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## Stressors across the life-course and preterm delivery: evidence from a pregnancy cohort

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### Abstract

**Objectives**—Growing evidence suggests that pre-conception stressors are associated with increased risk of preterm delivery (PTD). Our study assesses stressors in multiple domains at multiple points in the life course (i.e., childhood, adulthood, within 6 months of pregnancy) and their relation to PTD. We also examine heterogeneity of associations by race/ethnicity, PTD timing, and PTD clinical circumstance.

**Methods**—We assessed stressors retrospectively via mid-pregnancy questionnaires in the Pregnancy Outcomes and Community Health Study (1998-2004), a Michigan pregnancy cohort (n=2,559). Stressor domains included abuse/witnessing violence (hereafter “abuse”), loss, economic stress, and substance use. We used logistic and multinomial regression for the following outcomes: PTD (<37 weeks’ gestation), PTD by timing ( < 34 weeks, 35-36 weeks) and PTD by clinical circumstance (medically indicated, spontaneous). Covariates included race/ethnicity, education, parity, and marital status.

**Results**—Stressors in the previous 6 months were not associated with PTD. Experiencing abuse during both childhood and adulthood increased adjusted odds of PTD among women of white or other race/ethnicity only (aOR: 1.6, 95%CI: 1.1, 2.5). Among all women, abuse in childhood increased odds of late PTD (aOR: 1.5, 95%CI: 1.0, 2.2) while abuse in both childhood and adulthood non-significantly increased odds of early PTD (aOR: 1.6, 95%CI: 0.9, 2.7). Sexual, but not physical, abuse in both childhood and adulthood increased odds of PTD (aOR: 1.9, 95%CI: 1.0, 3.5).

**Conclusions**—Experiences of abuse—particularly sexual abuse—across the life-course may be important considerations when assessing PTD risk. Our results motivate future studies of pathways linking abuse and PTD.

### Keywords

preterm delivery; stress; abuse; life course

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## INTRODUCTION

Preterm delivery (PTD, <37 weeks gestation) is the leading cause of infant mortality, is associated with short- and long-term health and social outcomes of the infant, and is estimated to cost over \$25 billion annually in the U.S. (Behrman and Butler 2005; Blencowe et al. 2013; Pallotto and Kilbride 2006). Moreover, PTD is strongly patterned by race and socioeconomic status (SES) such that disadvantaged groups are at increased risk (Blumenshine et al. 2010; Bryant et al. 2010). These disparities are not easily explained by individual-level medical or behavioral factors (Goldenberg et al. 1996; Hummer et al. 1999; Lhila and Long 2012; McGrady et al. 1992), leading researchers to hypothesize a role for maternal psychosocial stress in the etiology of PTD, mediated by neuroendocrine, immune, vascular, or epigenetic pathways (Christian 2012; Wadhwa et al. 2011; Yao et al. 2014).

Empirical research investigating links between stressors during pregnancy and birth outcomes has generated inconsistent findings (Chen et al. 2011; Dunkel Schetter, 2011; Kramer et al. 2011; Laszlo et al. 2016). Due to increasing interest in viewing maternal and infant health through a life-course perspective (Holzman et al. 2006; Lu and Halfon 2003; Richardson et al. 2013), scholars have begun to examine the impact of stressors experienced *prior to* pregnancy on birth outcomes (Collins et al. 2011; Gawade et al. 2015; Harville et al. 2010; Khashan et al. 2009; Kramer et al. 2011; Love et al. 2010; Precht et al. 2007; Strutz et al. 2014; Witt et al. 2014a, 2014b).

Findings largely support an association between exposure to pre-conception stressors and increased risks of low birth weight and PTD (Harville et al. 2010; Khashan et al. 2009; Witt et al. 2014a, 2014b). Khashan and colleagues (2009) examined Danish national birth data (n=1.35 million) linked with hospital registry data to identify mothers who had experienced the death or serious illness of a close relative in the 6 months prior to conception or during pregnancy and found that exposure to this type of stressor prior to conception was associated with increased risk of PTD. Witt and colleagues (2014a, 2014b) also found that exposure to one of several pre-conception stressors (including death of a close relative, divorce or separation, and fertility problems) was associated with increased risks of both PTD and low birth weight. Witt et al. used a nationally representative U.S.-based sample, controlled for stressors during pregnancy, and identified that younger women (15-19 years old) were at highest risk.

Evidence suggests, however, that stressors across varied domains (e.g., abuse, economic hardship) may have differential health impacts and that measuring only a smaller set of life events may not capture the full extent of stress's health impacts (Thoits 2010). Moreover, timing of exposure to stress during the life course may matter with respect to perinatal health (Lu and Halfon 2003). Indeed, Witt and colleagues (2014b) report that events occurring within one year of conception were associated with higher risk of PTD among young women whereas events occurring more than a year prior to conception were associated with PTD among older women. Only one study of which we are aware has investigated pre-conception stressors across both multiple domains and time periods; Harville and colleagues, using data from Great Britain, report that violence/mental health and family structure issues in late childhood increased risk of PTD (2010).

Research that examines pre-conception stressors in multiple domains across multiple life-course periods in a racially diverse U.S. cohort will improve our understanding of the relationships between race/ethnicity, pre-conception stress, and PTD. Moreover, no prior work has considered potential differences by PTD timing (early vs. late) or PTD clinical circumstance (medically indicated vs. spontaneous); such heterogeneity could lend insight into pathways linking stressors to PTD due to the varying complications and etiologies of early vs. late and medically indicated vs. spontaneous PTD (Goldenberg et al. 2008).

To address these gaps, we examined associations between stressors in multiple domains over three life-course periods (i.e., childhood, adulthood, and around the time of the pregnancy) and PTD in a community-based, racially and socioeconomically diverse pregnancy cohort from Michigan. We selected four domains (abuse/witnessing violence, loss, economic stress, and substance abuse) based on prior work demonstrating their importance for pregnancy mental health in the same sample (Holzman et al. 2006). We hypothesized that stressors associated with pregnancy mental health may also be linked to PTD based on reports of associations between pregnancy anxiety and depression and adverse birth outcomes (Dunkel Schetter 2011; Gavin et al. 2009). We also investigated potential heterogeneity in these relationships by maternal race/ethnicity and by PTD timing (early, 34 weeks gestation, or late, 35-36 weeks) and clinical circumstance (medically indicated or spontaneous).

## METHODS

### Data and Study Population

Data came from the Pregnancy Outcomes and Community Health (POUCH 1998-2004) study, which enrolled women with singleton pregnancies at 52 clinics in 5 Michigan communities. Women were approached at the time of prenatal screening; those who did not decline further contact were contacted by study staff for enrollment and consent. POUCH enrolled 3,038 women and completed follow-up to delivery for 3,019. Participants met with a study nurse in the 16<sup>th</sup>–27<sup>th</sup> week of pregnancy and completed a detailed in-person and self-recorded interview that included questions about demographics, lifestyle, and a battery of psychosocial assessments, including the questions used to assess life stressors in this study. Comparisons of the POUCH study data and data from birth certificates in the 5 study communities indicated that the POUCH study sample was similar to the communities in terms of age, parity, education, Medicaid insurance coverage, PTD, and prior PTD; the percentage of African-American women over age 30 was lower in POUCH than in the communities as a whole. The detailed study protocol has been described elsewhere (Holzman et al. 2001). The institutional review boards at Michigan State University and all participating community hospitals approved this study. Because our study examines both childhood and adulthood stressors, we restricted our analysis to women 20 years (n=2,559).

### Measures

Our primary outcome measure was preterm delivery (PTD), defined as delivery <37 weeks gestation (vs. term delivery, 37 weeks). Gestational age was based on the mother's last menstrual period (LMP), unless it differed by >2 weeks from an ultrasound conducted before 25 weeks' gestation, in which case the ultrasound measure was used. We further

categorized PTD according to 1) timing: early PTD ( < 34 weeks) and late PTD (35-36 weeks) vs. term delivery ( > 37 weeks, reference category) and 2) clinical circumstance: spontaneous PTD and medically indicated PTD vs. term delivery (reference category). A physician and a labor and delivery nurse independently abstracted data from the prenatal and labor and delivery medical records to identify the clinical circumstances leading to PTD. We defined spontaneous PTD as spontaneous preterm labor (i.e., intact membranes, regular contractions, and cervical changes [ > 2 cm dilation] in the absence of labor induction) or preterm premature rupture of membranes and medically indicated PTD as induction of labor or a cesarean section before the onset of labor or PROM.

We define life stressors as events or circumstances that could potentially result in a perceived imbalance between demands and personal, societal, or environmental resources (Cohen et al. 1995). Life stressor questions were adapted from the Turner, Wheaton, and Lloyd Checklist (Turner et al. 1995). The first set of questions asked respondents how often a life stressor had occurred during the previous 6 months, a period that includes the first half of pregnancy, using a 5-point Likert scale to indicate “never”, “once or twice”, “several times”, “often”, and “very often”. A second, similar, set of questions asked respondents whether a life stressor had occurred “never”, “when you were a child”, “since you’ve grown up”, or “both as a child and an adult”. These questions differed slightly from those assessing the previous 6 months because we anticipated differences in the ability of participants to remember events and circumstances from the past 6 months compared to childhood.

In previously published work on the POUCH study, stressors were grouped into domains using an *a priori* approach with a confirmatory factor analysis (Holzman et al. 2006; Scheid et al. 2007). For stressors in the previous six months, domains included: abuse (2 questions: [1] shoved, hit, or physically abused; [2] raped, sexually molested, or forced to have sexual activity), economic problems (4 questions: [1] participant or someone she counted on for financial support had problems finding or keeping a job; participant or her family had problems with [2] housing or [3] transportation or [4] trouble keeping phone service), and substance use (alcohol or drug problems) in someone close. Due to clumping of responses near the low end of the Likert scale, responses within each domain were categorized as “never” (“never” for all questions in the domain), “once or twice” (“once or twice” for any 1 question in the domain), or “more than twice” (“once or twice” on >1 question in the domain or “several times”, “often”, or “very often” on any 1 question in the domain). (See Table 2.)

For stressors in adulthood and childhood, domains (Holzman et al. 2006) included: abuse and/or witnessing violence (hereafter “abuse/violence” 3 questions: [1] shoved, hit, or physically abused; [2] raped, sexually molested, or forced to have sexual activity; [3] saw something violent happen or saw someone killed), economic problems (5 questions: [1] participant or someone she counted on for financial support had problems finding or keeping a job; [2] participant or her family didn’t have enough money for necessities, [3] had problems with housing, [4] had trouble keeping phone service, or [5] had other problems about money), loss (4 questions: [1] divorce, [2] parent death, [3] death of someone close, and [4] someone close becoming unavailable), and substance use (participant or someone close to her had problems because of alcohol or drugs). Responses in these domains were

categorized as “never”, “childhood only”, “adulthood only” or “both childhood and adulthood”. (See Table 2.)

Maternal characteristics considered as covariates included age at enrollment in the POUCH study: educational attainment, (<12<sup>th</sup> grade, 12<sup>th</sup> grade and >12<sup>th</sup> grade), parity (number of pregnancies prior to the POUCH study pregnancy that ended in a live birth, categorized as 0 or 1), and marital status (married vs. unmarried). Race/ethnicity was also included as a covariate; women were categorized based on self-reported race/ethnicity as African American [AA] or white/other. Women of other race/ethnic groups were combined with whites to create a reference group because their numbers were small (57 Asian, 123 Hispanic, and 33 Native American or other) and their PTD rates were similar to that of whites. Models reported here use educational attainment as a measure of SES; substitution with other SES measures i.e., household income (which had more observations missing data) and insurance status (Medicaid vs. private), produced similar results.

### Statistical Analysis

We examined the distribution of maternal characteristics and life stressors overall and by PTD. We conducted bivariable chi-square tests comparing the probability of PTD across all life stressor variables. Following prior work (Holzman et al. 2006), we included life stressors in multivariable models if p-values from chi-square tests were <0.25. We used separate multivariable logistic regression models to assess associations between PTD and stressors in the previous 6 months and stressors in childhood/adulthood. Models were adjusted for maternal age, race/ethnicity, educational attainment, parity, and marital status. We tested for interactions between race/ethnicity and each life stressor domain using a Wald test with a threshold of  $p < 0.1$ . Observations with missing data (<1% of records) were dropped from the analysis. We used multinomial regression to examine relations between life stressors and the 3-level PTD timing and clinical circumstance variables. Analyses were weighted for the stratified sampling structure of the POUCH study. Five or less women were missing data for each stressor, 5 women were missing data for marital status, and no women were missing data on PTD or any other covariate; thus we conducted all analyses using only observations with available data. All analyses were conducted using SAS 9.4 (Cary, NC).

## RESULTS

Table 1 describes pregnancy outcomes, demographic and reproductive characteristics, and stress experiences of our sample (n=2,559). Approximately 11% of women had PTD, with 3.6% of all women delivering early preterm and 7.2% delivering late preterm. About 7% of all women had a spontaneous PTD and 4% had a medically indicated PTD. One-fifth of women were African American, 38% percent had a high school education or less, 36% were nulliparous and over 40% were unmarried. In the previous 6 months, approximately 11% of women experienced abuse, 31% experienced economic stress, and 22% experienced substance use in someone close to them. In either childhood, adulthood, or both, almost half of all women in the sample experienced abuse/violence, over 50% experienced economic problems, over 80% experienced loss, and about 45% experienced substance use problems in themselves or someone close to them.

Table 2 reports the number and percent of women with PTD by maternal demographic and reproductive characteristics and within the life stressor categories, with p-values from chi-square tests. Women who were African-American, unmarried, or had <12 years education were more likely to have a PTD compared to women who were white/other, married, or had 12 or more years of education, respectively.

Of stressors in the past 6 months, only economic problems was associated with PTD in the bivariable analyses with a p-value of <0.25 and therefore considered in multivariable analyses. Of stressors in childhood/adulthood, only abuse/violence and loss were significantly associated with PTD in bivariable analyses with a p-value of <0.25 and therefore considered in multivariable analyses. Almost 14% of women experiencing abuse/violence in both childhood and adulthood had a PTD compared to 9.8 to 11.7% of those experiencing abuse/violence during only one time period or not at all.

After adjusting for maternal covariates, economic problems in the previous 6 months were not significantly associated with PTD (data not shown). There was a significant interaction between race/ethnicity and abuse/violence ( $p=0.07$ ) such that white/other women who experienced abuse/violence in both childhood and adulthood had increased odds of PTD (OR 1.6, 95% CI 1.1, 2.5) (Table 3, column 1) whereas abuse/violence was not associated with PTD in African-American women. Loss during childhood/adulthood was not significantly associated with PTD in multivariable models.

Using multinomial regression, we further examined PTD by timing (early PTD and late PTD vs. term birth) and by clinical circumstance (spontaneous PTD and medically indicated PTD vs. term birth). African-American women had higher odds of early PTD compared to white women (OR: 1.9, 95% CI: 1.2, 3.2), and women with <12 years education had higher odds of both any PTD (OR: 1.6, 95% CI: 1.0, 2.4) and later PTD (OR: 1.9, 95% CI: 1.2, 3.1). Women experiencing abuse/violence in childhood only (compared to never) had higher odds of late PTD (OR: 1.5, 95% CI: 1.0, 2.2) (Table 3, column 2), and women experiencing abuse/violence during both childhood and adulthood (compared to never) had increased odds of early PTD (OR: 1.6, 95% CI: 0.9, 2.7), although this finding was not statistically significant at  $p<0.05$  (Table 3, column 3). The interaction between race/ethnicity and the abuse/violence variable was not significant in models of early/late PTD. There were no other significant associations between stressors and PTD divided by timing or circumstance.

Motivated by a growing body of literature implicating sexual abuse as a risk factor for adverse perinatal outcomes (Nerum et al. 2013; Noll et al. 2007; Schei et al. 2014; Seng et al. 2011), we conducted a post-hoc analysis examining sexual and physical abuse independently (instead of grouped within the abuse/violence domain). After adjustment, there were no significant associations between either sexual or physical abuse in the previous 6 months and PTD and no significant associations between physical abuse in childhood/adulthood and PTD. On the other hand, women experiencing sexual abuse in both childhood and adulthood (compared to never) had almost twice the odds of PTD (OR: 1.9, 95% CI: 1.0, 3.5) (Table 4, column 1). Moreover, sexual abuse in childhood only (OR: 1.5, 95% CI: 1.0, 2.2) and in both childhood and adulthood were associated with late PTD (OR:



2.2; 95% CI: 1.1, 4.5), but not early PTSD (Table 4, column 2 and 3). Due to limitations of sample size, we were unable to examine differences by race/ethnicity.

## DISCUSSION

Using data from a racially and socioeconomically diverse Michigan pregnancy cohort, we examined relations between stressors across multiple domains (abuse/witnessing violence, loss of someone close, economic stress, and substance abuse in someone close) and life-course periods (childhood, adulthood, and around the time of pregnancy) with PTSD, investigating both timing (early vs. late) and clinical circumstance (spontaneous vs. indicated) of PTSD. Women of white/other race/ethnicity who experienced abuse or witnessed violence in both childhood and adulthood had 60% higher odds of PTSD relative to women who never experienced abuse/violence, but we found no association among African-American women. Women of both race/ethnicities who experienced abuse/violence in childhood only had a 50% increase in odds of *late* PTSD, whereas women who experienced abuse/violence during both childhood and adulthood also had about a 60% increase in odds of *early* PTSD (though not statistically significant). Sexual abuse, in particular, in both childhood and adulthood was associated with a doubling of the odds of overall and late PTSD. We note that our sample size (n=2,559 women) resulted in confidence intervals that overlapped and/or were close to the null for many reported associations; these findings should therefore be interpreted with caution but indicate the potential importance of life-course exposure to abuse/violence on PTSD. In general, our findings indicate that cumulative exposure to abuse/violence (i.e., during both childhood and adulthood) is more strongly associated with PTSD compared to exposure at only one point in the life-course.

Although previous work has demonstrated associations between exposure to pre-conception stressors and adverse birth outcomes (Collins et al. 2011; Harville et al. 2010; Khashan et al. 2009; Love et al. 2010; Precht et al. 2007; Strutz et al. 2014; Witt et al. 2014a, 2014b), these studies did not examine stressors separately across multiple domains or specify exposure during childhood vs. adulthood. The only other study of which we are aware to examine stressors in multiple domains across the life course also found an association between violence/mental health issues in late childhood and PTSD (Harville et al. 2010), although these authors defined violence/mental health differently than in our study. Prior work in the POUCH Study reported that women who experienced abuse in the previous 6 months as well as in both childhood and adulthood had higher depressive symptoms during pregnancy (Holzman et al. 2006). Sexual abuse during childhood has recently emerged as a risk factor for adverse perinatal outcomes. Noll et al. found that women reporting childhood sexual abuse had a higher risk of PTSD and that this association was mediated by pathways marked by alcohol use during pregnancy (Noll et al. 2007). Other work found that sexual abuse in adulthood, but not childhood, was associated with increased risk of a cesarean delivery (Nerum et al. 2013; Schei et al. 2014), whereas physical abuse was not associated with type of delivery (Schei et al. 2014).

Proposed biological mechanisms hypothesized to link cumulative exposure to stress over the life course with PTSD include dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis, changes to immune function and inflammation, vascular problems, and epigenetics

(Christian 2012; Kramer et al. 2011; Wadhwa et al. 2011; Yao et al. 2014). For example, evidence suggests that exposure to early life adversity can have long-term impacts on HPA functioning (Gonzalez et al. 2009; Pesonen et al. 2010), and maternal HPA axis dysregulation may affect placental production of corticotrophin-releasing hormone (CRH), which in turn could influence timing of parturition (Challis 2000). Chronic stress is linked to elevated blood pressure (Roberts et al. 2008), which could affect placentation and blood flow to the placental/fetal compartments; long-term stress also impacts immune system activity, perhaps setting the stage for urogenital infections or conditions such as bacterial vaginosis, known risk factors for PTD (Culhane et al. 2001; Harville et al. 2005; Paul et al. 2008; although see: Trabert and Misra, 2007). Few studies, however, have explicitly examined the relationships between life-course stressors, proposed biological pathways, and PTD, due in part to the absence of large, prospective datasets including measures of both early life stressors and biological markers.

Cumulative stressors may also influence women's socioeconomic status, marital status, age at pregnancy, or behavioral factors associated with PTD (e.g., smoking, diet, physical activity, utilization of preventive care, or risky sexual behaviors), making it difficult to determine the most appropriate confounder vs. mediator variables in such analyses. Although we included education, parity, marital status, and maternal age as confounders, these variables may also be affected by early life stressors and thus function as mediators; we note that removing these variables from our models left the associations between stressors and PTD essentially unchanged (data not shown). Similarly, we chose not to include maternal smoking, body size, or pregnancy complications in our model because we hypothesized that these variables would function as mediators of the relationship between stressors and PTD.

The current study found that the association between abuse/violence and PTD was stronger among women of white or other race/ethnicity compared to African American women. One possible explanation is that stressor effects assessed in our study cannot be easily isolated against the backdrop of other stressors that may be more prevalent among African American compared to white women (e.g., discrimination, racism, or chronic stress due to poverty or living in segregated and/or disadvantaged neighborhoods) (Culhane and Goldenberg 2011; Nuru-Jeter et al. 2009; Williams and Collins 1999).

Limitations of these data include that all life course stressors were self-reported, which could have resulted in recall bias. Although validity of early life stressors is difficult to assess, evidence suggests that retrospective reports of serious early life events that are more objective than subjective (e.g., abuse, as compared to hardship) are reasonably valid (Hardt and Rutter 2004). Moreover, if recall bias was prominent, we would expect to find significant associations with more stressors, and we only found associations with abuse/violence. Women may also have interpreted questions regarding life course stressors differently, depending on community or cultural norms. Our data did not enable us to identify women who personally experienced violence (other than abuse) from those who witnessed violence, and we were not able to assess "dose" of stressors in childhood or adulthood (i.e., isolated incidence vs. chronic exposure). Such additional information on exposure and dose might lead to more precise estimates of the relationships between life



course stressors and PTD. Other limitations include that we were unable to control for stressors during pregnancy as has been done in prior studies (Witt et al. 2014a; 2014b); our reported associations between stressors and PTD are therefore not independent of pathways through stressors during pregnancy. Finally, we note that, despite a sample size of 2,559 women, both exposure to stressors and PTD were relatively rare (e.g., overall probability of PTD was 0.11), resulting in overlapping confidence intervals that were in some cases close to the null. Our ability to detect significant interactions by race/ethnicity for outcomes such as early vs. later PTD was limited by our sample size.

However, studies assessing stressors in multiple domains at multiple points prior to pregnancy are few. Our study therefore makes an important contribution to the literature on life course stressors and birth outcomes and is unique in our examination of PTD by both timing and clinical circumstance. Although our findings may not be generalizable to the entire U.S.—the rate of PTD in our study (11%) was higher than that for singletons in the entire U.S. in 2000 (8.7%) (Martin et al. 2002)—the POUCH study was representative of the 5 Michigan communities from which it was drawn and is a racially and socioeconomically diverse sample.

Links between childhood/adulthood abuse and PTD have both clinical and policy implications. In particular, these associations support calls from the Maternal and Child Health Bureau (2012) and others (Cheng et al. 2012; Lu and Halfon 2003) to shift clinical emphasis for prevention of PTD to the preconception period. Preventing abuse may help to lower PTD rates. In addition, clinicians who screen women for history of abuse during routine gynecological exams, at healthy child visits, and/or in early pregnancy may identify women at increased risk of PTD who would benefit from closer monitoring. Further research is needed to identify intervention strategies for high-risk women; such work could focus on testing factors thought to increase resilience to stressors, such as social support (Thoits 2010), or interventions that focus on reducing the impact of early abuse or trauma. Overall, our work and others' suggest that policies or programs to prevent sexual abuse may play an important role in women's long-term reproductive health.

In conclusion, our findings indicate that experiencing abuse and/or witnessing violence prior to pregnancy, and especially in childhood, may be linked to PTD. Stressors in the domains of economic hardship, loss, and substance abuse were, however, not associated with PTD. The relationship between abuse/violence and PTD appeared particularly salient among white women, and exposure during both childhood and adulthood is linked to early PTD. Moreover, our findings point to the unique importance of sexual abuse in childhood and across the life-course as a risk factor for PTD. Further research is needed to understand the observed heterogeneity in terms of race/ethnicity and timing of PTD and to elucidate possible biological mechanisms.

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## REFERENCES

- Behrman, R., Butler, A. Preterm birth: causes, consequences, and prevention. National Academies Press; Washington, DC: 2005.
- Blencowe H, Cousens S, Chou D, Oestergaard M, Say L, Moller AB, et al. Born too soon: the global epidemiology of 15 million preterm births. *Reprod Health*. 2013; 10(Suppl 1):S2. [PubMed: 24625129]
- Blumenshine P, Egerter S, Barclay CJ, Cubbin C, Braveman PA. Socioeconomic disparities in adverse birth outcomes: a systematic review. *Am J Prev Med*. 2010; 39(3):263–272. [PubMed: 20709259]
- Bryant AS, Worjloh A, Caughey AB, Washington AE. Racial/ethnic disparities in obstetric outcomes and care: prevalence and determinants. *Am J Obstet Gynecol*. 2010; 202(4):335–343. [PubMed: 20060513]
- Challis JRG. Mechanism of parturition and preterm labor. *Obstet Gynecol Surv*. 2000; 55(10):650–660. [PubMed: 11023206]
- Chen MJ, Grobman WA, Gollan JK, Borders AE. The use of psychosocial stress scales in preterm birth research. *Am J Obstet Gynecol*. 2011; 205(5):402–432. [PubMed: 21816383]
- Cheng TL, Kotelchuck M, Guyer B. Preconception women's health and pediatrics: an opportunity to address infant mortality and family health. *Acad Pediatr*. 2012; 12(5):357–359. [PubMed: 22658953]
- Christian LM. Psychoneuroimmunology in pregnancy: immune pathways linking stress with maternal health, adverse birth outcomes, and fetal development. *Neurosci Biobehav Rev*. 2012; 36(1):350–361. [PubMed: 21787802]
- Cohen, S., Kessler, RC., Gordon, LU. Measuring stress: a guide for health and social scientists. Oxford University Press; New York: 1995.
- Collins JW, Rankin KM, David RJ. Low birth weight across generations: the effect of economic environment. *Matern Child Health J*. 2011; 15(4):438–445. [PubMed: 20390329]
- Culhane JF, Rauh V, McCollum KF, Hogan VK, Agnew K, Wadhwa PD. Maternal stress is associated with bacterial vaginosis in human pregnancy. *Matern Child Health J*. 2001; 5(2):127–134. [PubMed: 11573838]
- Culhane JF, Goldenberg RL. Racial disparities in preterm birth. *Semin Perinatol*. 2011; 35(4):234–239. [PubMed: 21798403]
- Dunkel Schetter C. Psychological science on pregnancy: stress processes, biopsychosocial models, and emerging research issues. *Annual Review of Psychology*. 2011; 62:531–558.
- Gavin AR, Holzman C, Siefert K, Tian Y. Maternal depressive symptoms, depression, and psychiatric medication use in relation to risk of preterm delivery. *Womens Health Issues*. 2009; 19(5):325–34. [PubMed: 19733802]
- Gawade PL, Oeffinger KC, Sklar CA, Green DM, Krull KR, Chemaitilly W, et al. Lifestyle, distress, and pregnancy outcomes in the Childhood Cancer Survivor Study cohort. *Am J Obstet Gynecol*. 2015; 212(1):47.e41–10. [PubMed: 25068563]
- Goldenberg RL, Cliver SP, Mulvihill FX, Hickey CA, Hoffman HJ, Klerman LV, Johnson MJ. Medical, psychosocial, and behavioral risk factors do not explain the increased risk for low birth weight among black women. *Am J Obstet Gynecol*. 1996; 175(5):1317–1324. [PubMed: 8942508]
- Goldenberg RL, Culhane JF, Iams JD, Romero R. Epidemiology and causes of preterm birth. *Lancet*. 2008; 371(9606):75–84. [PubMed: 18177778]
- Gonzalez A, Jenkins JM, Steiner M, Fleming AS. The relation between early life adversity, cortisol awakening response and diurnal salivary cortisol levels in postpartum women. *Psychoneuroendocrinology*. 2009; 34(1):76–86. [PubMed: 18835661]
- Hardt J, Rutter M. Validity of adult retrospective reports of adverse childhood experiences: review of the evidence. *J Child Psychol Psychiatry*. 2004; 45(2):260–273. [PubMed: 14982240]
- Harville EW, Hatch MC, Zhang J. Perceived life stress and bacterial vaginosis. *J Womens Health (Larchmt)*. 2005; 14(7):627–633. [PubMed: 16181019]

- Harville EW, Boynton-Jarrett R, Power C, Hypponen E. Childhood hardship, maternal smoking, and birth outcomes: a prospective cohort study. *Arch Pediatr Adolesc Med.* 2010; 164(6):533–539. [PubMed: 20530303]
- Holzman C, Bullen B, Fisher R, Paneth N, Reuss L. Pregnancy outcomes and community health: the POUCH study of preterm delivery. *Paediatr Perinat Epidemiol.* 2001; 15(Suppl 2):136–158. [PubMed: 11520406]
- Holzman C, Eyster J, Tiedje LB, Roman LA, Seagull E, Rahbar MH. A life course perspective on depressive symptoms in mid-pregnancy. *Matern Child Health J.* 2006; 10(2):127–138. [PubMed: 16400535]
- Hummer RA, Biegler M, De Turk PB, Forbes D, Frisbie WP, Hong Y, Pullum SG. Race, nativity, and infant mortality in the United States. *Social Forces.* 1999; 77(3):1083–1117.
- Khashan AS, McNamee R, Abel KM, Mortensen PB, Kenny LC, Pedersen MG, et al. Rates of preterm birth following antenatal maternal exposure to severe life events: a population-based cohort study. *Hum Reprod.* 2009; 24(2):429–437. [PubMed: 19054778]
- Kramer MR, Hogue CJ, Dunlop AL, Menon R. Preconceptional stress and racial disparities in preterm birth: an overview. *Acta obstetrica et gynecologica Scandinavica.* 2011
- Laszlo KD, Li J, Olsen J, Vestergaard M, Obel C, Cnattingius S. Maternal bereavement and the risk of preterm delivery: the importance of gestational age and of the precursor of preterm birth. *Psychol Med.* 2016; 46(6):1163–1173. [PubMed: 26646988]
- Lhila A, Long S. What is driving the black-white difference in low birthweight in the US? *Health Econ.* 2012; 21(3):301–315. [PubMed: 21294220]
- Love C, David RJ, Rankin KM, Collins JW Jr. Exploring weathering: effects of lifelong economic environment and maternal age on low birth weight, small for gestational age, and preterm birth in African-American and white women. *Am J Epidemiol.* 2010; 172(2):127–134. [PubMed: 20576757]
- Lu MC, Halfon N. Racial and ethnic disparities in birth outcomes: a life-course perspective. *Matern Child Health J.* 2003; 7(1):13–30. [PubMed: 12710797]
- McGrady GA, Sung JF, Rowley DL, Hogue CJ. Preterm delivery and low birth weight among first-born infants of black and white college graduates. *Am J Epidemiol.* 1992; 136(3):266–76. [PubMed: 1415148]
- Martin JA, Hamilton BE, Ventura SJ, Menacker F, Park MM. Births: final data for 2000. *National Vital Statistics Report.* 2002; 50(5):1–101.
- Maternal and Child Health Bureau. Rethinking MCH: The Life Course Model as an Organizing Framework. Concept Paper. U.S. Department of Health and Human Services, Health Resources and Services Administration; 2010. 2016. <http://mchb.hrsa.gov/lifecourse/rethinkingmchlifecourse.pdf> Accessed May 5
- Nerum H, Halvorsen L, Straume B, Sorlie T, Oian P. Different labour outcomes in primiparous women that have been subjected to childhood sexual abuse or rape in adulthood: a case-control study in a clinical cohort. *BJOG: an international journal of obstetrics and gynaecology.* 2013; 120(4):487–495. [PubMed: 23157417]
- Noll JG, Schulkin J, Trickett PK, Susman EJ, Breech L, Putnam FW. Differential pathways to preterm delivery for sexually abused and comparison women. *J Pediatr Psychol.* 2007; 32(10):1238–1248. [PubMed: 17569710]
- Nuru-Jeter A, Dominguez TP, Hammond WP, Lue J, Skaff M, Egerter S, et al. “It’s the skin you’re in”: African-American women talk about their experiences of racism. An exploratory study to develop measures of racism for birth outcome studies. *Matern Child Health J.* 2009; 13:29–39. [PubMed: 18463971]
- Palotto EK, Kilbride HW. Perinatal outcome and later implications of intrauterine growth restriction. *Clin Obstet Gynecol.* 2006; 49(2):257–269. [PubMed: 16721105]
- Paul K, Boutain D, Manhart L, Hitti J. Racial disparity in bacterial vaginosis: the role of socioeconomic status, psychosocial stress, and neighborhood characteristics, and possible implications for preterm birth. *Soc Sci Med.* 2008; 67(5):824–833. [PubMed: 18573578]

- Pesonen AK, Raikkonen K, Feldt K, Heinonen K, Osmond C, Phillips DI, et al. Childhood separation experience predicts HPA axis hormonal responses in late adulthood: a natural experiment of World War II. *Psychoneuroendocrinology*. 2010; 35(5):758–767. [PubMed: 19963324]
- Precht DH, Andersen PK, Olsen J. Severe life events and impaired fetal growth: a nation-wide study with complete follow-up. *Acta obstetrica et gynecologica Scandinavica*. 2007; 86(3):266–275. [PubMed: 17364299]
- Richardson, L., Hussey, JM., Strutz, KL. A life course perspective on maternal and child health. In: Kotch, J., editor. *Maternal and Child Health: Programs, Problems, and Policy in Public Health*. 3rd ed.. Jones and Bartlett Publishers; Sudbury MA: 2013. p. 65-85.
- Roberts CB, Vines AI, Kaufman JS, James SA. Cross-sectional association between perceived discrimination and hypertension in African-American men and women: the Pitt County Study. *Am J Epidemiol*. 2008; 167(5):624–632. [PubMed: 18083714]
- Schei B, Lukasse M, Ryding EL, Campbell J, Karro H, Kristjansdottir H, et al. A history of abuse and operative delivery--results from a European multi-country cohort study. *PLoS One*. 2014; 9(1):e87579. [PubMed: 24498142]
- Scheid JM, Holzman CB, Jones N, Friderici KH, Nummy KA, Symonds LL, et al. Depressive symptoms in mid-pregnancy, lifetime stressors and the 5-HTTLPR genotype. *Genes Brain Behav*. 2007; 6(5):453–464. [PubMed: 16965382]
- Seng JS, Low LK, Sperlich M, Ronis DL, Liberzon I. Post-traumatic stress disorder, child abuse history, birthweight and gestational age: a prospective cohort study. *BJOG: an international journal of obstetrics and gynaecology*. 2011; 118(11):1329–1339. [PubMed: 21790957]
- Strutz KL, Hogan VK, Siega-Riz AM, Suchindran CM, Halpern CT, Hussey JM. Preconception stress, birth weight, and birth weight disparities among US women. *Am J Public Health*. 2014; 104(8):e125–132. [PubMed: 24922164]
- Thoits PA. Stress and health: major findings and policy implications. *J Health Soc Behav*. 2010; 51(Suppl):S41–53. [PubMed: 20943582]
- Trabert B, Misra DP. Risk factors for bacterial vaginosis during pregnancy among African American women. *Am J Obstet Gynecol*. 2007; 197(5):477.e471–478. [PubMed: 17980180]
- Turner RJ, Wheaton B, D.A. L. The epidemiology of social stress. *American Sociological Review*. 1995; 60:104–125.
- Wadhwa PD, Entringer S, Buss C, Lu MC. The contribution of maternal stress to preterm birth: issues and considerations. *Clin Perinatol*. 2011; 38(3):351–384. [PubMed: 21890014]
- Williams DR, Collins C. Racial residential segregation: a fundamental cause of racial disparities in health. *Public Health Rep*. 2001; 116(5):404–416. [PubMed: 12042604]
- Witt WP, Cheng ER, Wisk LE, Litzelman K, Chatterjee D, Mandell K, Wakeel F. Maternal stressful life events prior to conception and the impact on infant birth weight in the United States. *Am J Public Health*. 2014a; 104(Suppl 1):S81–89. [PubMed: 24354829]
- Witt WP, Cheng ER, Wisk LE, Litzelman K, Chatterjee D, Mandell K, Wakeel F. Preterm birth in the United States: the impact of stressful life events prior to conception and maternal age. *Am J Public Health*. 2014b; 104(Suppl 1):S73–80. [PubMed: 24354830]
- Yao Y, Robinson AM, Zucchi FC, Robbins JC, Babenko O, Kovalchuk O, et al. Ancestral exposure to stress epigenetically programs preterm birth risk and adverse maternal and newborn outcomes. *BMC Med*. 2014; 12:121. [PubMed: 25286408]

## SIGNIFICANCE

### **What is already known on this subject?**

Growing evidence suggests that exposure to pre-pregnancy stressors, such as death of a close relative, is associated with increased risks of low birth weight and preterm delivery (PTD).

### **What this study adds?**

We examine associations between PTD and stressors in multiple domains and life course periods (childhood, adulthood, and around the time of pregnancy). We find that abuse—particularly sexual abuse—in both childhood and adulthood emerges as a risk factor for PTD, with abuse at multiple time points linked to earlier PTD. Findings are stronger among white compared to African-American women.

**Table 1**

Distribution of pregnancy outcomes, maternal demographic and reproductive characteristics, and life stressors among women 20 years old in the Pregnancy Outcomes and Community Health (POUCH) study.

	n (%)
All	2559 (100)
Preterm delivery (PTD)	277 (10.8)
Timing of PTD	
Early (< 34 weeks)	92 (3.6)
Preterm (35-36 weeks)	185 (7.2)
Type of PTD	
Spontaneous	186 (7.3)
Medically indicated	91 (3.6)
Small for gestational age (SGA)	202 (7.9)
Maternal characteristics	
Race	
African-American	537 (21.0)
White/other	2022(79.0)
Age at enrollment	
20-29	1547 (60.5)
30-34	772 (30.2)
35	240 (9.4)
Education	
<12 years	264 (10.3)
12 years	715 (27.9)
>12 years	1580 (61.7)
Previous live births	
0	931 (36.4)
1	1628 (63.6)
Marital status	
Married	1502 (58.8)
Not married	1052 (41.2)
Stressors in the past 6 months	
Abuse	
Never	2272 (89.0)
Once or twice	156 (6.1)
More than twice	128 (5.0)
Economic problems	
Never	1750 (68.5)
Once or twice	282 (11.0)
More than twice	523 (20.5)
Substance use	
Never	2002 (78.3)



	n (%)
Once or twice	255 (10.0)
More than twice	299 (11.7)
Stressors in childhood/adulthood	
Abuse and/or see violence	
Never	1276 (50.0)
Childhood only	445 (17.4)
Adulthood only	393 (15.4)
Both childhood and adulthood	444 (17.4)
Economic problems	
Never	1221 (47.7)
Childhood only	450 (17.6)
Adulthood only	457 (17.9)
Both childhood and adulthood	430 (16.8)
Loss	
Never	480 (18.8)
Childhood only	497 (19.4)
Adulthood only	569 (22.2)
Both childhood and adulthood	1012 (39.6)
Substance use	
Never	1417 (55.5)
Childhood only	277 (10.9)
Adulthood only	425 (16.6)
Both childhood and adulthood	435 (17.0)

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**Table 2**

Percent preterm delivery (PTD, <37 weeks gestation) overall and by maternal characteristics and life stressor categories in POUCH.

	n(%)	p-value
All	277 (10.8)	
Maternal characteristics		
Race		<0.01
African-American	80 (14.9)	
White/other	197 (9.7)	
Age at enrollment		0.97
20-29	167 (10.8)	
30-34	85 (11.0)	
35	25 (10.4)	
Education		0.01
<12 years	42 (15.9)	
12 years	81 (11.3)	
>12 years	154 (9.8)	
Previous live births		0.77
0	103 (11.1)	
1	174 (10.7)	
Marital status(5 missing)		0.01
Married	143 (9.5)	
Not married	133 (12.6)	
Stressors in the past 6 months		
Abuse		0.48
Never	243 (10.7)	
Once or twice	16 (10.3)	
More than twice	18 (14.1)	
Economic problems		0.06
Never	172 (9.8)	
Once or twice	35 (12.4)	
More than twice	69 (13.2)	
Substance use		0.90
Never	214 (10.7)	
Once or twice	29 (11.4)	
More than twice	34 (11.4)	
Stressors in childhood/adulthood		
Abuse and/or see violence		0.11
Never	125 (9.8)	
Childhood only	52 (11.7)	
Adulthood only	39 (9.9)	
Both childhood and adulthood	61 (13.7)	

	n(%)	p-value
Economic problems		0.73
Never	124 (10.2)	
Childhood only	53 (11.8)	
Adulthood only	50 (10.9)	
Both childhood and adulthood	50 (11.6)	
Loss		0.06
Never	46 (9.6)	
Childhood only	40 (8.1)	
Adulthood only	67 (11.8)	
Both childhood and adulthood	124 (12.3)	
Substance use		0.38
Never	153 (10.8)	
Childhood only	30 (10.8)	
Adulthood only	38 (8.9)	
Both childhood and adulthood	55 (12.6)	

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**Table 3**

Multivariable adjusted associations between stressors in childhood and adulthood and odds of preterm delivery (PTD, <37 weeks gestation), early PTD (< 34 weeks gestation), and late PTD (35-36 weeks gestation) vs. term delivery (> 37 weeks gestation).

Stressor	Any PTD <sup>1</sup> (vs. term delivery)		Early PTD <sup>2</sup> (vs. term delivery)		Late PTD <sup>2</sup> (vs. term delivery)	
	OR	95% CI	OR	95% CI	OR	95%
Stressor						
Abuse/violence						
All race/ethnicities						
Never	--	--	Ref	Ref	Ref	Ref
Childhood only	--	--	0.6	(0.3, 1.3)	1.5	(1.0, 2.2)
Adulthood only	--	--	1.0	(0.5, 1.8)	0.9	(0.6, 1.5)
Both childhood and adulthood	--	--	1.6	(0.9, 2.7)	1.2	(0.8, 1.8)
African-American						
Never	Ref	--	--	--	--	--
Childhood only	1.4	(0.7, 2.7)	--	--	--	--
Adulthood only	1.2	(0.6, 2.3)	--	--	--	--
Both childhood and adulthood	0.8	(0.4, 1.5)	--	--	--	--
White/other						
Never	Ref	--	--	--	--	--
Childhood only	1.1	(0.7, 1.7)	--	--	--	--
Adulthood only	0.8	(0.5, 1.3)	--	--	--	--
Both childhood and adulthood	1.6	(1.1, 2.5)	--	--	--	--
Loss						
Never	Ref	--	Ref	--	Ref	--
Childhood only	0.8	(0.5, 1.2)	0.7	(0.4, 1.6)	0.8	(0.5, 1.4)
Adulthood only	1.2	(0.8, 1.8)	1.2	(0.6, 2.3)	1.2	(0.7, 2.0)
Both childhood and adulthood	1.2	(0.8, 1.8)	1.1	(0.6, 2.0)	1.3	(0.8, 2.0)
Maternal characteristics						
Race						
African-American	--	--	1.9	(1.2, 3.2)	1.2	(0.8, 1.8)
White/other	--	--	Ref	--	Ref	--
Age at enrollment	1.0	(1.0, 1.0)	1.0	(1.0, 1.1)	1.0	(1.0, 1.1)
Education						
<12 years	1.6	(1.0, 2.4)	1.0	(0.5, 2.2)	1.9	(1.2, 3.1)
12 years	1.2	(0.8, 1.6)	1.0	(0.6, 1.7)	1.2	(0.8, 1.8)
>12 years	Ref	--	Ref	--	Ref	--
Previous live births						

	Any PTD <sup>1</sup> (vs. term delivery)		Early PTD <sup>2</sup> (vs. term delivery)		Late PTD <sup>2</sup> (vs. term delivery)	
	OR	95% CI	OR	95% CI	OR	95%
0	Ref		Ref		Ref	
>=1	0.8	(0.6, 1.1)	0.7	(0.5, 1.2)	0.9	(0.6, 1.2)
Marital status						
Married	Ref		Ref		Ref	
Not married	1.1	(0.8, 1.5)	1.2	(0.7, 2.0)	1.1	(0.8, 1.6)

<sup>1</sup>Results from logistic regression models weighted for the stratified sampling structure of the POUCH study

<sup>2</sup>Results from multinomial regression models weighted for the stratified sampling structure of the POUCH study

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**Table 4**

Multivariable adjusted associations between physical and sexual abuse in childhood and adulthood and odds of preterm delivery (PTD, <37 weeks gestation), early PTD ( 34 weeks gestation), and late PTD (35-36 weeks gestation) vs. term delivery ( 37 weeks gestation).

Abuse variable	Any PTD <sup>1</sup> (vs. term delivery)		Early PTD <sup>2</sup> (vs. term delivery)		Late PTD <sup>2</sup> (vs. term delivery)	
	OR	95% CI	OR	95% CI	OR	95%
Abuse variable						
Physical abuse						
Never	Ref		Ref		Ref	
Childhood only	1.0	(0.7, 1.6)	1.5	(0.7, 2.9)	0.9	(0.5, 1.5)
Adulthood only	0.9	(0.6, 1.3)	0.8	(0.4, 1.6)	0.9	(0.5, 1.4)
Both childhood and adulthood	0.8	(0.5, 1.5)	1.3	(0.5, 3.1)	0.7	(0.3, 1.4)
Sexual abuse						
Never	Ref		Ref		Ref	
Childhood only	1.3	(0.9, 1.8)	0.9	(0.5, 1.7)	1.5	(1.0, 2.2)
Adulthood only	1.5	(0.9, 2.3)	1.8	(0.9, 3.6)	1.3	(0.7, 2.3)
Both childhood and adulthood	1.9	(1.0, 3.5)	1.4	(0.5, 4.1)	2.2	(1.1, 4.5)
Maternal characteristics						
Race/ethnicity						
African-American	1.5	(1.1, 2.1)	2.0	(1.2, 3.4)	1.3	(0.9, 1.9)
White/other	Ref		Ref		Ref	
Age at enrollment	1.0	(1.0, 1.1)	1.0	(1.0, 1.1)	1.0	(1.0, 1.1)
Education						
<12 years	1.6	(1.0, 2.4)	1.1	(0.5, 2.3)	1.9	(1.2, 3.1)
12 years	1.2	(0.9, 1.6)	1.1	(0.6, 1.8)	1.2	(0.8, 1.8)
>12 years	Ref		Ref		Ref	
Previous live births						
0	Ref		Ref		Ref	
>=1	0.8	(0.6, 1.1)	0.7	(0.5, 1.2)	0.9	(0.6, 1.2)
Marital status						
Married	Ref		Ref		Ref	
Not married	1.2	(0.8, 1.6)	1.3	(0.8, 2.2)	1.1	(0.8, 1.6)

<sup>1</sup>Results from logistic regression models weighted for the stratified sampling structure of the POUCH study

<sup>2</sup>Results from multinomial regression models weighted for the stratified sampling structure