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Corresponding Author:	Rebecca M Reynolds University of Edinburgh Edinburgh, UNITED KINGDOM
Corresponding Author Secondary Information:	
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First Author:	Theresia H Mina
First Author Secondary Information:	
Order of Authors:	Theresia H Mina
	Fiona C Denison
	Shareen Forbes
	Laura I Stirrat
	Jane E Norman
	Rebecca M Reynolds
Order of Authors Secondary Information:	
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Abstract:	Background Both maternal obesity and disordered mood have adverse effects on pregnancy outcome. We hypothesized that maternal very severe obesity (SO) is associated with increased anxiety and depression (A&D) symptoms during pregnancy, with adverse effects on gestational weight gain (GWG), postpartum mood and postpartum weight retention (PPWR) and explored any mediation by circulating glucocorticoids. Methods We measured A&D symptoms with validated questionnaires at week 17 and 28 pregnancy and 3 months postpartum in 135 lean (BMI ≤25 kg/m2) and 222 SO (BMI ≥40 kg/m2) pregnant women. Fasting serum cortisol was measured by radioimmunoassay; GWG and PPWR were recorded. Results A&D symptoms were higher in SO group during pregnancy and postpartum despite adjusting for multiple confounders including previous mental health diagnosis (p<0.05), and were non-linearly correlated with total GWG (R2 = 0.06, p=0.037; R2 = 0.09, p=0.001, respectively). In SO group only, increased maternal anxiety (β= 0.33, p=0.03) and depression (β=0.19, p=0.04) symptoms at week 17 pregnancy were associated with increased PPWR, independent of total GWG and breastfeeding. Anxiety symptoms at week 28 pregnancy, but not depression, were non-linearly correlated with serum cortisol level at week 36 pregnancy (R2 = 0.06, p=0.02). Cortisol did not mediate the link between A&D symptoms and GWG. Conclusions Maternal SO was associated with increased A&D symptoms, with adverse effects on GWG and PPWR independent of circulating glucocorticoids. Strategies to optimise GWG and postpartum weight management in SO women should include assessment

of maternal mood in early pregnancy.

Associations of mood symptoms with ante- and postnatal weight change in obese pregnancy are not mediated by cortisol

Theresia H Mina[1,3], Fiona C Denison[2,3], Shareen Forbes[1, 3], Laura I Stirrat[2,3], Jane E Norman[2,3] and Rebecca M Reynolds[1, 3*]

[1]University BHF Centre for Cardiovascular Sciences, Queen's Medical Research Institute, University of Edinburgh, 47 Little France, Edinburgh EH16 4TJ, Scotland, UK

[2]MRC Centre for Reproductive Health, Queen's Medical Research Institute, University of Edinburgh

[3] Tommy's Centre for Maternal and Fetal Health, Queen's Medical Research Institute, University of Edinburgh

Corresponding author: Rebecca M Reynolds

Telephone: +44 (0) 131 242 6762

Fax: +44 (0)131 242 6779

Email: r.reynolds@ed.ac.uk

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Abstract

Background

Both maternal obesity and disordered mood have adverse effects on pregnancy outcome. We hypothesized that maternal very severe obesity (SO) is associated with increased anxiety and depression (A&D) symptoms during pregnancy, with adverse effects on gestational weight gain (GWG), postpartum mood and postpartum weight retention (PPWR) and explored any mediation by circulating glucocorticoids.

Methods

We measured A&D symptoms with validated questionnaires at week 17 and 28 pregnancy and 3 months postpartum in 135 lean (BMI ≤ 25 kg/m^2) and 222 SO (BMI ≥ 40 kg/m^2) pregnant women. Fasting serum cortisol was measured by radioimmunoassay; GWG and PPWR were recorded.

Results

A&D symptoms were higher in SO group during pregnancy and postpartum despite adjusting for multiple confounders including previous mental health diagnosis (p<0.05), and were non-linearly correlated with total GWG ($R^2 = 0.06$, p=0.037; $R^2 = 0.09$, p=0.001, respectively). In SO group only, increased maternal anxiety ($\beta = 0.33$, p=0.03) and depression ($\beta = 0.19$, p=0.04) symptoms at week 17 pregnancy were associated with increased PPWR, independent of total GWG and breastfeeding. Anxiety symptoms at week 28 pregnancy, but not depression, were non-linearly correlated with serum cortisol level at week 36 pregnancy ($R^2 = 0.06$, p=0.02). Cortisol did not mediate the link between A&D symptoms and GWG.

Conclusions

Maternal SO was associated with increased A&D symptoms, with adverse effects on GWG and PPWR independent of circulating glucocorticoids. Strategies to optimise GWG and postpartum weight management in SO women should include assessment of maternal mood in early pregnancy.

Introduction

Depression during pregnancy is common, occurring in 6.5%- 12.9% of women worldwide (Gavin et al., 2005), though symptoms are often under- reported (Boots Family Trust Alliance, 2013). A recent meta-analysis showed that women with higher Body Mass Index (BMI) are at greater risk of anxiety and depression (A&D) symptoms (Odds Ratio (OR) [95% Confidence Interval] = 1.41 [1.10-1.80] and 1.43 [1.26-1.61], respectively) during pregnancy compared to normal-weight women (Molyneaux et al., 2014). This is of concern as 1 in 5 women in the UK are obese at antenatal booking (Heslehurst et al., 2010). Moreover, maternal obesity and mood disorders have been independently shown to associate with various obstetric complications, poorer birth outcomes, infant health (Lawlor et al., 2012; Alder et al., 2007), cognitive and behavioural development (Mina and Reynolds, 2014) and increased risk of postpartum depression (Molyneaux et al., 2014).

Excess gestational weight gain (GWG) is closely linked with maternal obesity (Institute of Medicine, 2009). Both maternal obesity and excessive GWG increase the risk of adverse obstetric outcomes such as gestational diabetes mellitus (GDM), macrosomia, stillbirth, and excessive postpartum weight retention (PPWR) (Norman and Reynolds, 2011). These in turn associate with increased risk of complications in further pregnancies, and risk of future metabolic and cardiovascular disorders in mother (McClure et al., 2013) and offspring (Reynolds et al., 2013). Nevertheless, approximately 20-40% of women exceed recommended international guidelines for GWG (Crozier et al., 2009).

Psychosocial and/or psychological factors may explain the limited outcomes identified in a meta-analysis of randomised trials of lifestyle interventions aimed at reducing excessive GWG in obese pregnancy (Gardner et al., 2011). Obese pregnant women also reported an unwillingness to discuss weight issues with health professionals (Strychar et al., 2000) and a negative attitude towards weight gain (DiPietro et al., 2003). Mood is known to

influence weight gain in non-pregnancy (Luppino et al., 2010) and GWG has been linked with increased risk of major depressive disorder during pregnancy (Bodnar et al., 2009), but most lifestyle interventions in pregnancy have not addressed maternal mood symptoms such as A&D.

Recently a randomised trial using a motivational interview in obese pregnant women was found to reduce both GWG and the level of anxiety (Bogaerts et al., 2013b). Although this strongly implies that maternal mood symptoms influence weight in obese pregnancy, these findings are in contrast with observations in populations of low-income women with lower rates of obesity, where higher psychosocial stress predicts lower GWG (Winkvist et al., 2002; Ota et al., 2011). Therefore in order to better understand how GWG and PPWR are influenced by mood symptoms, we need to simultaneously consider the effect of both maternal obesity and mood symptoms including A&D.

Mechanisms linking obesity with increased A&D remain unclear, but both are known to share many dysregulated biological pathways in non-pregnant individuals. These include altered homeostasis of neurotransmitters, metabolism, inflammation, clearance of oxidative stress, and altered hypothalamic pituitary adrenal (HPA) axis activity (Lopresti and Drummond, 2013). In healthy pregnancy, the maternal HPA axis undergoes dramatic changes with circulating cortisol levels rising three-fold higher than in non-pregnancy (Mastorakos and Ilias, 2003), yet our recent studies show cortisol levels are lower on obese pregnancy (Stirrat et al, 2014). Whether alterations in circulating glucocorticoids underpin the link between maternal obesity and mood symptoms in pregnancy is unknown.

We hypothesized that firstly, maternal obesity would be associated with increased A&D symptoms during pregnancy even after adjusting for an array of obesity-linked and/or mood-linked confounders. Secondly, the predicted increased A&D symptoms in obese

pregnancy would be associated with increased GWG, postpartum A&D symptoms and increased PPWR. Thirdly, the increased A&D symptoms in obese pregnancy would correlate with increased circulating cortisol levels. We aimed to test these hypotheses in a prospective case-control study of over 200 very Severely Obese (SO) women (WHO obese class III, BMI ≥ 40 kg/m^2) and lean controls who were assessed for symptoms of both A&D during the antenatal and postnatal period and were characterised in detail during pregnancy.

Methods

Participants

Women identified during their first community midwifery visit as having a BMI ≥40 kg/m^2 (SO) were referred to the Antenatal Metabolic Clinic (AMC), Simpson's Centre for Reproductive Health, Royal Infirmary of Edinburgh. These women, and lean controls with BMI ≤25 kg/m^2 at booking antenatal visit, were invited to participate in a prospective case-control study from 2008 to 2013. Ethical approval and written informed consent were obtained (reference: 08/S1101/39).

All women were weighed at week ~17, ~28 and ~36 of pregnancy and at 3 months postpartum (TANITA scales BC-418MA, TANITA Ltd). We defined total GWG as body weight at 36 − 17 weeks pregnancy, and used the 2009 IOM guidelines to categorise total GWG (obese women BMI ≥ 30 kg/m^2: recommended GWG = 4.9 -9.1 kg; normal weight women BMI 18-25 kg/m^2: recommended GWG = 11-16 kg). Women with SO were reviewed by a specialized dietician and advised about healthy eating and about how to maintain their weight during pregnancy. Community midwives discussed diet and exercise with lean controls during pregnancy. PPWR was defined as − (postnatal weight loss) = weight at 36 weeks gestation − weight at postnatal visit. A greater difference indicates lower PPWR.

We evaluated various demographic factors preceding pregnancy (collectively termed *maternal factors*) and those arising during pregnancy (collectively termed *pregnancy factors*) which potentially influence maternal mood during pregnancy and may confound the analyses of mood assessment through questionnaire and verified the data with hospital records. Questions about traumatic obstetric history (Mota et al., 2010), reproductive problems (Stanton et al., 2002), and inflammatory disorders (Rosenblat et al., 2014) were included as these have been independently shown to affect non-pregnant women's mood. Information

about major obstetric complications including gestational diabetes (GDM) and pre-eclampsia was extracted from the maternity records. Women identified their minor pregnancy complications from lists provided in the questionnaire: symphysis pubic dysfunction, chest infection, heartburn, headache, carpal tunnel syndrome, constipation, sciatica, hyperemesis and urinary tract infection.

Breastfeeding is known to reduce PPWR. Women were given a questionnaire about breast-feeding habits at the postnatal visit alongside mood assessments. A component of the questionnaire— responses to the question "*Are you breastfeeding your baby now? (yes/no)*"— was included for the subsequent analysis. A "yes" answer included both exclusive breastfeeding and a mix of breastfeeding and bottle-feeding with infant formula.

Mood assessments

Questionnaires were administered at the first study visit (~week 17 pregnancy; visit 1), ~week 28 of pregnancy (visit 2) and at the postpartum visit. The questionnaires comprised 5 previously validated self-rating items in printed format: 1) psychosocial risk factor assessment (Rosengren et al., 2004); 2) Satisfaction with Life Scale (SWLS) (Diener et al., 1985); 3) General Health Questionnaire (GHQ) (Goldberg, 1972); 4) Hospital Anxiety and Depression Scale (HADS) (Zigmond and Snaith, 1983) and 5) State-Trait Anxiety Index (STAI) (Spielberger, 1927). Total scores from each questionnaire and their clinical cut-offs were considered for further analysis.

The psychosocial risk factor assessment measures perceived stress at home, at work and financial stress using scales of "*never*", "*some of the time*", "*several periods*" and "*severe*". We also asked about the occurrence of stressful major life events such as divorce,

job dismissal, and bereavement. Participants' response to this section was later categorised into "none" or "1 and/or more major life events".

SWLS uses 1-7 Likert scale (1= *strongly disagree*, 7= *strongly agree*, range: 5-35), and was previously validated in a longitudinal pregnancy population (Dyrdal et al., 2010). Chronbach's α for the lean group was 0.929, 0.905, and 0.89 for 17 and 28 gestational weeks and postpartum respectively. A score ≤ 19 was used to define life satisfaction as "slightly below average".

GHQ-12 uses binary scoring (range: 0-15). A cut-off score of 3 and 4 was recommended by WHO for the UK population (Goldberg et al., 1997), but since a cut-off of 4 has been shown not to differentiate stress levels between pregnant and non-pregnant controls (Bussel et al., 2006), we used a cut-off of 3 in this study.

HADS evaluates A&D symptoms (range: 0-21 each) and has been reported to help in differentiating transient and enduring stress during pregnancy (Matthey and Ross-Hamid, 2012). A score ≥ 10 per component was used to indicate high risk of clinical A&D.

STAI evaluates both state (transient) and trait (persistent) anxiety (range: 20-80 each), and has been previously validated in pregnant women with SO (Gunning et al., 2010). A cut-off of 39 per component was used to indicate high risk of clinical anxiety.

A single question "*Have you consulted your General Practitioner (GP) about mood issues in the last 2 years?*" was included. Hospital records were used to verify previous history of mood disorders, and where applicable, the type and status of the diagnosis, counselling attendance and/or treatment with antidepressants or anxiolytic medication. At the same time-points, the risk of sleep apnoea and daytime sleepiness were evaluated using self-rating paper questionnaires containing Berlin Sleep Questionnaire (Netzer et al., 1999) and

Epworth Sleepiness Scale (ESS, Johns, 1991), respectively. This is because sleep disordered-breathing strongly associates with mood disorders (Alvaro et al., 2011), and increasingly observed in obese pregnancy (Maasilta et al., 2001).

The researcher (THM) was blinded to participants' SO/lean status during the scoring of mood questionnaires.

Serum cortisol measurement

Serum cortisol levels was measured with radioimmunoassay (RIA) using ImmuChem Cortisol ^{125}I kit (ICN Biomedicals, California, USA) as per the manufacturer's protocol in fasting maternal samples collected at 9am during the first visit (week 17), week 28 and 36 of pregnancy (Stirrat et al., 2014). The intra- and inter- assay coefficients of variation were 6.1% - 8.9% and 7.6%- 9.3% (low- high concentrations), respectively.

Statistical Analyses

Statistical analyses were performed using SPSS 19 (IBM, New York, USA) and figures drawn with SPSS 19 and Graphpad 6 (Graphpad Software Inc., La Jolla, USA). Prior to any analyses, data distribution was determined by Q-Q Plot and by histogram visualisation. Where required, the data were log-transformed. $P \leq 0.05$ was used as a cut-off of statistical significance for descriptive data.

Regression analyses were carried out with BMI as independent variable and each mood assessment scores and other potential confounders as dependent variable for each study time-point. Linear regression analyses were performed to adjust for demographic factors

preceding pregnancy (maternal factors, p^1), during pregnancy (pregnancy factors, p^2), and both (p^3). Previous history of mood diagnosis was further considered by: 1) omitting participants with a previous mental health diagnosis (p^4) and 2) performing further linear regression adjusting for history of mental health diagnosis (p^5). Mood assessments data were also analysed using clinical cut-offs for each questionnaire using logistic regression.

In testing the correlations among maternal mood, GWG, PPWR and serum cortisol levels, maternal mood outcomes were grouped into "anxiety symptoms" and "depression symptoms". Anxiety symptoms were represented by Hospital Anxiety (HA from HADS) and STAI, whilst depression outcomes were represented by Hospital Depression (HD, from HADS) and GHQ. To avoid multiple testing and the need for including a Bonferonni correction, the z-score was calculated for each outcome and we used averaged z-scores for each symptom group in the analysis. We confirmed that the z-scores reflected the general observations that A&D symptoms are highly correlated across week 17 and 28 pregnancy (all Pearson's correlation <0.7, $p \leq 0.0001$) and that generally the SO group displayed poorer mood outcomes (**S Table 1**).

Linear and quadratic curve-fitting were used to test whether there was any non-linear relationship between z-score anxiety and z-score depression with GWG and PPWR. MEDCURVE SPSS plug-in (http://www.afhayes.com/) was used to test whether there was any non-linear mediation by serum cortisol levels.

Results

Subject characteristics and confounding factors

The population of this study included all women with singleton pregnancies that completed mood assessments during pregnancy in the cohort—135 lean and 222 SO women. **Table 1** presents the characteristics of the participants. Although the SO group were heavier than the lean group at each time-point, they had significantly lower GWG.

SO group were younger, had higher parity, and were less affluent. They consumed less units of alcohol preceding pregnancy, but were more likely to smoke during pregnancy than the controls. There were no significant differences between lean and SO in other possible sources of maternal stress preceding the current pregnancy (**Table 1**). More participants in SO group developed GDM than in the lean group, but the rates of preeclampsia were similar. SO group reported a greater number of minor obstetric complications, and an increased risk of developing sleep disordered breathing than lean during pregnancy (**Table 1**).

More SO women had a history of a prior mental health diagnosis, which was dominated by depression (**Table 2**). However, the proportion of clinically active symptoms and antidepressants prescriptions at the first antenatal booking were similar between groups. The response to the direct question *"Have you consulted GP about mood issues in the last 2 years?"* was consistent with the hospital records (**Table 2**). Altogether SO group had more maternal and pregnancy factors which have been recognised to negatively influence maternal mood.

SO women had higher psychosocial stress and lower mood throughout pregnancy even after adjusting for confounding factors

SO mothers had a higher proportion of unemployment and higher finance-related stress (**Table 3**). When the unemployed individuals were excluded from the analysis, the work-related stress was higher among SO mothers (p=0.013). More SO mothers also experienced 1 or more traumatic life events preceding pregnancy.

In unadjusted analyses SO mothers were less satisfied with life and had higher A&D symptoms during pregnancy (P[1], **Table 3**). Adjusting for pregnancy factors reduced the significance of SWLS and HADS at visit 2 (P[3], **Table 3**), however the SO group generally displayed poorer results in mood assessment during pregnancy (P[4], **Table 3**). Analysing the data using clinical cut-off values of each questionnaire revealed that SO mothers were still at higher risks of A&D symptoms (P[1], **S Table 2**). Adjusting for maternal and/or pregnancy factors reduced the significance of SWLS, HADS and STAI (P[2], P[3], P[4], **S Table 2**), implying that maternal and/or pregnancy factors may play a larger role in influencing mood in SO participants with higher levels of anxiety. GHQ remained significant even after adjusting for both maternal and pregnancy factors (P[4], **S Table 2**).

Based on the results of the direct question and hospital records, we investigated whether the poorer mood assessment result in SO group was independent of participants' previous history of mental health diagnosis. We observed similar findings when we either included adjustment for- or excluded individuals with- a previous history of mental health diagnosis (**Table 3**). We concluded that SO prior to pregnancy was independently associated with higher A&D symptoms throughout pregnancy, independent of various demographic and pregnancy factors and previous history of mental health diagnosis.

Postpartum mood outcomes

The overall study attrition rate at postnatal follow-up for each group was approximately 30% (CONSORT table, **S Fig 1**). Women who attended for postnatal follow-up had better mood symptom scores during pregnancy than those who did not attend. In particular, SO women reported significantly better mood scores at the second visit in all domains other than HD than those who did not attend for follow-up (**S Table 3**). Despite this SO was associated with increased postpartum A&D symptoms compared to lean (P^4, **Table 3**) other than the perceived life satisfaction which increased following child birth in both groups (**S Fig 2**). The significance of the anxiety subsection of the HADS at the postpartum visit was reduced after adjusting for maternal factors (P^2, **Table 3**). Higher postnatal anxiety symptoms, in SO mothers were dependent on earlier anxiety symptoms during pregnancy, but not depression symptoms (P^7, **Table 3**).

Inverted U-shape relationship between GWG and maternal mood symptoms

No linear correlations between maternal mood symptoms at week 17 pregnancy and total GWG were found in either group. Mood symptoms formed an inverted U-shaped relationship with total GWG (**Fig 1**). At (z) anxiety and (z) depression symptoms = 0, GWG of both groups was within the 2009 IOM guideline recommendations, but were below the guideline with lower and higher levels of A&D symptoms. Both (z) anxiety and (z) depression symptoms were correlated significantly with GWG in SO group, whereas only the (z) depression symptoms were correlated significantly with GWG in the controls. The majority of the scatters with (z) depression symptoms ≤ 0 aggregated very tightly, implying that the majority of the correlation was due to participants with higher depression symptoms. Overall

Fig 1 implies that either low or high maternal symptoms of anxiety and/or depression result in lower total GWG than the 2009 IOM guideline, particularly in SO women.

Maternal mood symptoms are associated with increased PPWR in SO group, independent of total GWG and breastfeeding

SO group had significantly lower PPWR and lower proportion of breastfeeding at the postnatal visit as compared to the controls (**Table 1**). Increased PPWR was associated with increased maternal A&D symptoms at week 17 pregnancy in SO group, but not in the controls (**S Table 4**). Therefore regression analyses were performed in SO group only. **Table 4** shows that increased maternal A&D symptoms at week 17 pregnancy were associated with significantly increased PPWR in SO group, independent of total GWG and breastfeeding.

The associations of increased A&D symptoms in maternal SO with GWG and PPWR are independent of circulating glucocorticoids

Serum cortisol levels were lower in pregnancy with SO (**Table 1**), consistent with our previous observations (Stirrat et al., 2014). In SO group, anxiety symptoms at week 17 pregnancy formed an inverted U-shape correlation with serum cortisol level at late gestation such that cortisol levels were lowest in those with the lowest or highest anxiety symptoms (**Fig 2**). Serum cortisol level at week 28 pregnancy formed a U-shape relationship with total GWG in SO group such that lowest and highest cortisol levels were associated with greatest GWG (R^2=0.051, p=0.03). Increased serum cortisol level at week 36 pregnancy was associated with increased PPWR in SO group in adjusted analyses (β= -0.45, p=0.03). A

mediation analysis showed that serum cortisol level did not mediate the association of anxiety symptoms with total GWG (p=0.08) or with PPWR (p=0.50) in SO women.

Serum cortisol levels were not related to depression symptoms in SO, and no correlations were observed in lean group. Serum cortisol level at week 28 pregnancy was associated with reduced total GWG in controls in unadjusted and adjusted analyses (r=1.9, p<0.05; β=-2.2, p<0.05, respectively). There were no associations between cortisol levels and PPWR in lean women.

Discussion

In this prospective case-control study, we demonstrated for the first time that maternal SO is associated with higher antenatal and postnatal A&D symptoms compared with normal-weight controls, independent of a large number of confounders including several maternal and pregnancy factors and previous mental health diagnosis. We further showed the adverse associations between anxiety symptoms in early pregnancy and weight outcomes were not mediated by serum cortisol levels.

Many of the anxiety, but not depression outcomes, were attenuated after adjusting for pregnancy factors, implying that the majority of antenatal anxiety symptoms were pregnancy-specific, and can therefore be targeted for intervention during pregnancy. In contrast to findings in an intervention trial using motivational interview in an obese (BMI>30 kg/m^2) pregnant cohort from the Netherlands (Bogaerts et al., 2013b), we did not find significant changes in the STAI scores in SO women during the course of pregnancy. This was unlikely due to the higher severity of obesity in our cohort, as the mean STAI scores were similar to those of the women in the Netherlands cohort (Bogaerts et al., 2013b). A decrease of anxiety symptoms therefore seems achievable only when they are specifically addressed during antenatal care.

On the other hand, the higher antenatal GHQ scores in SO group as compared to controls, which remained significant following adjustments for multiple confounders, indicates that depression symptoms are not pregnancy-specific. Whilst the antenatal care given in our study and the motivational interview in the Netherland cohort (Bogaerts et al., 2013b) appear sufficient in preventing the aggravation of depression symptoms, it also implies that a more specific pharmacological or behavioural intervention such as counselling and/or cognitive behavioural therapy may be required to significantly reduce depression symptoms in obese pregnant women.

Our findings support the view that antenatal anxiety is one of the leading risk factors for postnatal anxiety disorders (Lancaster et al., 2010). Although antenatal depression symptoms remain a major risk factor for postpartum depression, our findings support the argument that postpartum depression has a distinct aetiology (birth and parenting) from antenatal depression (demographic factors). Ultimately antenatal mood symptoms in a vulnerable subpopulation such as SO pregnant women should be highlighted to health care professionals to help prevent possible postpartum mood disorders, and hopefully improve maternal and infant wellbeing.

In considering whether an intervention in early pregnancy could prevent the potential negative effect of antenatal mood symptoms, we evaluated the link between maternal mood symptoms at the first visit (week 17 pregnancy) and pregnancy outcomes. The non-linear correlation between maternal mood and GWG may partly explain the previous conflicting literature about mood and GWG in women with different levels of obesity (Rauh et al., 2013; Guelinckx et al., 2010). However, it appears to be more physiologically relevant in the SO group as the proportion of pregnant women with high mood symptoms and the magnitude of total GWG deviation from the IOM guidelines was greater in SO group as compared to controls. Mothers with SO and lower levels of A&D symptoms may have possibly invested greater effort in managing their diet, resulting in less GWG. Nevertheless, the management of obese pregnancies should strongly consider addressing A&D symptoms since the more extreme the mood symptoms, the further the total GWG deviated from that of women with average levels of mood symptoms.

The association between antenatal A&D symptoms and PPWR has not been previously reported in obese pregnancy. Bogaerts et al (2013a) recently reported the association between antenatal anxiety symptoms, but not depression symptoms, with increased PPWR in obese women. But unlike our study, Bogaerts et al (2013a) study lacked

healthy weight controls and the participants were less severely obese (BMI = 34.4 kg/m^2). Both the non-linear correlation between maternal A&D symptoms and GWG and the lack of a specific intervention for mood symptoms may explain why lifestyle interventions targeting GWG and/or PPWR have had limited success so far (Gardner et al., 2011).

The findings in a meta-analyses in a non-pregnant population, where acute stress promotes increased cortisol levels (Dickerson and Kemeny, 2004) but prolonged stress promotes blunted cortisol reactivity, resulting in lower systemic cortisol (Burke et al., 2005), may explain the inverted U-shape correlation between anxiety symptoms, but not depression, and serum cortisol level at late gestation. Such a time-specific correlation is likely to be due to the transforming maternal HPA axis during early pregnancy (Pasquali et al., 1993), together with a higher trajectory of cortisol level with anxiety in pregnancy (Kane et al., 2014) and the generally lower levels of circulating cortisol in SO women as compared to controls. The U-shape correlation between cortisol levels and GWG found in the SO group was unexpected and was in contrast to the inverse linear relation observed in the lean women. A recent observation showed obese pregnant women with excessive GWG had the highest evening cortisol levels as compared to lean women (Aubuchon-Endsley et al., 2014). However, we did not observe any direct mediation by cortisol of the links between A&D symptoms on either GWG or PPWR. Future studies should consider the assessment of free cortisol, daily profiling, and/or the circadian, placental and foetal effects on the maternal HPA axis.

The main strength of our study is the prospective study design. The detailed characterisation of women during pregnancy enabled us to adjust for multiple important risk factors that have not been considered simultaneously in pregnancy such as sleep disordered breathings, infertility and inflammation disorders. Furthermore, the very clear differences in obesity levels between our SO and control group enabled us to determine independent effects

of obesity, unlike other studies with overweight and less severely obese women (Molyneaux et al., 2014). The higher proportion of deprivation among the SO mothers than in the lean group is a limitation, nevertheless this is consistent with findings from the UK national survey where maternal obesity correlates with deprivation and income level (Heslehurst et al., 2010) and we adjusted all analyses for deprivation category. The total GWG, which as calculated between 17 and 36 weeks of gestation, may have underestimated the actual total GWG as defined by the IOM. However since the total GWG at (z) score anxiety and depression = 0 was within the IOM guideline in both groups, this did not seem to pose significant problems.

We were limited by the 30% attrition rate at postnatal follow-up, though this was similar in both lean and SO groups. Of note, those who did not attend for follow-up had poorer mood scores than those who did, particularly in the SO group and so it is likely that we may have underestimated the post-partum mood differences between groups. We were unable to define PPWR by subtracting postnatal weight with weight preceding the pregnancy as these data were unavailable. However our calculation of PPWR was free from any bias of maternal recall. We could not segregate exclusive breastfeeding from mixed breast/bottle feeding as the proportion of exclusive breastfeeding was very low, even in the controls. This has not been previously discussed (Bogaerts et al., 2013a).

In conclusion, SO during pregnancy is associated with significantly poorer antenatal and postnatal maternal mood symptoms. Both anxiety and depression symptoms formed an inverted U-shape relationship with total GWG where either few or several adverse mood symptoms was associated with less total GWG. This information should inform strategies to optimise GWG in SO women.

Conflict of Interest

None

Ethical Standards

The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008.

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Figure Captions

Figure 1 Anxiety and depression symptoms in week 17 pregnancy correlate non-linearly with total Gestational Weight Gain.

Total Gestational Weight Gain = Weight (kg) at week 36- week 17 pregnancy. (Z)Anxiety symptoms = average of (z) HA and (z) STAI. (Z)Depression symptoms = average (z) HD and (z) GHQ. The 2009 IOM guideline for lean group = 11-16 kg, and for SO group = 5-9 kg. SO: Severely Obese.

Figure 2 Anxiety symptoms are correlated non-linearly with the level of serum cortisol at week 36 pregnancy in severely obese women.

R^2 = the coefficient of correlation, the curve-fitting result of the quadratic function. No significant linear correlation was found.

Tables

Table 1 Maternal body composition, gestational age at visit and demographics [1]For further analysis the log-transformed serum cortisol levels were used. [2]Others include eczema, rheumatoid arthritis, multiple sclerosis and Crohn's disease. Bold-Italic texts are significant at 0.05 level, underlined texts are significant at 0.1 level. SO: Severely Obese; ESS: Epworth Sleepiness Scale; IVF: In Vitro Fertilisation; PCOS: Polycystic Ovarian Syndrome. P value for body composition measures changes during pregnancy. Statistical tests include [a] t-test, [b] chi-square, [c] Mann-Whitney, [d] Fisher's Exact. *Deprivation Category (McLoone, 2004), **One alcohol unit follows the NHS guideline. Bold-Italic texts are significant at 0.05 levels. Underlined texts are significant at 0.1 levels.

Table 2 Mental health demographics [1]The tabulation only includes participants with previous diagnosis of mental health disorders. [2]The tabulation only includes participants with active mental health disorders at 1st antenatal booking. SO: Severely Obese, p (χ^2): P value Chi-square and/or Fisher's- Exact test. Bold-Italic texts are significant at 0.05 levels

Table 3 Psychosocial stress, survey on consulting GP regarding mental health, and mood assessments of research participants throughout pregnancy and at postnatal stage

P^1 was obtained from [a] chi-square test, [b] Fisher's Exact test, [c] Mann-Whitney Test and [d] unpaired t-test. Linear regression was used to obtain P^2 P^3 and P^4. SO: Severely Obese, Preg: Pregnancy, PN: postnatal. Bold-Italic texts are significant at 0.05 levels. Underlined texts are significant at 0.1 levels.

[1] unadjusted

[2] adjusted for maternal factors **prior to** current pregnancy: age, smoking status, alcohol consumption (unit/week), parity, deprivation category

[3] adjusted for maternal factors arising **during** pregnancy: minor complications, GDM, risks of sleep apnoea, differences of gestational visit time between lean and obese groups at visit 1 and postnatal

[4] adjusted for factors in P^2 and P^3, [5] adjusted for previous history of mental health diagnosis, [6] after omitting individuals with previous history of mental health diagnosis.

[7] P^5 adjusted for the results of anxiety or depression symptom assessment in pregnancy

Table 4 Increased maternal anxiety and depression symptoms in week 17 pregnancy are associated with increased postpartum weight retention in Severely Obese (SO) group. Postpartum weight retention = - (Postnatal weight loss). P^1: All demographic factors as defined in the demographic table and time- points at postnatal visits; P^2: demographic factors + breastfeeding; P^3: demographic factors + breastfeeding + total Gestational Weight Gain. Bold-Italic texts are significant at 0.05 levels. Underlined texts are significant at 0.1 levels.

Table 1

Demographics		Lean (n = 135)	SO (n = 222)	P value
Body composition at visit 1, mean (SD)	Weight (kg)	63.3 (6.8)	119.3 (14.9)	≤ 0.0001[a]
	BMI (kg/m²)	22.8 (1.7)	44.2 (4.1)	≤ 0.0001[a]
	BP- systolic (mmHg)	105.9 (8.8)	117.3 (9.9)	≤ 0.0001[a]
	BP- diastolic (mmHg)	63.1 (6.8)	69.9 (7.3)	≤ 0.0001[a]
Gestational age (weeks) & postnatal age (months) at visit	Visit 1 (mean in weeks + days, CI[95%])	17+4 (17- 18)	18+4 (18+2- 19+2)	0.0004[a]
	Visit 2 (mean in weeks + days, CI[95%])	29 (28+4 - 29+3)	28+6 (28+2- 29+3)	0.646[a]
	Postnatal (mean in months, CI[95%])	3.9 (3.6- 4.1)	4.1 (3.8- 4.5)	≤0.0001[a]
Total Gestational Weight Gain (kg)	Mean (SD)	9.59 (3.85)	5.73 (5.07)	≤ 0.0001[a]
	According to the 2009 IOM recommendation, week 36-17 pregnancy — Below	88 (67.69)	84 (43.75)	≤ 0.0001[b]
	Within	34 (26.15)	63 (32.81)	
	Above	8 (6.15)	45 (23.44)	
Postpartum weight retention (kg)	Week 36 pregnancy- postpartum, mean (SD)	9.5 (3.65)	6.77 (6.17)	≤ 0.0001[a]
Serum cortisol level, nmol/l[1]	Week 17 pregnancy, mean (SD)	1555.29 (977.97)	1386.18 (1074.39)	0.007[c]
	Week 28 pregnancy, mean (SD)	2387.84 (3786.24)	1834.36 (1141.25)	0.001[c]
	Week 36 pregnancy, mean (SD)	2118.97 (924.19)	1867.11 (965.82)	0.001[c]
Age in years, mean (SD)		33.4 (4.5)	31.4 (5.2)	0.0003[a]
Parity, n (%)	0	85 (63)	106 (48)	0.02[b]
	1	40 (30)	76 (34)	
	≥2	10(7)	40 (18)	
Deprivation category*, n (%)	Affluent-intermediate (1- 3)	91 (67.4)	67 (30.3)	≤0.0001[d]
	Deprived – very deprived (4- 7)	54 (32.6)	155 (69.8)	
Ethnicity, n (%)	Caucasian	132 (97.8)	210 (94.6)	0.721[d]
	Others	3 (2.2)	12 (5.4)	
Smoking status during pregnancy, n (%)	Never	77 (57)	124 (56.1)	0.025[b]
	Ex-smoker	54 (40)	69 (31.2)	
	Currently smoking	4 (3)	28 (12.7)	
Alcohol consumption before pregnancy	Unit/week, median (range)**	6 (0-30)	2 (0-30)	≤0.0001[c]
	Undeclared, n (%)	7 (5.2)	85 (38.3)	≤0.0001[d]
Alcohol consumption during pregnancy	Not consuming, n (%)	125 (57)	181 (81.5)	0.001[d]
	Undeclared, n (%)	81 (37.5)	33 (14.9)	
	Unit/week, median (range)**	0 (0-11)	0 (0-10)	0.242[c]
Infertility factors, n (%)	Fertility drug	7 (6.7)	3 (1.4)	0.118[d]
	IVF	9 (5.2)	3 (1.4)	0.212[d]
	PCOS	8 (5.9)	20 (9)	0.593[d]
Previous pregnancy loss	Miscarriage ≥1, n (%)	40 (22.2)	109 (26.3)	0.629[d]
	Ectopic, molar, stillbirth ≥1, n (%)	1 (0.7)	6 (2.8)	0.626[d]
	Termination ≥1, n (%)	15 (11)	30 (14)	0.670[d]
Minor obstetric complications, ≥ 5 out of 9 syndromes, n (%)		10 (7.8)	46 (21.8)	0.012[b]
Preeclampsia, n (%)		4 (3)	21 (9.5)	0.082[d]
Gestational Diabetes Mellitus, n (%)		3 (2.2)	45 (20.4)	≤0.0001[d]
Medical disorders, n (%)	Asthma	19(14.1)	48 (21.6)	0.487[b]
	Hypothyroidism	1 (0.7)	15 (6.8)	
	Others[2]	2 (2.2)	6 (2.8)	
Risk of sleep disordered breathing, n (%)	Berlin Questionnaire	6 (6.4)	99 (73.6)	≤0.0001[d]
	ESS, cut-off <10 (47)	16 (16.8)	34 (24)	0.224[d]
	Both	2 (3.2)	30 (22.3)	≤0.0001[d]
Exclusive and mixed breastfeeding at postpartum visit of mood assessments, n (%)		94 (78)	56 (29)	≤0.0001[d]

Table 2

Previous mental health demographics		Lean (n = 135)	SO (n = 222)	P (χ^2)
	Previous diagnosis of mental health disorders, **n (%)**			
	Yes	23 (17)	78 (35.5)	***0.006***
	Types of mental health diagnosis**, n (%)**			
	Anxiety	4 (17.4)	9 (11.5)	
	Depression	8 (34.8)	47 (60.3)	
	Previous postnatal depression	4 (17.4)	13 (16.7)	***0.002***
	Anxiety & Depression	3 (13.0)	8 (10.3)	
	Anorexia and Bulimia	4 (17.4)	1 (1.3)	
	Status of mental health disorders at 1st antenatal booking [1]**, n (%)**			
	Inactive	7 (30.4)	18 (23.1)	
	Active	16 (69.6)	60 (76.9)	0.336
	Anti-depressant status at 1st antenatal booking [2]**, n (%)**			
	Discontinued	5 (31.3)	24 (40)	
	Continued	3 (18.8)	10 (16.7)	0.411
	Counselling only	8 (50)	26 (43.3)	
	"Have you consulted GP about mental health in the last 2 years?" **n (%)**			
	Yes	12 (9.25)	120 (54.1)	
	No	108 (80)	46 (20.7)	***≤ 0.0001***
	Did not answer	15 (10.75)	56 (25.25)	

(Left-side vertical labels: "Hospital records" spanning the first four sections; "Questionnaire" spanning the last section.)

Table 3

Psychosocial stress, n (%)		Lean		SO		P¹	P²	P³	P⁴	P⁵	P⁶
		Pregnancy	PN	Pregnancy	PN						
Work	Never	9 (7.5)	7 (9.6)	24 (14.65)	9 (11.5)	ᵃ*0.037*ᵖʳᵉᵍ ᵃ0.435ᴾᴺ	0.612ᵖʳᵉᵍ 0.461ᴾᴺ	0.079ᵖʳᵉᵍ 0.586ᴾᴺ	0.593ᵖʳᵉᵍ 0.461ᴾᴺ	0.618ᵖʳᵉᵍ 0.488ᴾᴺ	0.156ᵖʳᵉᵍ 0.943ᴾᴺ
	Some periods	64 (53.1)	40 (54.8)	61 (37.05)	37 (47.4)						
	Several periods	41 (34.05)	15 (20.5)	54 (33.1)	15 (19.2)						
	Permanently	3 (2.5)	1 (1.4)	7 (4.25)	4 (5.1)						
	Not working	3 (2.95)	10 (13.7)	18 (10.95)	13 (16.7)						
Home	Never	26 (22)	11 (15.1)	27 (16.6)	7 (9)	ᵃ0.164ᵖʳᵉᵍ ᵃ0.359ᴾᴺ	0.476ᵖʳᵉᵍ *0.048*ᴾᴺ	0.195ᵖʳᵉᵍ 0.137ᴾᴺ	0.769ᵖʳᵉᵍ *0.029*ᴾᴺ	0.506ᵖʳᵉᵍ *0.038*ᴾᴺ	0.606ᵖʳᵉᵍ *0.027*ᴾᴺ
	Some periods	78 (65.15)	48 (65.8)	99 (59.6)	51 (65.4)						
	Several periods	14 (12.05)	14 (19.2)	36 (21.95)	19 (24.4)						
	Permanently	1 (0.8)	0	3 (1.8)	1 (1.3)						
Finance	Little or none	70 (58.45)	40 (54.8)	67 (40.7)	28 (35.9)	ᵃ*0.011*ᵖʳᵉᵍ ᵃ*0.020*ᴾᴺ	*0.022*ᵖʳᵉᵍ *0.002*ᴾᴺ	*0.001*ᵖʳᵉᵍ *0.002*ᴾᴺ	*0.007*ᵖʳᵉᵍ *0.002*ᴾᴺ	*0.013*ᵖʳᵉᵍ *0.004*ᴾᴺ	0.249ᵖʳᵉᵍ *0.003*ᴾᴺ
	Moderate	47 (39.05)	30 (41.1)	78 (47.25)	43 (55.1)						
	High or severe	3 (2.5)	3 (4.1)	20 (12.05)	7 (9)						
Life events	None	90 (74.75)	55 (75)	91 (54.65)	43 (55)	ᵇ*0.005*ᵖʳᵉᵍ ᵇ*0.005*ᴾᴺ	0.233ᵖʳᵉᵍ *0.03*ᴾᴺ	0.118ᵖʳᵉᵍ *0.021*ᴾᴺ	0.633ᵖʳᵉᵍ *0.005*ᴾᴺ	0.982ᵖʳᵉᵍ *0.021*ᴾᴺ	0.545ᵖʳᵉᵍ *0.003*ᴾᴺ
	1 or more	30 (25.25)	18 (25)	75 (45.35)	35 (45)						

Mood assessments		Lean	SO	P¹	P²	P³	P⁴	P⁵	P⁶	P⁷
Satisfaction With Life Scale *in median (range), possible scores: 5-35*										
Visit 1		29 (7-35)	25 (5-35)	*≤ 0.0001*ᶜ	*≤ 0.0001*	*≤ 0.0001*	*≤ 0.0001*	*0.001*	0.22	-
Visit 2		30 (9-35)	26 (9-35)	*≤ 0.0001*ᶜ	*0.024*	0.225	<u>0.052</u>	*0.049*	<u>0.062</u>	-
Postnatal		30 (18-35)	28 (12-35)	*≤ 0.0001*ᶜ	*≤ 0.0001*	*≤ 0.0001*	*≤ 0.0001*	*≤ 0.0001*	*0.002*	0.319
Hospital Anxiety Depression Scale *in mean (SD), possible scores: 0-21 per component*										
Anxiety	Visit 1	5.16 (2.79)	5.82 (3.43)	0.081ᵈ	0.448	0.262	0.442	0.804	*0.033*	-
	Visit 2	4.97 (2.68)	5.98 (3.48)	*0.009*ᵈ	*0.018*	0.354	<u>0.085</u>	<u>0.077</u>	<u>0.086</u>	-
	Postnatal	4.39 (3.11)	5.77 (3.86)	*0.020*ᵈ	0.142	*0.004*	<u>0.088</u>	0.113	*0.028*	0.197
Depression	Visit 1	2.15 (2.13)	3.69 (3.22)	*≤ 0.0001*ᵈ	*0.006*	*≤ 0.0001*	*0.003*	*0.007*	0.202	-
	Visit 2	2.05 (1.74)	3.91 (3.13)	*≤ 0.0001*ᵈ	*0.019*	0.38	<u>0.092</u>	<u>0.085</u>	<u>0.084</u>	-
	Postnatal	2.07 (1.79)	3.32 (2.86)	*0.002*ᵈ	*0.02*	*0.001*	*0.01*	*0.013*	*0.012*	*0.043*
State- Trait Anxiety Index *in mean (SD), possible scores: 20-80 per component*										
State	Visit 1	28.78 (8.55)	33.83 (10.44)	*≤ 0.0001*ᵈ	*0.009*	*0.001*	*0.022*	<u>0.066</u>	<u>0.075</u>	-
	Visit 2	28.61 (7.84)	34.10 (10.37)	*≤ 0.0001*ᵈ	*0.006*	*≤ 0.0001*	*0.003*	*0.006*	*0.008*	-
	Postnatal	28.16 (7.7)	32.23 (9.73)	*0.006*ᵈ	*0.019*	*≤ 0.0001*	*0.011*	*0.014*	*0.007*	0.748
Trait	Visit 1	32.66 (8.99)	36.49 (11.55)	*0.003*ᵈ	0.119	*0.019*	0.1	0.26	0.19	-
	Visit 2	32.17 (7.91)	36.30 (11.3)	*0.001*ᵈ	0.142	*0.015*	<u>0.085</u>	0.13	*0.036*	-
	Postnatal	30.94 (8.41)	35.25 (10.81)	*0.009*ᵈ	*0.006*	*0.001*	*0.036*	0.056	*0.017*	0.817
General Health Questionnaire *in mean (SD), possible scores: 0-15*										
Visit 1		1.62 (1.92)	3.21 (2.75)	*≤ 0.0001*ᵈ	*≤ 0.0001*	*≤ 0.0001*	*≤ 0.0001*	*≤ 0.0001*	*0.039*	-
Visit 2		1.75 (1.79)	3.36 (2.92)	*≤ 0.0001*ᵈ	*0.001*	*≤ 0.0001*	*0.001*	*0.003*	*0.002*	-
Postnatal		1.29 (1.24)	2.74 (2.16)	*≤ 0.0001*ᵈ	*≤ 0.0001*	*≤ 0.0001*	*0.001*	*0.001*	*0.004*	*0.04*

Table 4

Postnatal weight loss (SO group), β (p)		P[1]	P[2]	P[3]
Week 17 pregnancy	(z) Anxiety symptoms	*-0.33 (0.04)*	*-0.33 (0.04)*	*-0.33 (0.03)*
	(z) Depression symptoms	*-0.21 (0.02)*	*-0.21 (0.02)*	*-0.19 (0.04)*

LEAN

SEVERELY OBESE

Serum cortisol level week 36

$R^2 = 0.001$
$p = 0.639$

$R^2 = 0.058$
$p = 0.017$

Z scores Anxiety symptoms
week 28 pregnancy

Z scores Anxiety symptoms
week 28 pregnancy
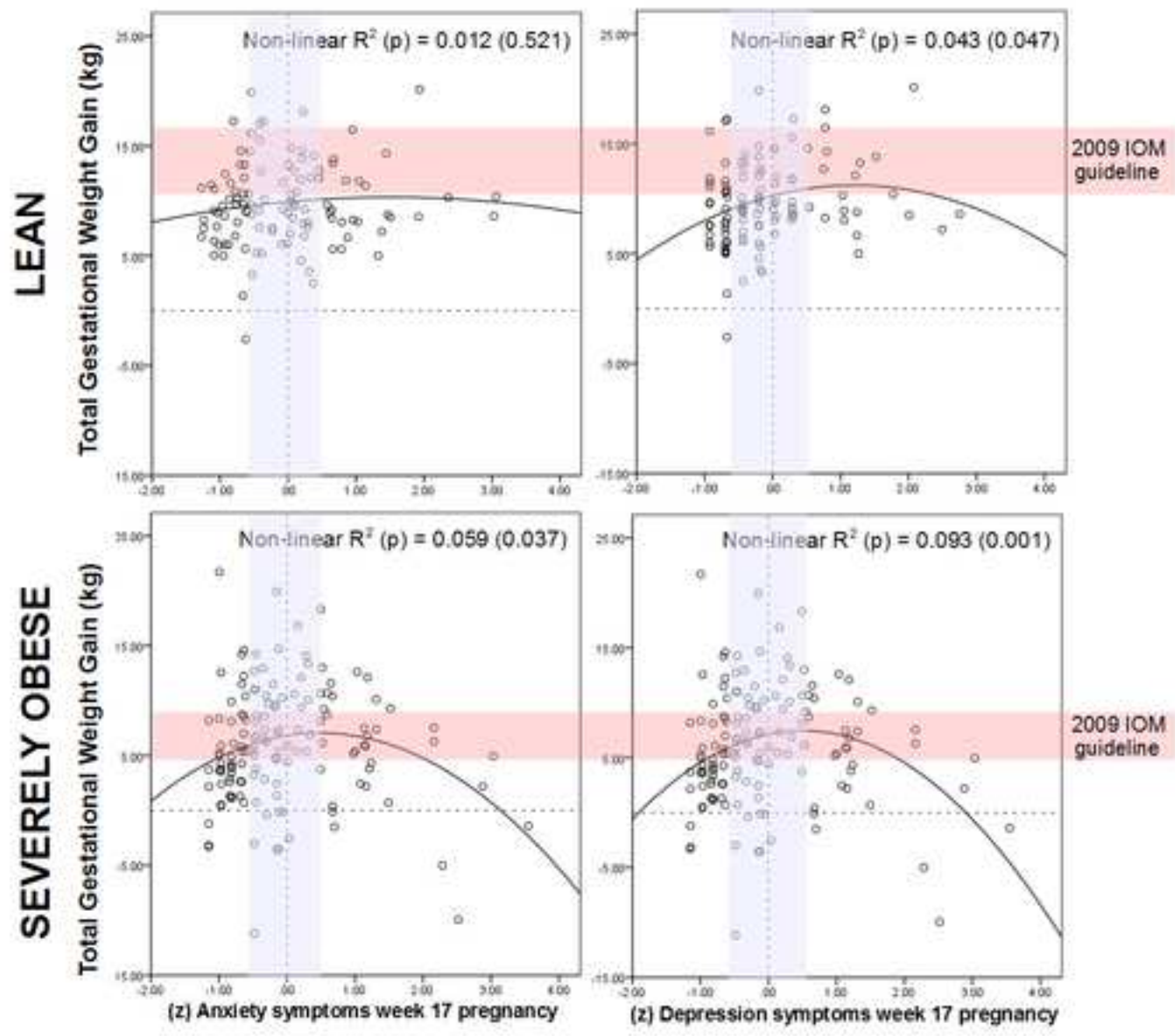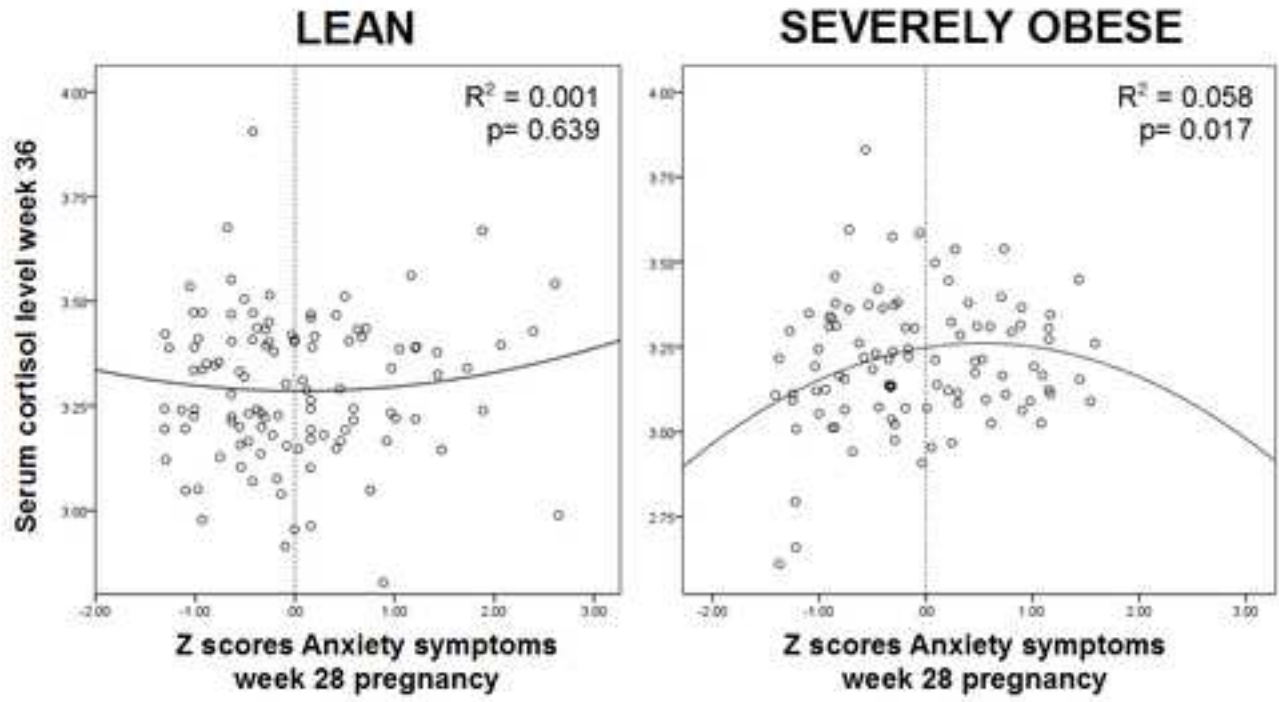
Supplementary

Supplementary Figure 1 CONSORT diagram of the study for the mood assessments during pregnancy and at postnatal. The upper limit of BMI is 60 kg/m2.

Supplementary Figure 2 Participants were more satisfied with life following pregnancy and delivery. The bottom and top line of the bar represents minimum and maximum SWLS score, respectively. * P≤0.05. SO: Severely Obese.

Supplementary Table 1 The poorer mood outcome in SO group was still observed in z-score format

Mean (SD)		week 17	week 28	p
Anx	Lean	-0.26 (0.81)	-0.29 (0.72)	
				≤0.0001
	SO	0.16 (0.96)	0.18 (0.98)	
Dep	Lean	-0.40 (0.72)	-0.42 (0.63)	
				≤0.0001
	SO	0.24 (0.96)	0.25 (0.99)	

HIP study pool (n = 344)

SO: Severely Obese. Anx: averaged z-scores of anxiety outcomes, Dep: averaged z-scores of depression outcomes.

Supplementary Table 2 Mood assessment cut-off scores of research participants throughout pregnancy.

Mood assessments	Lean	SO	P^1	P^2	P^3	P^4
Satisfaction with Life Scale score ≤19, slightly below average (41)						
visit1, n (%)	10 (8.2)	38 (22.89)	*0.001*	*0.015*	*0.002*	0.008
visit2, n (%)	5 (4.2)	30 (17.75)	*≤ 0.0001*	*0.032*	*0.025*	*0.039*
Postnatal, n (%)	2 (2.78)	6 (9.09)	0.152	0.075	0.095	0.925
Hospital Anxiety Depression Scale score ≥10 (38)						
Anxiety						
visit1, n (%)	10 (8.2)	24 (14.63)	0.139	0.44	0.242	0.202
visit2, n (%)	7 (6.25)	30 (17.86)	*0.004*	0.303	*0.028*	0.456
Postnatal, n (%)	3 (4.17)	13 (18.57)	*0.008*	0.659	*0.012*	0.49
Depression						
visit1, n (%)	2 (1.64)	10 (6.14)	0.076	0.887	0.238	0.684
visit2, n (%)	1 (0.84)	9 (5.36)	*0.05*	0.535	0.678	0.884
Postnatal, n (%)	0 (0)	4 (5.8)	0.055	0.165	0.13	0.978
State Trait Anxiety Index score ≥39, from validation study of female population (39)						
State						
visit1, n (%)	13 (10.83)	45 (27.78)	*0.001*	*0.023*	*0.005*	*0.033*
visit2, n (%)	15 (12.6)	46 (27.87)	*0.002*	*0.044*	*0.013*	*0.053*
Postnatal, n (%)	9 (13)	20 (25.97)	0.062	0.118	*0.002*	*0.017*
Trait						
visit1, n (%)	25 (21)	54 (33.13)	*0.031*	0.096	0.093	0.058
visit2, n (%)	24 (20.5)	59 (35.75)	*0.008*	0.428	*0.027*	0.399
Postnatal, n (%)	11 (16.18)	22 (28.57)	0.112	*0.033*	*0.029*	0.075
General Health Questionnaire score ≥3, a suggested cut-off for further screening (42)						
visit1, n (%)	23 (18.7)	87 (53.05)	*≤ 0.0001*	*≤ 0.0001*	*≤ 0.0001*	*≤ 0.0001*
visit2, n (%)	32 (26.89)	85 (50.3)	*≤ 0.0001*	*0.002*	*0.003*	*0.006*
Postnatal, n (%)	12 (17.14)	34 (50)	*≤ 0.0001*	*0.007*	*≤ 0.0001*	*0.023*

P^1 was obtained from Fisher's Exact Test. Logistic regression was used to obtain P^2 P^3 and P^4. SO: Severely Obese. OR: Odd Ratio, CI: Confidence Interval Bold-Italic texts are significant at 0.05 levels, underlined text are significant at 0.1 levels. The cut-off scores are recommended scores for further clinical diagnosis.

[1] unadjusted

[2] adjusted for maternal factors **prior to** current pregnancy: age, smoking status, alcohol consumption (unit/week), parity, deprivation category

[3] adjusted for maternal factors arising **during** pregnancy: minor complications, GDM, risks of sleep apnoea, differences of gestational visit time between lean and obese groups at visit 1 and postnatal

[4] adjusted for factors in P^2 and P^3,

Supplementary Table 3 Differences in mood scores during pregnancy between mothers who attended for follow-up and those who did not.

Mood Assessments		Attended postnatal follow-up			Declined postnatal follow-up			p value (t-test)		
		Lean	SO	All	Lean	SO	All	Lean	SO	All
visit 1	SWLS	28.05 (5.45)	24.94 (5.95)	26.34 (5.92)	27.73 (1.31)	22.76 (7.05)	24.47 (7.11)	0.806	*0.055*	*0.036*
	HA	5.05 (2.65)	5.64 (3.44)	5.38 (3.12)	5.73 (0.71)	6.33 (3.56)	6.11 (3.46)	0.307	0.283	0.112
	HD	1.91 (1.87)	3.52 (3.22)	2.8 (2.81)	3.27 (0.61)	4.25 (3.35)	3.9 (3.20)	*0.007*	0.223	*0.009*
	State	28.15 (7.69)	33.07 (10.50)	30.86 (9.64)	31.77 (2.45)	35.86 (10.48)	34.45 (10.93)	<u>0.076</u>	0.143	*0.012*
	Trait	32.45 (8.78)	35.52 (11.22)	34.15 (10.29)	34.09 (2.24)	39.17 (12.51)	37.48 (11.98)	0.455	0.083	*0.032*
	GHQ	1.5 (1.77)	2.97 (2.71)	2.31 (2.44)	2.27 (0.55)	3.95 (2.86)	3.37 (2.86)	<u>0.097</u>	*0.050*	*0.004*
visit 2	SWLS	28.64 (4.53)	25.64 (5.14)	26.99 (5.09)	30 (0.99)	23.19 (6.14)	25.27 (6.44)	0.232	*0.012*	*0.028*
	HA	5 (2.71)	5.76 (3.34)	5.42 (3.09)	5 (0.62)	6.58 (3.89)	6.1 (3.62)	1.000	0.191	0.144
	HD	2.01 (1.81)	3.28 (2.66)	2.7 (2.39)	2.26 (0.32)	5.63 (3.68)	4.6 (3.52)	0.567	*0.000*	*0.000*
	State	28.59 (8.00)	32.86 (9.70)	30.93 (9.20)	29.47 (1.63)	37.53 (11.62)	34.93 (10.99)	0.656	*0.013*	*0.005*
	Trait	32.18 (8.08)	35.20 (10.88)	33.85 (9.82)	33.17 (1.59)	39.7 (12.37)	37.67 (11.28)	0.629	*0.030*	*0.011*
	GHQ	1.68 (1.83)	3.05 (2.64)	2.44 (2.41)	2.16 (0.38)	4.19 (3.59)	3.56 (3.25)	0.295	*0.030*	*0.003*

Mothers who attended postnatal follow-up reported less mood symptoms during pregnancy as compared to those who did not. SO: Severely Obese, Bold-Italic texts are significant at 0.05 levels. Displayed values are mean (SD).

Supplementary Table 4 Increased maternal anxiety and depression symptoms in week 17 pregnancy were correlated with increased postpartum weight retention in Severely Obese (SO) group, but not in the controls. Postpartum weight retention = - (Postnatal weight loss), ** p≤ 0.01, *p ≤ 0.05.

Postnatal weight loss, Pearson's R (p)		Lean	SO
Week 17 pregnancy	(z) Anxiety symptoms	0.07	**-0.24****
	(z) Depression symptoms	0.06	**-0.22***

Assessed for Eligibility = 422

Excluded = 65
Declined mood assessments in HIP study = 56
BMI was extremely high = 1
Hospital and/or study numbers were lost,
demographic data unverified = 8

Lean = 135 — pregnancy — Very Severely Obese (SO) = 222

Lean = 103 — Postnatal 3 months — SO = 142

Lean = 82 — Postnatal 6 months — SO = 109

across visit-lean

across visit-SO

Wilcoxon Paired-Match Signed Rank Test

Wilcoxon Paired-Match Signed Rank Test