# Interaction of oxytocin level and past depression may predict postpartum depressive symptom severity

**Suena H. Massey, MD**[a,b], **Stephanie A. Schuette, BA**[a,b], **Hossein Pournajafi-Nazarloo, MD, PhD**[c], **Katherine L. Wisner, MD, MS**[a,d], and **C. Sue Carter, PhD**[c]

[a]Department of Psychiatry & Behavioral Sciences, Northwestern University Feinberg School of Medicine, Chicago, IL

[b] Department of Medical Social Sciences, Northwestern University Feinberg School of Medicine, Chicago, IL

[c] The Kinsey Institute and Department of Biology, Indiana University, Bloomington, IN, USA

[d]Department of Obstetrics and Gynecology, Northwestern University Feinberg School of Medicine, Chicago, IL

## Abstract

**Purpose**—We examined plasma oxytocin concentration and postpartum depression (PPD) symptom severity in women who were not depressed during pregnancy, and whether this differed by major depressive disorder (MDD) history.

**Methods**—We assessed psychiatric history and plasma oxytocin in 66 healthy pregnant women in the third trimester (M = 35 ± 3 weeks) and depressive symptoms at 6 weeks postpartum (M = 5.9 ± 0.8 weeks). Linear regression analysis was used to examine oxytocin and PPD symptom severity, and moderation of oxytocin and PPD by past MDD.

**Results**—Women with (n = 13) and without (n = 53) past MDD differed in third trimester depressive symptom severity, but not oxytocin level, demographic factors or birth outcomes. Controlling for third trimester depressive symptoms, oxytocin level was unrelated to PPD symptom severity [B(SE) = −.019(.084); β = −.025; t = −.227; p = .821]. However, oxytocin level interacted with past MDD to predict PPD symptom severity [(B(SE) = 7.489(2.429); β = .328; t = 3.084; p = .003]. Higher oxytocin predicted greater PPD symptom severity in women with past MDD (p = .019), but not in women without (p = .216).

**Corresponding Author:** Suena H. Massey, MD, 676 North Saint Clair Street, Suite 1000, Chicago, IL 60611, USA, (312) 695-6479 (office), (312) 695-5502 (fax), (202) 577-9286 (mobile), suena.massey@northwestern.edu.

**Conclusions**—Replication in a larger sample and methodologic challenges are discussed.

## Introduction

Major depressive disorder (MDD) occurring after birth, referred to as postpartum depression (PPD), is a common complication of childbearing, affecting some one in five mothers in the first postpartum year (Wisner et al. 2013). PPD has been associated with far-reaching adverse consequences to maternal and child health, including impaired maternal-infant bonding (McFarland et al. 2011), increased risk of recurrence of maternal depression (Yonkers et al. 2009), and the development of mental disorders and medical problems in children later in life (Wisner et al. 2006). A number of psychosocial predictors of PPD have been identified through systematic meta-analysis; these are a prior history of depression, depression during pregnancy, anxiety during pregnancy, general life stress, low social support, and low marital satisfaction (Robertson et al. 2004). As such, routine screening for PPD at the postpartum obstetric follow up visit is recommended by the American College of Obstetrics and Gynecology (ACOG 2015).

However, time constraints related to caring for a new infant, and social stigma associated with depression and mental health problems more broadly, still represent significant barriers to seeking professional help even among women who are identified with PPD (Goodman 2009). Many mothers with PPD feel that they are failing because they expect that they should be happy, which decreases the likelihood that they will seek or accept help (Dennis & Chung-Lee 2006). If women who are destined to develop PPD could be accurately identified during pregnancy, prevention could implemented (Zlotnick et al. 2006). Obstetricians routinely screen for non-psychiatric complications of child bearing with similar prevalence to PPD, such as gestational diabetes, using readily available biomarkers (Wen et al. 2000). The prevalence and far-reaching adverse effects of PPD justify the search for biomarker screening as well.

Oxytocin, a neuropeptide hormone produced primarily in the hypothalamus, and released from the pituitary into the peripheral circulation, long known for its role in delivery and lactation (Carter 1998, Carter et al. 2001) has also received substantial attention for its role in social affiliation and behavior, stress management (Carter & Altemus 1997; Feldman 2012), and increasingly, its potential for therapeutic benefit across a broad range of disorders (Meyer-Lindenberg et al. 2011), including PPD (Kim et al. 2014). There is also early evidence that measures related to oxytocin functioning, including plasma oxytocin concentration (Skrundz et al. 2011) and indices of oxytocin receptor availability (Bell et al. 2015), may represent promising biomarkers of elevated risk for PPD. Clarification of these processes could support the future use of oxytocin as a screening biomarker for PPD during pregnancy.

However, a substantial challenge to the study of peripheral oxytocin concerns its accurate measurement. Recent findings using mass spectrometry suggest that following release,

oxytocin is quickly bound or sequestered on components of blood. Only a small fraction of the oxytocin in peripheral circulation is detectable by conventional immunoassays (Martin-Protean 2015), although the oxytocin measured by immunoassay may represent a biologically relevant, or free component. Moreover, immunoassays—either enzyme immunoassays (EIA) or radioimmunoassays (RIA)—indicate that free oxytocin levels vary inter-individually, and that transient increases can be measured in response to social interactions and also nonsocial stressors (Feldman et al. 2011).

Further complicating matters, the relationship between plasma oxytocin concentration and PPD may not be linear. Seay and colleagues (2014) found that very high and very low plasma oxytocin concentrations predicted an increase in depressive symptoms 10 weeks later. Similarly, in a detailed study involving multiple serial measurements of plasma oxytocin by RIA before, during, and after affiliative and stressful tasks, Cyranowski and colleagues (2008) showed that depressed women exhibited greater increases in oxytocin concentrations following a one-hour affiliation task compared to non-depressed women. Thus, it is possible that prior to the manifestation of clinically detectable depressive symptoms, individuals might experience dysregulation in oxytocin function. This could be reflected by abnormal variation in measured plasma oxytocin levels, in some cases as the oxytocin system attempts to compensate for reduced receptor availability or rapid changes in the hormone. This early dysregulation of the oxytocin system may be detectable as increases in concentrations of the oxytocin peptide in response to affiliative interactions as this system attempts to compensate for lower levels of receptor availability.

Finally, the relationship between oxytocin and depressive symptoms may vary by past exposure to MDD via stable dynamic transcriptional alterations to genes, or epigenetic mechanisms (Sun et al. 2013; Klengel et al. 2014). For example, methylation of the oxytocin receptor gene (*OXTR*) has been linked to past exposure to acute psychological stress exposure that predates the onset of MDD (Unternmaehrer et al. 2012). Recently, methylation of *OXTR* at key regulatory sites, indicative of reduced receptor expression, was found to be associated with a greater risk for PPD among a subset of women who had not experienced depression during pregnancy (Bell et al. 2015). Taken together, these findings suggest that MDD prior to pregnancy may render certain women more vulnerable to PPD, possibly mediated by methylation of *OXTR*, and subsequent dysregulation of oxytocinergic systems. These systems may in turn regulate affect and resilience in the face of stress (Tops et al. 2013) which leads to increased vulnerability to PPD.

The first goal of this study was to determine the relationship between third trimester plasma oxytocin and PPD symptom severity. Based on findings by Skrundz et al., (2009) showing that women with lower third trimester oxytocin were at greater risk for developing PPD at 2 weeks postpartum, we expected to find an inverse relationship between third trimester plasma oxytocin and depressive symptoms at 6 weeks postpartum. Next, we secondarily explored how the relationship between oxytocin and PPD symptom severity might differ by lifetime history of MDD. Based on limited literature, we hypothesized that among women with a history of depression prior to pregnancy, higher oxytocin levels would predict greater PPD symptom severity.

## Materials and Methods

### Sample and Recruitment

Participants were 66 pregnant women recruited during their third trimester of gestation (M = 34.9 weeks, SD = 3.3 weeks, range = 29 – 40 weeks) using online advertisements placed on websites of a large urban university medical center in the Midwest region of the United States. Flyers and brochures were also placed throughout the medical center campus, affiliated clinics, and in nearby local businesses. In addition to advertisements, a research assistant recruited participants from the waiting area of the academic faculty obstetric clinic by assessing interest in "a study about oxytocin and mood." Informed consent was obtained from all individual participants included in the study. Potential participants were screened for the following preliminary inclusion criteria: age    18 years, English-literacy, and third trimester singleton pregnancy. Exclusion criteria were: (a) current mood disorder; (b) medical illness prior to or during pregnancy including diabetes, hypertension, sleep apnea, or thyroid disease; (c) current treatment for depression or anxiety; (d) fetal malformation or multiple gestation; (e) cigarette smoking beyond the $10^{th}$ week of gestation; and (f) pregravid body mass index (BMI) > 32 kg/m$^2$. Derivation of the final analytic sample is illustrated in Figure 1. Eligible women identified through initial screening who did not participate (n = 36) and participants lost to follow-up (n = 2) did not differ in any measured characteristics from those included in the analytic sample (n = 66).

### Study procedures

Women who met initial inclusion and exclusion criteria were invited for baseline assessments. At the baseline visit, after completing written informed consent procedures, demographic information, parity, breast feeding intention, and estimated pre-gravid weight were obtained by a combination of patient report and medical records. Women were evaluated for a current mood disorder using a modified Mini International Neuropsychiatric Interview (MINI) Version 5.0.0 (Sheehan et al. 1998), the Mood Disorders Questionnaire (Hirschfield et al. 2000), and study assessments of depressive symptoms severity described below. None of the women who met initial inclusion and exclusion criteria through screening were found to have MDD or bipolar disorder at the baseline visit.

Following these assessments, women were escorted to the clinical research unit by the research assistant for blood draws. Prior to the blood draw, height, weight, and vital signs were measured by a research nurse. Participants were scheduled for follow up visits approximately 6 weeks following their projected due date (M = 5.9 weeks, SD = 6 days). The study coordinator checked medical records for actual delivery dates, and adjusted the timing of postpartum assessments such that they occurred as close to 6 weeks following delivery as possible. Women were offered the option to complete postpartum assessments either in person or by telephone. All but one women (98.5 %, n = 65 out of 66) opted for the telephone assessment. Participants were asked about birth outcomes and complications, and assessed again for depressive symptom severity. Participants were given a $50 gift card following completion of the postpartum assessments. Data collection began in March 2014 and ended in June 2015. All participants were offered referrals for treatment at the end of the study. To ensure participant safety, all participants were urged to contact the study

coordinator or PI if they developed worsening or new depressive symptoms from the baseline visit until the postpartum follow-up. Any participant requesting support or treatment, regardless of their depressive symptom severity, were invited to obtain it from the study center. All procedures were approved by the Institutional Review Board of Northwestern University prior to conduct and were performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments.

## Measures

### Depressive symptoms

Depressive symptoms during the third trimester and postpartum visits were assessed using the Inventory for Depressive Symptoms – Self Report 30 ($IDS-SR_{30}$) (Rush et al., 2000). This 30-item questionnaire was designed to assess the severity of depressive symptoms in nine symptom domains using well-defined anchors. The $IDS-SR_{30}$ was chosen for use in this sample due to its sensitivity to change in the lower range of scores relative to other depression scales (Rush et al., 2005). The $IDS-SR_{30}$ contains the following cut points of symptom severity: 0 – 13 = no depression; 14 – 25 = mild depression; 26 – 38 = moderate depression; 39 – 48 = severe depression; 49 – 84 = very severe depression. In addition to the $IDS-SR_{30}$, the 10-item Edinburgh Postnatal Depression Scale (EPDS) was also administered during the postpartum follow-up. A score of 10 or greater of the EPDS was considered a positive screen for depression (Cox et al. 1996).

### Past Major Depressive Disorder

To evaluate a past history of major depressive disorder, Module A4 from the MINI, which assesses history of any past major depressive episodes (Sheehan et al. 1998), was administered. For participants meeting criteria for a past depressive episode, the length of time from resolution of the episode to the present time was recorded.

### Blood sample preparation

To minimize diurnal fluctuations and variability due to social context, visits were conducted in the aforementioned order (assessments, followed by blood draw); all participants had blood samples drawn between 11:00 am and 1:00 pm. A 3 mL blood sample was drawn from a peripheral upper extremity vein into chilled glass dipotassium EDTA tubes and placed immediately on ice. After collection, the sample was centrifuged at 3500 rpm for 10 minutes at 4° C. The plasma (supernatant) was collected as 400 μL aliquots into 1.5 ml Eppendorf tubes and immediately stored at −70° C until shipment. All samples were sent in one shipment packed in dry ice to the lab of Dr. Sue Carter at The Kinsey Institute of Indiana University for enzyme-linked immunosorbent assay (EIA)

### Measurement of oxytocin

The enzyme-immunoassay was based on kit ADI 901 153A from Enzo Life Sciences, Farmingdale, NY. Direct measurement of plasma was done following the manufacturers' protocols and samples were diluted 1:8 to obtain values on the most sensitive part of the standard curve. Samples were assayed without extraction in duplicate. The minimum detection limit for oxytocin was 15.6 pg/ml, with inter- and intra-assay

coefficients of less than 10%. The distribution of oxytocin concentrations in this sample are shown in Figure 2.

It is worthwhile to note that previous studies assaying unextracted plasma samples from our laboratory used EIA kits ADI 901 153 from the same company (Enzo, previously Assay Designs), but using an older antibody that has since been depleted. The previous kits yielded reliable and consistent, albeit lower oxytocin values averaging around 250 - 350 pg/ml in samples from thousands of healthy adults (Goldman et al. 2008; Gouin et al. 2010; Rubin et al. 2010; Feldman et al. 2012; Hammock et al. 2012), including pregnant women (MacKinnon et al. 2014; Zelkowitz et al. 2014). We and other laboratories found that the newer ENZO kit (ADI 901 153A) gave values that were approximately 2.5 to 3 fold higher than those obtained with kit ADI 901 153. The precise origins of this shift in peptide values are unknown. However, the inter- and intra-assay coefficients of variation with the new kit remain small. Because of the consistency across laboratories, we assume that the change in basal values reflects differences in the antibody used in the new kits.

### Data analysis

All variables were checked for normal distribution using both visual inspection and the Jarque-Bera goodness-of-fit test. Significantly skewed independent variables were transformed by natural logarithm prior to entry into the regression model. We examined data for outliers, defined as more than two standard deviations from the mean (none found). Participants were divided into those with a past MDD history and those without. Demographic and clinical characteristics were compared between these groups using t-tests and $\chi^2$ tests for continuous and binary variables, respectively. Variables were also examined for multi-co-linearity (defined *a priori* as r = .60) using bivariate correlation analysis (none found). The relationship between third trimester plasma oxytocin concentration and PPD symptom severity was examined using linear regression analysis, with third trimester depressive symptom severity as a covariate. Next, the relationship between oxytocin and PPD symptom severity was tested using past history of MDD as a moderator. In this second model, characteristics that differed between past MDD and no past MDD groups were entered as covariates.

## Results

Characteristics for the whole sample, and by past MDD history are shown in Table 1. Racial and ethnic breakdown was as follows: non-Hispanic Caucasian 72.7 % (n = 48); African-American 10.6% (n = 7); Asian 9.1 % (n = 6); Hispanic 7.6% (n = 5). The distribution of pre-gravid BMI in this sample was: Underweight (BMI < 18.5) = 4.5% (n = 3); normal weight (BMI 18.5 – 24.9) = 68.2% (n = 45); overweight (BMI 25 – 29.9) = 16.7% (n = 11); obese (BMI    30 - 32) = 10.6% (n = 7). Birth complications included preeclampsia (n = 2); infections (n = 2); prolonged labor/failure to progress n = 6; postpartum hemorrhage (n = 1); meconium stained amniotic fluid (n = 1), and breach presentation (n = 1).

Approximately one in five participants (n = 13) had a previous major depressive episode; the length of time between the most recent depressive episode and the current pregnancy ranged from 2.5 to 20 years (M = 10.3 years, SD = 6.8 years). Other past psychiatric diagnoses

detected by the MINI were: panic disorder (n = 2); post-traumatic stress disorder (n = 1); obsessive-compulsive disorder (n = 1); generalized anxiety disorder (n = 1); alcohol abuse (n = 1); alcohol dependence (n = 1), marijuana abuse (n = 1), antisocial personality disorder (n = 1). Women in both past and no past MDD groups scored in the "no depression" to "mild depression" range on the IDS-SR$_{30}$ in the third trimester and at 6 weeks postpartum. Mean EPDS scores were below the positive screening threshold of 10 in both groups. With the exception of past MDD and any past psychiatric history, no significant differences in third trimester measures, birth outcomes, or postpartum measures were found between past MDD and no past MDD groups. As shown in Figure 2, plasma oxytocin concentrations were normally distributed [skewness S(SE) = −.094 (.295); kurtosis C(SE) = −.664(.582)]. Scores from the third trimester IDS-SR$_{30}$ assessment were right-skewed [S(SE) = 3.623(.295)] and therefore natural log-transformed prior to entry into the regression model.

Plasma oxytocin levels were unrelated to PPD symptom severity in univariate (r = .086; p = .493) and multivariate [B(SE) = −.019(.084); β = −.025; t = −.227; p = .821] analyses. For the test of moderation of oxytocin and PPD symptom severity by past MDD history, regression coefficients are shown in Table 2 (F = 14.296 p < .001; *df* = 4; adjusted R$^2$ = .450). Third trimester depressive symptom severity predicted PPD symptom severity [(B(SE) = 4.219(.718); β = .554; t = 5.874; p < .001]. Third trimester plasma oxytocin concentration interacted with a history of past MDD to predict postpartum depressive symptom severity [(B(SE) = 7.489(2.429); β = .328; t = 3.084; p = .003]. Specifically, as illustrated in Figure 3, higher plasma oxytocin concentration measured in the third trimester predicted greater PPD symptom severity in women with a history of MDD (p = .019), but not in women without (p = .216).

## Discussion

In contrast to two similar studies to our knowledge (Skrundz et al. 2011; Eapen et al. 2014), we did not find an inverse relationship between third trimester plasma oxytocin level and PPD as hypothesized. Rather, we found a direct relationship between oxytocin and PPD symptom severity, though only among women with a lifetime history of depression. We carefully considered a number of potential explanations for our discrepant findings.

First, as transient increases in oxytocin levels have been shown following affiliative tasks (Cyranowski et al. 2008), it is important to note that in the current study, oxytocin was measured directly following approximately one hour of study assessments with the research assistant and study psychiatrist, followed by assessment of weight and vital signs by a study nurse. While not intended as such, these interactions among participants and research staff, could have simulated the effects of an affiliative task. Indeed the range of oxytocin levels in the current study were fairly narrowly, and normally distributed (Figure 2) in comparison to the very wide ranges and skewed distributions reported by others (Weisman et al. 2013; Lancaster et al. 2015). As very high or very low oxytocin concentrations have been predictive of depressive symptom severity 10 weeks later (Seay et al. 2014), and depressed individuals may experience greater oxytocin increases in response to affiliation relative to non-depressed individuals (Cyranowski et al., 2008), it is possible that measurement of oxytocin at the beginning of the visit (prior to 'affiliation') instead of at the end (following

'affiliation'), could actually have resulted in finding an inverse relationship between oxytocin and PPD symptom severity.

Next, earlier investigations were drawn from different populations, with different individual histories of both adversity and social support across their lifespans. PPD symptoms were assessed at two weeks postpartum in the Skrundz study (2011) compared to assessment at six weeks postpartum in the current study. Women in the Eapen study (2014) were recruited for a larger study on separation anxiety whereas we specifically recruited healthy women not receiving any treatment for a psychiatric condition. In the Zelkowitz study (2014), while an inverse relationship between oxytocin and depressive symptoms was found in their high stress group, a direct relationship (high oxytocin—greater depressive symptom severity) was observed in the low stress group, which roughly mirrors the direct relationship found in our sample. In summary, our present findings are tentative, and support the value of studying the predictive value of oxytocin in this context of past MDD history.

Next, interpretations of the functional effects of oxytocin must take into account cross-reactivity of oxytocin with other peptide receptors, including those for vasopressin (Albers 2015). At high levels oxytocin might stimulate vasopressin receptors, with effects that are contradictory to those typically attributed to oxytocin (Carter 2014). We have previously found that high levels of oxytocin in the third trimester could be associated with a long or painful labor, possibly through actions on the vasopressin receptor, which may slow labor (Prevost et al. 2014). Thus, the relationship of higher third trimester oxytocin levels to greater PPD symptom severity among women with prior MDD history could have been mediated by the stimulation of vasopressin receptors and associated depression symptoms (Frank & Landgraf 2008).

Variation in methods, including extraction of samples and different antibodies used for measuring oxytocin are another possible source of differences across studies. For this reason, direct comparisons of hormone values across studies are challenging. Of note, mass spectrometry methods to determine the true values for oxytocin in human plasma have recently led to the discovery that oxytocin is in fact available in concentrations as high as 1 ng/ml in human blood (Martin-Protean 2015) and that oxytocin is sequestered/bound to a variety of other molecules in plasma and in whole blood. Thus, assay methods that involve extraction, as well as separation of plasma from other components of blood, although recommended by some (Szeto et al. 2011; McCullough et al. 2013), greatly underestimate the levels of oxytocin in human blood. This putative carrier system might influence the presentation of the epitope (antibody binding site on the peptide), and explain differences among the values obtained with different antibodies.

A final factor that could contribute to discrepancies among studies is that different antibodies may recognize different forms of oxytocin. For example, in addition to the classical 9 amino acid form, these antibodies may recognize the 6 amino acid ring of oxytocin (tocinoic acid) or the precursor molecule, which contains 10-12 amino acids (Gainer 1982). As more reliable methods become available, individual differences in the oxytocin peptide and measures of receptor availability may offer new insights and more reliable methods for the prediction of vulnerability to postpartum depression.

## Limitations

While pregnancy, postpartum, and birth outcomes were not different between women with past MDD and women without, providing some support of the validity of findings, replication in a larger sample would be important. Next, depressive symptom severity was in the mild range, so it is unknown whether findings also apply to a broader range of depressive symptom severity. Finally, measures of the oxytocin receptor or the gene for this receptor were not available for the present study; these might have provided additional clues to individual genetic or epigenetic differences in the vulnerability to PPD (Bell et al. 2015).

## Conclusions

Confirmation of our findings in larger more representative samples can contribute to a more in-depth understanding of the etiology of perinatal depression, and may lead to improved prediction of PPD. In the future, availability of an "objective" blood test could help to challenge misperceptions or stigma associated with depression by providing biological evidence about risk for this condition. In light of the far-reaching consequences of untreated PPD to women and their children, the ability to predict which individuals are at greatest risk for developing PPD before it manifests yields the exciting possibility for prevention.

## Acknowledgements

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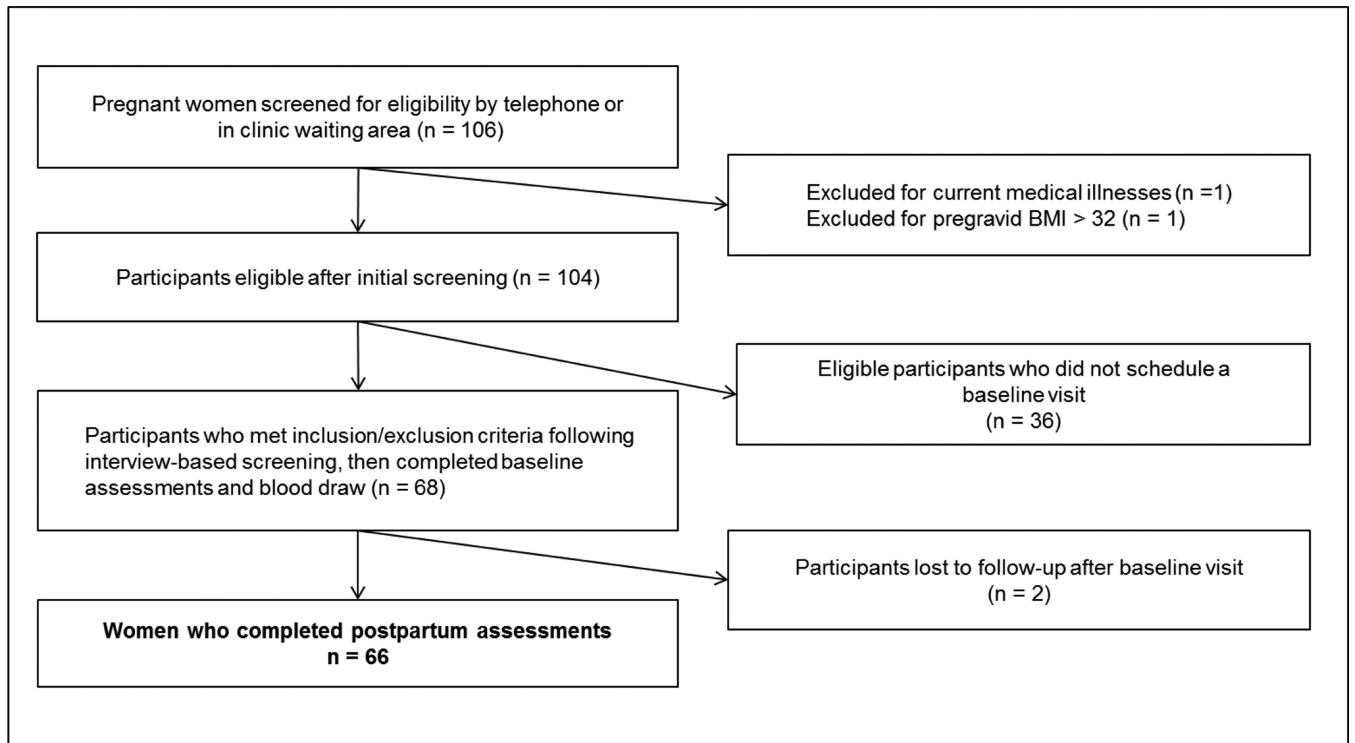
**Figure 1.**
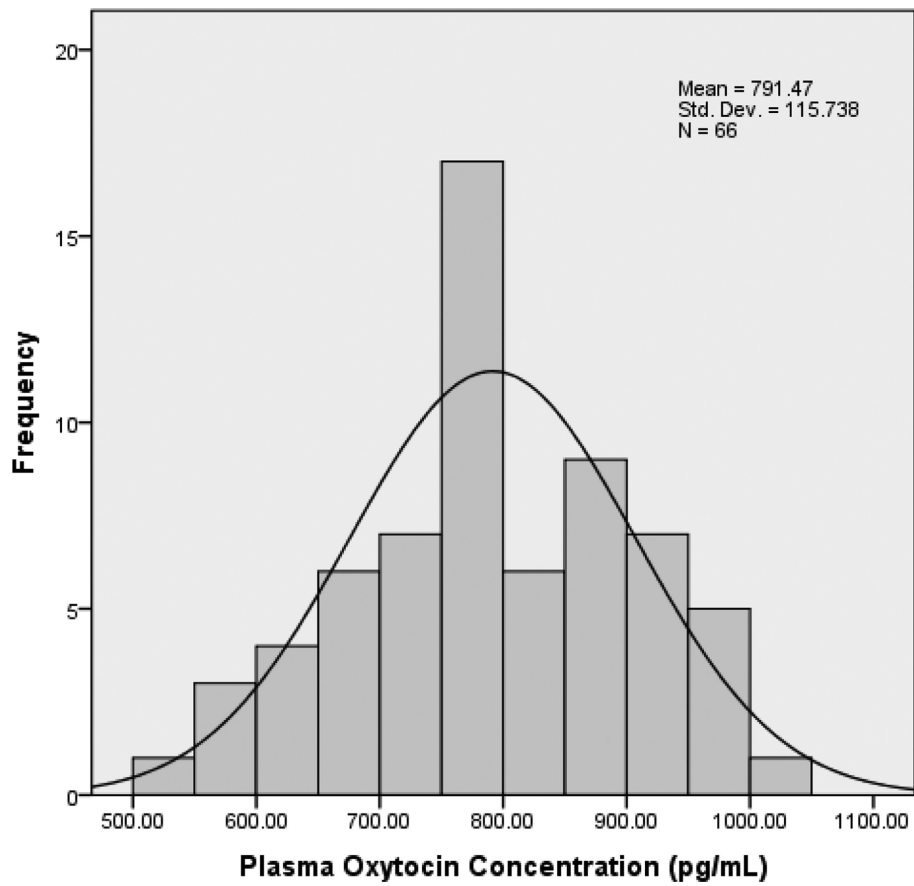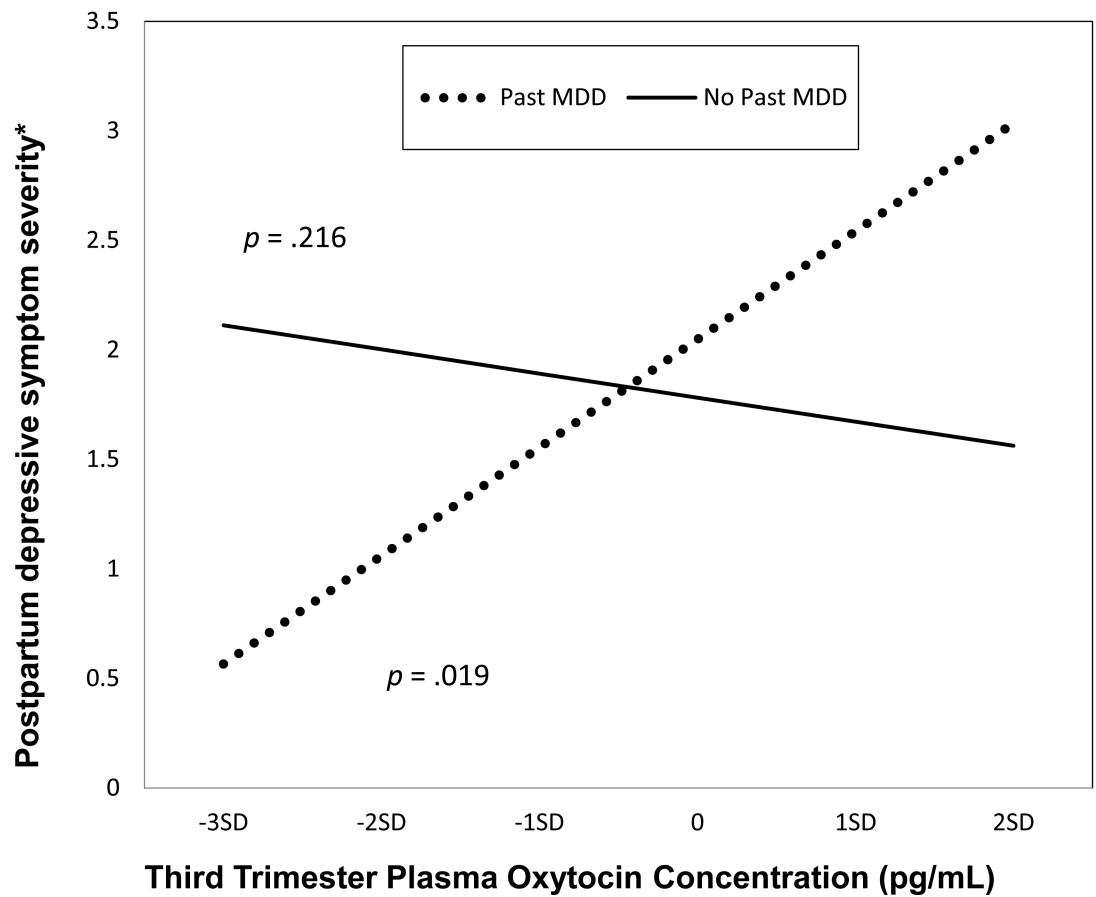Flow chart of potential participants to the analytic sample

**Figure 2.**
Distribution of Third Trimester Plasma Oxytocin Levels (N = 66)

*Natural log-transformed Inventory of Depressive Symptoms – Self Report 30 score
Covariates: Unmarried, multi-parity, natural log-transformed third trimester Inventory of Depressive Symptoms-30 Self Report score

**Figure 3.**
Interaction of third trimester plasma oxytocin concentration with past major depressive disorder to predict postpartum depressive symptom severity (N = 66).

**Table 1**

Descriptive characteristics of participants (N = 66)

| Third trimester measures | Mean (SD) or % | | |
| --- | --- | --- | --- |
| | Total sample N = 66 | Past MDD n = 13 | No Past MDD n = 53 |
| Age (years) | 33.1 (4.9) | 33.1 (5.4) | 33.1 (4.8) |
| Gestational age (weeks) | 35.0 (3.2) | 34.2 (3.1) | 35.2 (3.3) |
| Unmarried | 11.8% | 0.0% | 14.5% |
| Multiparous | 57.4% | 61.5 | 56.4% |
| Racial or ethnic minority | 29.4% | 30.8% | 29.1% |
| Pregravid BMI, (kg/m$^2$) | 23.3. | 22.2 (3.3) | 23.5 (3.9) |
| Gestational weight gain (lbs.) | 30.0 (10.0) | 31.2 (11.8) | 29.7 (9.7) |
| Intention to breastfeed | 98.5% | 100% | 98.2% |
| History of past MDD[a] | 19.1% | 100%[*] | 0%[*] |
| Any current psychiatric diagnosis[a] | 4.4% | 7.7% | 3.6% |
| Any past psychiatric diagnosis[a] | 27.9% | 100%[*] | 10.9%[*] |
| Family history of bipolar disorder[b] | 13.2% | 15.4% | 12.7% |
| IDS-SR$_{30}$ scored | 13.4 (9.3) | 15.7 (8.7) | 12.9 (9.5) |
| Oxytocin concentration (pg/mL) | 791.5 (115.7) | 835.3 (82.1) | 780.7 (120.8) |
| **Birth Outcomes** | | | |
| Gestational age at delivery (weeks) | 39.8 (1.1) | 39.9 (1.4) | 39.8 (1.1) |
| Timing of assessment since delivery (weeks) | 5.9 (0.8) | 5.8 (0.5) | 5.9 (0.9) |
| Birth weight in pounds | 7.6 (1.0) | 7.8 (0.9) | 7.6 (1.0) |
| Low birth weight (< 5lbs 5 oz.) | 1.5% | 0.0% | 1.9% |
| Prematurity | 1.5% | 7.7% | 0.0% |
| Gender of baby | | | |
| Boy | 51.5% | 61.5% | 49.1% |
| Girl | 48.5% | 38.5% | 50.9% |
| Caesarian delivery | 24.2% | 23.1% | 24.5% |
| Any birth complications | 19.4% | 7.7% | 22.2% |
| **Postpartum Measures** | | | |
| Current breast feeding | 89.4% | 100% | 86.8% |
| Estimated feedings per day | 8.6 (3.3) | 9.3 (1.8) | 8.4 (3.6) |
| Return of menses? | 14.3 % | 0.0% | 18.0% |
| IDS-SR$_{30}$ score[c] | 8.8 (7.6) | 14.1 (9.9) | 7.5 (6.4) |
| EPDS score[d] | 2.8 (3.4) | 3.8 (3.4) | 2.5 (3.4) |

[a]Modified Mini International Neuropsychiatric Interview Version 5.0.0

[b]Mood Disorders Questionnaire

[c]Inventory of Depressive Symptoms – Self Report 30

*d*Edinburgh Postnatal Depression Scale

\**p* < .05

**Table 2**

Factors associated depressive symptom severity[a] at 6 weeks postpartum (N = 66)

|  | B | SE | β | t | Sig. | 95% C.I. |
|---|---|---|---|---|---|---|
| Third trimester depressive symptom severity[a] | 4.219 | .718 | .554 | 5.874 | .000 | 2.783 – 5.655 |
| History of MDD[b] | 2.304 | 1.956 | .121 | 1.178 | .244 | −1.608 - 6.215 |
| Third trimester plasma oxytocin (pg/mL) | −.906 | .754 | −.119 | −1.202 | .234 | −2.413 - .602 |
| Oxytocin level × History of MDD | 7.489 | 2.429 | .328 | 3.084 | .003 | 2.633 - 12.346 |

[a]Inventory of Depressive Symptoms –Self Report 30 (IDS-SR$_{30}$)

[b]Modified Mini Neuropsychiatric Interview Version 5.0.0