depression risk even when adjusting for depression prior to and during pregnancy. Of note, in presenting adjusted odds ratios, we included variables that are causally related to depression, thus diluting the strength of the observed association. For clinicians selecting high-risk patients for monitoring, unadjusted odds ratios are likely the most accurate guide to overall risk assessment.

We identified the early postpartum as the period of greatest risk for onset of depression, as approximately half of the women who developed depression within 1 year of delivery presented within the first 2 months. While our dataset did not allow us to distinguish time of depression onset from time of recorded diagnosis, our comparison of the 2-month and 1-year prevalence does confirm that early postpartum is a period of elevated risk for clinical depression. The American Psychiatric Association recommends depression screening in early pregnancy for a range of preexisting psychiatric disorders. Our research supports this recommendation to allow for careful observation of high-risk women during the perinatal period.

Furthermore, women with prior psychiatric conditions were more likely to present in the early postpartum; for all prior psychiatric conditions, between one-half and two-thirds of women who developed postpartum depression presented in the first 2 months, compared to one-third of women without a psychiatric history who presented in the early postpartum. While prospective longitudinal data suggest that depression is greatest in the first few months postpartum, <sup>2,30</sup> this effect may be due to increased familiarity with the mental health care system in women with prior psychiatric diagnoses compared to women without psychiatric history. Maternal lack of knowledge about postpartum depression and inability to disclose feelings to health professionals are identified across studies as major barriers to seeking care. <sup>25</sup> These barriers may be diminished in women with experience

P values: \*P < .05, \*\*P < .01, \*\*\*P < .001; level of significance  $\alpha = 0.05$ .

Abbreviations: AOR = adjusted odds ratio, OCD = obsessive-compulsive disorder, PPD = postpartum depression,

PTSD = posttraumatic stress disorder.

recognizing depression symptoms as pathological. These data suggest that women with prior psychiatric history should be closely followed during the early postpartum period.

Pharmacologic treatment of depression for women diagnosed during pregnancy and postpartum was low with only 46.7% and 67.0% of depressed women receiving antidepressant treatment during pregnancy and postpartum, respectively; however, these results are consistent with treatment rates in other claims studies.<sup>27,31</sup> We did not have data on psychotherapeutic treatment. The US Preventive Services Task Force recommends counseling interventions, including cognitive behavioral therapy and interpersonal therapy, to prevent perinatal depression.<sup>32</sup> Survey data indicate that 55% of women prefer treatment with a combination of medications and counseling, compared to counseling alone (22%) and no treatment (8%).<sup>33</sup> Treatment involves careful risk-benefit analysis, particularly during pregnancy.<sup>34</sup>

All 336,522 pregnancies represent the first observed incidence of pregnancy per woman between 2003 and 2016. Prior births that occurred without Optum insurance would not be captured. As postpartum depression is a recurrent disorder, this is an important limitation. Additionally, these data are representative of commercially insured individuals. A database that included publicly insured and uninsured individuals may yield different baseline rates.

The 9.4% prevalence that we report is less than the 12%-13% prevalence documented in the literature. 1,2 Compared to clinical interview, the inexactness of chart diagnoses, which limits inclusion to individuals with formally recorded diagnoses, and pharmacy logs, in which antidepressants may be prescribed for alternative indications, is a limitation inherent to claims data that rely on provider billing. Psychiatric diagnoses may be underreported either because providers hesitate to document for fear of stigma or difficulty obtaining insurance coverage or because psychiatric care may be sought outside of insurance entirely. Only half of practicing psychiatrists in the United States accept insurance,<sup>35</sup> and prior to the passage of the Mental Health Parity and Addiction Equity Act in 2008, psychiatric care was often not covered or covered minimally under insurance. Thus, our numbers are an underrepresentation of the true prevalence of mental illness in our study population.

We attempted to address this limitation by including a range of depression diagnoses, including nonparity diagnoses which some providers may have preferred prior to 2010, when preexisting condition clauses for privately purchased health insurance were outlawed by passage of the Patient Protection and Affordable Care Act. Overall, these methods allow us to capture a broad range of mild to severe depression requiring treatment. The issue of treatment-seeking versus treatment-capture should be relatively constant across psychiatric diagnoses, so it is less likely to bias our analysis of psychiatric conditions as risk factors for postpartum depression.

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Some period of continuous insurance was required to adequately assess the maternal course, but this method selects against women who lose insurance. Variability in insurance coverage duration introduces additional underestimation into our assessment of psychiatric history. The 10-year period for identifying prior psychiatric diagnoses was selected because this period encompassed the entirety of an individual's coverage period for the majority of individuals. Most women did not have Optum insurance coverage for longer than 5 years, and women with previously existing psychiatric diagnoses who were not insured through Optum at the time of diagnosis would not be identified in our data, which biases our data toward underrepresenting the true prevalence of preexisting psychiatric illness. Nonetheless, this underestimation of the true population prevalence should not introduce systematic error into determination of risks conferred by preexisting mental illness, which is the focus of this article.

#### **Future Directions**

Given the many limitations of claims-based datasets, prospectively designed studies are needed. In addition, although recent years have brought extensive calls for increased monitoring of mental health in perinatal women, our understanding of what resources are offered or accepted by screen-positive women, and what benefits are conferred by these interventions, remains unclear. Future studies are needed to identify the most effective interventions for women with postpartum depression. In particular, improved understanding of how women with and without prior psychiatric diagnoses are able to navigate psychiatric care would help improve the provision of perinatal mental health care overall.

#### CONCLUSIONS

These data suggest that care providers should inquire about psychiatric history and carefully follow women with prior psychiatric history throughout the perinatal period.

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- Woody CA, Ferrari AJ, Siskind DJ, et al. A systematic review and meta-regression of the prevalence and incidence of perinatal depression. J Affect Disord. 2017;219:86–92.
- Gavin NI, Gaynes BN, Lohr KN, et al. Perinatal depression: a systematic review of prevalence and incidence. *Obstet Gynecol*. 2005;106(5 pt 1):1071–1083.
- American Psychiatric Association. Diagnostic and Statistical Manual for Mental Disorders. Fifth Edition. Washington, DC: American Psychiatric Association: 2013.
- Stewart DE, Vigod S. Postpartum depression. N Engl J Med. 2016;375(22):2177–2186.
- Committee on Obstetric Practice. The American College of Obstetricians and Gynecologists Committee Opinion No. 630: screening for perinatal depression. Obstet Gynecol. 2015;125(5):1268–1271.
- Earls MF; Committee on Psychosocial Aspects of Child and Family Health American Academy of Pediatrics. Incorporating recognition and management of perinatal and postpartum depression into pediatric practice. *Pediatrics*. 2010;126(5):1032–1039.
- Cox JL, Holden JM, Sagovsky R. Detection of postnatal depression: development of the 10-item Edinburgh Postnatal Depression Scale. Br J Psychiatry. 1987;150(6):782–786.
- Yawn BP, Dietrich AJ, Wollan P, et al; TRIPPD practices. TRIPPD: a practice-based network effectiveness study of postpartum depression screening and management. Ann Fam Med. 2012;10(4):320–329.
- Plana-Ripoll O, Pedersen CB, Holtz Y, et al. Exploring comorbidity within mental disorders among a Danish national population. *JAMA Psychiatry*. 2019;76(3):259–270.
- Howard LM, Molyneaux E, Dennis CL, et al. Non-psychotic mental disorders in the perinatal period. *Lancet*. 2014;384(9956):1775–1788.
- Guintivano J, Manuck T, Meltzer-Brody S. Predictors of postpartum depression: a comprehensive review of the last decade of evidence. Clin Obstet Gynecol. 2018;61(3):591–603.
- Suri R, Stowe ZN, Cohen LS, et al. Prospective longitudinal study of predictors of postpartum-onset depression in women with a history of major depressive disorder. J Clin Psychiatry. 2017;78(8):1110–1116.
- 13. Witt WP, Wisk LE, Cheng ER, et al. Poor prepregnancy and antepartum mental health predicts postpartum mental health problems

- population-based study. *Womens Health Issues*. 2011;21(4):304–313.
- Dennis CL, Brown HK, Wanigaratne S, et al. Determinants of comorbid depression and anxiety postnatally: a longitudinal cohort study of Chinese-Canadian women. J Affect Disord. 2018:227:24–30.
- Rasmussen MH, Strøm M, Wohlfahrt J, et al. Risk, treatment duration, and recurrence risk of postpartum affective disorder in women with no prior psychiatric history: a population-based cohort study. PLoS Med. 2017;14(9):e1002392.
- Turkcapar AF, Kadıoğlu N, Aslan E, et al. Sociodemographic and clinical features of postpartum depression among Turkish women: a prospective study. BMC Pregnancy Childbirth. 2015;15(1):108–115.
- Guintivano J, Sullivan PF, Stuebe AM, et al. Adverse life events, psychiatric history, and biological predictors of postpartum depression in an ethnically diverse sample of postpartum women. *Psychol Med.* 2018;48(7):1190–1200.
- Viguera AC, Tondo L, Koukopoulos AE, et al. Episodes of mood disorders in 2,252 pregnancies and postpartum periods. Am J Psychiatry. 2011;168(11):1179–1185.
- Bloch M, Rotenberg N, Koren D, et al. Risk factors for early postpartum depressive symptoms. Gen Hosp Psychiatry. 2006;28(1):3–8.
- Meltzer-Brody S, Zerwas S, Leserman J, et al. Eating disorders and trauma history in women with perinatal depression. J Womens Health (Larchmt). 2011;20(6):863–870.
- Micali N, Simonoff E, Treasure J. Pregnancy and post-partum depression and anxiety in a longitudinal general population cohort: the effect of eating disorders and past depression. J Affect Disord. 2011;131(1–3):150–157.
- 22. Tebeka S, Strat YL, Dubertret C. Developmental trajectories of pregnant and postpartum depression in an epidemiologic survey. *J Affect Disord*. 2016;203:62–68.
- Le Strat Y, Dubertret C, Le Foll B. Prevalence and correlates of major depressive episode in pregnant and postpartum women in the United States. J Affect Disord. 2011;135(1–3):128–138.
- Bauer AE, Maegbaek ML, Liu X, et al. Familiality of psychiatric disorders and risk of postpartum psychiatric episodes: a population-based cohort study. Am J Psychiatry. 2018;175(8):783–791.
- Dennis CL, Chung-Lee L. Postpartum depression help-seeking barriers and maternal treatment preferences: a qualitative systematic review. *Birth.* 2006;33(4):323–331.
- 26. Sword W, Busser D, Ganann R, et al. Women's

- postpartum depression. *Qual Health Res.* 2008;18(9):1161–1173.
- 27. Dietz PM, Williams SB, Callaghan WM, et al. Clinically identified maternal depression before, during, and after pregnancies ending in live births. *Am J Psychiatry*. 2007;164(10):1515–1520.
- Wisner KL, Sit DK, McShea MC, et al. Onset timing, thoughts of self-harm, and diagnoses in postpartum women with screen-positive depression findings. *JAMA Psychiatry*. 2013;70(5):490–498.
- Position Statement on Screening and Treatment of Mood and Anxiety Disorders During Pregnancy and Postpartum. American Psychiatric Association website. http://www. psychiatry.org/File%20Library/About-APA/ Organization-Documents-Policies/Policies/ Position-Screening-and-Treatment-Mood-Anxiety-Disorders-During-Pregnancy-Postpartum.pdf. 2018.
- Robakis TK, Williams KE, Crowe S, et al. Maternal attachment insecurity is a potent predictor of depressive symptoms in the early postnatal period. J Affect Disord. 2016;190:623–631.
- Geier ML, Hills N, Gonzales M, et al. Detection and treatment rates for perinatal depression in a state Medicaid population. CNS Spectr. 2015;20(1):11–19.
- Curry SJ, Krist AH, Owens DK, et al; US
   Preventive Services Task Force. Interventions to
   prevent perinatal depression: US Preventive
   Services Task Force recommendation
   statement. JAMA. 2019;321(6):580–587.
- Patel SR, Wisner KL. Decision making for depression treatment during pregnancy and the postpartum period. *Depress Anxiety*. 2011;28(7):589–595.
- Wisner KL, Zarin DA, Holmboe ES, et al. Riskbenefit decision making for treatment of depression during pregnancy. Am J Psychiatry. 2000;157(12):1933–1940.
- Bishop TF, Press MJ, Keyhani S, et al.
   Acceptance of insurance by psychiatrists and the implications for access to mental health care. JAMA Psychiatry. 2014;71(2):176–181.

Editor's Note: We encourage authors to submit papers for consideration as a part of our Focus on Women's Mental Health section. Please contact Marlene P. Freeman, MD, at mfreeman@psychiatrist.com.

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- You are treating a woman who is 8 months pregnant and has no prior recorded psychiatric history. According to nationwide cohort study results, which of the following factors in her history most strongly indicates that you should monitor her for postpartum depression?
  - a. Age over 35 years

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- b. Compulsive handwashing, although never diagnosed or treated
- c. Gestational diabetes
- d. Stressful managerial responsibilities at work
- 2. Which of the following conditions should raise the greatest concern for risk of postpartum depression?
  - a. Gestational diabetes
  - b. Gestational hypertension
  - c. Pre-eclampsia
  - d. Posttraumatic stress disorder
- 3. Among women with depression prior to pregnancy but not during pregnancy, what proportion will develop postpartum depression, according to cohort study results?

  - b. 20%
  - c. 30%
  - d. 65%
- Which of the following statements about postpartum depression is true, according to cohort study results?
  - a. Anxiety disorders are significantly positively associated with postpartum depression if the mother has comorbid depression
  - b. Anxiety disorders are significantly positively associated with postpartum depression even after controlling for comorbid depression
  - c. Postpartum depression diagnoses peak during the period of 4-6 months after delivery
  - d. Anxiety disorder diagnoses peak during the period of 4-6 months after delivery and have no effect on the risk for postpartum depression