Cortisol Level and Perinatal Outcome in Pregnant Women With Posttraumatic Stress Disorder: A Pilot Study

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Posttraumatic stress disorder (PTSD) affects 12% of women in the United States and could affect childbearing via behavioral and neuroendocrine mechanisms. This pilot study collected preliminary data about the extent to which the low cortisol profile found in patients with PTSD also occurs in the hormonal context of pregnancy, as well as the association between PTSD and less optimal processes and outcomes of pregnancy. Standardized psychiatric diagnostic telephone interviews, salivary cortisol assays, and medical records review were evaluated in a community sample of 25 women pregnant with their first child. Higher PTSD symptom counts correlated with worse overall perinatal outcomes summarized by an Optimality Index Score ($n = 22$; $r = -.725$; $P < .001$). The women whose symptoms met diagnostic criteria for PTSD or partial PTSD had lower peak basal salivary cortisol concentrations ($n = 14$; mean = .4584 versus .8123; $P = .010$). Further research on the effects of PTSD on pregnancy processes and outcomes is warranted. Differences in cortisol levels were consistent with the pattern seen in nonpregnant women with PTSD. This finding suggests that salivary cortisol would be a useful biological measure to include in perinatal research on PTSD and childbearing. J Midwifery Womens Health 2005;50:392–398 © 2005 by the American College of Nurse-Midwives.

keywords: stress disorders, posttraumatic, pregnancy, cortisol, perinatal outcomes, violence against women

INTRODUCTION

Clinical and epidemiologic literature over the past two decades has shown that both trauma and posttraumatic stress disorder (PTSD) are associated with poor health outcomes. PTSD affects women at twice the rate of men, is more likely to be chronic in women, and is associated with physical comorbidity.[1–5] PTSD has a point prevalence estimated at 4.6% among women, with a lifetime prevalence of 12.3%.[3] Two recent studies estimate higher point prevalence rates in pregnant women of 7.7% and 8.1%, respectively.[6,7] Although articles about the potential interaction of trauma history and childbearing difficulties have been published since at least the mid-1980s, there has been little research to date about the impact of posttraumatic stress on childbearing outcomes.

This article presents information on the proposed relationship between PTSD and possible effects on childbearing outcomes. The results of a pilot study that explores this relationship will be described to address two exploratory hypotheses related to PTSD and childbearing. The first is related to the hormonal changes that have been observed in PTSD patients but may or may not be present in pregnancy, and the second is related to negative childbearing outcomes in women with PTSD or PTSD symptoms.

POSTTRAUMATIC STRESS DISORDER

PTSD is a psychological syndrome with symptoms that include physical manifestations. It occurs as a sequela of exposure to an overwhelming trauma. The current diagnostic criteria are based on 17 core symptoms (shown in Table 1) and require experiencing one symptom from the "intrusive reexperiencing" cluster, three symptoms from the "avoidance or emotional numbing" cluster, and two symptoms from the "hyperarousal" cluster, all of which occur in relation to reminders of the trauma.[8] The symptoms must occur for longer than a month and cause clinically significant distress and impairment. These diagnostic criteria were established primarily with clinical samples of veterans who were receiving clinical mental health care in the aftermath of the Vietnam War. The optimal definition of the syndrome remains an open question,[9] especially in relation to women survivors of interpersonal trauma.[10,11] Because it appears that the *Diagnostic and Statistical Manual of Mental Disorders*, 4th Edition (DSM-IV) criteria may be too strict, partial or subsyndromal definitions are sometimes used, especially in cohorts from community or primary care populations (as opposed to psychiatric patients)[2,9] (Table 2). Thus, PTSD researchers measure symptoms, impairment, and distress in such a way to permit analyses using the strict diagnostic criteria, but dimensional measures, such as symptom counts or severity scores, are also used.

Hormonal Alterations of PTSD

Patients with PTSD have physiologic alterations in stress regulation systems, including dysregulation of the hypothalamic-pituitary-adrenal axis, which is one of the body's main stress response systems that regulates fight or flight reactions to a threat.[12] Cortisol levels increase in response to a threat or stressor to mobilize metabolic, circulatory, clotting, and immune responses. In addition, cortisol participates in a negative feedback mechanism to inhibit the

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1526-9523/05/$30.00 • doi:10.1016/j.jmwh.2005.04.024

stress response.[13] Basal cortisol concentrations have a diurnal pattern, peaking in the morning and declining late in the day.[13] In pregnancy, the diurnal pattern appears to be somewhat flatter,[14] and the basal concentrations of cortisol increase across the second half of gestation, peaking prior to labor.[15]

People with PTSD have dysregulated stress responses, reacting to reminders of trauma as though they were occurring again in reality and experiencing chronic autonomic arousal. Physiologic evidence of this dysregulation has been seen in the hypothalamic-pituitary-adrenal axis profiles of persons with PTSD in the form of lower peak cortisol levels and flatter diurnal curves,[16] lower rise in response to a new trauma,[3] and supersupression of endogenous cortisol release when an exogenous glucocorticoid (dexamethasone) is administered.[16] There has been no research to determine if the alterations in cortisol level seen in persons with PTSD remain discernible in the context of the hypothalamic-pituitary-adrenal axis changes in pregnancy. Thus, a goal of this pilot study was to generate preliminary data by depicting the diurnal patterns of women with PTSD and without PTSD, and to use the means of the peak levels as the effect size to calculate power for a larger study.

PTSD IN PREGNANCY

To date, there has been one descriptive epidemiologic analysis that associated a PTSD diagnosis with physical complications of pregnancy.[17] This study used Michigan Medicaid claims data to compare outcomes of 455 women diagnosed with PTSD with outcomes of 638 comparison women without a diagnosis of PTSD; all had diagnostic codes indicating they had been pregnant. The women with PTSD had more pregnancy complications, including more ectopic pregnancies, miscarriages, hyperemesis, preterm contraction episodes, and prenatal services related to large for gestational age (LGA) infants.[17]

PTSD may mediate the relationship between trauma and childbearing outcomes via behavioral and neuroendocrine pathways, including hypothalamic-pituitary-adrenal axis dysregulation.[16,18–20] There is some indirect evidence for this potential pathway from two studies[21,22] in which low cortisol levels were associated with worse labor processes and outcomes. To study such complex mechanisms, large-sample studies that combine psychological, biological, and outcomes data are needed. The pilot study reported here operationalized these 3 components by measuring PTSD symptoms, salivary cortisol, and a global indicator of processes and outcomes of maternity care, the Optimality Index-US.[23]

To summarize, the purpose of the pilot study reported here was to test instruments and procedures and generate preliminary data for future prospective, longitudinal epidemiologic and psychobiologic studies to understand the relationships between PTSD and childbearing outcomes. The two hypotheses explored were that 1) pregnant women with PTSD would have lower basal peak cortisol levels and 2) PTSD would be associated with worse overall perinatal outcomes, as evidenced by a summary measure, the Optimality Index Score.

Table 1. Definitions of the Six Required Components for Diagnosis of PTSD

Criterion A
Experiencing, witnessing, or being confronted with a traumatic event that involves
(a) actual or threatened death or serious injury or threat to physical integrity and
(b) where the person's response involved intense fear, helplessness, or horror
Criterion B
Intrusive reexperiencing of the trauma, manifesting in these 5 symptoms:
1. recurrent, intrusive, distressing recollections
2. recurrent distressing dreams
3. acting or feeling as if it were recurring
4. intense distress at exposure to cues
5. physiologic reactivity on exposure to cues
Criterion C
Emotional numbing and avoidance of internal and external reminders of the trauma, manifesting in these 7 symptoms:
1. avoiding thoughts, feelings, or talk
2. avoiding activities, places, or people
3. inability to recall an important aspect
4. diminished interest in significant activities
5. feeling of detachment or estrangement
6. restricted range of affect
7. sense of a foreshortened future
Criterion D
Autonomic hyperarousal, manifesting in these 5 symptoms:
1. difficulty falling or staying asleep
2. irritability or outbursts of anger
3. difficulty concentrating
4. hypervigilance
5. exaggerated startle response
Criterion E
Duration of symptoms occurring together is longer than 1 month
Criterion F
Person is experiencing clinically significant distress and impairment

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Table 2. Diagnostic Criteria for Full, Subsyndromal, and Partial PTSD

Diagnosis	Required Number of Symptoms From Specific Clusters				
DSM-IV PTSD (full syndrome) (symptoms in each cluster)	1 symptom from criterion B list	AND	3 symptoms from criterion C list	AND	2 symptoms from criterion D list
Subsyndromal PTSD (1 symptom per cluster)	1 symptom from criterion B list	AND	1 symptom from criterion C list	AND	1 symptom from criterion D list
Partial PTSD (DSM-IV required number of symptoms in 2 of the 3 clusters)	1 symptom from criterion B list	AND/OR	3 symptoms from criterion C list	AND/OR	2 symptoms from criterion D list

METHODS

The study protocol was approved by the institutional review boards of the 2 universities where it was conducted, and all participants gave informed consent. Because of the sensitive nature of the trauma history items, the procedures were informed by guidelines for research on violence against women.[24]

Participants were a nonpsychiatric sample of women who were English-speaking, age 18 or older, initiating prenatal care, and expecting their first child (but who may have had prior pregnancies). Thirty consecutive patients attending a new patient obstetric appointment who met eligibility criteria were invited by clinic nurses to be contacted by a survey research organization for a telephone interview as part of a study of "stressful life experiences, emotions, and pregnancy."

Data collected for this study included three components: 1) a standardized interview, which provided the data used to classify the cohort into 2 groups: PTSD and non-PTSD; 2) salivary cortisol samples; and 3) medical record information. The interview included eligibility verification, informed consent, and a structured psychiatric diagnostic interview, including the PTSD module from the National Women's Study.[3] Because of alterations in protein binding during pregnancy, salivary measurements of cortisol are the most valid.[25] Because cortisol levels rise during the second half of gestation,[15] all samples were collected prior to 20 weeks. The cortisol specimens were collected by using the Salivette system, at home, over 4 time periods, to approximate the diurnal curve: at bedtime (near 11 PM), upon awakening (near 8 AM), before eating lunch (near noon), and in the late afternoon (near 4 PM). Women were instructed at the end of the telephone interview about how to collect the specimens, and a written copy of the instructions were included in the collection kit. Instructions included how to time specimen collection in relation to sleeping, eating, and smoking. Specimen kits were returned via mail to the laboratory within 5 days of sampling and frozen at −80°F to await assay.[26] Medical records were abstracted approximately 2 weeks after expected date of delivery by a certified clinical research professional blind to the PTSD status of the women. Medical record data collection was structured to obtain information on the 52 items included in the Optimality Index-US.[23,27] Women were paid $20 for the interview and $10 for returning the cortisol kits by mail to the laboratory.

The standardized survey included several instruments; however, description here is limited to the measures related to the small number of variables used in the pilot analyses. Instruments with demonstrated reliability and validity were used.

The Life Stressor Checklist assesses 30 potential trauma exposures specific to women's experiences, including detailed assessment of childhood and adult abuse and potentially traumatic miscarriage, stillbirth, or abortion.[28] It includes follow-up items to determine if a traumatic event qualifies as a trauma exposure per DSM-IV criteria. It is not possible to determine validity of trauma history instruments, but this measure conforms to the consensus standards by using 1) behaviorally specific questions; 2) nonlegal language; and 3) the most comprehensive list of traumatic events, tailored to the population of interest that is feasible in the study.[29] Of the 5 instruments most frequently used in research to measure trauma exposures, this is the one with the highest sensitivity to trauma among women.[30]

The National Women's Study PTSD Module was used in the largest epidemiologic study of PTSD specific to women.[3] It is designed as a structured telephone diagnostic interview to be administered by lay interviewers. Compared with the gold standard, the Structured Clinical Interview for DSM-IV, the National Women's Study PTSD module has a sensitivity of 0.99 and specificity of 0.79.[29] It measures all 17 symptoms of PTSD, so that the number of symptoms in each of the 3 symptom clusters (Table 1) can be determined. It also measures time frame, consistent with criterion E, and distress and impairment, consistent with criterion F. Thus, this measure yields a dichotomous diagnosis based on DSM-IV criteria, a dimensional symptom count on a scale of 0 to 17, and the possibility of classifying respondents as having partial PTSD or subsyndromal PTSD.

The saliva specimens were returned by direct mail to the laboratory and frozen at −80°F for later assay. Assays were performed by using the commercially available Coat-a-Count radioimmune assay system, with which this laboratory achieves inter- and intra-assay variability near 5% and 3%, respectively.

The medical records data were summarized by using the Optimality Index-US, the main outcome measure used for the pilot. The Optimality Index score includes the Perinatal Background Index (demographic, medical, and obstetric history factors), and the Antepartum, Intrapartum, Neonatal, and Postpartum components.[23] This instrument serves as an interval-level global indicator of the "optimality" of processes and outcomes of maternity care. The 52 items are all dichotomous, indicating the item was "optimal" or "not optimal." The optimality concept has been elaborated and validated in the Netherlands[27] and the United States,[23] and was sensitive to expected differences by parity and in describing outcomes of a homebirth population.[23,27,31] The chart abstraction process and coding rules used were those published by the Dutch originators.[27] By this coding method, each item is scored as optimal or not, based on whether the risk, problem, or intervention was noted or not noted in the medical record. The index score is the sum of the optimal items and is typically presented as a percent, which represents the ratio of noted items compared with the potential items that could be noted in a study. (Note: Coding rules for the Optimality Index-US have evolved since this pilot was conducted. Current coding rules and scoring method are available from the authors.[23])

Demographic and psychiatric characteristics of the PTSD and comparison groups were compared by t tests, χ^2, or Fisher's exact test when cell sizes were smaller than 5. The correlation of PTSD symptom score with Optimality Index Score was analyzed by using Pearson product moment correlation. This small pilot was intended to generate preliminary data, and the study was not powered to show statistically significant differences.

RESULTS

Of the 30 women recruited, 3 could not be reached at the contact number they gave after 20 dialing attempts. One moved away from the study site. One experienced miscarriage. Thus, 25 women gave informed consent, were enrolled, and completed the telephone survey. Fourteen returned saliva specimens by mail (60% return rate in the PTSD group and 53% in the non-PTSD group). Medical records were available for 22 women who delivered at the research site hospitals.

Mean age during the first pregnancy was 27, and the majority of women were married (88%), had bachelor or graduate degrees (80%), and had household incomes greater than $25,000 (88%). More than half were European American (64%), but the sample included 8% African American, 16% Asian, and 4% (n = 1) each Latina, Native American, and other racial/ethnic identities. Compared by group, the PTSD group had less education. All participants in the comparison group had a college education, but half the women in the PTSD group did not have a bachelor's degree. This was the only significant demographic difference.

Twenty-three of 25 women disclosed one or more trauma exposures, but five of them declined to name a "worst trauma" because the event was "not troubling" at the time of the survey. Unexpected death of someone close to them was the most frequently endorsed worst trauma (n = 5), with violence trauma (sexual abuse, rape, and battering) forming the second most prevalent exposure (n = 4), consistent with epidemiologic and primary care studies.[1,3–5] Three women also endorsed prior abortion, miscarriage, and infertility as traumatic events, which may be particularly likely to affect subsequent pregnancy.[32] The 10 women in the PTSD group reported from 1 to 9 trauma exposures (mean 4.4; SD = 2.5), including "worst traumas" of childhood sexual abuse, assault, rape, family member being taken to jail, witnessing a robbery, unexpected death of a loved one, and a trauma not on the list that the participant declined to name. The 15 women in the comparison group reported from 0 to 4 trauma exposures (mean 1.7; SD = 1.1). Ten named a "worst trauma," including unexpected death of a loved one, traumatic miscarriage or abortion, sexual harassment, witnessing an accident, and death of a loved one (expected). Four declined to name a "worst" trauma because they were not significantly bothered by the trauma exposure(s) they reported experiencing. One reported no trauma exposure. This difference in means was statistically significant ($P = .001$).

Three women met criteria for lifetime PTSD using American Psychiatric Association (DSM-IV) criteria,[8] a proportion consistent with population prevalence estimates.[3] PTSD symptom counts ranged from 0 to 15, out of 17 possible symptoms. The mean number of PTSD symptoms reported in the entire sample was 4 of 17. By using the one-symptom-per-cluster criterion for subsyndromal PTSD, 7 women were classified in the PTSD group; by using the criterion for partial PTSD, 10 women were classified in the PTSD group. The results presented use the least restrictive classification of "partial PTSD." Comparisons of PTSD profile, including impairment, distress, depression and anxiety comorbidity, and mental health treatment are presented in Table 3.

The first hypothesis, that pregnant women with PTSD would have lower basal salivary cortisol levels, was supported. Mean peak cortisol concentration differed in the 2 groups, with the PTSD group having the lower profile (mean = .4584 versus .8123; $P = .01$; Figure 1).

The second hypothesis, that PTSD would be associated with worse overall perinatal outcomes, also was supported. The mean Optimality Index Score for the sample as a whole was 43 of 52 possible points (82.7%; range = 37–47). The correlation of the PTSD symptom count with the Optimality Index Score was very strong in the negative direction ($r = -.725$; $P < .000$; Figure 2).

Table 3. Comparison of PTSD Symptom Profiles, Comorbidity Scores, and Treatment Use of the 2 Groups

	PTSD* Group n = 10	Comparison Group n = 15	P†
Number of PTSD symptoms, mean (SD)	7.5 (3.6)	1.7 (1.8)	.000
DSM-IV diagnostic criterion met for			
Criterion A (trauma exposure, mean) (SD)	4.4 (2.5)	1.7 (1.1)	.001
Criterion B (intrusive reexperiencing) (%)	80	13.3	.001
Criterion C (avoidance and numbing) (%)	80	46.7	.105
Criterion D (hyperarousal) (%)	100	40	.002
Criterion E (lasting more than a month) (%)	90	13.3	.000
Criterion F-1 (with impaired functioning) (%)	30	6.7	.159
Criterion F-2 (with significant distress) (%)	50	20	.128
Comorbid disorder scores, mean (SD)			
Depression (range 8–24)	14.5 (2.8)	11.5 (2.6)	.012
Anxiety (range 1–10)	6.5 (3.3)	2.5 (2.2)	.001
Mental health treatment used (%)			
Individual psychotherapy	50	6.7	.023
Medication	30	6.7	.159

Total sample size from prenatal survey was 25.

*Women were classified in PTSD group if they met DSM-IV symptom count criteria in 2 of 3 symptoms (i.e., "partial" PTSD, the least restrictive grouping criterion).

†Chi-square significance was assessed by using Fisher's exact test when cell size was less than 5.

DISCUSSION

Preliminary data generated from this small pilot suggest that the hypothalamic-pituitary-adrenal axis dysregulation associated with PTSD appears to also occur in the hormonal context of pregnancy. The number of PTSD symptoms also correlated strongly with scores on a global summary index of perinatal outcomes; more symptoms were associated with worse outcomes.

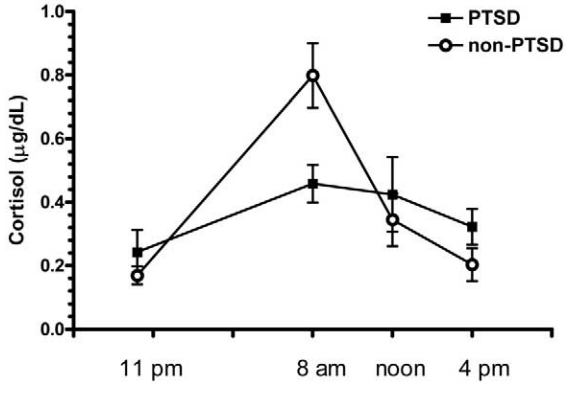

Figure 1. Diurnal cortisol concentration curves with standard error of the mean. Total sample returning cortisol samples was 14, 6 in the PTSD group, and 8 in the non-PTSD group.

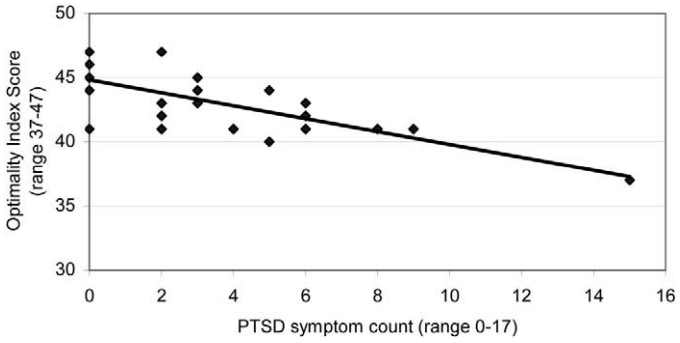

Figure 2. Correlation of PTSD symptom count with Optimality Index Score. Total sample in the medical records review was 22, 8 in the PTSD group and 14 in the non-PTSD group.

The findings from this pilot should be interpreted with caution. Data from survey mental health interviews are less reliable than face-to-face, clinician-administered diagnostic interviews, and our decision to group women with full and partial PTSD together in this small sample may have introduced additional error. The convenience sample for this pilot included some women of low socioeconomic status in prenatal care at academic medical centers. However, this sample overall is more educated and affluent than the US general population of women. Because poor women have greater rates of trauma exposure and poor and uninsured women have fewer resources for treatment, this pilot sample's results may underestimate the impact of PTSD on women who are medically disenfranchised. The strong and statistically significant negative correlation between PTSD symptom count and Optimality Index score in a sample size of 22 suggests that additional outcomes research is warranted.

The community-based saliva-sampling method has strengths and weaknesses. It permits assessment of the peak (on awakening) level, which the requirement to come to a laboratory setting precludes. But it also requires not smoking or eating prior to sample collection, and unmeasured factors (e.g., recent substance use or acute illness) could confound interpretation of cortisol results. The low return rate (14 sets of specimens out of 25 enrolled women) is another limitation. However, the rate of return did not differ by socioeconomic status or PTSD status. Obtaining these findings in this sample of 14 sets of specimens suggests that further biologic research also is warranted.

Women affected by PTSD in this small pilot came from a community (nonpsychiatric) sample with a relatively high socioeconomic status. They had levels of trauma exposure, PTSD, depression, and anxiety similar to those seen in clinical samples, yet only half reported ever using psychotherapy, and only one third reported having used medication. Half of the PTSD group rated their symptoms as "very distressing" and so might welcome attention to their posttraumatic stress-related needs. The distress, impairment, comorbidity, and treatment-seeking profile of the PTSD

group in this pilot suggests that using a partial or subsyndromal criterion for classifying cases of PTSD is appropriate. The mean peak cortisol level was significantly lower in the PTSD group, even though we used the most liberal criterion for assigning women to the PTSD group, which would be expected to decrease differences between the groups. By using the partial PTSD classification, the difference in group outcome score means approached a level of significance, which can be considered meaningful in small pilot samples. Thus, investigators studying community-based samples of women should continue to consider carefully the method used to assign subjects to the PTSD cohort. Because the clinical and epidemiologic importance of considering subsyndromal PTSD is gaining recognition,[1,2] analyses using both the full DSM-IV diagnostic criteria and partial, subsyndromal, or dimensional alternatives may be most informative.

The strong negative correlation between PTSD symptoms and the Optimality Index Score suggests that perinatal studies of PTSD's effect on childbearing processes and outcomes are urgently needed. There have been nearly two decades of clinical literature suggesting that trauma history, especially child sexual abuse, increases both psychological and physical challenges for the pregnant survivor of such trauma. This small pilot, conducted with a convenience sample of pregnant women, confirms that trauma exposure and a range of levels of posttraumatic stress are present in perinatal patients. In addition, biologic differences distinguish these women. Those with partial and full PTSD have worse overall perinatal outcomes on a summary outcome index. If further research confirms that complications and adverse outcomes of pregnancy are associated with PTSD, assessing for PTSD and providing pregnancy-specific PTSD interventions may be an important aspect of maternity care that has yet to receive scientific attention.

This research was funded by the University of Iowa Central Investment for Research Enhancement. The study was completed while Dr. Seng was a Pfizer Postdoctoral Fellow. It was supported in part by Building Interdisciplinary Research Careers in Women's Health (BIRCWH), US DHHS PHS, National Institutes of Health (1 K12 HD01438-01; Dr. Kane Low). The authors thank the prenatal clinic nurses who made this study possible: Ann Freyenberger, Julie Neuzil, Marti Kron, Becky Banks, and Ann Armstrong, as well as Suzanne Daley, CCRP, Elizabeth Lassiter, and the interview staff of the Iowa Social Science Institute.

REFERENCES

1. Stein MB, Walker JR, Hazen AL, Forde DR. Full and partial posttraumatic stress disorder: Findings from a community sample. Am J Psychiatry 1997;154:1114–9.

2. Marshall RD, Olfson M, Hellman F, et al. Comorbidity, impairment, and suicidality in subthreshold PTSD. Am J Psychiatry 2001;158:1467–73.

3. Resnick HS, Kilpatrick DG, Dansky BS, Saunders BE, Best CL. Prevalence of civilian trauma and posttraumatic stress disorder in a representative national sample of women. J Consult Clin Psychol 1993;61:984–91.

4. Breslau N, Davis GC, Peterson EL, Schultz L. Psychiatric sequelae of posttraumatic stress disorder in women. Arch Gen Psychiatry 1997;54:81–7.

5. Kimerling R, Clum G, McQuery J, Schnurr PP. PTSD and medical comorbidity. In Kimerling R, Ouimette P, Wolfe J, eds. Gender and PTSD. New York: Guilford Press, 2002:271–304.

6. Cook CAL, Flick LH, Homan SM, et al. Posttraumatic stress disorder in pregnancy: Prevalence, risk factors, and treatment. Obstet Gynecol 2004;103:710–7.

7. Ayers S, Pickering AD. Do women get posttraumatic stress disorder as a result of childbirth? A prospective study of incidence. Birth 2001;28:111–8.

8. American Psychiatric Association. Diagnostic and statistical manual of mental disorders, fourth edition. Washington (DC): APA, 1994.

9. Stein MB, Walker JR, Hazen AL, Forde DR. Full and partial posttraumatic stress disorder: Findings from a community survey. Am J Psychiatry 1997;154:1114–9.

10. Roth S, Newman E, Pelcovitz D, van der Kolk B, Mandel FS. Complex PTSD in victims exposed to sexual and physical abuse: Results from the DSM-IV Field Trial for Posttraumatic Stress Disorder. J Trauma Stress 1997;10:539–55.

11. van der Kolk BA, Pelcovitz D, Roth S, Mandel FS, McFarlane AC, Herman JL. Dissociation, somatization, and affect dysregulation: The complexity of adaptation to trauma. Am J Psychiatry 1996;153: 83–93.

12. Selye H. The stress of life. New York: McGraw-Hill, 1956.

13. Dickerson SS, Kemeny ME. Acute stressors and cortisol responses: Theoretical integration and synthesis of laboratory research. Psychol Bull 2004;130:355–91.

14. Challis JRG, Patrick JE. Changes in the diurnal rhythms of plasma cortisol in women during the third trimester or pregnancy. Gynecol Obstet Invest 1983;16:27–32.

15. Challis JRG, Sprague C, Patrick JE. Relation between diurnal changes in peripheral plasma progesterone, cortisol, and estriol in normal women at 30–31, 34–35, and 38–39 weeks of gestation. Gynecol Obstet Invest 1983;16:33–44.

16. Yehuda R. Biology of posttraumatic stress disorder. J Clin Psychiatry 2001;62(suppl 17):41–6.

17. Seng JS, Oakley DJ, Sampselle CM, Killion C, Graham-Bermann S, Liberzon I. Association of posttraumatic stress disorder with pregnancy complications. Obstet Gynecol 2001;97:17–22.

18. Seng JS. A conceptual framework for research on lifetime violence, posttraumatic stress, and childbearing. J Midwifery Womens Health 2002;47:337–46.

19. Petersen R, Saltzman LE, Goodwin M, Spitz A. Key scientific issues for research on violence occurring around the time of pregnancy. Atlanta, GA: Centers for Disease Control and Prevention, 1998. [accessed 10-21-01]. Available from: *http://www.cdc.gov/nccdphp/drh/wh_violenc.htm*

20. Friedman MJ, McEwan BS. Posttraumatic stress disorder, allostatic load, and medical illness. In Schnurr PP, Green BL, eds. Trauma and health: Physical health consequences of exposure to

extreme stress. Washington (DC): American Psychological Association, 2004:157–88.

21. McCool W, Susman E. Cortisol reactivity and self-report anxiety in the antepartum: Predictors of maternal intrapartal outcomes in gravid adolescents. J Psychosom Obstet Gynaecol 1994;15:9–18.

22. Mahomed K, Gulmezoglu AM, Nikodem VC, et al. Labor experience, maternal mood and cortisol and catecholamine levels in low-risk primiparous women. J Psychosom Obstet Gynaecol 1995; 16:181–6.

23. Murphy PA, Fullerton JT. Measuring outcomes of midwifery care: Development of an instrument to assess optimality. J Midwifery Womens Health 2001;46:274–84.

24. World Health Organization. Putting women first: Ethical and safety recommendations for research on violence against women. Geneva: WHO, 2001.

25. Vining RF, McGinley RA, Maksvytis JJ, Ho KY. Salivary cortisol: A better measure of adrenal cortical function than serum cortisol. Ann Clin Biochem 1983;20:329–35.

26. Clements AD, Parker CR. The relationship between salivary cortisol concentrations in frozen versus mailed samples. Psychoneuroendocrinology 1998;23:613–6.

27. Wiegers RA, Keirse M, Berghs G, van der Zee J. An approach to measuring quality of midwifery care. J Clin Epidemiol 1996;49: 319–25.

28. Wolfe J, Kimerling R. Gender issues in the assessment of posttraumatic stress disorder. In Wilson JP, Keane TM, eds. Assessing psychological trauma and PTSD. New York: Guilford Press, 1997:192–238.

29. Kilpatrick DG, Resnick HS, Freedy JR, et al. The posttraumatic stress disorder field trial: Emphasis on criterion A and overall PTSD diagnosis. DSM-IV sourcebook. Washington (DC): American Psychiatric Press, 1994.

30. Cusack K, Falsetti S, de Arellano M. Gender considerations in the psychometric assessment of PTSD. In Kimerling R, Ouimette P, Wolfe J, eds. Gender and PTSD. New York: Guilford Press, 2002: 150–76.

31. Wiegers RA, Keirse M, van der Zee J, Berghs G. Outcome of planned home and planned hospital births in low risk pregnancies: prospective study in midwifery practices in the Netherlands. Br Med J 1996;313:1309–13.

32. Turton P, Hughes P, Evans CD, Fainman D. Incidence, correlated and predictors of post-traumatic stress disorder in pregnancy after stillbirth. Br J Psychiatry 2001;178:556–60.