Temporal trends of co-diagnosis of depression and/or anxiety among female maternal and non-maternal hospitalizations: Results from Nationwide Inpatient Sample 2004–2013

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ABSTRACT

Perinatal depression/anxiety is considered the most underdiagnosed pregnancy complication in the US and is associated with poor maternal and fetal outcomes. However, despite its prevalence, most women who present with depressive symptoms are not screened and do not receive adequate treatment. We examined the clinical co-diagnosis of depression and/or anxiety among maternal and non-maternal hospitalizations among females aged 14–49 from the Nationwide Inpatient Sample (NIS) between 2004 and 2013 (*n* = 83,472,775). Meta-regression was used to determine annual change and presence of temporal trends. Survey logistic regression was used to examine the association with sociodemographic factors. Rates of diagnosis of depression and/or anxiety disorders demonstrated a temporal increase from 2004–2013, and this increase was mainly driven by non-maternal hospitalizations compared to maternal. Furthermore, non-maternal hospitalizations demonstrated a greater prevalence of depression and/or anxiety diagnoses compared to maternal hospitalizations over the same time period (21·7% versus 2·8%). Among all female hospitalizations, whites were roughly twice as likely as minorities to have a diagnosis of depression and/or anxiety. These results add to the evidence suggestive of the under-diagnosed depression/anxiety present among women of reproductive age, particularly pregnant women and minorities, and underscore the critical role of obstetricians in treating both physical and mental health.

1. Introduction

Major depressive disorder (MDD), is the second leading cause of disability worldwide and a major contributor to the burden of suicide and heart disease (Ferrari et al., 2013). Depression and anxiety are highly comorbid, with nearly 60% of those diagnosed as depressed also meeting diagnostic criteria for an anxiety disorder (Kessler et al., 2003). Women are consistently reported to have a greater prevalence of anxiety and depressive disorders than men (Weissman and Klerman, 1977; McLean et al., 2011; Wang et al., 2016). The reason for this is unclear, but is likely to be social as well as biological given that estimated depression heritability is 40–50% (Sullivan et al., 2000). There is evidence that the risk of depression and/or anxiety is greater during women's reproductive lives (Bebbington et al., 2003). Prepubescent boys are, if anything, more likely than girls to be depressed (Anderson et al., 1987; Angold and Rutter, 1992). However, during adolescence a dramatic shift occurs wherein between the ages of 11 and 13 years, this trend in depression rates is reversed (Cohen et al., 1993; Angold et al., 1998). By 15 years of age, females are approximately twice as likely as males to have experienced an episode of depression, and this gender gap persists for the next 35 to 40 years (Cyranowski et al., 2000; Frank and Young, 2000). This increased prevalence of depression correlates with hormonal changes in women, particularly during puberty, prior to menstruation, surrounding pregnancy and at perimenopause, and suggests that female hormonal fluctuations may be a trigger for depression (Albert, 2015).

Perinatal depression and/or anxiety is considered the most under-diagnosed pregnancy complication in the United States with more than

400,000 infants born to mothers who are depressed each year (Earls et al., 2010). Untreated depression during pregnancy has been associated with increased risk of miscarriage, low birth weight, and preterm birth, as well as poor infant attachment, early childhood developmental delays, and relationship strain (Bansil et al., 2010; Grote et al., 2010; Alhusen et al., 2013; Grigoriadis et al., 2013). Perinatal depression, defined as minor or major episodes of depression occurring during pregnancy or the first postpartum year, affects an estimated 7%–20% of women with rates as high as 35%–40% among low-income and minority women, as well as those with substance abuse disorders (Witt et al., 2011). Despite the prevalence of perinatal depression, most women who present with depressive symptoms are not screened and do not receive adequate treatment (Allbaugh et al., 2015).

A better understanding of the full scope of factors that affect perinatal depression rates may be of key importance in addressing disparities in birth and early developmental outcomes. However, the existing literature fails to assess the temporal trends and contributing factors of clinical co-diagnosis of depression and/or anxiety among women of reproductive age, including pregnant women. In this study, we examined the rates (and rates of change) of co-diagnosis of depression and/or anxiety in both maternal and non-maternal female hospitalizations using data from the Nationwide Inpatient Sample (NIS) from 2004 to 2013. Further, we assessed the associations between age, race, income level, substance abuse, comorbidities and other hospital factors with clinical diagnosis of depression and/or anxiety.

2. Methods

2.1. Data source

We used in-patient hospital administration data collected as part of the Healthcare Cost and Utilization Project of the Agency for Healthcare Research and Quality, the Nationwide Inpatient Sample (NIS) (HCUP, 2004-2013). NIS data are nationally representative and contain data on hospital stays in 1,000 hospitals sampled to represent a 20% stratified sample of US Community hospitals from 46 states. Each year of the NIS provides information on approximately 8 million inpatient stays from the 1000 sampled hospitals. Because the NIS is available yearly, beginning with 1988, analysis of trends over time is possible. Boston University IRB deemed this study exempt from federal regulations for the protection of human research participants.

2.2. Study population

NIS data sets from 2004 to 2013 were used in this analysis. Each survey year data was restricted to female patients of reproductive age (14–49 years old) and to those who had definitive information regarding sex and age, which was then pooled across 10 years (survey-weighted $N = 83,472,909$). Each record refers to a single hospitalization; as a result, a person may have multiple hospitalizations, and unique patient records may not be identified.

All maternal (pregnancy-related) hospitalizations were identified according to the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) diagnostic codes 640–677, V22, V23, V24, V28, and 792.3; ICD-9-CM procedure codes 72–75; and diagnosis-related group codes 370–384. These hospitalizations were further classified hierarchically into delivery, postpartum, and antenatal hospitalizations as previously described in detail elsewhere (Kuklina and Callaghan, 2010; Kuklina et al., 2011). Delivery hospitalizations were identified using a previously documented enhanced method that has been shown to improve the accuracy of identifying deliveries, especially those with severe complications (Kuklina et al., 2008). Hospitalizations for an abortion or an ectopic or molar pregnancy were excluded from the maternal population.

2.3. Exposure

We categorized all female hospitalizations between 14 and 49 years of age into two groups: 1) those identified as having a diagnosis of depression, or those having a diagnosis of anxiety, or those having a diagnosis of depression and anxiety during that particular hospitalization and 2) those who did not. Depression was diagnosed on the basis of the ICD-9 diagnosis codes as major depression (296•2, 296•3), depressive disorder NOS (311), unspecified episodic mood disorder (296•90), and dysthymic disorder (300•4). A clinical diagnosis of anxiety included ICD-9 codes for anxiety disorder NOS (300•00), panic disorder (300•01), generalized anxiety disorder (300•02), acute reaction to stress (308•0–308•9), post-traumatic stress disorder (309•81, 309•82, 309•83, 309•89), adjustment disorder (309•0, 309•1, 309•24, 309•28, 309•29, 309•3, 309•4, 309•9), and other anxiety states (300•09). The flow chart of inclusion and exclusion criteria and cohort development is presented in Supplementary Fig. 1. We will refer women hospitalized during pregnancy, childbirth or the postpartum as "maternal hospitalization" and women hospitalized during other timeframes as "non-maternal hospitalization."

2.4. Variables and definitions

Age was categorized into four groups: 14–19, 20–29, 30–39 and 40–49 years of age. Race/ethnicity was classified into five categories: white, black, Hispanic, other (Asian and all other race) and those missing race/ethnicity information (as a separate category). Those hospitalizations that were missing race/ethnicity were included in the analysis.

The type of primary insurance was dichotomized as either private/Medicare and all other insurance (self-pay/Medicaid/no charge/other source). Low income patients were identified based on NIS definitions of neighborhood annual income quartiles (low-income ≤ $24,999 and not low ≥ $25,000). The federal poverty line for a family of four in 2013 was $ 23,550 (Services, 2013). Substance abuse patients were identified by ICD-9 codes as those abusing alcohol (291•2, 291•5, 291•8, 291•9, 303•90–303•93, 305•00–305•03) and/or drugs (292•0, 292•82–292•89, 292•9, 304•00–304•93, 305•20–305•93, 648•30–648•34).

In addition, we also assessed pre-existing comorbidities (Elixhauser co-morbidity score calculated from ICD-9 diagnosis codes) and hospital characteristics such as teaching status (teaching and non-teaching), hospital bed size (small, medium and large), location (rural and urban) and region (Northeast, Midwest, South and West). The Elixhauser Comorbidity Index is a method for measuring 29 patient comorbidities based on ICD diagnostic codes categorized by the Agency for Healthcare Research and Quality (AHRQ) (Elixhauser et al., 1998). Specific co-morbidities, obesity, type 2 diabetes, and hypertension were selected as covariates in our analysis to understand the relationship between chronic disease and depression/anxiety with and without concurrent pregnancy (Cukor et al., 2007; Lassi et al., 2014).

2.5. Statistical analysis

First, we compared the demographic, co-morbidities, and hospital characteristics between the two exposure groups. Second, we assessed the temporal trends in the rate of clinical co-diagnosis of depression and/or anxiety disorders among maternal and non-maternal female hospitalizations. Survey analysis was performed using discharge weights and sixty strata that were defined depending on geographical region, teaching status, and hospital. Generalized linear models with Poisson family and year as a covariate was used to create predicted estimates of rates and standard error. Meta-regression was used to assess trends across survey years and to determine annual changes per 100,000 in predicted rates and standard errors (SE) of maternal and non-maternal female hospitalizations with the assumption of linearity

in trends. In estimation of annual change per 100,000, the year-specific rates were modeled as dependent variable and adjusted for survey year in meta-regression. *p*-values for trend (*p*-trend) across years for overall, age-, race/ethnicity-, payer-, income level-, substance abuse-, weight-, type 2 diabetes status-, and hypertension status-specific for maternal and non-maternal hospitalizations were derived from survey logistic regression where year was entered as a linear term in the model. *p*-interaction was calculated by adding an interactive term between year and the individual covariates in the model: age category, race/ethnicity, insurance payer, income level, substance abuse, weight, diabetes status, and hypertension status. This interaction indicates the significance of the difference in annual percent change.

Third, we used survey-weighted logistic regression to estimate odds ratios (OR) and 95% confidence intervals (95% CI). Crude estimates were derived for each covariate after adjusting for year of survey to account for the significant temporal trend. This was followed by multivariable logistic regression to assess the independent associations between clinically co-diagnosed depression and/or anxiety adjusted for age, race/ethnicity, type of insurance, neighborhood income, substance abuse, weight, diabetes status, hypertension status, comorbidities, region and location of hospital, and hospital bed size. All analyses were conducted using STATA 14•2 (StataCorp LP, College Station, Texas, USA; 2009).

3. Results

Out of the 83,472,909 hospitalizations of females age 14–49 in the NIS data between 2004 and 2013, we identified 43,889,296 maternal hospitalizations (52•6%) and 39,583,479 non-maternal hospitalizations (47•4%). Among these hospitalizations, 2•8% (*n* = 1,241,818) of maternal hospitalizations had a clinical co-diagnosis of depression and/or anxiety, while 21•7% (*n* = 8,567,854) of non-maternal hospitalizations had a clinical co-diagnosis of depression and/or anxiety.

The demographic and hospital characteristics by hospitalization type (maternal or non-maternal) and presence or absence of co-diagnosis of depression and/or anxiety are presented in Table 1 and Supplementary Table 1. Maternal hospitalizations during pregnancy or the postpartum period showed higher rates of comorbid depression and/or anxiety compared to delivery hospitalizations (*p* < 0•0001). The vast majority of maternal hospitalizations were aged 20–39 (87•2%), while non-maternal hospitalizations skewed older: 45•6% were aged ≥40 years (*p* < 0•0001). Older maternal and non-maternal patients also had higher rates of depression and/or anxiety compared to younger (*p* < 0•0001). Non-whites comprised a greater proportion of maternal compared to non-maternal hospitalizations (57•3% versus 50•1%, *p* < 0•0001). In both maternal and non-maternal hospitalizations, minorities were less likely to have a depression and/or anxiety diagnosis compared to whites (maternal: whites comprised 42•7% of total population but made up 58•8% of diagnoses, *p* < 0•0001; non-maternal: whites comprised 49•9% of total population but made up 59•9% of diagnoses, *p* < 0•0001). Among maternal hospitalizations, there was no significant difference in depression and/or anxiety rates by insurance payer; while among non-maternal hospitalizations, those without private insurance or Medicare showed higher rates. Additional diagnoses for maternal hospitalizations are listed in Supplementary Table 2.

Non-maternal hospitalizations had higher rates of comorbidities with 65•9% having at least one comorbidity compared to 23•1% among maternal hospitalizations (*p* < 0•0001). Diagnoses of depression and/or anxiety increased with increasing comorbidities (maternal: patients with at least one comorbidity comprised 23•1% of total population but made up 51•0% of diagnoses, *p* < 0•0001; non-maternal: patients with at least one comorbidity comprised 65•9% of total population but made up 77•4% of diagnoses, *p* < 0•0001). Considering specific comorbidities, those with obesity, diabetes, hypertension or substance abuse all had higher rates of depression and/or anxiety compared to patients without (*p* < 0•0001 for all).

The temporal trends of diagnosis of depression and/or anxiety from 2004–2013 among maternal and non-maternal hospitalizations is presented in Fig. 1. The rates of depression and/or anxiety among non-maternal hospitalizations ranged from 16,217•5 per 100,000 hospitalizations in 2004 to 28,233•1 per 100,000 hospitalizations in 2013, with a significant increase across the 10 years (annual change = 1372•4 per 100,000, *p*-trend < 0•0001). The rates of depression and/or anxiety among maternal hospitalizations ranged from 1760•2 per 100,000 hospitalizations in 2004 to 4101•0 per 100,000 hospitalizations in 2013, with a significant increase across the 10 years (annual change = 270•8 per 100,000, *p*-trend < 0•0001).

The year-specific rates and predicted annual change of depression and/or anxiety among maternal hospitalizations from 2004 to 2013 are presented in Fig. 2. There were temporal increases within each category of age groups, race/ethnicity, insurance type, income level, substance abuse, weight, diabetes status, and hypertension status (all: *p*-trend < 0•0001). The temporal trends were significantly different between categories of age (*p* < 0•0001), race/ethnicity (*p* = 0•01), income level (*p* = 0•005), substance abuse (*p* = 0.03), weight (*p* < 0•0001), type 2 diabetes status (*p* = 0•002), and hypertension status (*p* < 0•0001), whereas no significant difference was demonstrated by insurance payer categories. The p-interaction, calculated by adding an interactive term between the individual covariates and year in the model, indicates the significance of the difference in annual percent change.

The year-specific rates and predicted annual change of depression and/or anxiety among non-maternal hospitalizations from 2004 to 2013 are presented in Fig. 3. There were increasing temporal trends within each sub-group of age, race/ethnicity, insurance type, income level, substance abuse, weight, diabetes status, and hypertension status (all: *p*-trend < 0•0001). The temporal trends were significantly different between categories of insurance payer (*p* < 0•0001), substance abuse (*p* < 0•0001), weight (*p* < 0•0001), diabetes status (*p* < 0•0001), and hypertension status (*p* < 0•0001), whereas no significant difference was demonstrated between categories of age, race/ethnicity, or income level. The p-interaction, calculated by adding an interactive term between the individual covariates and year in the model, indicates the significance of the difference in annual percent change.

Table 2 presents the association between the socio-demographics, comorbidities and hospital characteristics and diagnosis of depression and/or anxiety among maternal and non-maternal hospitalizations. In a multivariable model, women hospitalized for a maternal diagnosis with a co-diagnosis of depression and/or anxiety were associated with older age (20–29 year olds (OR = 1•14, 95%CI = 1•11–1•16), 30–39 year olds (OR = 1•26, 95%CI = 1•23–1•29), and 40–49 years olds (OR = 1•86, 95%CI = 1•79–1•93)) as compared to teenagers (*p* < 0•0001). A co-diagnosis of depression and/or anxiety was less common among blacks (OR = 0•44, 95%CI = 0•43–0•46), Hispanics (OR = 0•37, 95%CI = 0•35–0•39), or other races (OR = 0•35, 95%CI = 0•34–0•37) as compared to whites (*p* < 0•0001). Low income women with a maternal diagnosis had a 9% decreased likelihood of diagnosis of depression and/or anxiety compared to higher income levels (OR = 0•91, 95%CI = 0•88–0•95, *p* < 0•0001). There was an increased likelihood of co-diagnosis of depression and/or anxiety with increasing comorbidities compared to those women with none (*p* < 0•0001). Women with either obesity (OR = 1•06, 95% CI = 1•03–1•09, *p* < 0•0001), type 2 diabetes (OR = 1•10, 95% CI = 1•06–1•13, *p* < 0•0001), hypertension (OR = 1•14, 95% CI = 1•11–1•17, *p* < 0•0001), or substance abuse (OR = 2•54, 95%CI = 2•45–2•64, *p* < 0•0001) were more likely for co-diagnosis of depression and/or anxiety. Maternal hospitalizations in the south and west were less likely to have a co-diagnosis of depression and or anxiety (OR = 0•70, 95%CI = 0•64–0•77) and (OR = 0.79, 95%CI = 0.71–0.87) than northeast (*p* < 0•0001). Non-maternal hospitalizations also followed a similar pattern as maternal hospitalizations, where those in the south were less likely to have a co-diagnosis of

Table 1

Demographic and hospital characteristics by diagnosis of depression and/or anxiety in female maternal and non-maternal hospitalizations, NIS 2004–2013.

	Maternal hospitalizations				Non-maternal hospitalizations			
	Total	Diagnosis of depression and/or anxiety			Total	Diagnosis of depression and/or anxiety		
		Yes	No	P		Yes	No	p
No. of cases	43,889,296	1,241,818 (2•8)	42,647,478 (97•2)		39,583,479	8,567,854 (21•7)	31,015,625 (78•4)	
Hospitalization type				<0•0001				
Pregnancy	3,568,041 (8•1)	208,525 (16•8)	3,359,516 (7•9)					
Delivery	39,611,223 (90•3)	981,005 (79•0)	38,630,218 (90•6)					
Postpartum	710,032 (1•6)	52,288 (4•2)	657,743 (1•5)					
Age group				<0•0001				<0•0001
14–19	4,250,863 (9•7)	90,813 (7•3)	4,160,050 (9•8)		3,140,256 (7•9)	671,287 (7•8)	2,468,969 (8•0)	
20–29	22,775,352 (51•9)	604,082 (48•6)	22,171,270 (52•0)		7,321,154 (18•5)	1,472,152 (17•2)	5,849,002 (18•9)	
30–39	15,514,053 (35•3)	471,687 (38•0)	15,042,366 (35•3)		11,066,490 (28•0)	2,394,328 (28•0)	8,672,162 (28•0)	
40–49	1,349,028 (3•1)	75,235 (6•1)	1,273,792 (3•0)		18,055,578 (45•6)	4,030,086 (47•0)	14,025,492 (45•2)	
Race/ethnicity				<0•0001				<0•0001
White	18,718,043 (42•7)	730,595 (58•8)	17,987,448 (42•2)		19,736,149 (49•9)	5,134,439 (59•9)	14,601,710 (47•1)	
Black	5,200,530 (11•9)	116,352 (9•4)	5,084,177 (11•9)		6,634,389 (16•8)	960,313 (11•2)	5,674,076 (18•3)	
Hispanic	8,353,132 (19•0)	116,603 (9•4)	8,236,528 (19•3)		4,074,033 (10•3)	577,705 (6•7)	3,496,327 (11•3)	
Other	3,789,192 (8•6)	53,426 (4•3)	3,735,766 (8•8)		1,918,837 (4•9)	298,413 (3•5)	1,620,424 (5•2)	
Unknown	7,828,400 (17•8)	224,842 (18•1)	7,603,558 (17•8)		7,220,071 (18•2)	1,596,982 (18•6)	5,623,088 (18•1)	
Insurance payer				0•37				<0•0001
Private/Medicare	22,144,398 (50•5)	621,146 (50•1)	21,523,252 (50•6)		23,037,406 (58•4)	4,848,544 (56•8)	18,188,862 (58•8)	
Self-pay/ Medicaid/ No charge/Other	21,670,618 (49•5)	618,078 (49•9)	21,052,540 (49•4)		16,439,559 (41•6)	3,695,378 (43•2)	12,744,181 (41•2)	
Low income	12,018,098 (27•9)	310,800 (25•5)	11,707,298 (28•0)	<0•0001	11,970,252 (31•1)	2,464,490 (29•5)	9,505,762 (31•5)	<0•0001
Elixhauser comorbidity Index								
Categories				<0•0001				<0•0001
0	33,743,444 (76•9)	608,365 (49•0)	33,135,079 (77•7)		13,514,583 (34•1)	1,934,434 (22•6)	11,580,148 (37•3)	
1	5,970,613 (13•6)	328,284 (26•4)	5,642,329 (13•2)		10,703,070 (27•0)	2,431,404 (28•4)	8,271,666 (26•7)	
2	3,157,812 (7•2)	187,274 (15•1)	2,970,538 (7•0)		7,211,283 (18•2)	1,926,552 (22•5)	5,284,731 (17•0)	
3	760,499 (1•7)	76,718 (6•2)	683,781 (1•6)		4,250,250 (10•7)	1,185,491 (13•8)	3,064,759 (9•9)	
4 +	256,928 (0•6)	41,177 (3•3)	215,751 (0•5)		3,904,294 (9•9)	1,089,972 (12•7)	2,814,322 (9•1)	
Obesity	1,488,283 (3•4)	100,912 (8•1)	1,387,371 (3•3)	<0•0001	4,691,180 (11•9)	1,223,040 (14•3)	3,468,140 (11•2)	<0•0001
Type 2 diabetes	563,603 (1•3)	40,159 (3•2)	523,445 (1•2)	<0•0001	4,505,634 (11•4)	1,069,002 (12•5)	3,436,632 (11•1)	<0•0001
Hypertension	1,006,852 (2•3)	76,934 (6•2)	929,918 (2•2)	<0•0001	8,527,074 (21•5)	2,173,498 (25•4)	6,353,576 (20•5)	<0•0001
Substance Abuse	752,438 (1•7)	112,150 (9•0)	640,288 (1•5)	<0•0001	4,862,831 (12•3)	1,809,916 (21•1)	3,052,916 (9•8)	<0•0001
Hospital Characteristics								
Location				<0•0001				<0•0001
Rural	4,853,443 (11•1)	138,609 (11•2)	4,714,834 (11•2)		4,409,688 (11•2)	1,068,945 (12•6)	3,340,743 (10•8)	
Urban, nonteaching	18,139,166 (41•6)	427,345 (34•6)	17,711,821 (41•8)		15,618,367 (39•7)	3,348,528 (39•2)	12,269,839 (39•8)	
Urban, teaching	20,656,021 (47•3)	668,689 (54•2)	19,987,332 (47•1)		19,345,334 (49•1)	4,097,791 (48•1)	15,247,543 (49•4)	
Bed size				0•013				0•36
Small	4,817,664 (11•0)	145,051 (11•8)	4,672,614 (11•0)		4,644,411 (11•8)	1,024,654 (12•0)	3,619,757 (11•7)	
Medium	11,517,760 (26•4)	300,964 (24•4)	11,216,795 (26•5)		9,784,167 (24•9)	2,084,902 (24•5)	7,699,265 (25•0)	
Large	27,313,206 (62•6)	788,627 (63•9)	26,524,579 (62•5)		24,944,811 (63•3)	5,405,709 (63•5)	19,539,103 (63•3)	
Region				<0•0001				<0•0001
Northeast	7,283,225 (16•6)	255,259 (20•6)	7,027,966 (16•5)		7,807,764 (19•7)	1,748,815 (20•4)	6,058,949 (19•5)	
Midwest	9,288,875 (21•2)	332,091 (26•7)	8,956,784 (21•0)		9,111,564 (23•0)	2,330,003 (27•2)	6,781,561 (21•9)	
South	16,672,619 (38•0)	397,396 (32•0)	16,275,223 (38•2)		15,537,601 (39•3)	3,116,481 (36•4)	12,421,120 (40•1)	
West	10,644,577 (24•2)	257,071 (20•7)	10,387,505 (24•4)		7,126,551 (18•0)	1,372,555 (16•0)	5,753,996 (18•5)	

All values are weighted frequencies and weighted percentages using survey analysis. *p*-value is derived from chi-square test for all comparisons.

depression and or anxiety (OR = 0•84, 95%CI = 0•80–0•88) as compared to northeast, in addition to west (OR = 0.79, 95%CI = 0.75–0.83).

Women hospitalized for reasons other than a maternal diagnosis with co-diagnosis of depression and/or anxiety were more likely to be teenagers 14–19 compared to older women: 20–29-year old (OR = 0•82, 95%CI = 0•78–0•85), 30–39 year olds (OR = 0•87, 95%CI = 0•83–0•91), and 40–49 years olds (OR = 0•86, 95%CI = 0•82–0•90, *p* < 0•0001). Diagnosis of depression and/or anxiety was less common among blacks (OR = 0•43, 95%CI = 0•42–0•44), Hispanics (OR = 0•51, 95%CI = 0•49–0•53), or women of other races (OR = 0•54, 95%CI = 0•52–0•56) compared to whites (*p* < 0•0001). Low income women were 6% less likely to have a co-diagnosis of depression and/or anxiety compared to higher income levels (OR = 0•94, 95%CI = 0•93–0•96, *p* < 0•0001 There was an increased likelihood of diagnosis of depression and/or anxiety with increasing comorbidities compared to those women with none (*p* < 0•0001). Women with either obesity (OR = 1•10, 95% CI = 1•09–1•11, *p* < 0•0001), hypertension (OR = 1•14, 95%

CI = 1•13–1•15, *p* < 0•0001), or substance abuse (OR = 1•97, 95%CI = 1•93–2•01, *p* < 0•0001) were at higher risk for co-diagnosis of depression and/or anxiety, while those with type 2 diabetes (OR = 0•94, 95% CI = 0•93–0•95, *p* < 0•0001) had a slightly lower risk. Urban hospitalizations were less likely to have a co-diagnosis of depression and/or anxiety than rural hospitalizations (urban non-teaching: OR = 0•90, 95%CI = 0•86–0•94, urban teaching: OR = 0•89, 95%CI = 0•85–0•93, *p* < 0•0001).

4. Discussion

In our analysis of nationally representative hospitalizations among women aged 14–49 between the years 2004 and 2013, we report four primary findings. First, we found that the rates of clinical co-diagnosis of depression and/or anxiety disorders among all female hospitalizations demonstrated a temporal increase during this time period. Second, the magnitude of co-diagnosis of depression and/or anxiety among maternal hospitalizations was almost one-tenth that of non-maternal hospitalizations. Third, there was significant variation in the rate of
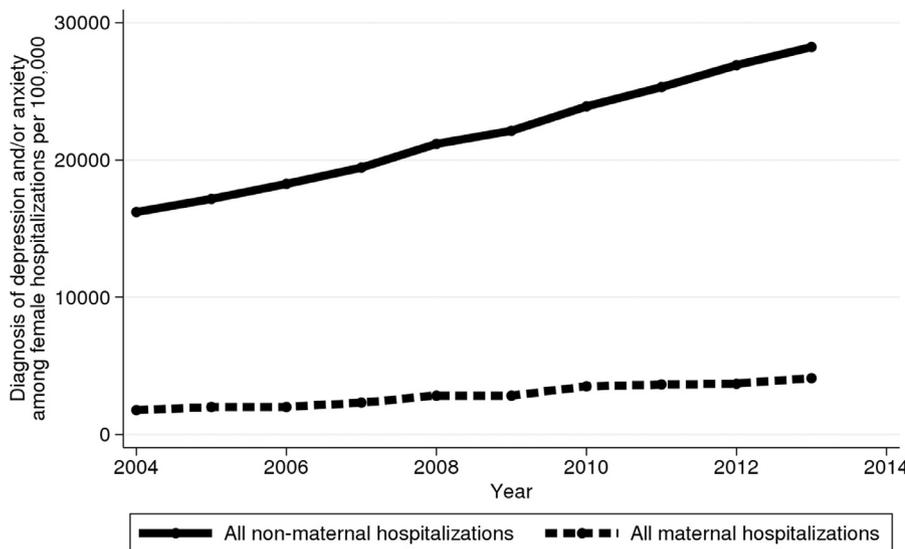
Fig. 1. Rate of diagnosis of depression and/or anxiety disorders among female maternal and non-maternal hospitalizations age 14–49, NIS 2004–2013

Temporal trend of depression and/or anxiety diagnosis among:

All non-maternal hospitalizations, Predicted annual change (SE) = 1372•4 (38•7), p-trend < 0•0001; All maternal hospitalizations, Predicted annual change (SE) = 270•8 (11•6), p-trend < 0•0001. p-interaction < 0•0001.

All rates are survey-weighted and per 100,000 hospitalizations. Change denotes annual change in rate per 100,000 hospitalizations and is calculated from predicted rates using a survey weighted Poisson regression model with year as a continuous covariate. A positive value indicates increase in annual change per 100,000 and standard error (SE) from 2004 to 2013. P-trend calculated using meta-regression indicates the significance of the increase in hospitalization rates of diagnosis of depression and/or anxiety from 2004 to 2013. P-interaction, calculated by adding an interactive term between the individual covariates and year in the model, indicates the significance of the difference in annual percent change.

	2004	2007	2010	2013	Predicted annual change		Annual % change	p-trend	p-interaction
Maternal hospitalizations	**1760.2**	**2305.1**	**3503.4**	**4101.0**	**270.8**		**10.1**	**<0.0001**	
By age									<0.0001
14-19 years	1484.0	1795.3	2716.0	3343.1	200.5		9.6	<0.0001	
20-29 years	1718.4	2241.1	3287.4	3792.3	236.6		9.3	<0.0001	
30-39 years	1870.4	2451.3	3702.7	4288.9	279.2		9.7	<0.0001	
40-49 years	2165.6	3619.3	7150.1	8204.0	769.4		15.6	<0.0001	
By race/ethnicity									0.001
									0.010*
White	2411.7	3325.9	4713.5	5463.9	338.3		9.3	<0.0001	
Black	1379.2	1661.4	2638.4	3150.0	221.0		10.9	<0.0001	
Hispanic	796.9	1128.9	1592.9	2105.9	156.1		12.1	<0.0001	
Other	770.8	1093.5	1737.0	1751.0	126.9		9.8	<0.0001	
Unknown	1884.5	2376.1	4495.0	5419.6	448.0		14.0	<0.0001	
By insurance payer									0.80
Private/Medicare	1722.2	2324.4	3521.9	4026.6	268.4		10.0	<0.0001	
Self-pay/ Other	1806.3	2276.6	3482.9	4170.2	273.0		10.1	<0.0001	
By income level									0.005
Low income	1435.5	1997.6	3467.7	3851.7	282.1		11.6	<0.0001	
Non-low income	1894.7	2424.7	3540.1	4210.1	267.6		9.6	<0.0001	
By substance abuse									0.03
Substance abuse +	9701.4	12,052.4	17,734.2	19,612.8	1174.7		8.5	<0.0001	
Substance abuse -	1656.1	2149.2	3231.5	3734.5	242.7		9.7	<0.0001	
By weight									<0.0001
obese	4709.4	4945.7	7474.2	8122.2	407.4		6.8	<0.0001	
Non-obese	1726.7	2231.9	3319.2	3827.8	243.7		9.5	<0.0001	
By diabetes status									0.002
diabetic	4173.4	4985.0	8829.7	9966.2	762.0		11.7	<0.0001	
Non-diabetic	1732.6	2272.3	3424.7	4015.5	262.6		10.0	<0.0001	
By hypertension status									<0.0001
hypertensive	3837.3	5172.7	9332.5	10,886.0	874.3		12.8	<0.0001	
Non-hypertensive	1721.4	2239.2	3350.6	3910.7	251.2		9.7	<0.0001	

Predicted annual change in rate per 100,000

Fig. 2. Temporal trends of co-diagnosis of depression and/or anxiety among maternal hospitalizations aged 14–49, NIS 2004–2013
All rates are survey-weighted and per 100,000 hospitalizations. Change denotes annual change in rate per 100,000 hospitalizations and is calculated from predicted rates using a survey weighted Poisson regression model with year as a continuous covariate. A positive value indicates increase in annual change per 100,000 and percent change from baseline (% change) from 2004 to 2013. P-trend calculated using meta-regression indicates the significance of the increase in hospitalization rates of diagnosis of depression and/or anxiety from 2004 to 2013. P-interaction, calculated by adding an interactive term between the individual covariates and year in the model, indicates the significance of the difference in annual percent change. * p-interaction excluding unknown race category.

increase in the clinical co-diagnosis of depression and/or anxiety disorders among maternal and non-maternal hospitalizations, with non-maternal hospitalizations displaying a rate five-times greater than maternal hospitalizations over the 10-year time period. Fourth, whites were roughly twice as likely to have a co-diagnosis of depression and/or anxiety compared to minority race/ethnicity groups and also displayed an increasing trend of diagnosis among both maternal and non-maternal hospitalizations.
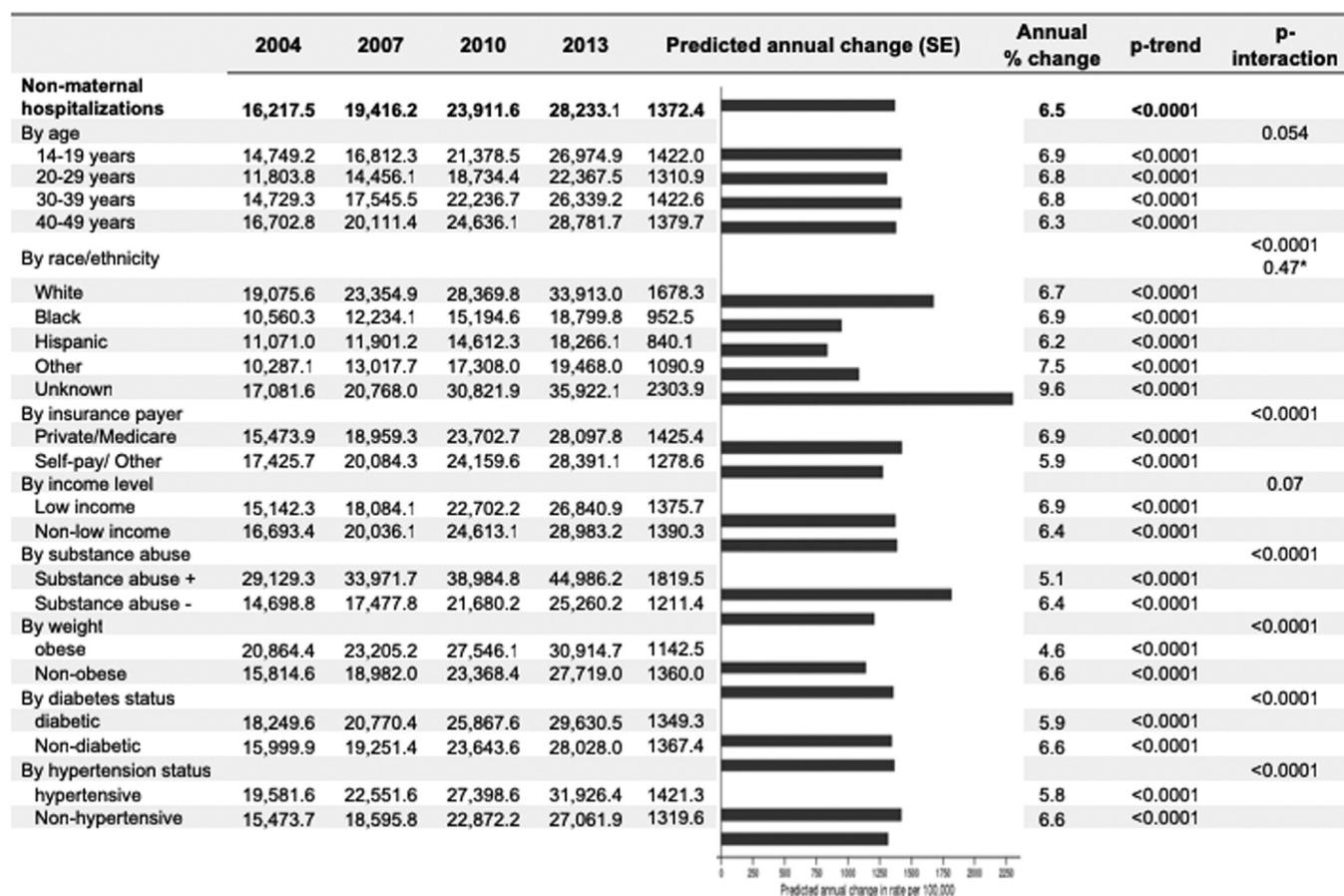
	2004	2007	2010	2013	Predicted annual change (SE)		Annual % change	p-trend	p-interaction
Non-maternal hospitalizations	**16,217.5**	**19,416.2**	**23,911.6**	**28,233.1**	**1372.4**		**6.5**	**<0.0001**	
By age									0.054
14-19 years	14,749.2	16,812.3	21,378.5	26,974.9	1422.0		6.9	<0.0001	
20-29 years	11,803.8	14,456.1	18,734.4	22,367.5	1310.9		6.8	<0.0001	
30-39 years	14,729.3	17,545.5	22,236.7	26,339.2	1422.6		6.8	<0.0001	
40-49 years	16,702.8	20,111.4	24,636.1	28,781.7	1379.7		6.3	<0.0001	
By race/ethnicity									<0.0001 0.47*
White	19,075.6	23,354.9	28,369.8	33,913.0	1678.3		6.7	<0.0001	
Black	10,560.3	12,234.1	15,194.6	18,799.8	952.5		6.9	<0.0001	
Hispanic	11,071.0	11,901.2	14,612.3	18,266.1	840.1		6.2	<0.0001	
Other	10,287.1	13,017.7	17,308.0	19,468.0	1090.9		7.5	<0.0001	
Unknown	17,081.6	20,768.0	30,821.9	35,922.1	2303.9		9.6	<0.0001	
By insurance payer									<0.0001
Private/Medicare	15,473.9	18,959.3	23,702.7	28,097.8	1425.4		6.9	<0.0001	
Self-pay/ Other	17,425.7	20,084.3	24,159.6	28,391.1	1278.6		5.9	<0.0001	
By income level									0.07
Low income	15,142.3	18,084.1	22,702.2	26,840.9	1375.7		6.9	<0.0001	
Non-low income	16,693.4	20,036.1	24,613.1	28,983.2	1390.3		6.4	<0.0001	
By substance abuse									<0.0001
Substance abuse +	29,129.3	33,971.7	38,984.8	44,986.2	1819.5		5.1	<0.0001	
Substance abuse -	14,698.8	17,477.8	21,680.2	25,260.2	1211.4		6.4	<0.0001	
By weight									<0.0001
obese	20,864.4	23,205.2	27,546.1	30,914.7	1142.5		4.6	<0.0001	
Non-obese	15,814.6	18,982.0	23,368.4	27,719.0	1360.0		6.6	<0.0001	
By diabetes status									<0.0001
diabetic	18,249.6	20,770.4	25,867.6	29,630.5	1349.3		5.9	<0.0001	
Non-diabetic	15,999.9	19,251.4	23,643.6	28,028.0	1367.4		6.6	<0.0001	
By hypertension status									<0.0001
hypertensive	19,581.6	22,551.6	27,398.6	31,926.4	1421.3		5.8	<0.0001	
Non-hypertensive	15,473.7	18,595.8	22,872.2	27,061.9	1319.6		6.6	<0.0001	

Predicted annual change in rate per 100,000

Fig. 3. Temporal trends of co-diagnosis of depression and/or anxiety among female non-maternal hospitalizations aged 14–49, NIS 2004–2013
All rates are survey-weighted and per 100,000 hospitalizations. Change denotes annual change in rate per 100,000 hospitalizations and is calculated from predicted rates using a survey weighted Poisson regression model with year as a continuous covariate. A positive value indicates increase in annual change per 100,000 and percent change from baseline (% change) from 2004 to 2013. P-trend calculated using meta-regression indicates the significance of the increase in hospitalization rates of diagnosis of depression and/or anxiety from 2004 to 2013. *P*-interaction, calculated by adding an interactive term between the individual covariates and year in the model, indicates the significance of the difference in annual percent change. * *p*-interaction excluding unknown race category.

Our central finding of a temporal increase in the rates of clinical diagnosis of depression and/or anxiety disorders among female hospitalizations was similar to other reports, including a study showing that during the time period between 1991–1992 and 2002, rates of depression in the overall population increased from 3•3% to 7•1% (Compton et al., 2006). Another investigation determined that between 1990 and 2010 in the US, major depressive disorder showed a 43% increase in disability-adjusted life years and anxiety disorders showed a 21% increase (Murray et al., 2013). At the same time, the female to male ratio of global disability from major depression remained unchanged at 1•7:1 (Albert, 2015). It is likely that, rather than being indicative of an emerging epidemic of mental health disorders, this overall increased rate of depression can mainly be explained by increasing acceptance of mental health disorders, less of a social stigma in seeking treatment, and new focus on treatment of psychiatric illnesses (Docherty, 1997; Kessler et al., 2007; Baxter et al., 2014). Another potential contributor to the rate increase in depression and/or anxiety is the increasing epidemic of obesity and its associated comorbidities, including diabetes and hypertension (Pickering et al., 2011). A meta-analysis of directional associations between obesity and depression provides strong support for a prospective obesity-to-depression link (Faith et al., 2011). Our data are also supported by other studies showing an increased risk of depression in obese women (Pickering et al., 2011; Pratt and Brody, 2014b). However, interestingly, our results indicating slightly reduced risk of non-maternal depression/anxiety in type 2 diabetes patients are in contrast to several published

analyses demonstrating that type 2 diabetes and depression are highly comorbid (Anderson et al., 2001; Rotella and Mannucci, 2013). Despite greater awareness and treatment of depression in primary care settings, the prevalence of depressive symptoms remains high while treatment levels remain low, suggesting that the current rates are an underestimate of the full magnitude of the disease (Shim et al., 2011).

We also found that the rate of clinical diagnosis of depression and/or anxiety was both more prevalent among non-maternal hospitalizations and displayed a greater rate increase over the 10-year time period than in maternal hospitalizations. Previous studies have shown that 10–16% of pregnant women fulfill the diagnostic criteria for depression, suggesting that our results actually reflect a severe under diagnosis of depression and/or anxiety among a vulnerable population, affecting both the woman and fetus (Brown and Solchany, 2004; Marcus and Heringhausen, 2009; Le Strat et al., 2011). Although novel, this finding is unsurprising for several reasons. Primarily, the NIS population of women hospitalized for maternal diagnoses skews younger than for non-maternal. There is an established age discrepancy between the peaks in the lifetime prevalence of depression (age 14–25) and the prevalence of antidepressant use (age >45) implying that young adults with depression may not always receive diagnosis and treatment until many years after the onset of illness (Pearson et al., 2013; Albert, 2015). Additionally, the hospitalized non-maternal population is generally less healthy than the maternal population, evident by more comorbidities (indicative of chronic disease) and more than an eight times greater rate of substance abuse, both risk factors for depression (Nunes

Table 2
Associations between diagnosis of depression and/or anxiety among female maternal and non-maternal hospitalizations, NIS 2004–2013.

| | Maternal hospitalizations | | | Non-maternal hospitalizations | | |
| | Depression and/or anxiety | Multivariable | | Depression and/or anxiety | Multivariable | |
	n (%)	OR (95%CI)	p	n (%)	OR (95%CI)	p
Age categories			< 0·0001			< 0·0001
14–19 years	90,813 (2·1)	Ref		671,287 (21·4)	Ref	
20–29 years	604,082 (2·6)	1·14 (1·11–1·16)		1,472,152 (20·1)	0·82 (0·78–0·85)	
30–39 years	471,687 (3·0)	1·26 (1·23–1·29)		2,394,328 (21·6)	0·87 (0·83–0·91)	
40–49 years	75,235 (5·6)	1·86 (1·79–1·93)		4,030,086 (22·3)	0·86 (0·82–0·90)	
Race/ethnicity			< 0·0001			< 0·0001
White	730,595 (3·9)	Ref		5,134,439 (26·0)	Ref	
Black	116,352 (2·2)	0·44 (0·43–0·46)		960,313 (14·5)	0·43 (0·42–0·44)	
Hispanic	116,603 (1·4)	0·37 (0·35–0·39)		577,705 (14·2)	0·51 (0·49–0·53)	
Other	53,426 (1·4)	0·35 (0·34–0·37)		298,413 (15·6)	0·54 (0·52–0·56)	
Unknown	224,842 (2·9)	0·81 (0·76–0·87)		1,596,982 (22·1)	0·87 (0·83–0·92)	
Insurance			< 0·0001			< 0·0001
Private/Medicare	621,146 (2·8)	Ref		4,848,544 (21·1)	Ref	
Self-pay/Medicaid/						
No charge/Other	618,078 (2·9)	1·19 (1·16–1·22)		3,695,378 (22·5)	1·07 (1·06–1·08)	
Low income	310,800 (2·6)	0·91 (0·88–0·95)	< 0·0001	2,464,490 (20·6)	0·94 (0·93–0·96)	< 0·0001
Elixhauser comorbidity index						
Categories			< 0·0001			< 0·0001
0	608,365 (1·8)	Ref		1,934,434 (14·3)	Ref	
1	328,284 (5·5)	2·62 (2·56–2·67)		2,431,404 (22·7)	1·57 (1·56–1·59)	
2	187,274 (5·9)	3·02 (2·94–3·10)		1,926,552 (26·7)	1·82 (1·79–1·85)	
3	76,718 (10·1)	4·46 (4·31–4·61)		1,185,491 (27·9)	1·87 (1·84–1·91)	
4 +	41,177 (16·0)	6·18 (5·90–6·47)		1,089,972 (27·9)	1·79 (1·75–1·83)	
Obesity	100,912 (6·8)	1·06 (1·03–1·09)	< 0·0001	1,223,040 (26·1)	1·10 (1·09–1·11)	< 0·0001
Type 2 Diabetes	40,159 (7·1)	1·10 (1·06–1·13)	< 0·0001	1,069,002 (23·7)	0·94 (0·93–0·95)	< 0·0001
Hypertension	76,934 (7·6)	1·14 (1·11–1·17)	< 0·0001	2,173,498 (25·5)	1·14 (1·13–1·15)	< 0·0001
Substance abuse	112,150 (14·9)	2·54 (2·45–2·64)	< 0·0001	1,809,916 (37·2)	1·97 (1·93–2·01)	< 0·0001
Hospital Characteristics						
Location			< 0·0001			< 0·0001
Rural	138,609 (2·9)	Ref		1,068,945 (24·2)	Ref	
Urban, nonteaching	427,345 (2·4)	0·96 (0·89–1·04)		3,348,528 (21·4)	0·90 (0·86–0·94)	
Urban, teaching	668,689 (3·2)	1·18 (1·09–1·28)		4,097,791 (21·2)	0·89 (0·85–0·93)	
Bed size			0·009			0·35
Small	145,051 (3·0)	Ref		1,024,654 (22·1)	Ref	
Medium	300,964 (2·6)	0·93 (0·85–1·00)		2,084,902 (21·3)	1·00 (0·96–1·04)	
Large	788,627 (2·9)	1·02 (0·94–1·10)		5,405,709 (21·7)	1·02 (0·98–1·06)	
Region			< 0·0001			< 0·0001
Northeast	255,259 (3·5)	Ref		1,748,815 (22·4)	Ref	
Midwest	332,091 (3·6)	0·94 (0·86–1·04)		2,330,003 (25·6)	1·05 (1·00–1·11)	
South	397,396 (2·4)	0·70 (0·64–0·77)		3,116,481 (20·1)	0·84 (0·80–0·88)	
West	257,071 (2·4)	0·79 (0·71–0·87)		1,372,555 (19·3)	0·79 (0·75–0·83)	

Survey weighted logistic regression model is used for estimating odds ratio (OR), 95% confidence intervals (95%CI) and p value. Both crude and multivariable models are adjusted for survey year.

and Rounsaville, 2006; Egede, 2007; Huang et al., 2010; Forray et al., 2014). However, even when comparing the depression and/or anxiety rates among maternal hospitalizations to rates of women in the general public (9·5%), there is evidence for an under diagnosis among pregnant and postpartum women (Pratt and Brody, 2014a). Our study also showed that maternal and non-maternal hospitalizations demonstrated similar geographic variation with those from the south less likely to have a co-diagnosis of depression and/or anxiety as compared to hospitalizations from northeast, may be indicative of inadequate medical care. This lower likelihood of diagnosis of depression in the southern part of the country may reflect the increased risk of mortality due to other diseases, which may also be driven at least partly by inadequate medical care.

Finally, we observed that among both maternal and non-maternal hospitalizations, white women were roughly twice as likely as minorities to have a diagnosis of depression and/or anxiety. Our results are similar to other findings in both pregnant and non-pregnant women showing that in the provision of medical care services, and resulting diagnosis and anti-depressant treatment, whites show higher rates of depression than minorities (Sclar et al., 2008; Huybrechts et al., 2013). However, this finding is in apparent contrast to several published studies of populations screened for depression, which concluded that ethnic minorities had both higher prevalence rates and an increased

burden of depression (Williams et al., 2007; Kim, 2014; Mukherjee et al., 2016). These combined results demonstrate that although depression and/or anxiety disproportionately affects minorities, it is usually untreated and is more severe and disabling compared to whites. The substantial racial/ethnic wealth gap between whites and minorities could potentially explain this phenomenon, with minorities more likely to be low income with less access to health care. Interestingly, in our analysis, neither insurance payer type or income level could account for the racial/ethnic disparities in diagnosis of depression and/or anxiety. Compared to privately insured women, those without private insurance actually had a 19% and 7% increased likelihood of diagnosis among maternal and non-maternal hospitalizations, respectively, while low income women only had a 9% and 6% decreased likelihood of diagnosis compared to women of higher income levels. These data and previously published reports (Huybrechts et al., 2013) suggest that the diagnostic and treatment disparities among minority women persist at all income levels for reasons still being explored. One potential explanation for these disparities is that minorities tend to under report symptom severity and avoid treatment due to both overt discomfort in talking about mental health and cultural mistrust of the health care system and majority white clinicians (Whaley, 2001; Ward et al., 2009). Minority pregnant women and mothers in particular may be hesitant to seek help due to past atrocities encountered by African Americans in mental

health institutional systems where children were taken from their mothers, and other stigmas regarding minority women's care of their children (Amankwaa, 2003; Bina, 2008).

4.1. Limitations

Our study results are subject to several limitations characteristic to the administrative nature of the data. First, NIS data does not provide patient-level data which makes it impossible to distinguish between incident hospitalization and recurrent admission. This is especially true among older populations as they are more likely to have multiple comorbidities increasing their overall risk of hospitalization (Karlamangla et al., 2007). Second, approximately one-fifth of the hospitalizations in the NIS have missing values for race. However, our results regarding racial disparities would prove valid because these missing values are likely non-differential and therefore our calculated measures of association would only be biased toward the null. Third, the analysis was limited to covariates available in the NIS database and thus we were unable to adjust our analyses for other potential confounders. Fourth, our results are based on the subgrouping of maternal and non-maternal hospitalizations in which we can assume the maternal population is healthy enough to be coded with a normal pregnancy outcome, while in the non-maternal population we can only assume that a mental or physical illness, chronic disease, trauma injuries, etc. were severe enough to warrant hospitalization. Fifth, although the postpartum period can be considered to span as long as six months to one year after giving birth, the nature of the NIS dataset allowed us to only capture hospitalizations for postpartum conditions or complications as specifically detailed in ICD-9 coding. Sixth, the elevated risk of postpartum depression may lead to either under diagnosis or over diagnosis of major depression. False positives may lead to lower rates of screening / assessment or the converse, false positive screens in the early postpartum period may lead to over diagnosis. Postpartum blues usually start 3–4 days after delivery and can last approximately 10–14 days. Although, the majority (90.3%) of the maternal hospitalization in our study are for delivery, that results in short-term hospitalization and only 1.6% of maternal hospitalizations are post-partum, we should consider that some post-partum hospitalizations with depression may have been post-partum blues.

4.2. Conclusion

We found that the rates of clinical co-diagnosis of depression and/or anxiety disorders among female hospitalizations demonstrated a temporal increase from 2004 to 2013, and this increase was mainly driven by non-maternal hospitalizations. Furthermore, non-maternal hospitalizations demonstrated a greater prevalence of depression and/or anxiety diagnoses compared to maternal hospitalizations over the same time period. Among all female hospitalizations, whites were roughly twice as likely as minorities to have a co-diagnosis of depression and/or anxiety. These results add to the evidence suggestive of the severely underdiagnosed depression and/or anxiety present among women of reproductive age, particularly minorities and pregnant women, and underscores the critical role of obstetricians in treating both physical and mental health concerns for improvement of fetal and maternal outcomes.

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Conflict of interest

Clinical trial registration

Not applicable.

Authorship statement

All authors have approved the manuscript, made significant contribution to the study, have read and approved the final version of the manuscript.

Supplementary materials

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