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Pregnancy-Related Anxiety: Evidence of Distinct Clinical Significance from a Prospective Longitudinal Study

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Abstract

Background—Pregnancy-related anxiety (PrA) has attracted considerable research attention, but questions remain about its distinctiveness from conventional constructs and measures. In a high psychosocial risk, ethnically diverse sample, we examine the degree to which PrA is distinct from continuous and diagnostic measures of anxiety and worry in terms of longitudinal course, associations with psychosocial and perinatal risk, and prediction of postnatal mood disturbance.

Methods—345 women oversampled for prenatal anxiety and depression were selected from an urban obstetrics clinic serving a predominantly low-income, ethnically diverse population. PrA was assessed at 20 and 32 weeks gestation; anxiety and depression symptoms were assessed from questionnaire and from clinical interview at 20 and 32 weeks gestation and again at 2 and 6 months postnatally. Data relevant to psychosocial and obstetric risks were ascertained from interview, medical exam, and chart review.

Results—Two distinct factors of PrA were identified, indexing specific concerns about the child's health and about the birth; these two PrA factors showed distinct longitudinal patterns in the prenatal period, and modest associations with general measures of anxiety and depression from questionnaire and clinical interview. PrA was also distinguished from conventional symptom measures in its associated features and prediction of birth weight and postnatal mood.

Limitations—The sample was at high psychosocial risk and ethnically diverse; findings may not generalize to other samples.

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Conclusions—PrA can be distinguished from general measures of anxiety in pregnancy in terms of longitudinal course, associated features, and prediction to postnatal mood disturbance, and may warrant specific clinical attention.

Keywords

Perinatal; Pregnancy related anxiety; obstetric outcomes

1. Introduction

Maternal prenatal anxiety and depression are recognized clinical and public health concerns because of the well-documented links with maternal somatic health in pregnancy (Kurki et al., 2000), obstetric outcomes (Ding et al., 2014), and behavioral and biological outcomes in the child and adolescent (O'Donnell et al., 2014; O'Donnell et al., 2013). Related phenotypes such as prenatal life events stress have comparable associations (Entringer et al., 2012; King et al., 2009; Li et al., 2012; Wadhwa et al., 2011). An important question that has emerged in this line of study – with implications for understanding both causal mechanisms and clinical application – is how best to characterize prenatal distress and, more specifically, if pregnancy-related anxiety (or “pregnancy-specific anxiety”) is a distinct clinical phenomena that can be differentiated from conventional symptom measures. We test this hypothesis in a large, ethnically diverse sample followed prospectively from pregnancy to 6 months postpartum.

Pregnancy-related anxiety refers to worry or distress particular to pregnancy, including the health of the developing child, changes in appearance, labor and birth, and future parenting concerns. Many measures of pregnancy-related anxiety and distress have appeared (Cote-Arsenault, 2003; DiPietro et al., 2008; Huizink et al., 2004; Lobel et al., 2008; Rini et al., 1999; Somerville et al., 2014; Van den Bergh, 1990), and several reviews of the research literature exist (Alderdice et al., 2012; Brunton et al., 2015; Dunkel Schetter and Tanner, 2012; Meades and Ayers, 2011). A key tenet of these studies is that pregnancy-related anxiety does more than describe the content of pregnant women's worries; that is, pregnancy-related anxiety is proposed as a distinct clinical entity with construct and discriminant validity. Reviews of the available research, e.g., (Brunton et al., 2015) imply that these conditions may not yet be met.

We test the hypothesis that pregnancy-related anxiety is a distinct clinical phenomena according to several criteria. The first is the degree to which symptoms of pregnancy-related anxiety can be empirically distinguished. Existing studies suggest modest-moderate overlap between measures of pregnancy-related anxiety and conventional self-report questionnaire measures of anxiety, worry, depression and stress (Huizink et al., 2004; Lobel et al., 2008). We consider this further by examining the overlap with diagnostic measures of anxiety and depression from clinical interview. Second, we examine if pregnancy-related anxiety can be distinguished from conventional symptoms measures by its course in pregnancy. At least some features of pregnancy-related anxiety may diminish significantly across pregnancy (Lobel et al., 2008), perhaps reflecting greater confidence in the health of the baby in response to ultrasound findings or because of a decreased risk of miscarriage with longer

gestation (Ekelin et al., 2009; Tsartsara and Johnson, 2006). Whether or not this trend is particular to pregnancy-related anxiety is not clear, as some but not other reports of conventional symptoms of anxiety report changes within pregnancy, e.g., (Heron et al., 2004; van Bussel et al., 2009).

Third, we investigate the extent to which pregnancy-related anxiety and conventional symptom measures can be discriminated by differential associations with external factors. Evidence of this type would provide an important kind of evidence that pregnancy-related anxiety is a distinct phenomenon. Research of this type is limited and it is not clear which risks or experiences should relate differentially to pregnancy-related anxiety and conventional symptom measures. For example, women who experienced a previous miscarriage might experience significant pregnancy-related anxiety, but they also show (perhaps comparable) significant elevations on conventional symptom measures (Blackmore et al., 2011; DeBackere et al., 2008). One of the few factors that may be more closely associated with pregnancy-specific anxiety is parity. First-time mothers may report greater pregnancy-related anxiety than parous women (Huizink et al., 2015); it is not clear if that is also so for conventional symptoms measures, or if the effect is driven by the subset with histories of miscarriage. In the current study we consider if pregnancy-related anxiety and conventional symptoms measures can be differentiated by external correlates, particularly psychosocial stress and pregnancy experiences.

Fourth, the hypothesis that pregnancy-related anxiety is a distinct clinical syndrome would also be supported if it predicted external outcomes independently of conventional symptom measures. Pregnancy-related anxiety is associated with obstetric outcomes, but few studies have formally tested the hypothesis that pregnancy-related anxiety predicts obstetric outcome more strongly than, and independently of, conventional symptom measures. For example, Lobel (Lobel et al., 2008) reported that a measure of pregnancy-specific distress predicted gestational age independent of a composite measure of general stress measures. Mancuso and colleagues (Mancuso et al., 2004) and Kramer and colleagues (Kramer et al., 2009) also found that pregnancy-related anxiety was particularly associated with preterm birth. It may be that pregnancy-related anxiety is a more sensitive index of maternal distress than conventional symptoms measures (Dunkel Schetter and Tanner, 2012; Huizink et al., 2004). We build on and extend these results in the current study, assessing those obstetric outcomes most widely studied, birth weight and gestational age at birth.

Finally, we conduct a more novel analysis to consider if pregnancy-related anxiety predicts unique variability in postnatal mood disturbance. Previous studies demonstrate substantial stability of mood disturbance from the prenatal to the postnatal period (Robertson et al., 2004) and that prenatal anxiety increases the risk for postnatal depressive symptoms (Heron et al., 2004). Demonstrating that pregnancy-related anxiety predicts unique variance in postnatal mood disturbance would further support its status as a distinct clinical entity with clinical significance. Alternatively, pregnancy-related anxiety would not predict postnatal maternal mood disturbance if it were limited to pregnancy or was subsumed by general mood disturbance. We contrast these predictions in the current study.

In summary, the current study tests the hypothesis that pregnancy-related anxiety is a distinct clinical phenotype according to several construct and discriminant validity criteria. Novel and notable features of the research include a longitudinal design, diagnostic measures throughout the perinatal period, detailed measures of psychosocial risk, and a large ethnically diverse sample.

2. Methods

2.1 Participants

The data are derived from two related prospective longitudinal studies that used parallel clinical protocols. Pregnant women receiving obstetrical care from a hospital-based practice serving a predominantly low-income, inner-city population were approached by nursing staff in the clinic, informed about the study and, if eligible, invited to participate. Inclusion criteria were a confirmed singleton pregnancy of less than 18 weeks gestation; 19–34 years of age; low to medium obstetric risk determined by the medical team using standardized definitions (NIH, ACOG); fluent in English; no current substance or alcohol abuse; no past or current diagnosis of bipolar disorder or schizophrenia or presence of psychotic features; ability to provide informed consent. Study team members met with 627 eligible women who completed a screening assessment that included the Edinburgh Postnatal Depression Scale (EPDS) and Penn State Worry Questionnaire (PSWQ). 497 women (79% of those eligible) were subsequently consented for participation, oversampling for women who scored high on affective symptoms as measured by the EPDS or PSWQ. Of these, for the main analyses we subsequently excluded women who did not experience a live birth or delivered a baby of very low birth weight (<2500g) because we were interested in studying normal-risk pregnancies and to avoid, for some mothers, reverse causality in which maternal prenatal anxiety or worry was induced by significant suspected or confirmed health concerns for the baby or pregnancy (see supplemental analyses); we also excluded women with a history of psychosis or significant drug use, or were lost to contact prior to study enrollment. This resulted in a sample of 372 women on whom we obtained clinical data; a further 37 were not consented for postnatal assessments, leaving a final sample for analysis of 345. Ethical approval was obtained from the university IRB and all participants provided written informed consent.

2.2 Procedures

Assessments were conducted on four occasions: approximately 20 and 32 weeks gestation and at approximately 8 weeks and 6 months postnatally. At each assessment participants completed a clinical diagnostic interview and a battery of health and psychosocial questionnaires. All questionnaires were read aloud to participants to pre-empt problems in literacy and to insure understanding of each question. Detailed medical, clinical and socio-demographic data were collected via interview and chart notes.

2.3 Measures

Pregnancy-related anxiety was assessed from seven questions about their level of worry or fear about themselves during various aspects of pregnancy and birth (e.g., “I am worried about the pain of delivery,” “I am worried about not being able to control myself during

labor”), and the baby’s health and development (e.g., “I am worried that something will be wrong with my baby physically,” “I am worried that something will be wrong with my baby mentally”). The measure is composed of items that are most frequently included across existing measures, e.g. (Huizink et al., 2004; Van den Bergh, 1990); none of the items were based on prior pregnancy and birth experiences, consistent with recent studies (Huizink et al., 2015). Responses were given on a 5-point Likert scale ranging from not at all, a little, somewhat, quite a bit, and very much. Factor structure and reliability data are reported below and in Appendix I.

Conventional measures of maternal symptoms were based on several instruments. Clinically significant anxiety was assessed using the Structured Clinical Interview for DSM-IV (SCID) (First, 1995); the SCID was administered by trained clinical interviewers at each of the four assessments. Women were classified according to whether or not they met DSM-IV diagnostic criteria for Generalized Anxiety Disorder (GAD) and, secondly, whether or not they satisfied criteria for clinically significant anxiety but did not meet formal diagnostic requirements, i.e., “subsyndromal” cases or Anxiety Disorder NOS. Both the narrow and broad phenotypes are considered in analyses. We note that the diagnostic criterion for GAD is that symptoms persisted for 6 months, which means that some diagnostic assessment periods are overlapping (e.g., the two prenatal assessment periods overlap).

Continuous measure of anxiety or worry was based on the PSWQ (Meyer et al., 1990), a 16-item index of worry with considerable evidence for reliability and validity, including in the perinatal period (O’Connor et al., 2013; Swanson et al., 2011); evidence for its link with anxiety disorders has also been established (Behar et al., 2003). The PSWQ was chosen because it is a relatively brief and focused measure of worry, a core feature of anxiety and stress, and because it has established clinical prediction, as noted above. We also included the state subscale of the State-Trait Anxiety Inventory (Spielberger et al., 1983), a 20-item index of current anxiety-related items with considerable validity and reliability that has been used in studies of prenatal maternal anxiety, e.g. (O’Donnell et al., 2012). Depression was measured according to a continuous rating of depressive symptoms based on the Edinburgh Postnatal Depression Scale (EPDS) (Cox et al., 1987), a 10-item self-report questionnaire measure that is widely used in the pre- and post-natal period with extensive reliability and validity (Murray and Carothers, 1990).

Obstetric outcomes included birth weight (as a continuous variable), gestational age at birth, pregnancy complications (a composite dichotomous index based on obstetrician exam), and mode of birth (vaginal versus cesarean section). In addition, pregnancy-related factors included parity, pre-pregnancy BMI, smoking and alcohol intake in pregnancy (given the limited distribution, these were coded yes/no). Psychosocial and socio-demographic factors included maternal education (number of years completed), marital status (married/cohabiting versus single), race/ethnicity (coded as African American vs non-African American), and Medicaid recipient status.

2.4 Statistical analyses

After reporting demographic data, we report analysis of the pregnancy-related anxiety items, including factor and reliability analysis. This is followed by analyses comparing pregnancy-

related anxiety to conventional symptom measures, and longitudinal analyses to compare the course of symptom measures across pregnancy. Several different sets of analyses were undertaken to test the distinctiveness of pregnancy-related anxiety. Cross-sectional analyses examine if pregnancy-related anxiety is differentially associated with psychosocial risk variables and pregnancy-related experiences compared with conventional symptom measures. To test whether these dependent correlations were statistically significantly different from one another, correlation coefficients were converted to *z*-scores using Fisher's *r*-to-*z* transformation, and asymptotic covariances of the estimates were calculated following Steiger (Steiger, 1980). This information was used to conduct *z*-tests to determine whether the correlation between e.g., pregnancy-related anxiety and a given psychosocial risk variable was significantly different from the correlation between the conventional symptom measure and the same psychosocial risk variable. Next, path analysis was used to test the incremental prediction of pregnancy-related anxiety and other symptom measures of obstetric outcomes and postnatal mood. Path models were estimated using *Mplus* 7.0. Missing data were handled using full information maximum likelihood (Enders and Bandalos, 2001).

The key measures of anxiety are the diagnostic data from clinical interview (given the novelty of diagnoses in this line of research) and the PSWQ as a continuous measure; analyses of the STAI are broadly comparable to results with the PSWQ, and so are not discussed in much detail because of space limitations (details available from the authors). Although the pregnancy-related symptom measure focuses on anxiety and worry, we nonetheless also include the EPDS as an index of continuous depressive symptoms.

For analyses predicting obstetric outcome and postnatal mood disturbance, we focus on prenatal measures at the 32-week assessment. That is based on the tendency in past research to focus on predictors in the third trimester and the absence of a strong *a priori* hypothesis about timing; analyses using the mood measures at the 20-week assessment were broadly consistent with the analyses of the 32-week measures (details available from the authors). Finally, for analyses predicting postnatal mood disturbance, we focus on the 6-month assessment given the evidence that not all postnatal disturbance may be evident at the earlier prenatal assessment.

3. Results

Descriptive data (Table 1) indicate ethnic/racial diversity and the high psychosocial risk status of the sample. Factor analysis of the pregnancy-related anxiety items indicated two clear factors, 4 items indicating worry about the child's health (PrA-child; "I am worried that something will be wrong with my baby physically") and three items focused on concerns of the self in relation to birth (PrA-self; e.g., "I am worried about the pain of delivery"). The factor solution was identical at each prenatal assessment and internal consistencies (Cronbach alpha) were sound for both subscales at both time points in pregnancy (20 weeks gestation, PrA-child = .85; PrA-self = .82; for 32 weeks gestation, PrA-child = .86; PrA-self = .83; see Appendix I).

Associations between the two PrA scales and other symptom measures, provided in Table 2, indicate modest-moderate overlap at the prenatal assessments; there also modest overlap between the PrA-child and PrA-self scales. Diagnostic measures of anxiety did detect pregnancy-related anxiety (i.e., without asking directly about pregnancy-related concerns and experiences); the stronger correlations with continuous measures may be explained by the generally greater sensitivity of continuous over categorical measures. There was similarly modest overlap between PrA and the EPDS in mid-gestation (r 's = .36 for PrA-child and .21 for PrA-self, p 's <.01) and in the third trimester (r 's = .37 for PrA-child and .23 for PrA-self, p 's <.01) (not tabled).

Longitudinal analyses indicated a significant decrease in PrA-child from 20 ($m = 1.63$, $SD = .93$) to 32 ($m = 1.40$, $SD = .74$) weeks gestation ($t(293) = 5.12$, $p < .0001$). No significant change in PrA-self was detected ($m = 2.50$, $SD = 1.26$ and $m = 2.55$, $SD = 1.23$ at 20 and 32 weeks, respectively; $t(293) = -1.06$, $p = .29$). Neither was there a significant decrease in anxiety symptoms on the PSWQ or depressive symptoms on the EPDS (not tabled). Longitudinal change in GAD diagnostic status in pregnancy was confounded by the requirement that symptoms persist for 6 months (i.e., the assessment at 32 weeks overlapped with the 20-week assessment).

Table 2 presents the external correlates with pregnancy-related anxiety and the clinical diagnostic data and the PSWQ; correlations that are significantly different from one another at $p < .05$ according to the Fisher r -to- z transformation for dependent correlations are highlighted. Several of the external correlates were differentially associated with PrA and conventional symptom measures (most notably anxiety from clinical interview), with several consistencies noted. For example, in mid-gestation, parity was more strongly associated with pregnancy-related anxiety than conventional symptom measures: PrA-child at 20 weeks was more strongly associated with parity than was the narrow ($z = 3.32$, $p < .001$) and broader ($z = 2.69$, $p < .01$) GAD phenotype; the same was true for age at first pregnancy ($z = 2.62$, $p < .01$ for the narrow and $z = 2.05$, $p < .05$ for the broader phenotype) and maternal race ($z = -2.64$, $p < .01$ for the narrow and $z = -2.55$, $p < .05$ for the broader phenotype). Additionally, PrA-child at 20 weeks and the broader GAD phenotype were differentially associated with maternal education ($z = 2.53$, $p < .05$), though neither PrA nor GAD were significantly correlated with education on the bivariate level. In late gestation, PrA-child at 32 weeks and the narrow GAD phenotype were differentially associated with parity ($z = 2.55$, $p < .05$) and age at first pregnancy ($z = 2.55$, $p < .05$); PrA-child at 32 weeks and the broader GAD phenotype were also differentially associated with maternal education ($z = 2.50$, $p < .05$), although neither bivariate correlation was significant.

Differences between PrA-self and GAD were also noted: PrA-self at 20 weeks was more closely associated with parity ($z = 6.37$, $p < .0001$ for the narrow and $z = 5.53$, $p < .0001$ for the broader phenotype), number of miscarriages ($z = -2.65$, $p < .01$ for the narrow and $z = -2.10$, $p < .05$ for the broader phenotype), age at first pregnancy ($z = 2.93$, $p < .01$ for the narrow and $z = 2.24$, $p < .05$ for the broader phenotype), and age at the interview ($z = -2.81$, $p < .01$ for the narrow and $z = -2.26$, $p < .05$ for the broader phenotype). Finally, PrA-self at 32 weeks was more strongly associated with parity ($z = 6.05$, $p < .0001$ for the narrow and z

= 5.04, $p < .0001$ for the broader phenotypes) and maternal age at interview ($z = -3.19$, $p < .01$ for the narrow and $z = -2.55$, $p < .05$ for the broader phenotype).

Findings from Table 2 also indicate that both pregnancy-related anxiety (PrA-child) and the broader GAD phenotype were significantly associated with birth weight; associations with other symptom measures, including the PSWQ and the more narrow anxiety disorder phenotype, were weaker but in the same direction. Table 2 also indicates that the prediction of obstetric outcomes was most reliable for birth weight; associations with gestational age at birth were generally weak and non-significant.

Based on the correlations in Table 2, we constructed a path model predicting birth weight and gestational age at birth from PrA-child, PrA-self, and the broader GAD phenotype; we included GAD from the clinical interview at the 32-week assessment and PrA-child and PrA-self from the same assessment. Also included in the model, on *a priori* basis, were maternal education, race/ethnicity, pre-pregnancy BMI, prenatal smoking, and Medicaid recipient status. Measures of prenatal anxiety were allowed to covary; additionally, a correlation was estimated between infant birth weight and gestational age at birth, given their interdependence. Results indicated that PrA-child was significantly associated with infant birth weight ($\beta = -.11$, $p < .05$) independently of GAD, which was also negatively associated with birth weight ($\beta = -.11$, $p < .05$); PrA-self was not associated with birth weight when included in a model with PrA-child and GAD. PrA-child was also associated with lower gestational age at birth, $\beta = -.13$, $p < .05$; neither GAD nor PrA-self predicted gestational age at birth in the model. These effects were adjusting for maternal education, race/ethnicity, pre-pregnancy BMI, prenatal smoking, and Medicaid recipient status. Model fit statistics and parameter estimates are provided in Figure 1.

The final set of analyses examine if pregnancy-related anxiety predicted postnatal mood disturbance from the clinical interview at 6 months. Results (Figure 2) indicate that, after controlling for prenatal GAD and PrA-self, PrA-child predicted an increased likelihood of 6-month GAD ($\beta = .17$, $p < .05$; OR = 1.69). This was also above and beyond the influence of maternal education, race/ethnicity, pre-pregnancy BMI, prenatal smoking, and Medicaid recipient status.

Supplemental analyses

A series of supplementary analyses were carried out to test the robustness of the predictors and consider exploratory hypotheses. We found no evidence of a significant interaction between pregnancy-related anxiety and conventional symptom measures in predicting outcomes; neither did we detect any evidence that the prediction from PrA to obstetric or postnatal mood outcomes varied significantly by race/ethnicity. Also, all analyses were repeated without children who were born at less than 37 weeks gestation, as well as with mode of birth and obstetric complications considered as covariates; the same pattern of findings emerged in all of these models. We also re-ran analyses including children who weighed less than 2500g at birth ($n = 30$) and obtained broadly identical findings (details available from the authors).

4. Discussion

The perinatal period is a particular target for research on affective disorders because it poses significant public health and clinical challenges and opportunities (Glover et al., 2010; Wisner et al., 2009) and because this period may provide leverage for understanding causal mechanisms (Blackmore et al., 2014; Schiller et al., 2015). One persisting notion in this line of study is that the expression of affective disorders may take a particular form or require a particular assessment. The construct of pregnancy-related anxiety is a leading example. Findings from the current study replicate and extend prior work in demonstrating that pregnancy-related anxiety a) is modestly associated with conventional symptom measures, including diagnostic measures; b) shows a different longitudinal course in pregnancy from conventional symptom measures; c) can be differentiated from conventional symptoms in terms of external correlates; d) has distinct prediction to birth weight, gestational age at birth, and postnatal mood disturbance that is independent of conventional symptom measures. The findings are additionally notable given that the study assessed an ethically and racially diverse sample at high psychosocial (but not medical) risk; this a population for whom concerns about prenatal affective symptoms are most significant but who are nevertheless underrepresented in clinical research.

The construct of pregnancy-related anxiety has gained considerable influence as judged, for example, by the number of proposed measures and reviews of the topic (cited above). Although there is inherent value in describing the content of a pregnant woman's worry, e.g., for clinical purposes, the scientific and clinical impact of the pregnancy-related anxiety construct would be substantial to the extent that it is distinguished from conventional measures and also provides incremental value in predicting, for example, obstetric outcome or postnatal mood disturbance – two clinically important outcomes that are closely associated with mood disturbance in pregnancy.

Notwithstanding the modest-moderate overlap between pregnancy-related anxiety and other symptom measures in the 2nd and 3rd trimesters, we found that one subset of pregnancy-related anxiety items dealing with fear about the child significantly decreased with gestation. We are not alone in documenting this decrease (Lobel et al., 2008), but this is a significant observation in this study because no such decrease was found for conventional symptom measures using multiple assessment strategies. This de-coupling of worries about the child's health and general worry in pregnancy is evidence that the former is not merely a component of the latter. We were not able to identify the basis for the decrease in worry about the child's health. It may be that typical prenatal care (experienced by all women in this study) is an emollient for some worries and fears, even if it does not address worries about labor and birth or less-circumscribed distress captured in conventional symptom measures.

Pregnancy-related anxiety could also be differentiated from conventional symptom measures in terms of external correlates. Parity, age at first pregnancy, number of miscarriages, and maternal age differentiated PrA-self or PrA-child from conventional anxiety symptom measures (e.g., from clinical interview). The finding that first-time mothers display more pregnancy-related anxiety than experienced mothers has been reported by others (Huizink et

al., 2015); a somewhat consistent pattern of other differential correlates implies that this distinct is not limited to parity.

By far the most important findings concerning pregnancy-related anxiety were that it predicted birth weight and gestational age at birth independently of conventional symptom measures and, the more novel finding, unique variance in postnatal maternal clinical disturbance. Previous studies reported that pregnancy-related anxiety is associated with obstetric outcomes; a much smaller subset of these shows that it predicts independently of other symptom or stress measures (Dunkel Schetter and Tanner, 2012; Kramer et al., 2009; Mancuso et al., 2004). The broader literature of stress and affective symptoms associates prenatal stress and affective symptoms with both birth weight and gestational age, e.g. (Wadhwa et al., 1993). However, as recent meta-analyses indicate (Grote et al., 2010; Littleton et al., 2007), there remain conflicting findings as to the robustness of the link between maternal prenatal affective symptoms and obstetric outcomes, and the risk phenotype involved. Results of this and prior studies may clarify inconsistent findings by suggesting that pregnancy-related anxiety may be the psychological marker that is a more sensitive and robust predictor of obstetric outcome. Why that would be is not yet clear, however. For example, pregnancy-related anxiety may capture immediate mood levels and mood variability more sensitively than more generic and less context-dependent questions, which dominate conventional symptom measures. On the other hand, there are many examples in this literature of seemingly similar measures having different predictive value, as in the case of life events stress versus emotional stress and child outcome (Tegethoff et al., 2011). It is not clear if this implies genuinely distinct mechanisms, or a less than robust effect. In any event, evidence that pregnancy-related anxiety is a more sensitive index of the biological mechanisms underlying obstetric outcomes (e.g., CRH or inflammation) has not yet been amply demonstrated. Associations between affective symptoms or other measures of stress are generally only weakly associated with biological factors that may explain pre-term birth or low birth weight. The available evidence that pregnancy-related anxiety is a distinct clinical syndrome does not imply that it has a privileged influence on stress circuits affecting the mother or developing child.

The most novel finding in the study is the prediction of postnatal mood disturbance. Most striking was the prediction of clinically significant anxiety assigned from clinical interview at 6 months from pregnancy-related anxiety about the child at 32 weeks, after accounting for stability of clinical syndrome. That observation helps further establish that pregnancy-related anxiety has *bona fide* clinical value, is not reducible to general(ized) anxiety, and is not resolved by the birth of the child. As with most associations reported in the paper, the effect size was modest.

We note several limitations of the current study. One is that the study was based on a high psychosocial risk but average medical risk sample; the results may not extend to other, less psychosocially at-risk samples. The generally high and somewhat restricted range of psychosocial risk may explain the lack of association with psychosocial variables, although other studies have similarly found modest to negligible associations between psychosocial risk and pregnancy-related and other anxiety measures (van Bussel et al., 2009). Second, the analyses were conducted on a particular measure of pregnancy-related anxiety, although the

measure assesses similar items to the many existing measures proposed – and there is substantial content overlap across most measures. We note that our focus was not the structure of an existing measure *per se*, but rather on pregnancy-related anxiety as a distinct clinical phenotype. Also, we did not include assessments of all forms of symptoms associated with pregnancy and birth, such as women with an excessive fear or phobia of childbirth. Finally, there are other factors that may be used to distinguish pregnancy-related anxiety from conventional symptom measures, and further research on neurobiology, genetics, and other factors is needed to complement and extend our results. These limitations were offset by several strengths of the paper, including a comparatively large, ethnically diverse sample; multiple occasions of measurement from mid-pregnancy to 6 months postpartum; detailed symptom measures, including psychiatric diagnostic interviews; consideration of key obstetric outcomes and postnatal maternal mood.

Several clinical applications may be derived from our results. The first is the potential value in a surprisingly brief measure of affective symptoms that may be seen as relevant and accessible to pregnant women. Reviews of psychometric properties of pregnancy-related anxiety measures, e.g. (Alderdice et al., 2012) indicate the availability of several tools that are brief, easy to use, have good psychometric properties, and can be readily incorporated into clinical care. One further advantage may be that they may be met with less skepticism or resistance and so perhaps more accurate self-disclosure than conventional measures of psychopathology. Further clinical work is needed to examine in greater detail how and if specific pregnancy-related fears and worries change across pregnancy, and which are genuinely transient and which may index a more lasting disturbance. Finally, we cannot determine from this study if pregnancy-related anxiety is as responsive to interventions as general measures of anxiety. There is a significant and growing research base on prenatal interventions for maternal distress (O'Connor et al., 2014), but these have not yet systematically considered pregnancy-related anxiety and worry. The collective findings strongly suggest that pregnancy-related measures also be included in clinical interventions to reduce prenatal maternal stress in order to benefit the mother and child.

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Appendix I. Pregnancy-related anxiety scale and factor results

20 weeks	Factor 1	Factor 2
I am worried about the pain of contractions	.09	.93
I am worried about the pain of delivery	.17	.86
I am worried about not being able to control myself during labor	.29	.57
I am afraid that something will be wrong with my baby physically	.82	.26

20 weeks	Factor 1	Factor 2
I am afraid that something will be wrong with my baby mentally	.85	.21
I am afraid that my baby will be stillborn	.66	.07
I worry that my child will be in poor health	.77	.12
Scale Reliability:	$\alpha = .85$	$\alpha = .82$
32 weeks	Factor 1	Factor 2
I am worried about the pain of contractions	.20	.87
I am worried about the pain of delivery	.21	.93
I am worried about not being able to control myself during labor	.28	.57
I am afraid that something will be wrong with my baby physically	.86	.24
I am afraid that something will be wrong with my baby mentally	.92	.27
I am afraid that my baby will be stillborn	.63	.21
I worry that my child will be in poor health	.75	.14
Scale Reliability:	$\alpha = .86$	$\alpha = .83$

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Highlights

- Pregnancy-related anxiety (PrA) has attracted considerable research attention, but questions remain about its distinctiveness from conventional constructs and measures.
- Two PrA factors showed distinct longitudinal patterns in the prenatal period, and modest associations with general measures of anxiety and depression from questionnaire and clinical interview.
- PrA was distinguished from conventional symptom measures in its associated features and prediction of birth weight and postnatal mood disturbance.
- PrA may warrant specific clinical attention.

Figure 1. Path Model Relating Child Birth Weight and Gestational Age at Birth to 32 Week Assessments of Maternal Anxiety

Note: χ^2 (15, N = 336) = 18.74, $p = .23$, CFI = .94, TLI = .93, RMSEA = .03. * $p < .05$, ** $p < .01$. w = weeks, m = months. Gray dashed lines indicate an association that was estimated but was not statistically significant. Pra Child = pregnancy-related anxiety concerning child health, Pra Self = pregnancy-related anxiety concerning pregnancy and delivery. GAD = Generalized anxiety disorder (the broader phenotype), assessed using the Structured Clinical Interview for DSM-IV. GA = gestational age.

Figure 2. Path Model Relating Maternal GAD at 6 months Postpartum to 32 Week Assessments of Maternal Anxiety

Note: $\chi^2(15, N = 319) = 9.87, p = .89, CFI = 1.00, TLI = 1.37, RMSEA = .00$. * $p < .05$, ** $p < .01$, ⁺ $p < .10$. w = weeks, m = months. Gray dashed lines indicate an association that was estimated but was not statistically significant. Pra Child = pregnancy-related anxiety

Table 1

Sociodemographic and Clinical Characteristics of the sample.

Characteristic	N (%) or mean (SD), range
Maternal age at interview (years)	24.40 (3.64), 19–34
Ethnicity	
White/Caucasian	109 (31.59)
Black/African American	164 (47.54)
Other	71 (20.58)
Education (years)	12.58 (2.05), 8–26
Marital Status	
Single	185 (53.62)
Cohabiting/Married	159 (46.09)
Receiving Medicaid	247 (71.59)
BMI at 20 weeks gestation	
Underweight (<18.5)	11 (3.19)
Normal (18.5–24.9)	128 (37.10)
Overweight (25.0–29.9)	82 (23.77)
Obese (>30)	123 (35.65)
Age at first pregnancy	19.64 (3.83), 11–34
Birth weight (grams)	3371 (449), 2505–4735
Gestational age at birth (weeks)	39.40 (1.22), 33–42
Number of previous pregnancies	1.70 (1.63), 0–8
History of miscarriage	
0	255 (73.91)
1	70 (20.29)
2+	16 (4.64)
Met criteria for depression (MDD) during pregnancy	94 (27.25)
Met criteria for anxiety (narrow band GAD) during pregnancy	130 (37.68)

Table 2

Associations between Pregnancy-related Anxiety and Conventional Symptom Measures ($N = 345$).

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
<i>Anxiety measures</i>																		
1. PrA 20Weeks: Child	–																	
2. PrA 32 Weeks: Child	.65**	–																
3. PrA 20 Weeks: Self	.21**	.23**	–															
4. PrA 32 Weeks: Self	.23**	.26**	.74**	–														
5. PSWQ 20 Weeks	.32**	.38**	.22**	.22**	–													
6. PSWQ 32 Weeks	.33**	.42**	.25**	.30**	.80**	–												
7. SCID GAD narrow	.09	.23**	.11	.24**	.46**	.39**	–											
8. SCID GAD broad	.22**	.20*	.12*	.22**	.41**	.36**	.65**	–										
<i>Demographic and Pregnancy Measures</i>																		
9. Parity ^a	.15**	.08	.35**	.30**	.02	–.07	–.09	–.03	–									
10. Number of Miscarriages	.02	–.03	–.11*	–.05	–.02	.05	.08	.04	–.33**	–								
11. Age at First Pregnancy	.10	.08	.12*	.04	.07	–.02	–.09	–.04	.53**	–.24**	–							
12. Education (years)	.08	.08	–.09	–.13*	.00	.01	–.05	–.09	.16**	–.08	.36**	–						
13. Marital Status ^b	.03	.03	–.07	–.05	–.03	.03	–.04	–.02	.01	.04	.04	.13**	–					
14. Race ^c	–.19**	–.10	.03	.08	–.08	.06	.00	–.02	–.22**	.12*	–.20**	–.22**	–.25**	–				
15. Maternal Age	.02	.07	–.19**	–.20**	.05	.07	.01	–.03	–.19**	.18**	.24**	.24**	.12**	.00	–			
16. Medicaid Recipient ^d	–.01	–.06	.05	.02	–.03	–.02	.02	–.01	–.13*	.04	–.19**	–.28**	–.03	.09	–.13**	–		
<i>Birth Outcomes</i>																		
17. Birth weight	–.13*	–.12*	–.06	–.03	–.11*	–.11	–.13	–.13*	–.06	.02	.00	.01	.06	–.09	–.01	.02	–	
18. Gestational Age	–.11	–.06	.06	.07	.06	–.02	–.03	.01	.11*	–.13*	.02	–.05	.07	–.06	–.05	.03	.32**	–

Note:

* $p < .05$,** $p < .01$.

PrA Child = pregnancy-related anxiety concerning child health, PrA Self = pregnancy-related anxiety concerning pregnancy and delivery.

PSWQ = Penn State Worry Questionnaire, SCID = Structured Clinical Interview for DSM-IV, GAD = Generalized Anxiety Disorder, narrow = narrow phenotype, broad = broad phenotype. For both SCID
GAD variables, 0 = did not meet criteria during pregnancy, 1 = met criteria during pregnancy.

θ_0 = second or later pregnancy, 1 = first pregnancy;
 θ_1 = unmarried, 1 = married;
 θ_2 = not African American, 1 = African American;
 θ_3 = not receiving Medicaid, 1 = receiving Medicaid.