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Maternal depression and medication exposure during pregnancy: comparison of maternal retrospective recall to prospective documentation

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Abstract

Objective—Outcome investigations of prenatal maternal depression and psychotropic exposure rely extensively on maternal retrospective recall. This study compared postnatal recall to prospective documentation of illness and medication exposures.

Design—Prospective cohort and retrospective case-control studies.

Setting—Emory Women's Mental Health Program (prospective study) and Emory University Department of Psychology (retrospective study).

Sample—A total of 164 women who participated in both the prospective and retrospective studies.

Methods—Women with a history of mental illness were followed during pregnancy for prospective prenatal assessments of depression and medication exposures. At 6 months postpartum, some of these women also participated in a retrospective study during which they were asked to recall prenatal depression and medication use. Agreement between prospective and retrospective documentation of exposures was analysed.

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Contribution to authorship

Z.N.S. and D.J.N. conceived and designed the prospective study. Z.N.S., D.J.N., P.G., N.M., and B.T.K. participated in the acquisition of data for the prospective study. P.A.B. conceived and designed the retrospective study. P.A.B. and D.I. participated in the acquisition of data for the retrospective study. All of the authors participated in (1) the conception and design of the planned comparative analysis of findings from these two studies, (2) the actual analysis of the data, and (3) the drafting and editing of the manuscript. All authors provided approval of the final manuscript.

Details of ethics approval

The Emory University Institutional Review Board approved the activities of both the prospective (IRB#: 107-2003; date approved: 27 June 2007) and the retrospective (IRB#: 530-99; date approved: 19 June 2007) studies.

Main outcome measures—Occurrence of maternal depression during pregnancy and maternal use of pharmacological agents during pregnancy.

Results—There was only moderate agreement ($k = 0.42$) in prospective versus retrospective reporting of prenatal depression. Positive predictive value for recalling depression was 90.4%; however, negative predictive value for denying depression was only 53.8%. Participants accurately recalled psychotropic use but significantly underreported use of nonpsychotropic medications.

Conclusions—Studies using retrospective data collection may be susceptible to systematic recall bias with underreporting of maternal depression and use of nonpsychotropic agents during pregnancy.

Keywords

Depression; postpartum; pregnancy; recall bias; retrospective recall

Introduction

The treatment of mental illness during pregnancy remains a widely debated clinical conundrum, particularly if pharmacological intervention is considered. Treatment guidelines and review articles repeatedly uphold ‘a careful risk/benefit assessment’ as the cornerstone of prenatal clinical decision-making.^{1–3} This calls for women, their families, and clinicians to weigh the extant data on the impact of *in utero* exposure to both maternal medication and maternal psychiatric illness. Recent prospective studies have demonstrated high rates of recurrence of maternal depression and bipolar disorder during pregnancy in association with discontinuation of psychopharmacological treatment proximate to conception,^{4,5} suggesting that treatment decisions during pregnancy often constitute an either/or fetal exposure.

The volume of perinatal psychiatric research data addressing psychotropic exposure and obstetric outcome is rapidly expanding; however, these investigations have produced discordant results. Major potential confounds of prenatal medication outcome investigations that limit definitive conclusions include the following: (1) many outcome measures (e.g. timing of delivery and birthweight) can be influenced both by medication^{6–18} and by maternal mental illness;^{19–30} (2) psychotropic outcome investigations have incorporated limited assessment of the potentially confounding impact of the maternal mental illness they are being used to treat; and (3) immediately germane to the present investigation, there has been widespread reliance on maternal retrospective recall to determine fetal exposure to medications, environmental toxins including alcohol and tobacco, and maternal psychiatric illness.

Whereas this dependence on retrospective recall is self-evident in inherently retrospective reports (e.g. case-control studies), often overlooked is the widespread reliance on retrospective data collection in many self-proclaimed prospective perinatal studies. For example, ‘prospective’ reports from pregnancy registers and teratology control centres, although they use subjects who were prospectively identified and enrolled during pregnancy, typically collect the bulk of their pregnancy exposure data in a single postnatal interview

that is conducted months and, in some instances, years after delivery. This extensive reliance on retrospective data collection raises concern that much of the existing perinatal psychiatric literature, encompassing both the retrospective and prospective studies, has been susceptible to *recall bias*. Notably, the potential for recall bias has received scant attention in prenatal antidepressant studies.^{31,32}

Previous investigations of postnatal maternal recall focusing on obstetric course, complications, and outcome have produced mixed results. Whereas some have found that maternal recall is reliable compared with the medical record for pregnancy-related events such as complications, method of delivery, and preterm delivery,^{33–35} others have raised questions regarding the reliability of maternal recall.^{36,37} Furthermore, a recent investigation using maternal recall (median 10 weeks postpartum) found that 60% of mothers failed to recall accurately at least one major labour management event.³⁸ The reliability of maternal recall of medication exposures and psychiatric illness during pregnancy, as well as the influence of active maternal psychiatric symptoms on recall, remains obscure.

In nongravid samples, depression is associated with alterations in memory processing that stand to impact the accuracy of participant recall. Of particular concern is the observation that depressed individuals recall negative events more readily than positive ones,^{39,40} unlike healthy controls who preferentially recall positive memories. Whereas recollection is normally positively biased because the affect associated with negative events seems to fade faster, Walker *et al.*⁴⁰ found that the fading of negative memories was reduced in individuals who were mildly dysphoric to clinically depressed. Depressed participants rated negative events at recall almost as intensely as when they originally experienced them, but healthy controls experienced a reduction in the intensity of the unpleasant memory across time.⁴⁰ This is consistent with research indicating that memory for previous events is congruent with current mood.⁴¹

The focus of the current enquiry is to investigate the reliability of *retrospective recall* in perinatal psychiatric research with respect to (1) the course and severity of maternal depression during pregnancy and (2) the use of psychotropics and other pharmacological agents during gestation. In the current study, we compare the agreement of maternal recall at 6 months postpartum with prospective documentation of depression and use of medications and other substances during pregnancy. We hypothesise that (1) recall of depression will not demonstrate a high level of agreement with prospective reporting, (2) recall of depression will be affected by the current clinical status such that women who are depressed at the time of the 6-month postpartum visit will be more likely to report having been depressed during pregnancy, and (3) recall of prenatal psychotropic use will demonstrate a high level of agreement but use of other agents will be underreported retrospectively. The prenatal use of psychotropic medications will, in our estimation, be recalled more accurately than that of other agents because (1) women are conditioned to be particularly attentive to the use of psychotropic agents during pregnancy by the arguably disproportionate media coverage regarding the effects of fetal exposure to psychotropic agents relative to other medications and (2) participants in this study, as in other studies for which the current investigation holds relevance, have completed a protocol specifically constructed to examine the impact of fetal psychotropic exposure.

Methods

Women presenting to the Emory Women's Mental Health Program, from community referrals by obstetric or psychiatric care providers, were enrolled in a prospective observational study of the perinatal course of psychiatric illness and the pharmacokinetics of psychotropic medications during pregnancy. Pregnant women with any past or present history of mental illness were eligible for participation. Only those with acute suicidality or homicidality were excluded from participation. During this prospective longitudinal study, following an initial diagnostic assessment using the Structured Clinical Interview for DSM-IV (SCID),⁴² participants were evaluated at 4- to 6-week intervals throughout pregnancy for symptoms of depression using the Beck Depression Inventory (BDI).⁴³ In addition, participants completed a clinician-administered week-by-week prospective assessment of exposure to medications and other substances during pregnancy. Participants in the prospective study were subsequently recruited to participate in a 1-day study of infant stress reactivity at 6 months postpartum. During this postpartum study, conducted by a separate research team, women were asked to recall their prenatal mood state and the use of medications and other substances on a monthly basis during pregnancy. Women who participated in both the prospective prenatal study and the postpartum study were included in the current analysis. Written informed consent was obtained prior to study enrolment. The prospective and postpartum studies were approved by the Emory University Institutional Review Board.

The first step in the analysis was to evaluate the level of agreement between prospective documentation and retrospective recollection of maternal depression. Prospectively, the presence of depression was defined *a priori* as a BDI score of 14 or greater at any point during the prospective prenatal study. This has been confirmed by our group as an appropriate cutoff score for depression during pregnancy.⁴⁴ To be included in this analysis, it was also decided that the BDI must have been completed at least three times during pregnancy. Retrospectively, the occurrence of prenatal depression was defined in the postpartum study by maternal self-report and recorded as a dichotomous variable. Frequency tests, including calculation of a kappa coefficient, were performed to assess the level of agreement between the prospective and retrospective reporting of depression.

To test our hypothesis that maternal mood at the time of the 6-month postpartum assessment would impact recall, additional frequency tests were conducted to assess the relationship between the postpartum mood (i.e. current diagnosis of major depression as measured by the SCID administered at the post-partum study visit) and the postpartum recollection of mood during pregnancy. These tests were stratified by the prospective documentation of prenatal mood to provide a clearer delineation of the impact of current mood on the likelihood of false-positive and false-negative recollections. To complete our analysis of the determinants of recall of depression, we performed a multivariate logistic regression to assess the clinical and demographic predictors of maternal recall. The outcome modelled in the logistic regression was a maternal report at 6 months postpartum of having been depressed during pregnancy. Candidate predictors included race, marital status, maternal age, education, lifetime SCID diagnosis of a depressive, bipolar, and/or anxiety disorder, maternal mood at

the time of the postpartum study, and the prospective report of maternal mood during pregnancy. Stepwise selection was performed to determine the final reduced logistic model.

Next, the agreement of prospective documentation versus retrospective recollection of maternal use of pharmacological agents during pregnancy was evaluated. For both the prospective and retrospective data collection, the agents were classified as prescription psychotropic (e.g. antidepressants, mood stabilisers, and hypnotics), prescription nonpsychotropic (e.g. antibiotics, antiemetics, and narcotic analgesics), over-the-counter (e.g. analgesics and antihistamines), and habit-forming (e.g. tobacco, alcohol, and illicit drugs). Pharmacological exposure data were operationalised in two ways: (1) as a dichotomous variable for each category indicating whether an agent in each category was used during pregnancy and (2) as a continuous (integer) variable for each category indicating the number of agents in each category used during pregnancy. Frequency tests, including calculation of kappa coefficients, were performed to assess the level of agreement between the prospective and retrospective reporting as operationalised by the dichotomous variables. Paired *t* tests were performed to assess the agreement with respect to pharmacological exposure as operationalised by the continuous variables.

Results

A total of 179 women completed both the serial prospective assessments during pregnancy and the retrospective evaluation at 6 months postpartum. During the prospective study, these 179 participants completed 960 visits. The BDI was completed at least three times during pregnancy by 164 of the 179 participants. These 164 participants were included in the analyses of recall of depression.

The mean age of these 164 participants was 33.9 ± 4.4 years with 40.2% fulfilling criteria for advanced maternal age (i.e. age ≥ 35 years). The racial composition of the sample was 93.9% ($n = 154$) white/Caucasian, 3.7% ($n = 6$) black/African American, and 2.4% ($n = 4$) multiracial. The mean level of education was 15.9 ± 1.9 years. 90.9% ($n = 149$) of the participants were married, whereas 5.5% ($n = 9$) were never married and 3.6% ($n = 6$) were divorced or separated. 85.4% ($n = 140$) of the participants fulfilled lifetime SCID criteria for depression, 11.0% ($n = 18$) for bipolar disorder, and 41.5% ($n = 68$) for an anxiety disorder. Among those with an anxiety disorder, 77.9% ($n = 53/68$) had co-morbid depression, 13.2% ($n = 9/68$) co-morbid bipolar disorder, and 8.8% ($n = 6/68$) no co-morbid mood disorder.

The analysis of prospective versus retrospective reporting of depression included all 164 participants who completed the BDI at least three times during pregnancy and the postpartum assessment. Mean peak BDI scores during pregnancy in the overall sample equalled 19.0 ± 10.4 , with mean scores equalling 24.5 ± 8.4 among those fulfilling the *a priori* prospective criteria for depression and 8.4 ± 3.4 among those who failed to do so. Mean postpartum BDI scores equalled 15.1 ± 9.2 .

Whereas 65.9% of the women ($n = 108$) fulfilled the *a priori* prospective criteria for depression, only 44.5% ($n = 73$) at 6 months postpartum recalled having been depressed during pregnancy. Incidentally, only 12.2% ($n = 20$) of the participants were depressed at the

time of the 6-month postpartum visit. Table 1 shows the comparative frequencies of maternal depression during pregnancy as determined by prospective documentation versus retrospective recall. The kappa coefficient ($k = 0.42$, 95% CI 0.30–0.55) indicates that there was only moderate agreement between the prospective and retrospective measures of maternal depression. The positive predictive value of recalling depression at 6 months postpartum was 90.4%; however, the negative predictive value of not recalling depression was only 53.8%. Put differently, 46.2% ($n = 42/91$) of those who at 6 months postpartum denied having been depressed during pregnancy represented false negatives. Conversely, only 9.6% ($n = 7/73$) of those who at 6 months postpartum reported having been depressed during pregnancy were false positives.

Consistent with our *a priori* hypothesis, women who were determined prospectively to have been depressed during pregnancy were significantly less likely to recall having been depressed prenatally if they were not depressed at the time of the postnatal evaluation (Fisher's exact: $P < 0.008$; Table 2). Indeed, 95.2% ($n = 40/42$) of the false negatives were euthymic at the postnatal assessment. However, this association did not hold for the false-positive recall of prenatal depression (Fisher's exact: $P = 1.00$).

Logistic regression analysis further confirmed our hypothesis that recall was influenced by the maternal mood at the time of the postpartum visit. The reduced model, after stepwise selection, demonstrated that women who were depressed at the time of the postpartum visit were more likely (OR = 4.0) to recall having been depressed during pregnancy (Table 3); however, recall was more strongly associated with the prospective report of depression during pregnancy (OR = 10.1). The log likelihood of the main effects model was 225.72 ($\chi^2 = 50.63$, $df = 3$, $P < 0.001$). The Hosmer and Lemeshow goodness-of-fit statistic was 2.02 ($df = 3$, $P < 0.57$), indicating that the logistic model fit the data adequately.

The analysis of prospective versus retrospective reporting of use of pharmacological agents during pregnancy included 143 women for whom such data were collected in both studies. Kappa scores indicate that there was moderate agreement with respect to use of psychotropic agents (comparing mono-therapy versus polytherapy) and tobacco during pregnancy, fair agreement with respect to use of nonpsychotropic prescription medications and habit-forming substances (when considered collectively), and poor agreement with respect to use of alcohol and over-the-counter medications (Table 4). The total number of agents, number of over-the-counter medications, and number of nonpsychotropic prescription medications as determined by retrospective recall was significantly lower than that determined by prospective assessment (Table 5). As hypothesised, there was no significant difference in determination of the number of psychotropic agents by the two methods.

Discussion

These data raise critical concerns regarding the validity of existing perinatal studies that have relied solely on retrospective data collection. Our data demonstrate two distinct modes of *systematic bias* in the pattern of erroneous retrospective recall. First, some exposures were remembered more accurately than others. Whereas participants were generally accurate in their recollection of prenatal psychotropic use, they were far less accurate in their

recollection of prenatal depression, and use of nonpsychotropic agents (i.e. prescription agents, over-the-counter medications, and habit-forming substances) during gestation. Second, the errors in recall consistently represented false negatives more often than false positives. An unmistakable pattern emerged in which the participants were far more likely to *underreport* (rather than *overreport*) depression and the use of nonpsychotropic agents.

There was one noteworthy exception to this pattern of disagreement between the prospective and retrospective data collection methods. Prenatal alcohol use was reported more often at the postnatal assessment than it had been during the prospective visits during pregnancy. This higher rate of reporting alcohol use by retrospective recall might represent a false-positive report; however, it is also possible that the retrospective report is accurate and that women deliberately withheld details on alcohol use during the prospective assessments due to fear of recrimination. If so, having later seen that their children had been born in good health and at 6 months of age were developing normally, we suspect that women who had withheld reporting their alcohol use prospectively might have felt more comfortable doing so during the postpartum interview.

The current study has several limitations that warrant attention. First, the study population was extremely homogeneous precluding adequate subject diversity to assess extensively the impact of socio-economic or demographic factors on recall accuracy. Most participants were Caucasian, married, older than 30 years of age, and highly educated. At least one investigation of recall found that these demographic characteristics were associated with the highest level of retrospective recall accuracy for obstetric events.³⁶ Second, higher than typical rates of recall accuracy might have been anticipated in this highly compliant sample who successfully completed a high burden longitudinal clinical investigation comprised of serial evaluations of both prenatal mood and pharmacological exposures. Taken together, these limitations suggest that the current study, if anything, underestimates the weaknesses of postnatal recall. Third, the lack of a healthy volunteer comparator group affords no opportunity to compare recall between patient and control groups. Finally, the prospective determination of depression was made using a symptom rating scale rather than a diagnostic instrument. However, as noted above, we have previously reported that a BDI cutoff of 14 is a reliable determinant of depression in gravid subjects.⁴⁴

Despite these limitations, the implications of the current study for perinatal psychiatric research should not be underestimated. In pregnancy outcome studies, it is critically important to provide adequate control for the potential confounding and/or interacting effects of the myriad pathophysiological and pharmacological exposures that can impact maternal and fetal wellbeing. Univariate analyses of the effect of maternal stress, maternal depression, or maternal ingestion of a particular pharmacological agent obviously fail to provide such control. The current study indicates that even multivariate analyses, that is those that endeavour to assess the concomitant effects of fetal exposure to maternal medication and maternal illness, to the extent to which they have relied on retrospective data collection, may also fail to provide adequate control. Given this evidence that retrospective recall systematically underestimates the exposure to maternal psychiatric illness and nonpsychotropic agents (relative to psychotropic exposure), the impact of psychotropic exposure on various outcomes may have been overestimated.

It is equally important that no investigation to date has incorporated the maternal mood state at the time of the post-natal interview as a potential moderator of recall. Data from the current study suggest that the current maternal mood state might contribute to recall bias. This is consistent not only with previous reports regarding the impact of depression on recall in nonperinatal samples^{40,41} but also with earlier evidence that the current maternal mood state can bias maternal assessment of children's behaviour.⁴⁵

The ideal pregnancy outcome study would require prospective masked assessments of maternal symptoms and exposures complemented by laboratory confirmation of potential exposures (e.g. urine drug screen, urine cotinine, and maternal plasma medication concentrations). The importance of masked assessments coupled with laboratory confirmation in pregnancy outcome investigations is underscored by the current investigation. However, whereas the predominant finding was of retrospective underreporting of prenatal exposures and illness, the pattern of recall bias proved to be variable. It is important, therefore, to consider the exception with alcohol exposure in the present study. Ultimately, it is the lack of well-controlled investigations that most likely contributes to the disparity in the conclusions posited by past studies, precluding definitive treatment guidelines. Whereas the cost of completing well-designed prospective prenatal studies is considerable, the failure to do so has resulted in a literature replete with inconsistent methodologies that has produced sweeping changes in clinical practice based solely on retrospective data that have failed to address both the possibility of recall bias and potential confounding exposures such as nonpsychotropic agents and maternal illness, for example paroxetine, carbamazepine, and lithium. The current study provides evidence that maternal postnatal recall in those with mental illness may provide a biased estimate of maternal mood state and pharmacological exposures during pregnancy. Future investigations should incorporate prospective measures, and at the very least, note the potential bias of retrospective recall and the lack of laboratory confirmation, and temper conclusions accordingly.

Acknowledgments

Conflict of interests

D.J.N. has received research support from Eli Lilly, Glaxo-SmithKline (GSK), Janssen, the National Alliance for Research on Schizophrenia and Depression, the National Institutes of Health (NIH), and Wyeth. He has served on speakers' bureaus and/or received honoraria from Astra-Zeneca, Eli Lilly (GSK), Pfizer, and Wyeth. P.A.B. has received research support from NIH. P.G. has received research support from NIH. D.I. has received research support from NIH. T.H.W. has received research support from Astra-Zeneca and NIH. N.M. has received research support from NIH. B.T.K. has received research support from Bristol-Myers-Squibb (BMS), Cyberonics, Eli Lilly, Forest, Janssen, NIH, Novartis, and Wyeth. She has not served on speakers' bureaus or advisory boards. She does not hold equity positions in biomedical or pharmaceutical corporations. One of her family members, an employee of GSK, does hold GSK stock options. Z.N.S. has received research support from GSK, NIH, Pfizer, and Wyeth. He has served on advisory boards for BMS, GSK, and Wyeth. He has served on speakers' bureaus and/or received honoraria from Eli Lilly, GSK, Pfizer, and Wyeth.

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References

1. Wisner KL, Gelenberg AJ, Leonard H, Zarin D, Frank E. Pharmacologic treatment of depression during pregnancy. *JAMA*. 1999; 282:1264–9. [PubMed: 10517430]
2. Stowe ZN, Ragan K. Use of psychiatric medications during pregnancy and lactation. ACOG Practice Bulletin No. 87, Clinical Management Guidelines for Obstetrician-Gynecologists. 2007:1–20.
3. Austin MP, Priest SR. Clinical issues in perinatal mental health: new developments in the detection and treatment of perinatal mood and anxiety disorders. *Acta Psychiatr Scand*. 2005; 112:97–104. [PubMed: 15992390]
4. Cohen LS, Altshuler LL, Harlow BL, Nonacs R, Newport DJ, Viguera A, et al. Relapse of major depression during pregnancy in women who maintain or discontinue antidepressant treatment: a prospective study. *JAMA*. 2006; 295:499–507. [PubMed: 16449615]
5. Newport DJ, Stowe ZN, Viguera AC, Calamaras MR, Juric S, Knight B, et al. Lamotrigine in bipolar disorder: efficacy during pregnancy. *Bipolar Disord*. 2008; 10:432–6. [PubMed: 18402631]
6. Pastuszak A, Schick-Boschetto B, Zuber C, Feldkamp M, Pinelli M, Sihm S, et al. Pregnancy outcome following first-trimester exposure to fluoxetine (Prozac). *JAMA*. 1993; 269:2246–8. [PubMed: 8474204]
7. Goldstein DF, Corbin LA, Sundell KL. Effects of first-trimester fluoxetine exposure on the newborn. *Obstet Gynecol*. 1997; 89:713–18. [PubMed: 9166307]
8. Nulman I, Rovet J, Stewart DE, Wolpin J, Gardner HA, Theis JG, et al. Neurodevelopment of children exposed in utero to antidepressant drugs. *N Engl J Med*. 1997; 336:258–62. [PubMed: 8995088]
9. Kulin NA, Pastuszak A, Sage SR, Schick-Boschetto B, Spivey G, Feldkamp M, et al. Pregnancy outcome following maternal use of the new selective serotonin reuptake inhibitors: a prospective controlled multicenter study. *JAMA*. 1998; 279:609–10. [PubMed: 9486756]
10. Ericson A, Kallen B, Wiholm B. Delivery outcome after the use of anti-depressants in early pregnancy. *Eur J Clin Pharmacol*. 1999; 55:503–8. [PubMed: 10501819]
11. Cohen LS, Heller VL, Bailey JW, Grush L, Ablon JS, Bouffard SM. Birth outcomes following prenatal exposure to fluoxetine. *Biol Psychiatry*. 2000; 48:996–1000. [PubMed: 11082474]
12. Nulman I, Rovet J, Stewart DE, Wolpin J, Pace-Asciak P, Shuhaiber S, et al. Child development following exposure to tricyclic antidepressants or fluoxetine throughout fetal life: a prospective, controlled study. *Am J Psychiatry*. 2002; 159:1889–95. [PubMed: 12411224]
13. Casper RC, Fleisher BE, Lee-Ancas JC, Gilles A, Gaylor E, DeBattista A, et al. Follow-up of children of depressed mothers exposed or not exposed to antidepressant drugs during pregnancy. *J Pediatr*. 2003; 142:402–8. [PubMed: 12712058]
14. Hendrick V, Smith LM, Suri R, Hwang S, Haynes D, Altshuler L. Birth outcomes after prenatal exposure to antidepressant medication. *Am J Obstet Gynecol*. 2003; 188:812–15. [PubMed: 12634662]
15. Suri R, Altshuler L, Hendrick V, Lee E, Mintz J. The impact of depression and fluoxetine treatment on obstetrical outcome. *Arch Womens Ment Health*. 2004; 7:193–200.
16. Oberlander TF, Misri S, Fitzgerald CE, Kostaras X, Rurak D, Riggs W. Pharmacologic factors associated with transient neonatal symptoms following prenatal psychotropic medication exposure. *J Clin Psychiatry*. 2004; 65:230–7. [PubMed: 15003078]
17. Kallen B. Neonate characteristics after maternal use of antidepressants in late pregnancy. *Arch Pediatr Adolesc Med*. 2004; 148:312–16. [PubMed: 15066868]
18. Malm H, Klaukka T, Neuvonen PJ. Risks associated with selective serotonin reuptake inhibitors in pregnancy. *Obstet Gynecol*. 2005; 106:1289–96. [PubMed: 16319254]
19. Steer RA, Scholl TO, Hediger ML, Fischer RL. Self-reported depression and negative pregnancy outcomes. *J Clin Epidemiol*. 1992; 45:1093–9. [PubMed: 1474405]
20. Hoffman S, Hatch MC. Depressive symptomatology during pregnancy: evidence for an association with decreased fetal growth in pregnancies of lower social class women. *Health Psychol*. 2000; 19:535–43. [PubMed: 11129356]

21. Kurki T, Hiilesmaa V, Raitasalo R, Mattila H, Ylikorkala O. Depression and anxiety in early pregnancy and risk for preeclampsia. *Obstet Gynecol.* 2000; 95:487–90. [PubMed: 10725477]
22. Allister L, Lester BM, Carr S, Liu J. The effects of maternal depression on fetal heart rate response to vibroacoustic stimulation. *Dev Neuropsychol.* 2001; 20:639–51. [PubMed: 12002098]
23. Chung TK, Lau TK, Yip AS, Chiu HF, Lee DT. Antepartum depressive symptomatology is associated with adverse obstetric and neonatal outcomes. *Psychosom Med.* 2001; 63:830–4. [PubMed: 11573032]
24. Field T, Diego M, Dieter J, Hernandez-Reif M, Schanberg S, Kuhn C, et al. Depressed withdrawn and intrusive mothers' effects on their fetuses and neonates. *Infant Behav Dev.* 2001; 24:27–39.
25. Orr ST, James SA, Prince CB. Maternal prenatal depressive symptoms and spontaneous preterm births among African-American women in Baltimore, Maryland. *Am J Epidemiol.* 2002; 156:797–802. [PubMed: 12396996]
26. Larsson C, Sydsjo G, Josefsson A. Health, sociodemographic data, and pregnancy outcome in women with antepartum depressive symptoms. *Obstet Gynecol.* 2004; 104:459–66. [PubMed: 15339754]
27. Rahman A, Lovel H, Bunn J, Iqbal Z, Harrington R. Mothers' mental health and infant growth: a case-control study from Rawalpindi, Pakistan. *Child Care Health Dev.* 2004; 30:21–7. [PubMed: 14678308]
28. Patel V, Prince M. Maternal psychological morbidity and low birth weight in India. *Br J Psychiatry.* 2006; 188:284–5. [PubMed: 16507972]
29. Rahman A, Bunn J, Lovel H, Creed F. Association between antenatal depression and low birthweight in a developing country. *Acta Psychiatr Scand.* 2007; 115:481–6. [PubMed: 17498160]
30. O'Connor TG, Heron J, Golding J, Beveridge M, Glover V. Maternal antenatal anxiety and children's behavioural/emotional problems at 4 years. Report from the Avon Longitudinal Study of Parents and Children. *Br J Psychiatry.* 2002; 180:502–8. [PubMed: 12042228]
31. Louik C, Lin AE, Werler MM, Hernandez-Diaz S, Mitchell AA. First-trimester use of selective serotonin-reuptake inhibitors and the risk of birth defects. *N Engl J Med.* 2007; 356:2675–83. [PubMed: 17596601]
32. Alwan S, Reefhuis J, Rasmussen SA, Olney RS, Friedman JM. National Birth Defects Prevention Study. Use of selective serotonin-reuptake inhibitors in pregnancy and the risk of birth defects. *N Engl J Med.* 2007; 356:2684–92. [PubMed: 17596602]
33. Tomeo CA, Rich-Edwards JW, Michels KB, Berkey CS, Hunter DJ, Frazier AL, et al. Reproducibility and validity of maternal recall of pregnancy-related events. *Epidemiology.* 1999; 10:774–7. [PubMed: 10535796]
34. Sou SC, Chen WJ, Hsieh WS, Jeng SF. Severe obstetric complications and birth characteristics in preterm or term delivery were accurately recalled by mothers. *J Clin Epidemiol.* 2006; 59:429–35. [PubMed: 16549266]
35. Quigley MA, Hockley C, Davidson LL. Agreement between hospital records and maternal recall of mode of delivery: evidence from 12 391 deliveries in the UK Millennium Cohort Study. *BJOG.* 2007; 114:195–200. [PubMed: 17166217]
36. Kristensen P, Irgens LM. Maternal reproductive history: a registry based comparison of previous pregnancy data derived from maternal recall and data obtained during the actual pregnancy. *Acta Obstet Gynecol Scand.* 2000; 79:471–7. [PubMed: 10857871]
37. Rao MR, Levine RJ, Wasif NK, Clemens JD. Reliability of maternal recall and reporting of child births and deaths in rural Egypt. *Paediatr Peri-natal Epidemiol.* 2003; 17:125–31.
38. Elkadry E, Kenton K, White P, Creech S, Brubaker L. Do mothers remember key events during labor? *Am J Obstet Gynecol.* 2003; 189:195–200. [PubMed: 12861162]
39. Dalgleish T, Watts FN. Biases of attention and memory in disorders of anxiety and depression. *Clin Psychol Rev.* 1990; 10:589–604.
40. Walker WR, Skowronski JJ, Gibbons JA, Vogl RJ, Thompson CP. On emotions that accompany autobiographical memories: dysphoria disrupts the fading affect bias. *Cogn Emot.* 2003; 17:703–23.

41. Eich E, Macaulay D. Are real moods required to reveal mood-congruent and mood-dependent memory? *Psychol Sci.* 2000; 11:244–8. [PubMed: 11273411]
42. First, MB.; Spitzer, RL.; Gibbon, M.; Williams, JBW. Structured Clinical Interview for DSM-IV-TR Axis I Disorders, Research Version, Patient Edition (SCID-I/P). Biometrics Research, New York State Psychiatric Institute; New York, NY: 2002.
43. Beck AT, Ward CH, Mendelson M, Mock J, Erbaugh J. An inventory for measuring depression. *Arch Gen Psychiatry.* 1961; 4:561–71. [PubMed: 13688369]
44. Bruce, B.; Berg, JP.; Ragan, KA.; Stowe, ZN.; Newport, DJ. An item analysis of the Beck Depression Inventory to assess symptoms of perinatal depression.. American Psychiatric Association 159th Annual Meeting; Toronto, Canada. May 2006; Abstract NR759
45. Najman JM, Williams GM, Nikles J, Spence S, Bor W, O'Callaghan M, et al. Bias influencing maternal reports of child behaviour and emotional state. *Soc Psychiatry Psychiatr Epidemiol.* 2001; 36:186–94. [PubMed: 11518032]

Table 1

Frequency distribution of prospective versus retrospective determination of depression during pregnancy

Prospective documentation of depression during pregnancy	Retrospective recall of depression during pregnancy		Total
	Depressed	Not depressed	
Depressed	66	42	108
Not depressed	7	49	56
Total	73	91	164
Statistics	Fisher's exact: $P < 0.0001$, $k = 0.42$ (95% CI 0.30–0.55)		

Table 2

Frequency distributions of retrospective recall of prenatal depression controlling for mood at time of postpartum assessment—stratified by prospective determination of depression during pregnancy

Mood at time of postpartum assessment	<u>Prospectively depressed during pregnancy</u>			<u>Prospectively not depressed during pregnancy</u>		
	<u>Retrospective recall</u>		Total	<u>Retrospective recall</u>		Total
	Depressed	Not depressed		Depressed	Not depressed	
Depressed	16	2	18	0	2	2
Not depressed	50	40	90	7	47	54
Total	66	42	108	7	49	56
Statistics	Fisher's exact: $P < 0.008$			Fisher's exact: $P = 1.00$		

Table 3

Results of logistic regression analysis of factors influencing retrospective recall of depression during pregnancy

Factors predicting retrospective recall of having been depressed during pregnancy	OR (95% CI)	Wald chi-square
Fulfilled prospective criteria for depression during pregnancy	10.1 (4.1–25.0)	$\chi^2 = 25.2, P < 0.0001$
Depressed at time of postpartum assessment	4.0 (1.1–13.7)	$\chi^2 = 4.7, P < 0.03$
Lifetime SCID diagnosis of major depression	3.5 (1.1–11.1)	$\chi^2 = 4.8, P < 0.03$

Candidate predictors that were excluded in the reduced logistic regression model include race, marital status, age, level of education, lifetime SCID diagnosis of bipolar disorder, and lifetime SCID diagnosis of an anxiety disorder.

Table 4

Frequency distributions of prospective versus retrospective determination of use of various classes of pharmacological agents during pregnancy

Class of agent	Prospective	Retrospective		Statistical analysis
		Yes	No	
Psychotropic monotherapy vs polytherapy	Yes	73	20	$k = 0.52$ (95% CI 0.38–0.67), PPV: 85.9% NPV: 65.5%
	No	12	38	
Nonpsychotropic (prescription)	Yes	47	42	$k = 0.28$ (95% CI 0.13–0.42), PPV: 79.7% NPV: 50.0%
	No	12	42	
Over-the-counter	Yes	24	64	$k = 0.05$ (95% CI –0.07 to 0.17), PPV: 66.7% NPV: 40.2%
	No	12	43	
Habit-forming (any)	Yes	6	16	$k = 0.23$ (95% CI 0.02–0.44), PPV: 40.0% NPV: 87.5%
	No	9	112	
Tobacco	Yes	5	6	$k = 0.53$ (95% CI 0.24–0.82), PPV: 71.4% NPV: 95.6%
	No	2	130	
Alcohol	Yes	1	5	$k = 0.08$ (95% CI –0.15 to 0.30), PPV: 10.0% NPV: 96.2%
	No	9	128	

k , Kappa coefficient; NPV, negative predictive value (i.e. 'No' per retrospective recall is accompanied by 'No' per prospective determination); PPV, positive predictive value (i.e. 'Yes' per retrospective recall is accompanied by 'Yes' per prospective determination).

Table 5

Results of paired *t* tests comparing prospective versus retrospective determination of number of pharmacological agents of various classes used during pregnancy

Class of agent	Number of agents used during pregnancy (mean [95% CI])		Paired <i>t</i> test
	Prospective	Retrospective	
Psychotropic	1.49 [1.33–1.65]	1.56 [1.41–1.71]	$t = 0.94, df = 142, P < 0.36$
Nonpsychotropic (prescription)	1.31 [1.04–1.57]	0.71 [0.47–0.94]	$t = -4.35, df = 142, P < 0.0001$
Over-the-counter	1.24 [1.02–1.47]	0.35 [0.24–0.46]	$t = -7.23, df = 142, P < 0.0001$
Habit-forming	0.20 [0.11–0.28]	0.12 [0.06–0.18]	$t = -1.77, df = 142, P < 0.08$
Total	4.24 [3.76–4.71]	2.73 [2.39–3.08]	$t = -6.37, df = 142, P < 0.0001$