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Human Lactation**Breastfeeding, Antidepressants and Depression in the Mercy
Pregnancy and Emotional Wellbeing Study**

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Review

Key Messages:

- Although depression is consistently linked to lower rates of breastfeeding, fewer studies have shown breastfeeding can protect against depression.
- Despite a cohort selected to include women with depressive disorders, the overall rates of breastfeeding intention, initiation, partner support and duration were high.
- Mothers being treated with antidepressants and reporting longer breastfeeding durations (in months), on average reported significantly lower depressive symptoms at 12 months postpartum.
- There are potential benefits to breastfeeding to 12 months post-partum for depressed, medicated women.

Abstract

Background: Depression is consistently shown to predict lower rates of breastfeeding. In a handful of studies, breastfeeding has predicted lower depression symptoms. However, studies demonstrating the latter are limited in their measurement of both depression and breastfeeding and have not followed participants from pregnancy across the postpartum.

Research Aims: Describe the breastfeeding intentions and behaviors for the first 12-months postpartum for non-medicated depressed, antidepressant-exposed, and a control group. The secondary aim was to examine group differences in the association between depressive symptoms and breastfeeding duration up to 12-months postpartum.

Methods: First trimester women ($N = 212$) were recruited into a prospective longitudinal study. Depressive disorders at baseline were diagnosed using the SCID-IV and depressive symptoms were measured at first and second trimesters, and six and 12 months postpartum using the Edinburgh Postnatal Depression Scale. We measured breastfeeding duration, support from family and employers, and perceptions of their experience.

Results: Depressed women and antidepressant-exposed women reported a trend towards lower rates of intention, initiation and duration but this did not reach statistical significance. There was a statistically significant difference on depressive symptoms for women taking antidepressants during pregnancy, compared to controls, when they continued to breastfeed for 12 months postpartum.

Conclusions: Our study did not find a strong association between depression or antidepressant use and intention to breastfeed, partner breastfeeding support, initiation or duration of breastfeeding. However, for women who took antidepressants, there was evidence that breastfeeding for 12 months was associated with lower depressive symptoms.

Background

Improving breastfeeding rates and reducing depression in the postpartum have been identified as key areas of focus for public health policy and initiatives for postpartum health. Worldwide initiatives to boost breastfeeding have included the WHO (2009) Baby Friendly Hospital Initiative (BFHI) and a *Call to Action* (2012) by the Surgeon General in the United States of America. Equally, improving identification of perinatal depression has led to many centers introducing universal screening programs for perinatal depression (Siu et al., 2016). In the USA, the United Kingdom and Australia, the frequency of difficulties with breastfeeding and the high prevalence of postnatal depression have led some researchers to suggest there may be common factors associated with increased risk for both (Homewood, Tweed, Cree, & Crossley, 2009; Shakespeare, Blake, & Garcia, 2004) and indeed, the relationship may be bidirectional (Stuebe, Grewen, & Meltzer-Brody, 2013; Stuebe, Grewen, Pedersen, Propper, & Meltzer-Brody, 2012).

In both experimental and observation studies, breastfeeding has been shown to reduce stress, anxiety and negative mood symptoms (Mezzacappa & Katlin, 2002; Mezzacappa, Kelsey, & Katkin, 2005). Furthermore, researchers have used case studies to identify weaning as a risk for relapse in depression (Sharma & Corpse, 2008; Susman & Katz, 1988). There is also some evidence that breastfeeding is protective against sleep disruption of the early postpartum through altering maternal sleep structure (Blyton, Sullivan, & Edwards, 2002; Butte, Jensen, Moon, Glaze, & Frost, 1992). Indeed, sleep quality and disruption have been identified as factors that increase the likelihood of depressive and anxiety symptoms seen in women in the postpartum (Hiscock, Canterford, Ukoumunne, & Wake, 2007). Therefore, several plausible pathways exist to explain an association between breastfeeding and mood.

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Understanding the relationship between depression and breastfeeding also has led researchers to examine physical, physiological and endocrine differences in lactating women with depression. For instance, maternal depression has been associated with lower milk intake and weight gain, and poorer latch (Hart, Jackson, & Boylan, 2011). Women with depression are more likely to dislike breastfeeding and report pain (Watkins, Meltzer-Brody, Zolnoun, & Stuebe, 2011). Researchers have linked depression and breastfeeding with the endocrine system, demonstrating that women who are depressed release lower oxytocin while breastfeeding (Stuebe et al., 2013). Given the role oxytocin plays in reducing the experience of stress and anxiety (Heinrichs, Baumgartner, Kirschbaum, & Ehlert, 2003; Uvnas-Moberg, Widstrom, Nissen, & Bjorvell, 1990), this pathway may explain the earlier findings of negative experiences of breastfeeding in depressed women. Finally, in a recent large study, women ($N = 1447$) with depression were more likely to breastfeed infrequently, add cereal to infant formula and introduce solid foods earlier compared to non-depressed women (Gaffney, Kitsantas, Brito, & Swamidoss, 2014). Collectively, these findings indicate variation in breastfeeding practices and experiences between depressed and non-depressed women.

The relationship between depression and aspects of breastfeeding is examined in two systematic reviews. The first review included 49 articles relevant to depression and breastfeeding up to 2007 and demonstrated a unidirectional relationship between postpartum depression and reduced likelihood of both breastfeeding initiation and duration of exclusivity (Dennis & McQueen, 2009). In the second review, researchers identified 48 studies up to 2013, including both pregnancy and postpartum depression (Dias & Figueiredo, 2015). Women with depression had shorter breastfeeding duration compared to women without depression; however, they did not differ for initiation or intention to breastfeed.

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3 In both reviews, methodological variability was identified as a concern when interpreting
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5 the relationship between depression and breastfeeding. For instance, in the latest review, only
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7 five of the 48 studies included a diagnostic measure of depression and only four of these
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9 demonstrated depression was associated with reduced duration of breastfeeding (Field,
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11 Hernandez-Reif, & Feijo, 2002; Hamdan & Tamim, 2012; Imbula, Okitundu, & Mampunza,
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13 2011; Yonkers et al., 2001). Following women ($N = 168$) only to 12 weeks postpartum limited
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15 the one study that did not report changes for breastfeeding (Bogen, Hanusa, Moses-Kolko, &
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17 Wisner, 2010). Indeed, women were followed to 12 months or more in the postpartum in only 11
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19 studies in the review (Dias & Figueiredo, 2015). In this review, studies were excluded if
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21 antidepressant exposure was assessed.
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27 While antidepressants are becoming a more frequently used treatment for depression
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29 across the perinatal period, research into antidepressants and breastfeeding is mostly limited to
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31 drug level excretion studies and adverse effects on the infant due to exposure (Cooper, Willy,
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33 Pont, & Ray, 2007; Gentile, 2005; A. J. Lewis, Bailey, & Galbally, 2012; Ververs et al., 2006).
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35 This is due to concerns about the potential risk of ongoing exposure of the baby to
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37 antidepressants through mother's milk. In the limited studies that have examined antidepressants
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39 and breastfeeding, women taking antidepressant reported lower initiation rates (Gorman, Kao, &
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41 Chambers, 2012; Leggett, Costi, Morrison, Clifton, & Grzeskowiak, 2016; B. A. Lewis et al.,
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43 2016). There is also some suggestion that serotonergic antidepressants, such as the Selective
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45 Serotonergic Reuptake Inhibitors (SSRIs), may have the potential to increase oxytocin, but may
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47 also influence lactation directly through serotonergic pathways (Marshall, Hernandez, &
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49 Horseman, 2014; Uvnas-Moberg, Bjorkstrand, Hillegaard, & Ahlenius, 1999). Conversely,
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51 serotonin is shown to influence milk production through a negative feedback system via
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3 serotonin and serotonin receptors located within the mammary glands (Marshall et al., 2014).
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5 Therefore, it is unclear if the use of antidepressants may be beneficial or detrimental to
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7 establishing lactation. Given the importance clinically for both woman and child of treating
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9 maternal depression as early as possible, understanding the influence that antidepressants may
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11 have on lactation and breastfeeding behavior is an important focus for research (Hale & Rowe,
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13 2016).
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17 In this paper, we explore the relationship between breastfeeding, depression and
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19 antidepressant use in pregnancy using data from the [study name withheld to maintain the
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21 integrity of the review process]. Specifically, we aim to describe the breastfeeding intentions and
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23 behaviors of three groups of women comprising the [study name withheld to maintain the
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25 integrity of the review process] cohort: those with a diagnosed major depressive disorder but not
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27 taking medication; those taking antidepressant medication; and, those not diagnosed with
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29 depression and not taking antidepressants. In addition, we aim to describe the depressive
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31 symptoms of the three groups during pregnancy and the first year postpartum. Finally, we
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33 examine the association between breastfeeding duration and depressive symptoms in the
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35 postpartum, and investigate whether the association differs between the three groups of women.
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40 41 42 **Methods**

43 44 **Design**

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46 [Study name withheld to maintain the integrity of the review process] is a selected cohort
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48 study with an observational and longitudinal prospective design that recruited women before the
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50 20th week of pregnancy across three groups: women on antidepressant medication in pregnancy
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52 (AD), women with depression not on antidepressants (NMD), and healthy control women
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54 (control group). The study received ethical approval by the [HREC reference withheld to
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maintain the integrity of the review process]. Further details of the design, procedure and participants, including STROBE diagram of the obtained sample, are described in the published study protocol [citation withheld to maintain the integrity of the review process].

Setting

Participants were recruited between September 2012 and October 2014 with the last participant delivering in late May 2015. There are approximately 6000 deliveries per annum at this metropolitan tertiary maternity hospital in [location withheld to maintain the integrity of the review process], which is an accredited Baby Friendly health facility (World Health Organisation & UNICEF, 2009).

Sample

Of the 212 study participants, 35 women were taking antidepressant medication in pregnancy, and 21 were non-medicated but meeting diagnostic criteria for depression or dysthymia at recruitment using SCID-IV. Only three women with current depression met diagnostic criteria for dysthymia. Women were included in the study if they were less than 20 weeks pregnant and proficient in English. Exclusion criteria included psychotic and bipolar disorders, substance abuse disorder, intellectual disability, serious preexisting physical or psychiatric illness requiring acute inpatient admission, and child protection involvement. There were 212 women who completed relevant measurements at 12 months postpartum included in this study from the original 282 recruited into the overall study; attrition was distributed relatively evenly across the groups. With this sample size and using conventional power (.80) and alpha level (.05), a between-groups omnibus F -test can detect an effect as small as $\eta_p^2 = .04$, and a within-between interaction effect (three by four) can detect the smallest effect by conventional standards ($\eta_p^2 < .02$).

Measurement

Demographics and covariates. A range of demographics and key covariates were collected in first and third trimester and at delivery. Information about all constructs and their administration during the period of the study is available in the published study protocol [citation withheld to maintain the integrity of the review process].

Maternal Mental Health. A diagnostic measure was undertaken at recruitment in first trimester of pregnancy to evaluate depressive disorders, the Structured Clinical Interview for DSM-IV (SCID) Mood disorders schedule (First, Spitzer, Gibbon, & Williams, 1997). A screening measure for depressive symptoms was also undertaken at two-time points in pregnancy and then two-time points in the postpartum to examine changes in symptoms over time. The measure chosen was the Edinburgh Postnatal Depression Scale (EPDS), administered in first and third trimester of pregnancy and 6 and 12 months postpartum (Cox, Holden, & Sagovsky, 1987). The EPDS is a 10-item scale measuring depressive symptom severity during a seven-day period. A 4-point (0 - 3) scale is used to produce a total score ranging between 0 and 30. Cox et al. (1987) have demonstrated this tool as internally consistent and valid. In addition, the EPDS is a valid scale for use with Australian women during the perinatal period (Boyce, Stubbs, & Todd, 1993).

Antidepressant Use. Antidepressant type, usage, dosage and timing were assessed by a self-report questionnaire at recruitment and in the third trimester, as well as obtained from hospital records at delivery. Maternal blood was also collected following delivery and assayed for antidepressant drug levels. All women reporting ongoing antidepressant use in pregnancy had commensurate blood drug levels confirming usage [citation withheld to maintain the integrity of the review process]. Thirty-two women on antidepressant medication in pregnancy, who

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3 provided information about infant feeding at 12 months of age, were included in the analyses. Of
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5 these 32 women, 24 (75%) women remained on the same medication from first trimester in
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7 pregnancy through 12 months postpartum; four (17%) of these women increased their dose
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9 during this period.
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12 **Breastfeeding.** Breastfeeding intentions and behaviors were collected at four points
13 during the study period (i.e., Trimesters 1 and 3, and at 6 and 12 months postpartum). The
14 measured variables via self-report were antenatal feeding intentions, partner support of feeding
15 intentions, breastfeeding initiation and length of time to first feed, breastfeeding status at both 6-
16 and 12-months, baby's age (in weeks) at breastfeeding cessation, satisfaction with breastfeeding
17 duration, and for those who continued to breastfeed the nighttime feed frequencies during 6
18 through 12 months. This is the number of feeds overnight and was also recorded for those who
19 did not breastfeed. Maternal perception of partner, employer, mother and health professional
20 support of breastfeeding was also recorded in the postpartum. Breastfeeding was the provision of
21 the mother's milk to the baby and could be via expressed milk or directly from the mother.
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36 **Data Collection**

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38 Researchers approached women who were booked to deliver at [hospital and location
39 withheld] during their initial antenatal appointment. Using a HREC-approved participant
40 information and consent form, participants provided informed consent. Questionnaires were
41 administered at first and third trimesters, and six and 12 months postpartum, by the research
42 coordinator, an investigator or by mail when necessary.
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50 **Data Analysis**

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52 To address the first aim of the paper, we present descriptive statistics for breastfeeding
53 variables to investigate whether breastfeeding behaviors are homogenous between the three
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3 study groups. We present frequencies (n , %) for categorical breastfeeding variables, using z -tests
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6 to compare inferentially the proportional differences between the groups. We present central
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8 tendency measures (mean and standard deviation) for continuous breastfeeding variables, testing
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10 group differences using one-way analysis of variance (ANOVA) tests.

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12 **For the second aim**, we present each group's unadjusted EPDS scores at each point in the
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14 study period and test for a significant interaction using a three by four mixed-plot ANOVA. **For**
15
16 **the third aim**, we examined associations between breastfeeding duration in the first 12 months
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18 postpartum (entered at block 2) and EPDS at 12 months to test for significant differences
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20 between the groups using separate hierarchical regression models, controlling for first trimester
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22 EPDS (entered at block 1). Supporting the regression models, we present group-specific zero-
23
24 order bivariate correlations, and means and standard deviations for each variable in the model.
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26 Together, the three identical regression analyses comprise a multiple-groups pairwise-
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28 comparison framework, which allows for comparisons between groups **by converting the raw**
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30 **difference of coefficients into standardized scores (z -score)** (Hair, Anderson, Babin, & Black,
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32 2010). Data were analyzed using *SPSS* version 24 (IBM Corporation, 2016).
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39 Results

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42 **Women across the three groups did not differ on average in their age, educational**
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44 **attainment and annual household income reported at recruitment. BMI at recruitment was**
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46 **marginally higher in the AD ($M = 27.36$, $SD = 4.77$) group compared to the control ($M = 25.52$,**
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48 **$SD = 4.43$) group; BMI in the NMD ($M = 27.27$, $SD = 5.41$) did not differ to the other groups.**

51 Breastfeeding Characteristics of the Sample

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54 **When comparing groups on their perception that breastfeeding was an enjoyable**
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56 **experience for them, the women did not differ; in fact, the average response was agreeable.**
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3 There were also no significant proportional differences between the groups in support for
4 breastfeeding from partner, mother, their doctor, and their employer. Furthermore, there were
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6 also no significant proportional differences between the groups in mode of delivery and whether
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8 their child was given a pacifier.
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12 Most of the sample initiated breastfeeding (Table 1). For women who reported initiating
13 breastfeeding, the number of minutes to first feed did not differ between the groups (Control: M
14 $= 3.97$, $SD = 10.17$; NMD: $M = 7.34$, $SD = 20.17$; AD: $M = 6.02$, $SD = 11.74$). While the AD (M
15 $= 7.08$, $SD = 4.78$) and NMD ($M = 7.46$, $SD = 4.32$) groups showed a trend towards fewer
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17 months spent breastfeeding, compared to the control group ($M = 8.49$, $SD = 3.92$), there were no
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19 significant differences across the three groups for any of the domains of breastfeeding, including
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21 duration. The groups also reported similar levels of support from their partner for their
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23 breastfeeding intentions (Control: $M = 4.84$, $SD = .59$; NMD: $M = 4.80$, $SD = .41$; AD: $M = 4.91$,
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25 $SD = .39$). Nighttime feed frequency between six and 12 months postpartum was captured
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27 retrospectively in the 12-month questionnaire. At 6, 7, 9 and 11 months, nighttime feeding
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29 frequencies did not differ significantly between the groups (see Figure 1). For both control and
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31 NMD women, the majority were no longer feeding overnight at 12 months of age; however,
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33 significantly more women taking antidepressants (40%) continued to breastfeed overnight.
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44 **Patterns in EPDS for AD, NMD and Control**

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46 Figure 2 presents unadjusted EPDS scores for each group at each of the four
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48 measurement points. The interaction term in the model was significant using a Greenhouse-
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50 Geisser epsilon-corrected test, $F(5.61, 527.59) = 2.80$, $p = .013$, $\eta_p^2 = .03$, *observed power* = .87.
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52 Probing of the interaction term showed that the repeated measurement of time was not significant
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54 for any group using a more conservative alpha (.01) to adjust for family-wise error. However,
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3 groups did differ significantly within measurement points. At Trimesters 1 and 3, both NMD and
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5 AD mothers reported significantly higher EPDS compared to control mothers. At six months
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7 postpartum, the NMD and AD group reported significantly higher EPDS than the control group
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9 and at 12 months postpartum, only the NMD group reported significantly higher EPDS than the
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11 control group.
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13 14 **Breastfeeding Duration and Depression**

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16 The distribution of breastfeeding duration deviated from normality in each group as
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18 indicated using Shapiro-Wilk tests ($p < .05$). Observation of group histograms revealed a non-
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20 normal, bimodal distribution; both six and 12 months were frequent responses. The high
21
22 frequency of mothers reporting 12-month breastfeeding duration indicates that breastfeeding to
23
24 one year is common in the cohort. As a result, we bootstrapped (i.e. resampling with
25
26 replacement) model estimates using 1000 samples and present 95% bias-corrected confidence
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28 intervals to provide an approximation of the accuracy of our estimates. There were strong and
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30 significant associations between all model variables for the AD group and no significant
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32 associations among any model variables for the NMD group (Table 2). AD and NMD mothers'
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34 EPDS scores measured at both times did not differ significantly, but were both significantly
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36 higher than the control group ($p < .05$).
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44 For the AD and control groups, EPDS during Trimester 1 accounted for a significant one-
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46 quarter of the variance in EPDS at 12 months postpartum; higher EPDS scores during Trimester
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48 1 were associated with higher EPDS scores at 12 months (Table 3). In the second block,
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50 breastfeeding duration accounted for significant unique variance in the EPDS scores of AD
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52 mothers. Controlling for their first trimester depression scores, each additional month of
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54 breastfeeding reported by an AD mother was associated with a decrease of half of one point in
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3 12-month postpartum EPDS scores. Pairwise comparisons between each group's breastfeeding
4 duration coefficient demonstrated that only one pair differed significantly: duration was a
5 stronger negative predictor of 12-month postpartum depression scores for AD compared to
6 control women ($z = 2.18, p = .03$).
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12 Although the pairwise comparisons did not show a significant difference between the AD
13 group and the NMD group, the significance of these groups' coefficients from zero was different.
14 There was a clear trend in predicted EPDS scores at 12-months postpartum for mothers in the
15 NMD group, such that they remained relatively constant and sub-threshold (using a clinical
16 screening cut-off of 13) across the range of months (see Figure 3). However, for mothers in the
17 AD group, the trend differed: women ceasing breastfeeding early reported EPDS scores in the
18 clinical range and were similar to NMD mothers. Though with every month longer they
19 breastfed, EPDS scores reduced by half of one point. Over 12 months, this equates to an average
20 6 points lower EPDS score, aligning AD mothers with control mothers who were neither
21 depressed nor taking antidepressants. We tested the difference in EPDS at 12 months postpartum
22 between the three groups, selecting only those mothers still breastfeeding at completion of the
23 12-month survey. Both the control ($n = 73; M = 5.49, SD = 4.30$) and the AD ($n = 12; M = 4.92,$
24 $SD = 3.65$) groups reported significantly lower 12-month postpartum EPDS compared to the
25 NMD group ($n = 8; M = 9.50, SD = 5.88$), $F(2, 90) = 3.29, p = .042, \eta_p^2 = .07$.
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48 Discussion

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50 We found that for women with depression who take antidepressant medication during
51 pregnancy, the duration of their breastfeeding was associated with reduced depressive symptoms
52 at 12 months postpartum. Specifically, each month they continued to breastfeed was associated
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3 with a reduced EPDS score. For those who breastfed to 12 months their level of depressive
4 symptoms was in a comparable range to the control group, in contrast to women on
5 antidepressants who ceased feeding earlier. The contrast in depressive symptoms across the
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with a reduced EPDS score. For those who breastfed to 12 months their level of depressive symptoms was in a comparable range to the control group, in contrast to women on antidepressants who ceased feeding earlier. The contrast in depressive symptoms across the postpartum between women on antidepressants who continued to breastfeed to 12 months and who did not was clear. However, using this observational data, it is unable to be determined whether this is the result of breastfeeding on depressive symptoms or that women who were receiving effective treatment can breastfeed longer.

Despite observational data and few women in the sample who did not breastfeed, treatment for women on antidepressants mostly remained stable on agent and dose across the postpartum. This suggests any additional benefits of treatment were unlikely and we further controlled for in our analyses by including repeat EPDS scores. Women on antidepressants in pregnancy continued to show lower depressive symptoms the longer they breastfed into the postpartum. Women in the non-medicated depressed group did show a downward trend, although not significant, in their depressive symptoms when they continued to breastfeed. Whereas for those women in the control group, depressive symptoms remained low however long they breastfed across the postpartum.

Despite our cohort being a sample selected to include women with depressive disorders, the overall rates of breastfeeding intention, initiation, partner support and duration were high. This is reassuring and suggests public health campaigns to improve breastfeeding in Australia have been effective across the whole population. Across all three groups, most initiated breastfeeding, sustained breastfeeding to six months postpartum, and between one-quarter and one-fifth continued to breastfeed to 12 months postpartum. While this still falls short of WHO recommendations, the result is higher than historical rates and is consistent with overall findings

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3 from recent population surveys (Amir & Donath, 2008), and this is despite our study including a
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5 larger proportion of women with depression and women taking antidepressants than would be
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7 found in a community sample.
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10 An interesting difference identified in this sample was the frequency of night feedings
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12 across the groups. Previous research has shown that the majority of breastfed babies have night
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14 feeds at six months of age (Galbally, Lewis, McEgan, Scalzo, & Islam, 2013; Hörnell, Aarts,
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16 Kylberg, Hofvander, & Gebre-Medhin, 1999). In this study over one-third of women across all
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18 three groups were feeding their infants overnight at 12 months. Women on antidepressant
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20 medication continued to have more frequent night feedings than the other groups. The reason for
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22 this is unclear. However, animal research in cows has shown administration of serotonin caused
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24 inhibition of lactation and conversely the administration of a 5-HT antagonist, methysergide,
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26 increased milk production (Hernandez et al., 2008). Furthermore, these same researchers
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28 administered fluoxetine to cows and showed a decline in milk production (Hernandez, Collier,
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30 Vomachka, Collier, & Horseman, 2011). Given concerns raised that serotonergic agents affect
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32 milk production, it could be postulated that for women taking antidepressant medication more
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34 frequent night feedings may be required to maintain supply (Marshall et al., 2014). Equally, it
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36 may be that women on antidepressants with lower depressive symptoms, similar to controls, are
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38 more able and motivated to feed at night. Ensuring women are getting adequate sleep may be an
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40 important component of clinical care for women with depression on antidepressants that are
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42 breastfeeding.
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50 Taken together, these results suggest there may be an interaction between antidepressant
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52 treatment and breastfeeding that is beneficial for maternal mood, breastfeeding duration, or both.
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54 Given the well-established association between maternal depression and poorer infant, child and
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3 now adult outcomes, these findings can be weighed as part of the careful individual decision to
4 commence or continue treatment with antidepressants while breastfeeding. These findings also
5 suggest that breastfeeding patterns, particularly night feeding, may differ for those with
6 depression and those on antidepressant medication and tailored support and advice may be
7 helpful for these women. For mental health clinicians and researchers, these findings suggest the
8 importance of building the evidence base for safety of antidepressants in lactation and ensuring
9 women with depression are provided with information and support if they choose to breastfeed.
10 For midwives and lactation consultants, this study suggests the importance of the specific
11 consideration of women with depression when designing and developing models of care around
12 breastfeeding support. It may be that women with depression require tailored information that
13 considers antidepressants, but also the specific challenges and benefits of breastfeeding for them.

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29 The mechanisms by which depression and breastfeeding may be related (e.g.,
30 psychological and social processes and biological mechanisms) remain unexplored. For instance,
31 successfully breastfeeding to 12 months postpartum may be associated with cognitive
32 attributions of self-efficacy and confidence, which will be protective for depressive symptoms.
33 For women with depression taking antidepressants in pregnancy, their sense of confidence at
34 becoming parents may be lower and achieving this aspect of early parenting care may be
35 protective for their wellbeing. Equally, biological aspects including both hormonal and genetic,
36 may underpin any relationship between depression and breastfeeding. Future studies examining
37 the relationship between depression and breastfeeding ideally should include genetics, hormonal,
38 psychosocial risk and protective factors as well as robust measures of depression and
39 breastfeeding.

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Limitations

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3 As some women will continue to feed beyond 12 months, a limitation of the study is that
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5 we only follow up to this point. In addition, several wider risk factors to breastfeeding were not
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7 considered, including a woman's own history of being breastfed and history of breast surgery
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9 Finally, breastfeeding information between birth and six months was collected by retrospective
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11 report at 6 months and at 12 months; future research should look to collect this data more
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13 frequently and during the early critical period for breastfeeding in the postpartum.
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18 Conclusion

20 While previous research on antidepressants and breastfeeding has been limited in scope,
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22 our findings suggest an expanded focus for future research. For infants potentially exposed
23
24 through milk, establishing that these medications are safe is vital for clinicians to be able to
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26 prescribe them confidently for breastfeeding women. The long-term implications of this
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28 exposure remain relatively unknown. It is important that researchers continue to untangle the
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30 relationship between depression and breastfeeding, as a potential modifiable risk factor for
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32 postnatal depression. Breastfeeding does not require the addition of costly pharmacological or
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34 psychological interventions and could be a focus where women at risk for depression and
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36 breastfeeding difficulties could be targeted for specific support within the maternity and early
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38 parenting contexts.
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Declaration of Conflicting Interests

One author has previously received honorarium for speaking from Lundbeck in 2015 and 2016. The other authors declare that they have no competing interests.

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3 Figure 1. Nighttime feeding frequency between 6 and 12 months inclusive, for each of the three
4 groups of mothers.
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10 Figure 2. Total EPDS scores at each Wave of data collection for the three groups of mothers who
11 reported initiating breastfeeding. Error bars represent Standard Error of the Mean. Within time-
12 point between-groups pairwise comparison tests, using $p < .01$: Trimester 1 and 3, and 6m
13 Postpartum, AD, NMD > Control; 12m Postpartum, NMD > Control.
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20 Figure 3. Predicted individual 12-month postpartum EPDS scores (adjusted for First Trimester
21 EPDS) by breastfeeding duration in months for all three groups.
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Table 1. Frequency Distribution of Breastfeeding Variables by Groups.

Breastfeeding variables	Non-		
	Control (<i>n</i> = 156)	medicated Depressed (<i>n</i> = 21)	Antidepressant -Exposed (<i>n</i> = 35)
	<i>n</i> (% ^a)	<i>n</i> (% ^a)	<i>n</i> (% ^a)
<i>Intention to Breastfeed at W1</i> ^b			
Mother's milk	123 (79.4)	16 (76.2)	26 (76.5)
Formula	0 (0)	0 (0)	2 (5.9)
Mother's milk and Formula	26 (16.8)	5 (23.8)	5 (14.7)
No Plan Yet	6 (3.9)	0 (0)	1 (2.9)
<i>Intention to Breastfeed at W2</i> ^c			
Mother's milk	141 (90.4)	19 (95.0)	29 (82.9)
Formula	1 (.6)	0 (0)	2 (5.7)
Mother's and Formula	11 (7.1)	1 (5)	3 (8.6)
Don't Know	3 (1.9)	0 (0)	1 (2.9)
Breastfeeding Initiation	153 (98.1)	20 (95.2)	33 (94.3)
Still Breastfeeding at 6 Months ^d	117 (80.1)	15 (78.9)	21 (70.0)
Still Breastfeeding at 12 months ^e	54 (42.2)	4 (26.7)	10 (37.0)
Satisfied with Breastfeeding Duration (valid %) ^f	102 (71.8)	13 (65)	17 (56.7)

Note. No significant differences found between groups for all tabulated descriptive statistics presented above ($p < .05$) using *F*-test to compare means and *z*-scores to compare column proportions.

^a Valid percentage shown.

^b Missing, $n = 2$

^c Missing, $n = 1$.

^d Missing, $n = 17$.

^e Missing, $n = 42$.

^f Missing, $n = 20$.

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Table 2. Group^a Correlations, Means and Standard Deviations For Each Regression Model.

	1	2	3	M	SD
1. EPDS 12 Months Postpartum	-	.47** (.19)	-.60*** (-.10)	8.19 (10.00)	5.02 (4.71)
2. EPDS Trimester 1	.50***	-	-.32* (-.34)	9.88 (10.33)	6.61 (5.19)
3. Breastfeeding Duration	-.06	.08	-	7.21 (7.68)	4.69 (4.32)
Mean	5.49	5.19	8.52		
Standard Deviation	4.34	3.65	3.89		

^aAD above the diagonal (NMD parenthesis), Control below the diagonal.

p* < .05 *p* < .01 ****p* < .001

Table 3. Results by Group for Regression Models predicting 12-month Postpartum Depression, with 95% Bias-corrected Bootstrapped Estimates Path Coefficients.

	Control (<i>n</i> = 154)				Non-medicated Depressed (<i>n</i> = 21)				Antidepressant Exposed (<i>n</i> = 32)			
	95%				95%				95%			
	<i>B</i>	<i>SE B^a</i>	β	<i>C.I.'s^a</i>	<i>B</i>	<i>SE B^a</i>	β	<i>95% C.I.'s^a</i>	<i>B</i>	<i>B^a</i>	β	<i>C.I.'s^a</i>
Step 1												
Constant	2.35	0.53		1.50, 3.19	8.25	2.36		3.08, 12.91	4.63	1.21		.24, 7.23
Trimester 1 EPDS	0.61***	0.08	0.50	.45, .76	0.17	0.21	0.19	-.13, .50	0.36**	.11	.47	.17, .59
<i>R</i> ²		0.25***					.04			.23*		
Step 2												
Constant	3.25	0.83		1.43, 5.34	8.73	3.73		2.15, 15.67	9.68	2.20		6.21, 14.04
Trimester 1 EPDS	0.62***	0.08	0.51	.46, .78	0.16	0.22	0.17	-.14, .45	0.24*	.12	.32	.01, .52
Breastfeeding												
Duration	-0.12 _b	0.08	-0.10	-.27, .03	-0.05	0.27	-0.04	-.62, .55	-0.53** _b	.17		-.89, -.24
ΔR^2			.01				.00			.23*		
<i>R</i> ²		.25***					.04			.45***		

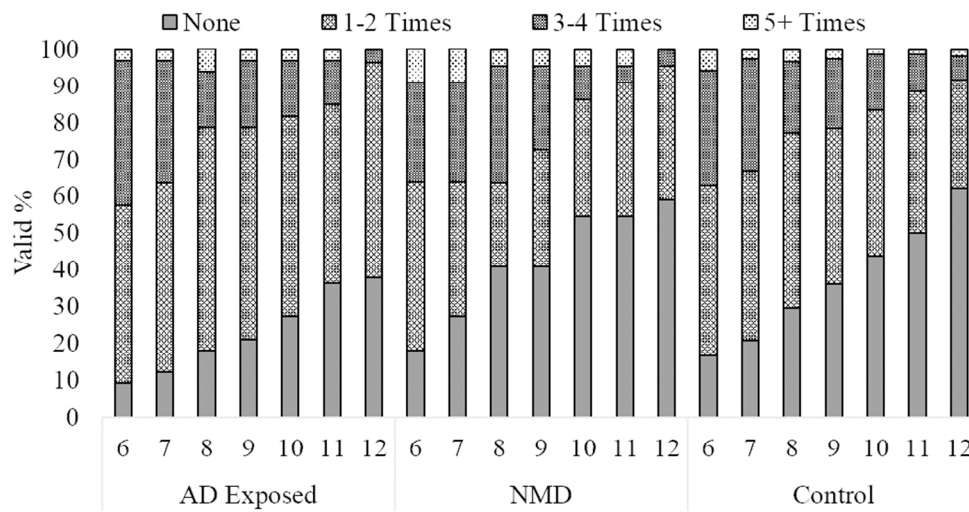
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^a1000 bootstrapped sample estimates

^bGroup coefficients differ significantly ($p < .05$) using pairwise parameter comparison z-test.

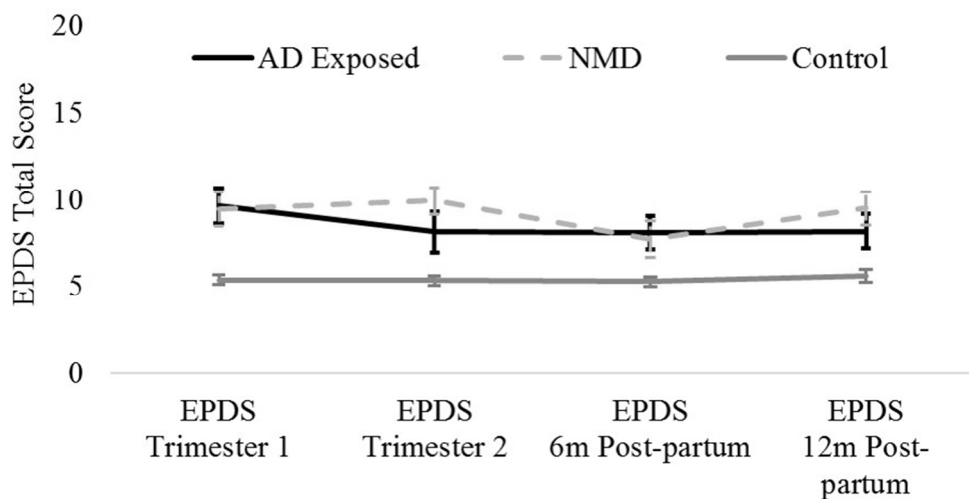
* $p < .05$ ** $p < .01$ *** $p < .001$

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Nighttime feeding frequency between 6 and 12 months inclusive, for each of the three groups of mothers.

92x49mm (300 x 300 DPI)



Total EPDS scores at each Wave of data collection for the three groups of mothers who reported initiating breastfeeding. Error bars represent Standard Error of the Mean. Within time-point between-groups pairwise comparison tests, using $p < .01$: Trimester 1 and 3, and 6m Postpartum, AD, NMD > Control; 12m Postpartum, NMD > Control.

78x40mm (300 x 300 DPI)

Review

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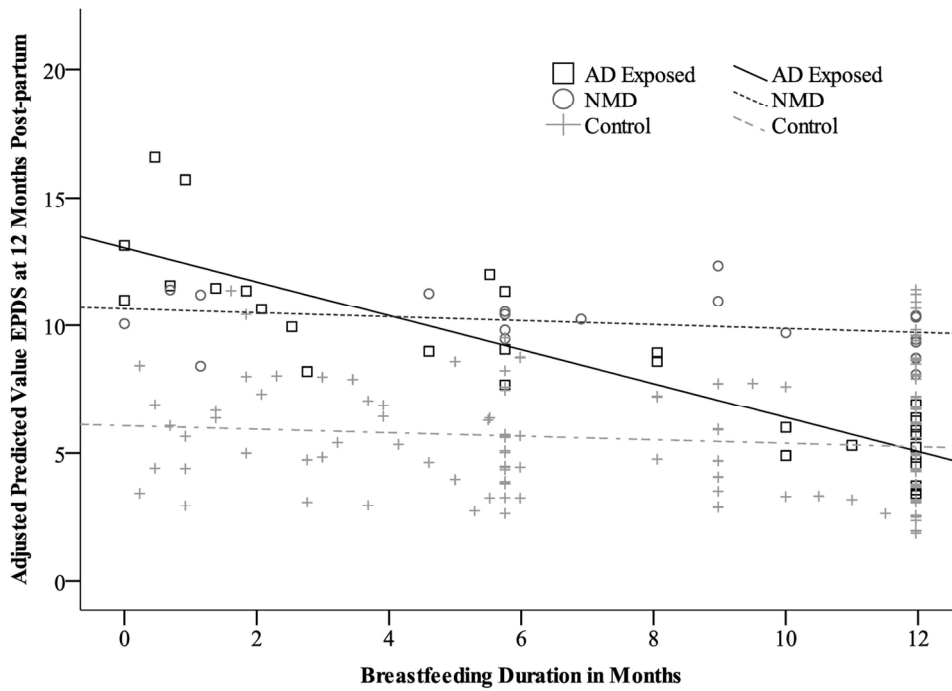


Figure 3. Predicted individual 12-month postpartum EPDS scores (adjusted for First Trimester EPDS) by breastfeeding duration in months for all three groups.

131x92mm (300 x 300 DPI)