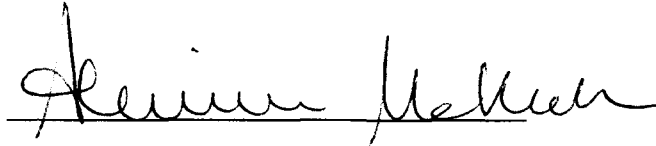


ELEVATED PREVALENCE OF MINOR DEPRESSION IN PREGNANT WOMEN:
ASSOCIATION WITH SOMATIC SYMPTOMS OF DEPRESSION.

Except where reference is made to the work of others, the work described in
this thesis is my own or was done in collaboration with my advisory committee. This

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Adrienne Brett McMahon

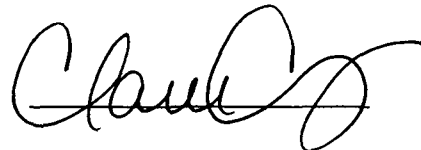
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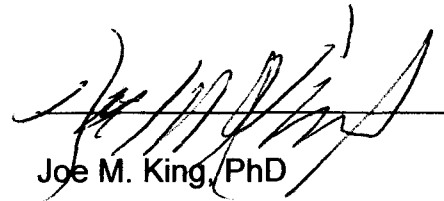
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Elevated Prevalence of Minor Depression in Pregnant Women:

Association with Somatic Symptoms of Depression

by

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A thesis submitted to the Graduate Faculty of
Auburn University Montgomery
in partial fulfillment of the
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[Antenatal, Minor Depression, Pregnancy, Somatic Symptoms]

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Abstract

A previous study of the prevalence of depression (Ashley, 2010) found that pregnant women were more likely to have minor depression compared to women who were not pregnant. The present study is designed to investigate if somatic symptoms associated with both pregnancy and depression was responsible for this increased prevalence of minor depression. A sample of pregnant women experiencing minor depression ($n = 432$) was compared to women who also had minor depression but were not pregnant. Comparisons of depressive symptoms were based on participant's responses to the Patient Health Questionnaire- 8 Depression Scale. Results indicate that of the somatic symptoms of depression involving appetite, sleep, and energy level, only changes in energy level accounted for the elevated prevalence of minor depression in pregnant women compared to women who are not pregnant. Further analysis indicated that of the emotional symptoms assessed, feeling down and feeling like a failure were more likely to occur among women who were not pregnant compared to women who are pregnant. When the energy level item was removed from analysis, there was no longer a significant difference in mean number of symptom days between the two groups. However, a smaller but significant number of pregnant women meet the criteria for minor depression with the energy level symptom removed. Implications for screening for depression during pregnancy are discussed.

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List of Abbreviations

BDI	Beck Depression Inventory
BRFSS	Behavioral Risk Factor Surveillance System
CDC	Centers for Disease Control
DSM-IV	<i>Diagnostic and statistical manual of mental disorders (4th ed., text revision)</i>
EPDS	Edinburgh Postnatal Depression Scale
PHQ	Primary Care Evaluation of Patient Health Questionnaire
PHQ-8	Patient Health Questionnaire-8 Depression Scale
PHQ-9	Patient Health Questionnaire-9 Depression Scale

Antenatal depression is defined as major and minor depressive episodes during pregnancy (Leung & Kaplan, 2009). According to the World Health Organization, depression is now recognized as one of the most burdensome diseases in the world and also one of the leading causes of disease related disability among women (Kessler, 2003). Research regarding the prevalence of antenatal depression shows a higher prevalence of minor depression in pregnant women, and a higher prevalence of major depression in women who are not pregnant (Ashley, 2010). The current study uses a population-based sample to investigate the hypothesis that endorsement of somatic symptoms of depression in pregnant women explains the higher prevalence of minor depression among pregnant women.

Antenatal depression has sparked considerable concern given its potential impact on both mother and fetus (Gaynes et al., 2005). Several studies have estimated the prevalence of antenatal depression; however, most limit their research to major depression alone. Other studies neglect to distinguish between major and minor depression, estimating a mixed prevalence from 8.5% (Gaynes et al., 2005) to 20% (Leung and Kaplan, 2009). Bowen and Muhajarine (2006) found a prevalence range as high as 50% of pregnant women with lower socioeconomic status (SES) experiencing either major or minor depressive episodes. Of the few limited sources that cover the prevalence of minor depression, Marchesi, Bertoni and Maggini (2009) found a prevalence of 18% among pregnant women.

The large range in prevalence may be explained by several factors including the “variations in definitions (major depression, minor depression, and elevated depressive symptomology), rating scales and timing of the assessments” (Banti et al., 2011). The most accepted form of diagnostic criteria for depression is currently taken from the Diagnostic and Statistical Manual, Fourth Edition, Text Revision (DSM IV- TR). The DSM IV-TR defines a major depressive episode as experiencing five or more of the nine listed symptomatic criteria within a two week period, with at least one symptom being either the symptom of experiencing a depressed mood, or loss of pleasure and/or interest in activities. Minor Depression is defined as fewer than five of the symptoms within a two week period to be considered, with at least one symptom being either experiencing a depressed mood, or loss of pleasure and/or interest in activities.

Several measures have been used in research to screen for depression, including the Edinburgh Postnatal Depression Scale (EPDS), which has been validated as a method for screening major depression (Smith et al., 2010; Gaynes et al., 2005), the Beck Depression Inventory-Second Edition (BDI-II) (Whisman, Davila & Goodman, 2011), and various versions of the Patient Health Questionnaire including the PHQ-9, PHQ-8 (Ashley, 2010; Kroenke, Spitzer & Williams, 2001; Kroenke et al., 2009) and the PHQ-2 (Smith, Gotman, Lin & Yonkers, 2010). All are supported as valid measures for screening depression.

These instruments may be problematic when used to screen pregnant women for depression. Specifically there is a relationship between normal symptoms of pregnancy and the diagnostic criteria of depression, particularly the somatic symptoms. Yonkers, Smith, Gotman and Belanger (2009) found that a pregnant woman is likely to experience “alterations in sleep, appetite/weight, energy and possibly concentration”, which are similar to several of the somatic symptoms in the criteria associated with both major and minor depression. Matthey and Ross-Hamid (2011) also show that a woman's physical changes have face validity, meaning it is reasonable that a pregnant woman would be likely to have a change in her weight as well as a decrease in her energy due to the hormonal changes in pregnancy.

The similarity between physical symptoms of pregnancy and somatic symptoms of depression has led to debate about under diagnosis of depression because depressive symptoms are construed as part of pregnancy, or over diagnosing because physical changes associated with pregnancy increase scores on depression screening inventories.

Research has suggested that women tend to “endorse depressive symptoms that [are] just due to the physical changes of pregnancy [causing] more women [to be] referred (for mental health services) than necessary” (Matthey et al., 2011). It is clear that the overlapping of somatic symptoms of depression and physical changes of normal pregnancy has created difficulty in the ability to accurately diagnose women who are pregnant with depression.

A recent study, using a representative sample comparable of the U.S. population, determined the prevalence of major and minor depression among pregnant women compared to those who are not pregnant. The study found that pregnant women have a higher prevalence of minor depressive episodes and a lower prevalence of major depressive episodes compared to women who are not pregnant (Ashley, 2010). Minor depression requires fewer than 5 symptoms for diagnosis. Three of the symptoms of depression are somatic and similar to physical changes associated with pregnancy. It is important to determine if minor depression is more prevalent among pregnant woman because of physical changes of depression and not those of a depressive disorder.

To date, there is limited research about the prevalence of minor depression among pregnant women, as opposed to the extensive literature on major depression among pregnant women. There has also been no research to determine endorsement of somatic symptoms and account for elevated levels of minor depression among pregnant women.

As minor depression is meeting only three to five of the criteria for depression, and four of the criteria for depression are physical symptoms similar to those of normal pregnancy, it is hypothesized that the reason behind elevated minor depression in pregnant women is due primarily to the symptoms of normal pregnancy, not to minor depression.

This study uses the 2006 BRFSS data, which includes data for the PHQ-8 for a large subset of the sample. The results of this study have the

potential to provide rational behind the ongoing debate of depression being over diagnosed or under diagnosed in pregnant women, as well as generate future research into more accurate depression screening methods and treatment options for pregnant women with depressive symptoms.

Method

Participants

All participants were drawn from the BRFSS of 2006, which is a random digit dialing telephone survey conducted on a yearly basis. With proper weighting, the BRFSS is a representative sample of the adult U.S. population. Interviewers gather data using a standard questionnaire administered to a sample of participants whose telephone numbers are in the United States (Kroenke et al., 2009), District of Columbia, Guam, Puerto Rico, and the U.S. Virgin Islands (Ashley, 2010). The BRFSS statistically controls for sampling bias by weighting the sample for non-coverage (houses that do not have telephones), non-response (houses where individuals do not answer their phones), and the number of telephones in a household. The weighting formula as well as the BRFSS data are publicly available and may be downloaded at the Centers for Disease Control (CDC, 2006a; CDC, 2006b).

The study uses the responses of women between the ages of 18 to 44, an age range selected to reflect the women who are of child-bearing age. The 2006 BRFSS encompasses a total sample who meet this age criteria for minor depression of 6,829 women, 390 of whom reported being pregnant at the time of the survey (Table 1).

Materials and Procedure

The Patient Health Questionnaire (PHQ-8) is comparable to PHQ-9, a measure of depression used in clinical settings (Kroenke et al., 2009). The PHQ-9 items are based on the nine criteria for depression as outlined in the DSM-IV, with the PHQ-8 excluding the question pertaining to thoughts of death and suicidal ideation. This item is omitted from the PHQ-8 because telephone interviewers would be unable to intervene with survey respondents who acknowledge suicidal ideation during the interview. This question may be omitted without detrimental effects to validity and reliability when used to “assess depressive symptoms in individuals with either medical or non-psychiatric conditions because suicidal ideation [is] less common in a primary care depressed population” (Kroenke & Spitzer, 2002). Further research has also supported that depressed pregnant women show fewer intense feelings of suicide compared to women who are not pregnant, suggesting that pregnancy may be a protective factor for the symptom of suicidal ideation (Banti et al., 2009).

Kroenke et al. (2001), demonstrated the construct and criterion validity of the PHQ-9 based on several studies conducted when the instrument was first released. The PHQ-8 is valid and reliable like the PHQ9 and both have been referred to as the “gold standard” for depression screening in general medical settings with adults (Smith et al., 2010). The PHQ-8 has both specificity and sensitivity for each depression categorization, making it both a

valid diagnostic and severity measure in clinical populations (Kroenke et al., 2002; Kroenke et al., 2009).

Each PHQ-8 question asks respondents the number of days during the past two weeks the individual had experienced a particular depressive symptom. For each item, valid responses may range from zero to 14 days.

The PHQ- 8 item responses are converted to scores based on the number of days responded for each question, 0-1 day (“not at all”) = 0 points; 2-6 days (“several days”) =1 point, 7-11 days (“more than half the days”) = 2 points and 12-14 days (“nearly every day”) = 3 points (Jiang & Hesser, 2011). The number of points is summed to produce a PHQ-8 total score. No depression = 0 – 4 points; minor depression = 5 – 9 points; moderate depression = 10 -14 points; moderately severe depression = 15 – 19 points; severe depression = 20 – 24 points (Kroenke et al., 2001), with major depression encompassing moderate to severe categories. If a response to any of the eight questions is missing, a score is not calculated.

The PHQ-8 total scores were used to identify women who met the criteria for minor depression. The study sample is restricted to both pregnant and women who are not pregnant whose PHQ-8 scores were between 5 and 9, inclusive.

Design

The design is a binary logistic regression model with pregnancy status as the outcome variable. Reported symptom days on the eight PHQ-8 items are the predictor variables. Age in years is also included in the model as a

covariate. Odds ratios of symptom frequencies are used to determine differences between women based on their pregnancy status. An alpha level of 0.05 is used for all comparisons between symptoms to verify significance.

The SAS surveylogistic module was used to analyze the data.

Surveylogistic allows for the analysis of complex survey data and accounts for design effects. In addition, the results of the logistic regression model were weighted to better approximate population values. As mentioned above, the BRFSS data set includes a variable (final weight) that corrects for sample bias attributable to telephone non-response, non-coverage and the number of telephones in the household.

Results

The likelihood ratio test was significant indicating that the model fit is significantly better than the null model ($\chi^2 [9] = 385,968.957, p < .0001$). The weighted percent of each symptom of depression experienced by pregnant women was compared to women who were not pregnant (Table 2). Table 3 shows that the Wald χ^2 values indicate that the only symptom pregnant women were more likely to report than women who were not pregnant was a decreased energy level. Wald χ^2 values of the somatic symptoms of appetite change and sleep disturbance were unrelated to pregnancy status. Women who were not pregnant were more likely than pregnant women to report symptoms of feeling down and feeling like a failure. Furthermore, there were no other symptoms that differentiated pregnant from non-pregnant women.

These are Type III effects, meaning that each parameter estimate takes into account the effects of other variables in the model.

The adjusted odds ratio estimates for each depressive symptom indicate that pregnant women were 1.9 times more likely to report a decreased energy level compared to women who are not pregnant (95% CI 1.5, 2.3). Odds ratios for the other somatic symptoms of appetite change and sleep disturbance indicated no significant relationship to pregnancy status. Pregnant women were 0.5 times less likely to report feeling down (95% CI, 0.37, 0.73) and 0.61 times less likely to report feelings of worthlessness (95% CI, 0.37, 1.0) compared to women who are not pregnant. Furthermore, the adjusted odds ratio estimates for the remaining depressive symptoms did not indicate any significant difference between pregnant women and women who are not pregnant (Table 4).

The preceding analysis focused on women aged 18-44 years with minor depression. Two additional analyses were conducted to determine if the removal of the item related to energy level would eliminate differences in mean depression symptom days between pregnant women and women who are not pregnant. As the original finding was based on all women aged 18-44 (Ashley, 2010), this follow-up analysis was performed on the same sample. Table 5 indicates this sample consisted of 47,568 women, 1980 who are pregnant and 45,588 who are not pregnant.

Using all 8 items of the PHQ-8 yielded a significant difference in mean number of symptom days reported by the two groups. Specifically, pregnant

women reported an average of 3.5 symptom days and women who were not pregnant reported an average 3.3 symptom days. A t-test with Satterthwaite correction for unequal variance comparing these means was significant ($t_{[2188.4]} = 3.1, p < .005$). With the energy level symptom removed from the PHQ-8, the average number of symptom days drops to 2.3 for pregnant women and 2.4 for women who are not pregnant. A t-test comparison with Satterthwaite correction for unequal variances indicates no significant difference in mean symptom days reported by the two groups ($t_{[2206.8]} = -1.08, p = n.s.$)

Excluding the energy level item eliminates the mean symptom day difference between pregnant and women who are not pregnant. It is perhaps more important to document how the elimination of this item affects the numbers of women identified as minor depression cases. Using all PHQ-8 items to determine minor depression, 6.95% of pregnant women met the criteria compared to 4.3% of women who were not pregnant. A Chi-Square test of independence was used to determine the extent to which pregnancy and minor depression were associated. The Chi-Square test was significant ($p < 0.0001$), and yielded a Phi Coefficient of -0.0545.

The same analysis was conducted on the basis of PHQ-8 scores calculated without including the energy level item. The weighted percent of pregnant women who met the criteria for minor depression using the 7-item PHQ-8 score was 5.21%, and 4.95% of the women who were not pregnant met the criteria. Chi-Square test for independence was significant ($p < 0.001$),

but produced a smaller Phi Coefficient of -0.0049. With the energy level item included in the PHQ-8 score, the Phi Coefficient is approximately 11 times larger than when that item is excluded from scoring. Although the relationship between minor depression and pregnancy status remains statistically significant with the removal of the energy level item, frequency of case identification for both groups becomes more similar.

Discussion

The goal of this study was to determine if a higher prevalence of minor depression in pregnant women compared to women who are not pregnant was related to an increase in somatic symptoms among pregnant women. The results indicate that of the somatic symptoms involving appetite, sleep, and energy level, only changes in energy level accounted for the elevated prevalence of minor depression in pregnant women compared to women who are not pregnant. When this symptom was removed from analysis, there was no longer a significant difference in mean number of symptom days between the two groups. Our results were further supported by an analysis of the frequency of minor depression in pregnant women compared to women who are not pregnant. Changes in energy level accounted for an elevated frequency of minor depression in pregnant women. When the energy level symptom was removed, the relationships remained significant; however, the group became more similar. The results further indicate that of the emotional symptoms, feeling down and feeling like a failure were more likely to occur among women who were not pregnant. The results support the hypothesis

that a somatic symptom does account for the increased prevalence of minor depression in pregnant women. We can further conclude that pregnant women are less likely to experience key emotional symptoms associated with minor depression

Based on these findings, there is a risk of over-diagnosis of pregnant women with minor depression in routine screenings using the PHQ-8 because some of the physical changes associated with pregnancy resemble the somatic symptoms of depression. Additionally, there is a risk the somatic symptoms of pregnancy being amplified when depressed (Kelley, Russo & Katon, 2001), causing difficulty to distinguish between symptoms associated with pregnancy and symptoms associated with depression. According to the DSM-IV-TR, to be diagnosed with minor depression, a woman would need to report fewer than 5 of the depressive symptoms. Three of the symptom criteria for depression are somatic complaints, and results of this study indicate that the higher prevalence of minor depression in pregnant women is attributable to the somatic symptom of low energy. Therefore, it is likely that some pregnant woman diagnosed with minor depression using the PHQ-8 or similar instruments may be experiencing somatic symptoms related to pregnancy rather than symptoms of minor depression. Over-diagnosis of minor depression in pregnant women may result in unnecessary treatment, which is costly and not without risk.

Common depression treatment methods include medication and/or counseling. Research supports that pregnant women are more likely to elect

a method involving both medication and therapy versus therapy alone if diagnosed with depression (Patel & Wisner, 2011). As a result, intake of antidepressants may have both positive and negative effects. The risk and benefits must be carefully weighed in each case. Antidepressants may increase the risk of major malformations, neonatal toxicity, withdrawal symptoms and neuropsychological behavioral impairment to the fetus (Field, 2010). According to Greco, Eckert and Kreonke (2001), antidepressants have also been shown to relieve depressed patients who are not pregnant of somatic complaints within the first month. Further research should be conducted to verify the benefits and effects of antidepressants on somatic complaints specifically in pregnant women compared to the benefits and effects of counseling or psychotherapy as an alternative. This comparison should take into consideration overall cost of medication versus cost of therapy, including time costs.

The predominant limitation involved with this study is the restriction of data available from the BRFSS and the PHQ-8. The PHQ-8 neglects to verify which stage each pregnant woman is in. Stage of pregnancy may have an effect on the overall mental stability and physical wellness for a pregnant woman. It is possible that the prevalence of all symptoms of minor depression change during pregnancy and thus prevalence of minor depression in pregnant women compared to women who are not pregnant may also vary by stage. Additional research is suggested to verify symptom prevalence by pregnancy stage of each symptom of depression in pregnant

women, particularly the somatic symptoms overlapping both pregnancy and minor depression.

The BRFSS does not provide information on whether the woman is multiparous (one or more prior pregnancies), experiencing pregnancy complications, or having a multiple birth pregnancy. These pregnancy differences could be associated with depression. For example, a women may have pregnancy complications such as Hyperemesis Gravidarum (extreme nausea, vomiting and weight loss) (Fejzo, Poursharif, Much & MacGibbon, 2009), preeclampsia, or anemia, all associated with higher rates of fatigue.

The BRFSS also does not provide a complete medical or psychological history. Some prior experiences may increase the risk of developing depression during pregnancy. According to Klein and Essex (1994), such variables include past history of depression, marital distress, and neuroticism or emotional instability

In summary, this study contributes to the future accurate assessment of minor depression in pregnant women with the PHQ-8, as well as future research in developing better screening models that differentiate minor and major depression in all women. Currently the PHQ-8 is an acceptable method for diagnosing minor depression within the pregnancy population; however, the prevalence of the symptom energy level is often endorsed more so by pregnant women compared to women who are not pregnant. When this

symptom is removed, the prevalence of minor depression drops down to a level seen by women who are not pregnant.

In order to make the PHQ-8 more adaptable for diagnosis, the scoring structure should be adjusted to account for the effects of the energy symptom. Raising the cut off score is not a satisfactory solution to control for the difference in prevalence, as this would affect all of the symptoms, not just energy level. As such, this study supports removing the energy item when calculating the total score for assessing minor depression with the PHQ-8.

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Table 1

Weighted Demographic and Risk Factor Comparison of Pregnant Women with Minor Depression ($5 \geq \text{PHQ-8} \leq 9$) and Women Who Are Not Pregnant with Minor Depression.

Variable	Pregnant		Not Pregnant	
	Frequency	Weighted Percent	Frequency	Weighted Percent
Age Group				
18-24	116	40.38	1058	31.58
25-34	243	47.14	2603	34.05
35-44	73	12.48	3506	34.37
Marital Status				
Married	290	63.93	3555	49.20
Divorced	14	2.82	926	7.75
Widowed	0	0.00	78	0.68
Separated	10	1.17	345	3.06
Never Married	84	20.52	1872	31.46
Cohabiting	34	11.56	380	7.75
Unknown	0	0.00	11	0.10
Race				
White	279	64.86	4656	57.15
African American	64	13.20	1005	11.83
Hispanic	52	15.52	640	25.41
Other Race (Non-Hispanic)	26	4.86	345	3.91
Multiracial (Non-Hispanic)	11	1.55	187	1.69

Table 1 Continued

Weighted Demographic and Risk Factor Comparison of Pregnant Women with Minor Depression ($5 \geq PHQ-8 \leq 9$) and Women Who Are Not Pregnant with Minor Depression.

Variable	Pregnant		Not Pregnant	
	Frequency	Weighted Percent	Frequency	Weighted Percent
Education				
Did Not Graduate High School	42	12.65	685	13.30
Graduated High School	121	34.69	2184	28.88
Attended College	123	22.84	2340	33.66
College Graduate	146	29.81	1952	24.06
Unknown	0	0.00	6	0.10
Employment				
Employed	251	57.38	4810	59.53
Unemployed	37	7.98	474	7.28
A Homemaker	104	27.28	1101	18.45
A Student	20	2.99	447	11.17
Retired	0	0.00	11	0.17
Unable to Work	20	4.37	307	3.16
Refused to Answer	0	0.00	17	0.23

Table 1 Continued

Weighted Demographic and Risk Factor Comparison of Pregnant Women with Minor Depression ($5 \geq PHQ-8 \leq 9$) and Women Who Are Not Pregnant with Minor Depression.

Variable	Pregnant		Not Pregnant	
	Frequency	Weighted Percent	Frequency	Weighted Percent
Income Level				
Less than \$10,000	47	13.10	909	13.82
\$10,000 to \$14,999	72	19.44	1313	17.53
\$15,000 to \$19,999	54	13.05	916	11.48
\$20,000 to \$24,999	75	16.48	1160	14.05
\$25,000 to \$34,999	146	31.08	2210	30.02
Refused to Answer	38	6.84	659	13.10

Table 2

Weighted Percent of Pregnant Women Reporting Depression Symptoms (12-14 Days), Compared to Women Who Are Not Pregnant Reporting Depression Symptoms (12-14 Days).

Variable	Pregnant	Not Pregnant
Sleep	33.9	21.5
Energy	47.2	23.6
Appetite	15.9	11.6
Pleasure	10.6	6.8
Down	0.8	1.8
Failure	0.1	2.02
Concentration	1.1	3.7
Movement	.03	1.5

Table 3

Analysis of Maximum Likelihood Estimates of Pregnant Women with Minor Depression Compared to Women who are Not Pregnant with Minor Depression.

Parameter	Estimate	Wald Chi-Square	Pr > Chisq
Age	-0.06	33.45	<0.0001
Sleep	0.13	1.57	0.2097
Energy	0.63	32.72	<0.0001
Appetite	0.02	0.05	0.8238
Pleasure	0.22	3.11	0.0780
Down	-0.65	14.44	0.0001
Failure	-0.49	3.84	0.0500
Concentration	-0.26	3.78	0.0520
Movement	-0.22	1.43	0.2317

Table 4

Adjusted Odds Ratio Estimates of Pregnant Women with Minor Depression Compared to Women who are Not Pregnant with Minor Depression.

Variable	Adjusted Odds Ratio	95% Confidence Interval
Age	0.94	0.92-0.96
Sleep	1.1	0.90-1.4
Energy	1.9	1.5 -2.3
Appetite	1.02	0.85-1.2
Pleasure	1.25	0.98-1.6
Down	0.5	0.37-0.73
Failure	0.61	0.37-1.0
Concentration	0.77	0.60-1.0
Movement	0.8	0.56-1.2

Table 5

Weighted Prevalence Estimates for Minor Depressive Episode (PHQ 8 $5 \geq x \leq 9$), Major Depressive Episode (PHQ 8 ≥ 10) and No Depressive Episode (PHQ 8 ≤ 4) in Pregnant Women Respondents vs. Women Respondents Who Are Not Pregnant.

Variable	Pregnant (n = 1980)	Not Pregnant (n = 45,588)	χ^2, p
Minor Depressive Episode	24.4 (n = 432)	17.6% (n=7,167)	54410 <.001
Major Depressive Episode	9.1%	10.7%	
No Depressive Episode	66.6%	71.7%	